the original document of hippocrates' oach

Journal of Preventive Medicine and Hygiene

journal of preventive medicine and hygiene

http://www.jpmh.org

Volume 63 - Issue 2 June 2022

Contents

COVID-19

Analysis of the correlation between mortality in nursing homes and among elderly population in Italy during the first phase of COVID-19 pandemic

ANTONIO SEBASTIANO[1], UMBERTO RESTELLI[1,2], SOFIA SILVOLA[1], ROBERTO PIGNI[1]
[1] Center for Health Economics, Social and Health Care Management, Università Carlo Cattaneo - LIUC, Castellanza, Italy;
[2] School of Public Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Keywords

COVID-19 • Mortality • Nursing homes • Elderly

Summary

Introduction. *The objective of the analysis is to investigate whether there is a correlation between deaths occurred within nursing homes in Lombardy Region and those related to the whole elderly population residing in the municipalities of their location at the beginning of the COVID-19 pandemic.*

Methods. *The analysis considered a sample of 17 nursing homes belonging to the same legal entity (with a total of 2,197 beds). The changes occurred in the trend of deaths in 2020 between January the 1st and February the 20th, and between February the 21st and April the 4th, compared with the average number of deaths occurred in the same time intervals of the previous three-year period (2017-2019) were investigated. To verify the presence of a correlation between deaths occurring within nursing homes*

and those related to the whole elderly population residing in the municipalities of their respective locations, Pearson correlation index was calculated, distinguishing between elderly over 65 years of age and elderly over 85 years of age.

Results. *A statistically significant correlation was identified between the number of deaths among the overall population and the number of deaths among nursing homes residents between February the 21st and April the 20th, while no correlations were identified between January the 1st and February the 20th.*

Conclusions. *The number of deaths occurred in the nursing homes of the sample considered shows similar trends to those of the elderly population of the municipalities in which they are located.*

Introduction

Year 2020 will be remembered as that in which SARS-CoV-2 related infections pandemic started. On December the 31st 2019 the first cases of SARS-CoV-2 related pneumonia emerged in the city of Wuhan (Hubey Province, China). SARS-CoV-2 reached 210 countries and territories spreading quickly and widely [1].

Italy is one of the first European countries in which cases of COVID-19 were diagnosed. The first case was diagnosed in Lombardy Region (in February 2020) and further diagnoses followed in other Northern Italian regions, spreading then throughout the whole national territory [2].

Through an analysis of death registry data within 4,100 municipalities in Northern Italy between January the 1st and May the 15th 2020, Ciminelli and colleagues (2020) estimated COVID-19 to be responsible for the death of almost 45,000 persons, more than 0.15% of local residents, during the so called "first wave" of the pandemic [3].

At the beginning of the pandemic, Lombardy was the most affected Italian region, with 37% of total COVID-19 national cases (73,348) and 53% of total COVID-19 related deaths, with a case-fatality rate of 18.3, compared with a national rate of 1.6% [2].

In Italy a broad media emphasis was given between March and April 2020 to the fact that nursing homes

were one of the main sites of COVID-19 spread, however it seems to have ignored that, in the same period, the entire elderly population has been affected by a staggering increase in deaths compared to previous years. This phenomenon involved mainly the regions most affected by the pandemic, as Lombardy, and often with an earlier onset within the communities than within nursing homes.

As reported by Trabucchi and De Leo (2020), in Lombardy, Veneto and Emilia-Romagna (three regions located in Northern Italy with a cumulative population in 2021 of more than 19 million inhabitants, representing more than 32% of the Italian resident population) during the first half of 2020, nursing homes reported commonly "10-15 deaths due to COVID-19 out of 70 guests" [4, 5].

Furthermore, a study conducted by the Italian National Institute of Health showed that between February the 1st and May the 5th 2020, in a sample of 1,356 nursing homes, among 97,521 elderly residents (78% of which in Northern Italy and 28% in Lombardy) 3,092 deaths were attributable to the COVID-19 (48% of which in Lombardy) [6].

The Italian 2020 mortality data, progressively made available by the Italian Institute of Statistics (ISTAT), further supported the hypothesis that the official pandemic data represented only the "tip of the iceberg",

Tab. I. Percentage variation and total number of deaths between February the 21st 2020 and April the 4th 2020 *vs* mean value of the 3 previous years in each Italian Region (Source: reprocessing of data published by ISTAT).

Region	Number of deaths between 21st February and 04th April				Δ number of deaths (%)
	Years 2017-2019 (mean)		Year 2020		
	Number	% of subjects over 65 years of age	Number	% of subjects over 65 years of age	
Abruzzo	1,770	90.2%	2,045	89.7%	275 (15.5%)
Basilicata	708	88.1%	735	91.4%	27 (3.8%)
Calabria	2,452	88.7%	2,574	89.7%	122 (5.0%)
Campania	6,404	85.3%	6,565	86.2%	161 (2.5%)
Emilia-Romagna	6,113	91.2%	9,819	91.7%	3,706 (60.6%)
Friuli-Venezia Giulia	1,755	90.6%	2,018	92.1%	263 (15.0%)
Lazio	6,593	88.7%	6,516	89.3%	-77 (-1.2%)
Liguria	2,612	91.4%	3,934	93.8%	1,322 (50.6%)
Lombardy	12,212	89.9%	30,962	92.5%	18,750 (153.5%)
Marche	2,034	91.5%	2,940	92.3%	906 (44.5%)
Molise	399	89.5%	396	90.2%	-3 (-0.7%)
Piedmont	6,215	90.2%	9,240	92.2%	3,025 (48.7%)
Apulia	4,742	89.2%	5,236	89.0%	494 (10.4%)
Sardinia	1,919	87.3%	2,197	88.7%	278 (14.5%)
Sicily	6,189	89.1%	6,316	89.5%	127 (2.1%)
Tuscany	5,342	91.4%	5,996	92.4%	654 (12.2%)
Trentino-Alto Adige	1,108	90.1%	1,845	92.2%	737 (66.5%)
Umbria	1,264	91.9%	1,328	92.5%	64 (5.0%)
Valle d'Aosta	171	89.7%	284	93.7%	113 (66.1%)
Veneto	5,681	89.9%	7,021	91.2%	1,340 (23.6%)
Total	75,683	89.6%	107,967	91.2%	32,284 (42.7%)

underestimating the real extent of COVID-19 and subsequent deaths [3, 7].

While an increase in the number of deaths occurred in 2020 compared with previous years, it might not be attributable exclusively to the spread of SARS-CoV-2, the mortality trends observed in the peak period of the pandemic suggests that deaths directly or indirectly attributable to COVID-19 were more than those reported in official data (i.e. people who died at their domicile or in nursing homes not being diagnosed through a swab and a subsequent molecular biology testing).

Starting from these premises, the objective of the analysis presented is to investigate whether there is a statistical correlation between the deaths occurred within 17 nursing homes, belonging to the same legal entity, located in Lombardy (Northern Italy) and those related to the whole elderly population residing in the municipalities of their location.

Methods

The analysis conducted adopted a cumulative approach. The sample of 17 nursing homes considered includes 2,197 beds, with an average number of 130 beds per each nursing home (with a minimum number of beds of 60 and a maximum number of beds of 204). From a territorial point of view, the analysis involved 13 municipalities located in Lombardy (including Milan),

located in 5 different provinces (Bergamo, Brescia, Como, Milan, and Monza e Brianza).

Specifically, the changes that occurred in the trend of 2020 deaths in the period between January the 1st 2020 and February the 20th 2020, and in the period between February the 21st 2020 and April the 4th 2020, compared with the average number of deaths occurring in the same time intervals of the previous three-year period (2017-2019) were studiedanalysed. The choice to operate a focus on Lombardy is because it was the Italian Region most affected by the pandemic in the first half of 2020.

As reported in Table I, between February the 21st 2020 and April the 4th 2020, the total number of deaths increased by 153.5% compared with the mean number of deaths in the same period in 2017-2019 and 92.5% of cases were represented by subjects with more than 65 years of age. Data reported refers to the 7,270 Italian municipalities included in the "*Anagrafe Nazionale della Popolazione Residente*" and the total number of subjects included is equal to 93.5% of the Italian resident population on January the 1st 2019. At a regional level, the percentage of subjects included in the data reported in Table I is between 98.6% (Lombardy) and 78.7% (*Molise*) of the regional resident population.

The total number of daily deaths occurring in Lombardy from the beginning of the year 2020 to May the 15th 2020 and the average number of daily deaths in the same period in the previous three years (2017-2019) is reported in Figure 1.

Fig. 1. Number of daily deaths in Lombardy between January the 1st 2020 and May the 15th 2020 *vs* mean value of the previous 3 years (Source: reprocessing of data published by ISTAT).
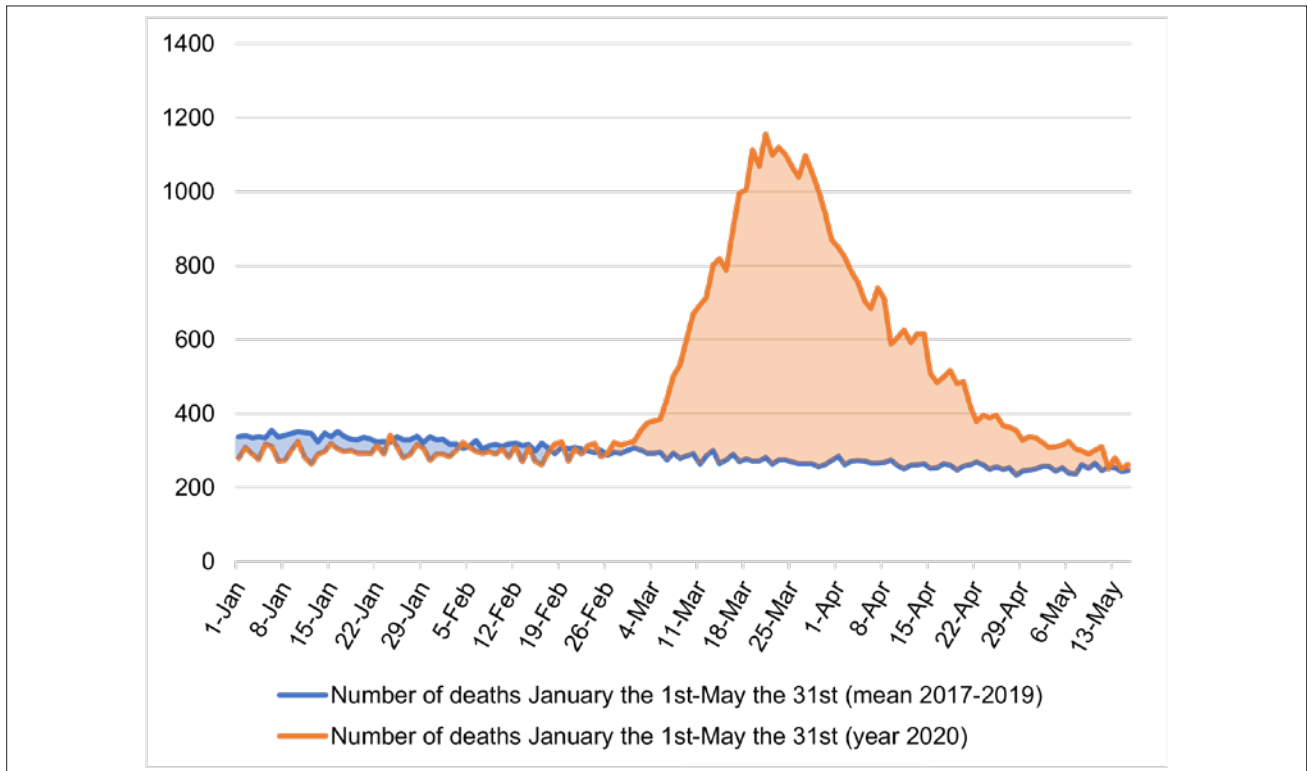
Concerning the observation period, the choice to stop the analysis on April the 4th 2020 is due to the fact that after this date the variations in deaths on a weekly basis show the consolidation of a trend of continuous and significant decrease, until it returns to values close to those of the previous three years in the last week of May, as reported in Figure 2 (weeks are defined as seven consecutive days intervals starting from the first seven days of March 2020; May the 15th 2020 is the last day in 2020 for which data were available at the time of the analysis from the Italian Institute of Statistics).

With the aim of verifying the presence of a correlation between deaths occurring within nursing homes and those related to the whole elderly population residing in the municipalities of their respective locations, Pearson correlation index was calculated. The index was calculated as the percentage ratio between deaths that occurred in the nursing homes of the sample in 2017-2019 and 2020 (pre-pandemic and pandemic periods), and the percentage ratio between deaths recorded in the overall elderly population of the respective municipalities in 2017-2019 and 2020 (pre-pandemic and pandemic periods), distinguishing between elderly over 65 years of age and elderly over 85 years of age. This choice is due to the fact that the latter is the main catchment area of nursing homes. In this regard, data published by the Sectorial Observatory on Nursing Homes at LIUC University reports an average age at admission to Nursing Homes in Lombardy of 84.6 years between 2013 and 2018 [8].

The comparison between the number of deaths occurred

in the elderly population within the municipalities in which the nursing homes included in the sample are located is presented in Table II, along with the number of deaths occurred in the nursing homes, between January the 1st and February the 20th, and between February the 21st and April the 4th in the pre-pandemic period (mean value 2017-2019) and pandemic period (2020).

Results

The correlation coefficients between the number of deaths in the overall resident population and the number of deaths among the residents of the nursing homes included in the sample between January the 1st and February the 20th, and between February the 21st and April the 4th in the pre-pandemic period (mean value 2017-2019) and pandemic period (2020) are reported in Table III, both considering subjects over 65 years of age and subjects over 85 years of age.

In the period prior to the outbreak of the pandemic there is no statistically significant correlation between the number of deaths among the overall population and the number of deaths among nursing homes residents (both considering subjects over 65 years and over 85 years).

On the contrary, these correlations are both statistically significant between February the 21st and April the 4th, even assuming a rather significant intensity, especially with reference to the segment of the subjects over 85 years, as reported in Figure 3. Given that the correlation index does not express a causal link, it is plausible

Fig. 2. Percentage variation in the number of weekly deaths between March the 1st 2020 and May the 15th 2020 *vs* the mean value of the 3 previous years.
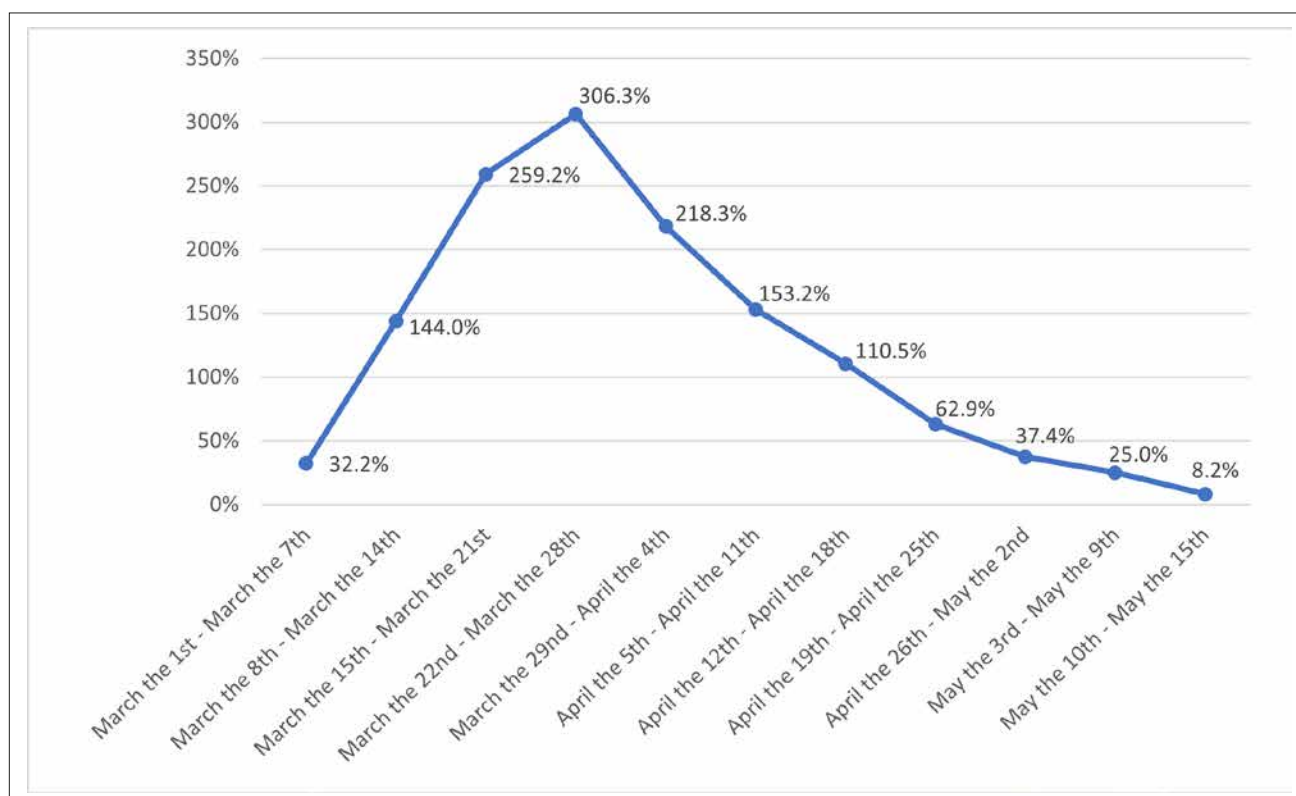
Tab. II. Number of deaths occurred in the nursing homes, between January the 1st and February the 20th, and between February the 21st and April the 4th in the pre-pandemic period (mean value 2017-2019) and pandemic period (2020).

	Resident population (age ≥ 65)		Resident population (age ≥ 85)		Nursing home residents (age ≥ 65)	
	January 1st - February 20th	February 21st - April 4th	January 1st - February 20th	February 21st - April 4th	January 1st - February 20th	February 21st - April 4th
Number of deaths 2017 - 2019 (mean)	2,974	2,105	1,694	1,148	139	95
Number of deaths 2020	2,478	4,199	1,415	2,304	146	265
Δ 2020 / mean 2017-2019 (N)	-496	+ 2,094	-279	1,156	7	170
Δ 2020 / mean 2017-2019 (%)	-16.68%	99.51%	-16.47%	100.70%	4.78%	177.97%

to suppose that mortality within each nursing home was conditioned by the spread of the pandemic in the relative municipalities of location and that the guests of the nursing homes were exposed to a greater risk of contagion and, consequently, of mortality, in the areas in which there was a greater spread of the SARS-CoV-2.

The underlying hypothesis is reinforced by two relevant aspects. The first is the absence of statistical correlations between the number of deaths in the overall resident population and the number of deaths among nursing homes residents in the pre-pandemic period (January the 1st - February the 20th).

The second aspect is to be found in the fact that all the nursing homes included in the sample, can be traced back to a common legal entity that managed at a unitary level the adoption of every single measure of prevention and contrast to the spread of the pandemic from the definition of protocols and safety procedures to the procurement of personal protective equipment (surgical masks/FPP2, disposable gowns, disposable gloves, visors/glasses, etc.). The decision-making discretion of each nursing home was therefore reduced to a minimum, and they therefore faced the pandemic with a homogeneous approach and equal resources at their disposal.

Discussion and conclusions

Nursing homes residents are mainly elderly (over 85 years) non-self-sufficient subjects, with several comorbidities and frequent cognitive impairment, and prognostic indicators compatible with a reduced life expectancy. As confirmed in literature, elderly patients, patients with

Tab. III. Correlation coefficients between the number of deaths in the overall resident population and the number of deaths among nursing homes residents between January the 1st and February the 20th, and between February the 21st and April the 4th in the pre-pandemic period (mean value 2017-2019) and pandemic period (2020).

	Correlation coefficient of the number of deaths	
	Pre-pademic period January the 1st - February the 20th	Pademic period February the 21st - April the 4th
Subjects over 65 years of age - overall population / nursing homes residents	0.40	0.67**
Subjects over 85 years of age - overall population / nursing homes residents	0.47	0.81**

Fig. 3. Scatter plot on the percentage variations of deaths in the two periods considered among the overall population over 85 years and residents of the nursing homes included in the sample.
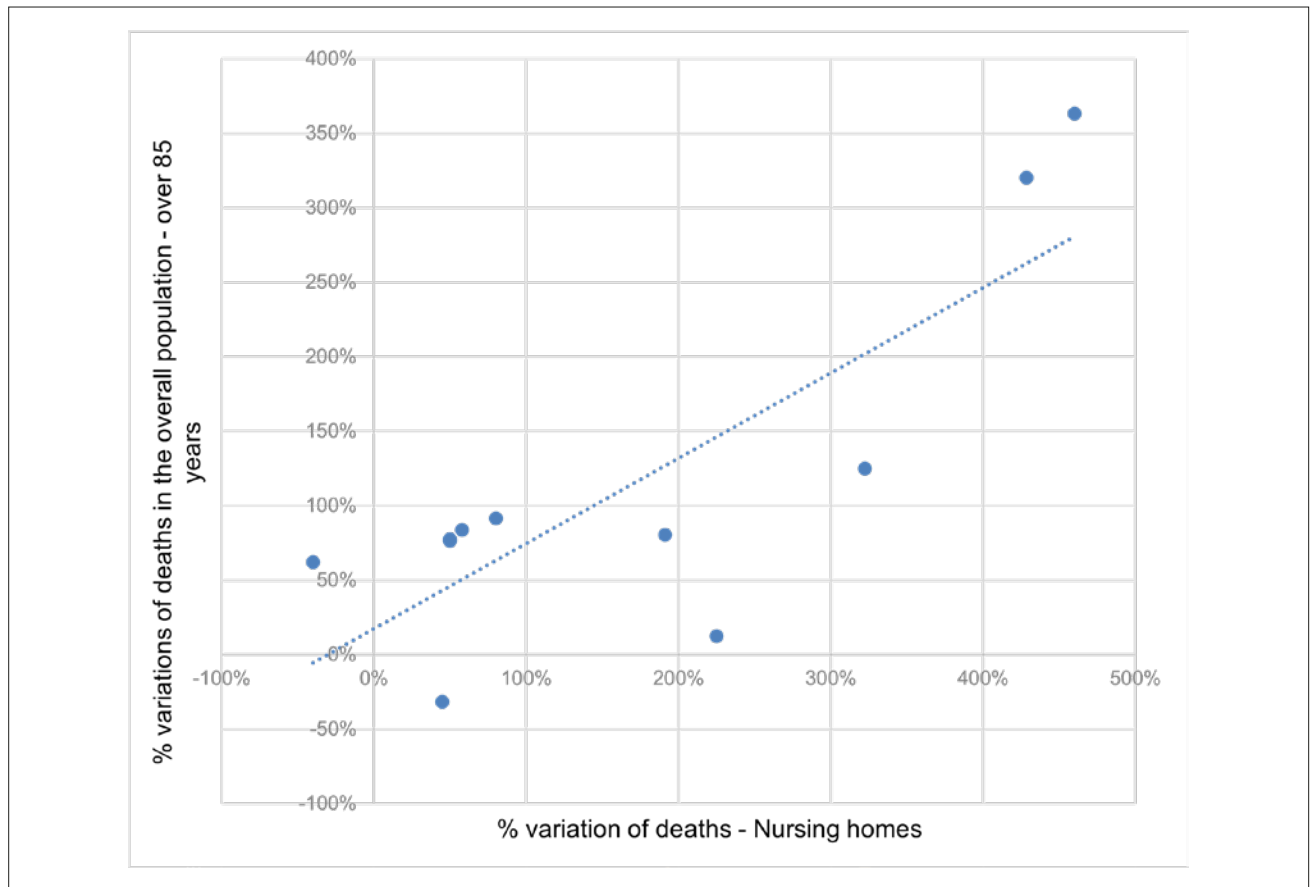
comorbidities (chronic obstructive pulmonary disease, cardiovascular disease, hypertension) and patients with dyspnoea are more vulnerable to more severe morbidity and mortality related to COVID-19 [9, 10]. These elements might explain the high level of lethality of SARS-CoV-2 infection within nursing homes, also considering that they are not designed for isolation, but, on the contrary, they are integrated into the communities in which they are located, as well as strongly oriented to ensure frequent moments of socialization between residents.

Despite this, the number of deaths occurred in the nursing homes of the sample considered shows similar trends to those of the elderly population of the municipalities in which they are located.

A retrospective study conducted by Veronese and colleagues (2021) confirmed that, considering different degrees of frailty of nursing home residents, COVID-19 was associated with a higher risk of all-cause mortality than those not infected [11].

Moreover, as reported in Table IV, extending the period of observation to May the 15th, the highest variations in the number of deaths between 2020 and 2017-2019 are observed in the 75-85 years age group (+ 128.1%) and in the 65-74 years age group (+ 126.0%), the latter being under-represented among nursing homes residents due to younger age. The deaths of subjects in the 65-74 years age group are likely to have been occurred at domicile, which should then not be considered a safer place than nursing homes and/or other residential services for the elderly population.

Tab. IV. Percentage variation and number of deaths in Lombardy per age group between February the 2nd 2020 – May the 15th 2020 and the mean value of the previous 3 years (2017-2019)-

Age group	Number of deaths February the 2nd - May the 15th		Δ number of deaths (%)
	Mean 2017-2019	Year 2020	
0-14 years	69	61	-8 (-11.6%)
15-64 years	2,315	3,705	1,390 (60.1%)
65-74 years	2,960	6,690	3,730 (126.0%)
75-84 years	6,799	15,511	8,712 (128.1%)
85 years and more	10,537	22,636	12,099 (114.8%)
Total	22,680	48,603	25,923 (114.3%)

The most important interventions to protect nursing homes residents from COVID-19 reported in literature are the implementation of clear procedures to contain the virus, the ability to isolate any positive case and the availability of personal protection equipment [10]. On this topic, Kosar and colleagues (2021) conducted a study in the United States among 12,271 nursing home residents, and reported that mortality rates among nursing home residents declined from March 2020 to November 2020 identifying as potential explanatory factors the improvements in personal protective equipment supply and use, and specific changes in the clinical management of COVID-19 [12].

Furthermore, a study conducted in the Spanish context found a statistical correlation between mortality in nursing homes and a lower staff to a resident ratio, showing "a 0.44 percentage point reduction in the share of nursing home fatalities for each additional staff per place" [13]. Finally, a study conducted in the United States confirmed these latest findings by stating that "nursing homes with higher registered nurse staffing have the potential to better control the spread of the novel coronavirus and reduce deaths" [14].

The results of the analysis conducted should be taken into due consideration while re-organizing the actual territorial system of long-term care, in order to avoid distorting prematurely and in an unjustified way the role of nursing homes within the supply chain of services for non-self-sufficient subjects.

Acknowledgements

Conflict of interest statement

Authors declare no conflict of interest.

Authors' contributions

AS: study conception and design, data collection, data analysis, interpretation of data, drafting of the manuscript; RP: data collection, data analysis, interpretation of data, editing and critical revision of the manuscript; SS, UR: support on data collection, support on interpretation of data, editing and critical revision of the manuscript. All authors have read and approved the final manuscript.

References

[1] Keni R, Alexander A, Nayak PG, Mudgal J, Nandakumar K. COVID-19: Emergence, Spread, Possible Treatments, and Global Burden. Front Public Health 2020;8:216. https://doi.org/10.3389/fpubh.2020.00216

[2] Romagnoli S, Peris A, De Gaudio AR, Geppetti P. SARS-CoV-2 and COVID-19: From the Bench to the Bedside. Physiol Rev 2020;100:1455-66. https://doi.org/10.1152/physrev.00020.2020

[3] Ciminelli G, Garcia-Mandicó S. COVID-19 in Italy: An Analysis of Death Registry Data. J Public Health 2020;42:723-30. https://doi.org/10.1093/pubmed/fdaa165

[4] Trabucchi M, De Leo D. Nursing homes or besieged castles: COVID-19 in northern Italy. Lancet Psychiatry 2020;7:387-8. https://doi.org/10.1016/S2215-0366(20)30149-8

[5] ISTAT – Istituto Nazionale di Statistica. Popolazione residente al 1° gennaio 2021. Available at: http://dati.istat.it/Index.aspx?QueryId=18460 (Accessed on: July 27, 2021).

[6] ISS. Survey nazionale sul contagio COVID-19 nelle strutture residenziali e sociosanitarie, Istituto Superiore di Sanità. Epidemia COVID-19, Final report: May 5th, 2020. Available at: https://www.e picentro.iss.it/coronavirus/pdf/sars-cov-2-survey-rsa-rapporto-fina le.pdf (Accessed on: November 1, 2020).

[7] ISTAT – Istituto nazionale di Statistica. Rapporto Annuale 2020 – La situazione del paese. 2020. https://www.istat.it/storage/rapporto-annuale/2020/Rapportoannuale2020.pdf (Accessed on: July 27, 2021).

[8] Osservatorio Settoriale sulle RSA, LIUC Business School. Andamento dei decessi periodo 21 febbraio-15 aprile 2020 vs.21 febbraio-15 aprile 2015-2019 (media), 13 maggio 2021.

[9] Wynants L, Van Calster B, Collins GS, Riley DR, Heinze G, Schuit E, Bonten MMJ, Dahly LD, Damen JAA, Dabray TPA, De Jong VMT, De Vos M, Dhiman P, Haller MC, Harhay MO, Henckaerts L, Heus P, Kammer M, Kreuzberger N, Lohmann A, Luijken K, Ma J, Martin GP, McLernon DJ, Andaur Navarro CL, Reitsma JB, Sergeant JC, Shi C, Skoetz N, Smits LJM, Snell KIE, Sperrin M, Spijker R, Steyerberg EW, Takada T, Tzoulaki I, Van Kuijk SMJ, Van Bussel B, Van der Horst ICC, Van Royen FS, Verbakel JY, Wallisch C, Wilkinson J, Wolff R, Hooft L, Moons KGM, Van Smeden M. Prediction models for diagnosis and prognosis of COVID-19: systematic review and critical appraisal. BMJ 2020;369:m1328. https://doi.org/10.1136/bmj.m1328

[10] Oliva C, Di Maddaloni F, Marcellusi A, Favato G. Cross-regional variations of Covid-19 mortality in Italy: an ecological study. J Public Health 2021;43:261-9. https://doi.org/10.1093/pubmed/fdaa248

[11] Veronese N, Koyanagi A, Stangherlin V, Mantoan P, Chiavalin M, Tudor F, Pozzobon G, Tessarin M, Pilotto A. Mortality attributable to COVID-19 in nursing home residents: a retrospective study. Aging Clin Exp Res 2021;33:1745-51. https://doi.org/10.1007/s40520-021-01855-6

[12] Kosar CM, White EM, Feifer RA, Blackman C, Gravenstein S, Panagiotou OA, McConeghy K, Mor V. COVID-19 mortality rates among nursing home residents declined from March to November 2020. Health Aff 2021;40:655-63. https://doi.org/10.1377/hlthaff.2020.02191

[13] Costa-Font J, Jiménez Martin S, Viola A. Fatal Underfunding? Explaining COVID-19 Mortality in Spanish Nursing Homes. J Aging Health 2021;33:607-17. https://doi.org/10.1177/08982643211003794

[14] Li Y, Temkin-Greener H, Shan G, Cai X. COVID-19 Infections and Deaths among Connecticut Nursing Home Residents: Facility Correlates. J Am Geriatr Soc 2020;68:1899-906. https://doi.org/10.1111/jgs.16689

Active surveillance of adverse events after immunization (AEFI) from the Local Health Unitof Ferrara, Italy

ANNA MARRA[1], ADRIANA DONZELLI[2], CATERINA FLORESCU[3], ANDREA RAUZINO[3], ANTONELLA MATTEI[4],
MARIA MARGHERITA SBARBATI[5], FABIANA FIASCA[4], ARMANDO STEFANATI[6], GIOVANNI GABUTTI[6]

[1] Hospital Pharmacy OU, Azienda Ospedaliera Universitaria di Ferrara, University of Ferrara, Ferrara, Italy;
[2] Hospital Pharmacy OU, Azienda USL di Ferrara, Ferrara, Italy; [3] Post-Graduate School of Hygiene and Preventive Medicine,
University of Ferrara, Ferrara, Italy; [4] Department of Life, Health & Environmental Sciences, University of L'Aquila, L'Aquila, Italy;
[5] Regional Health Unit, Department of infectious diseases-vaccinations, SISP Unit AV1, Fano, Italy;
[6] Department of Medical Sciences, University of Ferrara, Ferrara, Italy

Keywords

Summary

Introduction. *Vaccine vigilance implies the collection, evaluation, analysis and communication of adverse events following immunization (AEFI) and is a useful tool for vaccine monitoring allowing, even after approval and marketing, to check its safety/tolerability. The multiregional project "Active surveillance of adverse vaccine reactions", joined by the AUSL of Ferrara, is aimed at making parents of children, who have undergone at least one vaccination provided by the regional vaccination calendar in the first 24 months of life, aware of the reporting of any AEFI via mobile phone-SMS.*

Methods. *An analysis of the project data, collected in the period March 2018 - May 2019, was carried out, to evaluate the effectiveness of the reporting tool and the type and frequency of AEFI. Anonymized data were analyzed by number, gender, distribution by age, type of vaccine, adverse event, severity and outcome.*

Results. *A total of 1,494 consents and 983 SMS messages were obtained from parents. The vaccine doses carried out were 1,984 (28.3% hexavalent, 28% PCV13, 17% anti-rotavirus, 14.3% Men-B). Almost all (99.5%) AEFI were classified as "not serious". Based on the Organ System Class (SOC), most reports are related to "General Disorders and Administration Site Conditions" (52.3%), followed by "Psychiatric Disorders" (26.5%) and "Metabolic and nutrition disorders" (12.5%).*

Conclusions. *The reported AEFI are in line with the ones reported in the literature. Reporting via SMS is a valid vaccine surveillance tool contributing to the qualitative and quantitative improvement of the information transmitted.*

Introduction

In recent years, the safety of vaccines has aroused particular interest, also following the important changes in the management of vaccinations introduced with law no. 119 of 31 July 2017 [1]. In this context, vaccine vigilance is configured as a tool of fundamental importance to deepen knowledge on the safety of vaccines [2]. Vaccine vigilance is the set of pharmacovigilance activities related to the collection, evaluation, analysis and communication of adverse events following immunization.

An adverse event following a vaccination (Adverse Events Following Immunization, AEFI) is defined as "any adverse clinical event that occurs after the administration of a vaccine and which does not necessarily have a causal relationship to it. The adverse event could be an unfavorable or unintended sign, an abnormal laboratory result, a symptom or a disease" [3].

The only relation between the carried-out vaccination and the harmful event could be the temporal one, considering that the greater the interval between vaccination and the event, the lower the plausibility of a possible causal link between the two [3].

Vaccine vigilance therefore has the dual purpose of guaranteeing the safety of the vaccination act and keeping up to date the evaluation of the risk/benefit ratio, verifying that the latter remains favorable over time, especially in consideration of the fact that vaccination is offered to a healthy population [4].

Monitoring is mainly carried out through two methods: passive vaccine vigilance, that is the spontaneous reporting of adverse events following vaccination, and active one, which is stimulated reporting through independent studies.

In particular, active vaccine surveillance consists in the monitoring and evaluation of reports of suspected adverse reactions to vaccines performed by healthcare professionals or particular categories of users in specific situations stimulated by appropriate independent studies; these studies are conducted by the Regions in collaboration with the Italian Medicines Agency (AIFA) and other international regulatory bodies [5].

Since the main limitation of spontaneous reporting is represented by under-reporting, i.e. the failure to report

Tab. I. Pediatric vaccination calendar of the Emilia-Romagna Region, in force since 1 January 2018.

Calendar	0-30 days	3rd month	4th month	5th month	6th month	7th month	11th month	13th month	14th month	6 years	12th month	13-14 years
DTaP		x		x			x			x		x
IPV		x		x			x			x		x
HBV	x *	x		x			x					
HiB		x		x			x					
MMR								x		x		
V**								x		x		x °
PCV		x		x			x					
Men B			x		x	x			x			
Men ACWY								x				x
RV		x		x								
HPV											x	
Flu§												

Vaccines: DTaP: diphtheria, tetanus and acellular pertussis; IPV: inactivated poliovirus; HBV: hepatitis B; HiB: *Haemophilus influenzae* type b; MMR: measles, mumps and rubella; V: varicella; PCV: conjugate pneumococcal; Men B: meningoccal B; Men ACWY: quadrivalent conjugate meningococcal; RV: rotavirus; HPV: human papillomavirus; Flu: influenza.
* Newborns from HBsAg positive mother. ** Newborns since 2017. ° 2 doses provided to susceptible subjects. § Starting from 6th month, only for at risk children.

Tab. II. Pediatric vaccination calendar of the Emilia-Romagna Region, in force since 1 January 2019.

Calendar	0-30 days	3rd month	4th month	5th month	6th month	7th month	11th month	13th month	14th month	6 years	12th month	13-14 years
DTaP		x		x			x			x		x
IPV		x		x			x			x		x
HBV	x *	x		x			x					
HiB		x		x			x					
MMR								x		x		
V**								x		x		x °
PCV		x		x			x					
Men B			x		x				x			
Men ACWY								x				x
RV		x	x	x								
HPV											x °°	
Flu§												

Vaccines: DTaP: diphtheria, tetanus and acellular pertussis; IPV: inactivated poliovirus; HBV: hepatitis B; HiB: *Haemophilus influenzae* type b; MMR: measles, mumps and rubella; V: varicella; PCV: conjugate pneumococcal; Men B: meningoccal B; Men ACWY: quadrivalent conjugate meningococcal; RV: rotavirus; HPV: human papillomavirus; Flu: influenza.
* Newborns from HBsAg positive mother. ** Newborns since 2017. ° 2 doses provided to susceptible subjects. °° 2 doses (6 months of interval between doses). § Starting from 6th month, only for at risk children

a certain number of adverse reactions that hinders an estimation of the real incidence of adverse events, it is desirable to promote active vaccine surveillance programs in order to increase the awareness of patients and healthcare professionals to the issue of vaccine safety [6, 7].

In 2017, the Local Health Unit of Ferrara, Italy, together with the Provincial Center for Pharmaco-vigilance, joined the multiregional project "Reporting of adverse events after vaccination by parents", promoted by the Veneto Region, which also involved other regions as Sicily, Marche, Calabria, Piedmont and the Autonomous Province of Bolzano.

The context in which the project is inserted, looks at a national data with most of the reports related to immunization from health districts (which remain a very important point in the observation of adverse events) especially in the first two years of life, a period in which, according to the national vaccination calendar, immunization sessions are fairly close in time.

The proposed primary objective of this intervention is to increase the reporting rate of adverse events after immunization. Another goal of primary importance, but more difficult to quantify, is the involvement of citizens (parents) in the reporting of adverse events after immunization.

The tool to pursue this objective has been identified in the use of the SMS (short message service) mobile phone system in order to facilitate the adhesion of parents and, at the same time, to reduce the workload of health professionals in filling out the reporting.

The secondary objective is to speed up the management of reports by Pharmaco-vigilance Managers and to improve the collection of reports and the organization of the vaccine vigilance system, through the use of the *VigiFarmacoVax* platform.

Tab. III. Specific adverse events following immunization (AEFI).

Specific AEFIs	(n[1])	(%)
Pyrexia	468	37.5
Mood disorders	331	26.5
Gastrointestinal disorders	156	12.5
Local disturbances	116	9.3
Sleep disturbances	104	8.3
Crying	38	3.0
General malaise, asthenia, weakness, sweating	17	1.4
Hyperpyrexia	14	1.1
Upper respiratory tract infection, pneumonia, acute otitis	3	0.2
Seizures, ocular congestion	1	0.1
[1] The sum of the values does not equal the total of the AEFI.		

Methods

The project "Reporting of adverse events after vaccination by parents", to which the Local Health Unit of Ferrara has joined with the participation of the Community Pediatrics of the central-northern district, took place over 15 months, from March 2018 to May 2019, preceded by a pilot phase in May 2017.

The study population was represented by all children aged ≤ 2 years who underwent a vaccination according to the regional vaccination calendar in the period March 2018 - May 2019 (Tabs. I, II).

During each vaccination session, after having explained to the parents the methods and purposes of the active vaccine surveillance project, they were given the information letter, shared with the coordinating center and the pediatricians of the vaccination center, and the informed consent to participate in the study, in which, they were also asked to indicate a mobile number, in order to be subsequently contacted via SMS. Data gathering was conducted following the principles of the Declaration of Helsinki, according to current national legislation and in compliance with the protection of personal data. All data were anonimyzed.

Within 7 or 21 days from the vaccination session, depending on the type of administered vaccine (inactivated or live attenuated vaccine), an SMS was sent to the parent asking for the description of any adverse events occurring in the days after vaccination - "Did any adverse events occur after the vaccine administered on dd/mm/yy? If yes, please describe them by indicating the date of onset of symptoms. Thanks, the District".

The tools used included an informatic platform, *VigiFarmacoVax*, and a mobile phone system. *VigiFarmacoVax* is a specific software platform that allows the collection of data of vaccinated children (name, surname, sex, date of birth, vaccination clinic, vaccination date, type of vaccine and mobile phone number) and the automatic sending of the message to the parent who joined the project; even the return information, received via SMS from the parents, is managed by the same platform.

The parent can respond to the message without a time limit from receiving the same and the response, in the case of vaccinations performed at different times, was always attributed to the last vaccine administered. The text of the message was controlled by the platform through an algorithm that makes it possible to recognize the messages that describe adverse events and if these are to be considered serious. This recognition occurred by searching for the terms contained in a list of clinical events considered serious (IME LIST). If the text of the message contained one or more of these terms, then the system inserted an alert symbol next to the text of the message and placed this alert at the top of the list, awaiting confirmation from healthcare professionals.

All reports, to be sent to the *VigiFarmacoVax* platform, must be validated; validation requires the presence in the message of at least one adverse event and the assessment of the seriousness proposed by the system, also allowing the inclusion of additional information in the "comments of the reporter". Following validation, the messages were classified into 3 classes:

- messages without adverse events;
- messages with adverse events not reported in *VigiFarmacoVax* (discarded, that is, the message is saved and archived, without sending data to *VigiFarmacoVax*);
- messages with adverse events reported in *VigiFarmacoVax* (validated).

When the doctor validates the report in the *VigiFarmacoVax* platform, the same is automatically transferred to *VigiFarmacoVax*, where the project manager enters any missing information such as: ethnic origin of the child, coding of adverse events (using MedDRA terminology), AEFI outcome (complete resolution, hospitalization, not yet cured, etc.), date of onset of reaction (corresponding to the date of the vaccine administration), actions taken (administration of therapy, consultation with the pediatrician, etc.), batch and expiration of the vaccine, date, time, site of administration and pharmaceutical form (suspension for injection, powder for suspension for injection, powder for solution for injection, oral suspension). Finally, all the information entered is transferred, in a computerized manner, to the National Pharmaco-vigilance Network (RNF).

The received reports have been analyzed by number, gender, age distribution, type of suspected vaccine, adverse event, severity and outcome.

Data were anonymized and subsequently analyzed using Microsoft Excel 2007 software.

Given the limited number of MMR vaccine administrations, the latter was considered in the count of MMRV vaccines.

Adverse events characterized by the involvement of the same apparatus, or by a similar clinical presentation, were classified as belonging to the same group (for example, fever and low-grade fever were coded as "pyrexia").

Results

During the considered period, 1,494 consents were obtained for participation in the active vaccine vigilance project from the parents of 1,130 children, aged between 0 and 2 years.

Almost 66% (983; 65.8%) of those who gave their consent replied to the SMS.

A total of 1,984 doses of vaccine were given to these children; the highest number of administrations was recorded for the hexavalent vaccine (561; 28.3%), the 13-valent conjugated pneumococcal (555; 28%), the anti-rotavirus (338; 17%), and the meningococcal B (283; 14.3%) vaccines.

Of the 983 responses received from parents, 561 were validated as AEFI and reported a total of 1,248 adverse events.

Considering the defined criteria to establish the severity of a suspected adverse vaccine event, it emerges that almost all AEFI (558; 99.5%) were classified as "not serious"; 0.5% were classified as "severe" including upper respiratory tract infection, acute otitis and seizure. Adverse events were grouped accordingly to Organ-Systemic Classification - SOC (MedDRA7 terminology), and this subdivision highlighted that most of the received reports were related to "General disorders and conditions related to the administration site" (653; 52.3%), followed by "Psychiatric disorders" (331; 26.5%) and by "Metabolism and nutrition disorders" (156; 12.5%). Considering in detail the specific types of AEFI, pyrexia was the most frequent adverse event (468; 37.5%), followed by mood disorders (331; 26.5%), gastrointestinal disorders (156; 12.5%), local disturbances (116; 9.3%) and sleep disturbances (104; 8.3%) (Tab. III).

Conclusions

The study of the AEFI during the reporting period has allowed us to demonstrate how the start of an active surveillance project has led to a significant increase in reports.

However, it must be considered that the increase in reports and in awareness on the issue of vaccine safety may also be related to the increase in vaccination coverage and to the intense debate following the introduction of the mandatory vaccination law [8].

The innovative aspect of this project consists in the reduction of reporting times. Thanks to the use of mobile messaging (SMS), the time between the event following vaccination and reporting is reduced, especially in the case of minor events. The reduction of the time required for reporting can thus contribute to the qualitative and quantitative improvement of the transmitted information [9, 10].

Raising the awareness of health professionals and parents is of fundamental importance for the implementation of an effective vaccine vigilance system, especially at this time when the debate on vaccines is very active. In this context, the use of a direct and informal means of communication, such as messaging, for the reporting of adverse events, has proven to be a valid tool for involving users, as it makes parents perceive the health institution as a reference that is interested in the health of children even after the vaccination session.

The limits of the study concern the impossibility of knowing the outcome of the adverse event at the time of reporting, especially as regards the adverse events reported as "serious" and the lack of guarantee of equity in adhering to the study, given the need to know the Italian language and the need to be able to use mobile telephony as a reporting tool. However, the number of participants in the project and of the responses sent indicate the wide participation of parents. These data allow to speculate the possibility to extend this project to other realities of the national territory.

Continuous monitoring of vaccine safety and implementation of surveillance plans play a key role in achieving greater confidence in immunization programs and optimal vaccination coverage rate. Therefore, it is hoped that pharmacovigilance activity will increasingly become an essential part of the normal clinical practice; however, continuous training of health professionals is required to ensure greater willingness in communicating with citizens and make them more and more involved in monitoring activities.

Acknowledgements

Conflicts of interest statement

The other authors declare no conflict of interest related to this manuscript. GG declares that he does not have a specific conflict of interest related to this paper; however, he reports grants from Sanofi Pasteur MSD, GSK Biologicals SA, Pfizer, Sanofi Pasteur Italy, MSD Italy, Emergent BioSolutions and Seqirus for taking part to advisory boards, expert meetings, for acting as speaker and/or organizer of meetings/congresses and as principal investigator and chief of O.U. in RCTs.

Authors' contributions

All the named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole and have given their approval for this version to be published.

References

[1] Decreto legge 7 giugno 2017, n. 73, Disposizioni urgenti in materia di prevenzione vaccinale, modificato dalla Legge di conversione 31 luglio 2017, n. 119.

[2] Agenzia Italiana del Farmaco (AIFA). Rapporto vaccini 2018 – Sorveglianza post marketing in Italia. Available at: https://www.aifa.gov.it/documents/20142/241056/Rapporto+Vaccini+2018.pdf/62975a0e-a836-da32-f7b9-1e39196374dd (Accessed on: June 20, 2020).

[3] WHO. Causality assessment of an adverse event following immunization (AEFI). User manual for the revised classification (second edition). Available at: https://apps.who.int/iris/bitstream/handle/10665/259959/9789241513654-eng.pdf;jsessionid=697D60B13988EB4549AEC1E3876016DC?sequence=1. (Accessed on: June 18, 2020).

[4] WHO. Global Vaccine Safety. Adverse event following immunization. Available at: https://www.who.int/vaccine_safety/initiative/detection/AEFI/en/ (Accessed on: June 18, 2020).

[5] Agenzia Italiana del Farmaco (AIFA). La vaccinovigilanza in Italia: ruolo e obiettivi. Available at: http://www.agenziafarmaco.gov.it/sites/default/files/La_Vaccinovigilanza_in_Italia_18.04.2017.pdf (Accessed on: June 20, 2020).

[6] Bollaerts K, De Smedt T, Donegan K, Titievsky L, Bauchau V. Benefit-risk monitoring of vaccines using an interactive dashboard: a methodological proposal from the ADVANCE project. Drug Saf 2018;41:775-86. https://doi.org/10.1007/s40264-018-0658-y

[7] Westphal DW, Williams SA, Leeb A, Effler PV. Continuous active surveillance of adverse events following immunisation using SMS technology. Vaccine 2016;34:3350-5. https://doi.org/10.1016/j.vaccine.2016.05.015

[8] Scavone C, Rafaniello C, Brusco S, Bertini M, Menditto E, Orlando V, Trama U, Sportiello L, Rossi F, Capuano A. Did the new Italian law on mandatory vaccines affect adverse event following immunization's reporting? A pharmacovigilance study in Southern Italy. Front Pharmacol 2018;9:1003. https://doi.org/10.3389/fphar.2018.01003

[9] Pillsbury A, Quinn H, Cashman P, Leeb A, Macartney K; AusVaxSafety consortium. Active SMS-based influenza vaccine safety surveillance in Australian children. Vaccine 2017;35:7101-6. https://doi.org/10.1016/j.vaccine.2017.10.091

[10] Regan AK, Blyth CC, Tracey L, Mak DB, Richmond PC, Effler PV. Comparison of text-messaging to voice telephone interviews for active surveillance of adverse events following immunisation. Vaccine 2015;33:3689-94. https://doi.org/10.1016/j.vaccine.2015.06.022

HEALTH PROMOTION

Lebanese University Students and COVID-19: A Survey on their Related-Knowledge, Practice, and Behaviors

ZEINA NASSER[1], YOUSSEF JAMALEDDINE[2], OMAR ISMAIL[2], ABDALLAH SAAB[1], RAMA DAOUD[2], YOUSSEF FARES[1], LINDA ABOU-ABBAS[1]

[1] Neuroscience Research Center, Faculty of Medical Sciences, Lebanese University, Lebanon;
[2] Faculty of Medical Sciences, Lebanese University, Hadath, Lebanon

Summary

Introduction. *Young adults are at the epicenter for preventing the progression of COVID-19 pandemic and must be targeted for education to impede any potential transmission of the disease. This study aimed to assess the knowledge, practice and behaviors of Lebanese university students regarding COVID-19.*

Methods. *A cross-sectional study was carried out among university students at the Lebanese University between March 30, 2020, and April 4, 2020. Information on socio-demographic data, knowledge, practice, and additional information concerning COVID-19 were collected.*

Results. *Our survey showed that the majority of the students had good knowledge 90.8%, and more than two third of the respondents 78.6% reported good practice regarding COVID-19. Gradu-ate students were more knowledgeable compared to undergraduate students (unstandardized beta 0.349 with a 95% confidence interval (CI) of 0.165 to 0.533; p-value < 0.0001). Moreover, male students had a negative impact on good practice compared to females (unstandardized beta -0.280 with a 95% confidence interval (CI) of -0.402 to -0.159; p-value < 0.0001). Nearly half of the students (55.2%) reported that their food intake has increased, and 82.5% of the students didn't practice sport during the quarantine. The most common information source of the students was the television (63.3%) followed by social media (53.9%).*

Conclusions. *This study offers useful insights into the knowledge and practices of Lebanese university students towards COVID-19. Our findings support the importance to deliver health education campaign by the ministry of public health through television and social media to improve the knowledge on disease transmission and preventive measures.*

Introduction

Coronavirus disease 2019 (COVID-19) first emerged in December 2019 in Wuhan, in China, and then rapidly spread all over the world [1]. In late January 2020, the World Health Organization (WHO) declared COVID-19 as a public health emergency of international concern [2]. At present, no COVID-19 vaccine has been successfully developed and no effective treatment has been established. Hence, implementation of protective measures such as good hygienic practices including washing hands with soap and water or using hand sanitizers frequently, avoiding touching the face, mouth, nose, eyes with hands, and maintaining social distance is of utmost importance to reduce the spread of the disease. Public adherence to these preventive measures is affected by their knowledge, attitudes, and practices (KAP) towards this pandemic. Thus, assessment of KAP is important in identifying gaps and can guide decision makers in implementing adequate educational interventions to limit the spread of this outbreak.

Lebanon is one of the countries fighting the novel virus. The first Lebanese case was reported on February 21, 2020. Since then, the number of COVID-19 cases has risen considerably. As of November 5th 2020, this outbreak resulted in 87097 cases [3] with the highest incidence of COVID-19 occurring among young adults aged 20-29 years old (26.9%) [4] who are often an asymptomatic carrier of the SARS-COV-2 [5]. As a consequence, a high transmission of COVID-19 to the vulnerable group could occur and cause potential outbreak. In addition, the virus has high fatality rates in the elderly people with underlying health conditions [6, 7]. Thus, young adults are at the epicenter for preventing the progression of COVID-19 pandemic and must be targeted for education to impede any spread or potential transmission of the disease.

Given that a large number of young adults are enrolled in Lebanese public and private universities, assessment of their KAP levels will roughly reflect their awareness regarding COVID-19 which will constitute a general reference to guide the local authorities in identifying gaps, strengthening ongoing prevention efforts and planning the required educational interventions. Thus, there is an urgent need to understand the students' awareness of COVID-19 at this critical moment. Therefore, it is essential to evaluate their knowledge, practice, and behavior response towards COVID-19.

Methods

STUDY DESIGN AND POPULATION

A cross-sectional study was carried out among university students at the Lebanese University between March 30, 2020, and April 4, 2020. It includes Lebanese students from 15 faculties (Faculty of Letters and Human Sciences, Faculty of Law and Political and Administrative Sciences, Faculty of Sciences, Faculty of Fine Arts and Architecture, Faculty of Pedagogy, Faculty of Information, Faculty of Economics and Business Administration, Faculty of Engineering, Faculty of Agronomy, Faculty of Public Health, Faculty of Medical Sciences, Faculty of Dental Medicine, Faculty of Pharmacy, Faculty of Tourism and Hospitality Management, and Faculty of Technology). All eligible Bachelor, Masters and Doctor of Philosophy Ph.D. students registered at Lebanese University for the academic year 2019-2020 are enrolled in our study.

ETHICAL CONSIDERATION

The study protocol was reviewed and approved by the scientific committee of the Neuroscience Research Center (NRC), Faculty of Medical Sciences at the Lebanese University (Reference number 240/2020). The study was conducted following the Declaration of Helsinki [8]. Students had to answer a yes-no question to confirm their willingness to participate voluntarily.

SAMPLE SIZE CALCULATION

The sample size was calculated using the online Raosoft sample size calculator designed specifically for population surveys. Assuming 80000 students are registered in the Lebanese university, the required calculated sample size was 383 with a confidence level of 95% and a 5% margin of error. A total number of 2140 of students were recruited in the present study. The response acceptance was closed in April 4, 2020.

DATA COLLECTION

The questionnaire was created and designed by the authors after a thorough search in the literature and a link was sent to the participants including a brief introduction on the background, the aim of the study, voluntary nature of participation, declarations of confidentiality and anonymity, and instructions for filling in the questionnaire. Content validity of the resulting version was assessed by a panel of three experts with expertise in public health and epidemiology. They were asked to evaluate the relevance of the items in assessing the knowledge and practices of university students towards COVID-19. A consensus was reached after omitting three items that were rated irrelevant. Then, the items were translated and adapted to the Arabic language by three translators. A final questionnaire was generated and was divided into five sections:

1. socio-demographic characteristics included: Age, gender, faculty, level of education, marital status (single, married, divorced, or widowed);

2. the knowledge section consisted of 11 questions of triple choice response (true, false, and don't know) to assess the knowledge of students about symptoms, mode of transmission, and the current treatment of COVID-19, as well as the management of people who have been in contact with COVID-19 positive cases. A correct answer was assigned 1 point and an incorrect/don't know answer was assigned 0 points. The total knowledge score was 11 ranged from 0 to 11 with a higher score indicating a better knowledge. Students with knowledge score above 60% were regarded as having good knowledge, while those who scored below 60% were considered having poor knowledge based on Bloom's cut off point [9]. In addition to one question regarding their main sources of information regarding COVID-19. On this question, multiple responses from the participants were allowed;

3. the practice section included 8 questions regarding their protective measures to prevent getting the infection such as avoiding crowded places, using hand sanitizer, washing their hands, wearing a mask and gloves and avoiding shaking hands and kissing when meeting other peoples.

The answer (always) was assigned 1 point while answers (occasional and never) were assigned 0 points. The overall practice score, obtained by the sum of the scores, ranged between 0 and 8. Participants with scores >80% were classified as having acceptable preventive practice, while those with scores < 80% were considered having an unacceptable preventive practice based on Bloom's cut off point [10].

Behavior section included questions focusing mainly on the change in their daily habits and behavior during the quarantine, for example religion practices, smoking, sports and eating habits, and behavior.

STUDY PROCEDURE

As the Lebanese Government closed the public and private universities, the potential respondents were electronically invited to participate. The data was collected using an online survey. After adding the questionnaire into the Google forms, a link was sent to eligible students for responding to the questionnaire. To assess the clarity and readability of the questionnaire it was piloted on a total number of 30 participants sampled from the target population and subsequently excluded from the data analysis. The estimated time required for the completion of the survey was 5 minutes.

STATISTICAL ANALYSIS

Statistical analysis was carried out using the statistical software SPSS (Statistical Package for Social Sciences), version 22.0. Descriptive statistics were reported using means and standard deviations (SD) for continuous variables and frequency with percentages for categorical variables. Multivariate linear regression was used to identify factors associated with knowledge and practice scores as dependent variables. Unstandardized regression coefficients (β) and their 95% confidence

Tab. I. Demographic characteristics of the study participants (N = 2140).

Variable	Frequency	Percentage
Age (mean ± SD)[a] years (20.8 ± 3.9)		
Gender		
Male	488	22.8
Female	1652	77.2
Education		
Undergraduate	1785	83.4
Graduate	355	16.6
Marital status		
Single	1856	86.7
Others	284	13.3

[a] SD: Standard Deviation.

intervals (CIs) were reported. All tests were two-tailed, with a significance level of $p < 0.05$.

Results

DEMOGRAPHIC CHARACTERISTICS OF THE STUDY PARTICIPANTS

The demographic data is shown in Table I. A total of 2140 students were recruited from 15 faculties at Lebanese University. Their mean age was 20.8 ± 3.9 years and 77.2% of them were females. Among them, the majority 83.4% was undergraduate and 86.7% were single.

STUDENT'S KNOWLEDGE TOWARDS COVID-19

Out of the 2140 students, the majority 90.8% had good knowledge. Table II describes students' answers towards COVID-19 knowledge items. Poor knowledge was more apparent in the 2 items related to the transmission of the

disease in which the correct responses rates were low 31.3%, and 33.3 % respectively. The result indicates that the overall understanding about the virus was good, knowledge about the major symptoms namely fever, cough and difficulty in breathing was appreciated by 95.9% the students. Moreover 85.0% and 96.0% of the students were aware about the unavailability of specific treatment and about the management of COVID-19 positive contact respectively. The mean total knowledge score was 8.54 ± 1.54.

SOURCE OF INFORMATION

Table III showed the various sources of knowledge about COVID-19 among the students. Television 63.3% was the commonest source followed by Social media 53.9%, internet 49.1%, World Health Organization (WHO) 44%, Ministry of Health 42.7%, and friends 29.4%.

PRACTICE RELATED TO COVID-19 AMONG UNIVERSITY STUDENTS

In order to assess the practices followed by the students to prevent COVID-19 infection, 8 items were used. Table IV shows the answers collected from the students regarding their practice during the epidemic. The overall mean practice score was 7.15 ± 1.23 and more than half of the studied sample 78.6% reported good practice and 21.4 % reported poor practice toward COVID-19. Most of the students practiced appropriate protective measures in their daily life. The majority 96.6% agreed to avoid going to crowded places, 98.3% abided by cleaning hands with soap and water when back to home, 84.8% supported washing hands frequently, 93.5% shared their agreement on avoiding handshaking and 96.8% reported abiding by the lockdown rules. A negative practice of not wearing face masks while going out in public places was observed among 31.8% of the students.

Tab. II. COVID-19 knowledge among university students.

Knowledge items	Students'answers		
	Correct	Wrong	Do not know
K1. The main symptoms of Corona are fever > 38°C, cough, sore throat, runny nose and shortness of breath	2052 (95.9)	37 (1.7)	51 (2.4)
K2. There is no currently effective cure for COVID-19, but early symptomatic and supportive treatment can help most patients recover from the infection	1820 (85.0)	109 (5.1)	211 (9.9)
K3. Only the elderly, or who suffer from chronic diseases or obesity (overweight) are more likely to severe infection	1706 (79.7)	257 (12.0)	177(8.3)
K4. Contact of COVID-19 positive case must be isolated immediately for 14 days. If symptoms appear during this period, the patient must undergo a PCR[a] test	2055 (96.0)	50 (2.3)	35 (1.6)
K5. The disease will be transmitted from pets to the human	137 (6.4)	1674 (78.2)	329 (15.4)
K6. Coronavirus spreads via respiratory droplets of infected individuals	1726 (80.7)	184 (8.6)	230 (10.7)
K7. No need for children and young adults to take action to prevent Coronavirus	20 (0.9)	2076 (97.0)	44 (2.1)
K8. The disease cannot be transmitted from asymptomatic patients	77 (3.6)	1907 (89.1)	156 (7.3)
K9. The coronavirus can survive for many hours or many days in the environment	1525 (71.3)	202 (9.4)	413 (19.3)
K10. COVID-19 can be transmitted through eating undercooked meat/chicken	832 (38.9)	669 (31.3)	639 (29.9)
K11. COVID-19 can be eliminated with at least 60% alcohol (Yes)	712 (33.3)	1081 (50.5)	347 (16.2)

[a] PCR: polymerase chaine reaction.

Tab. III. Source of information regarding COV-ID-19.

Source of information*	n (%)
TV	1355(63.3)
Social media	1154(53.9)
Internet	1051(49.1)
WHO	941(44.0)
MOPH	913(42.7)
Friends	629(29.4)

* Multiple Responses, TV television, WHO World Health Organization, MOPH Ministry of Public health, n frequency, % percentage.

Tab. IV. Good Practice Related to COVID-19 among university students.

	n	%
P1. I don't visit a crowded place	2067	96.6
P2. I take a hand sanitizer with me when I go out	1730	80.8
P3. I wash my hands with soap and water when I am back home	2104	98.3
P4. I Frequently wash my hands	1815	84.8
P5. I put on mask when I go out	1460	68.2
P6. I avoid shaking hands	2001	93.5
P7. I avoid kissing	2054	96.0
P8. Abide by the lockdown rules	2071	96.8

n: frequency; %: percentage.

Behaviors of university students towards COVID-19 during quarantine

Of all the university students, only 6.9% of them reported that they increased their amount of smoking and 41.9% of them reported that they increased their religion practice since the start of the corona pandemic. On the other hand, near half of the students reported that their food intake has increased and agreed to cook their own food to minimize the risk to contract the infection during the quarantine 55.2% and 89.4% respectively. Our results showed that 82.5% of the students didn't practice sport during the quarantine (Tab. V).

Factors associated with knowledge and practices regarding COVID-19

Results of multiple linear regression analysis showed that graduated students were more knowledgeable compared to ungraduated students (unstandardized beta 0.349 with 95% CI of 0.165 to 0.533; p-value < 0.0001). Our results also showed that knowledge is positively associated with age (unstandardized beta 0.032 with 95% CI of 0.014 to 0.049; p-value < 0.0001) and male students were less knowledgeable compared to female students (unstandardized beta -0.281 with 95% CI of -0.435 to -0.126; p-value < 0.0001).

Multiple linear regression also showed that high level of knowledge and age were highly associated with good practice (unstandardized beta 0.172 with 95% CI of 0.138 to 0.205; p-value < 0.0001, unstandardized beta 0.014 with 95% CI of 0.002 to 0.027; p-value < 0.0001 respectively). On the other hand, male students had a negative impact on good practice (unstandardized beta -0.280 with 95% CI between -0.402 to 0.159; p-value < 0.0001) compared to female (Tab. VI).

Discussion

In this survey, we provided an insight to the knowledge, preventive measures of the students of Lebanese university towards COVID-19. The study also highlighted

Tab. V. Student's behavior during quarantine.

	Frequency	Percentage
Do you smoke (cigarettes, waterpipe, vape)? If you answered yes, how did quarantine affect your smoking pattern?		
I don't smoke	1678	78.4
I reduced my smoking after the start of the corona epidemic	217	10.1
I still smoke the same amount since the start of the corona epidemic	147	6.9
I increased the amount since the start of the corona epidemic	98	4.6
Does quarantine affect your Religion practice		
Yes, my religion practice has increased	896	41.9
Yes, my religion practice has decreased	32	1.5
No, my religion practice did not change	1212	56.6
Does quarantine affect your food intake?		
Yes, my food intake has increased	1181	55.2
Yes, my food intake has decreased	285	13.3
No, my food intake did not change	674	31.5
Does quarantine affect the number of food deliveries that you order?		
Yes, food deliveries have decreased	1913	89.4
Yes, food deliveries have increased	20	0.9
No change	207	9.7
Have you practice sport during the quarantine?		
No	375	82.5
Yes	1765	17.5

Tab. VI. Results of linear regression analysis on factors significantly associated with good knowledge and practices towards COVID-19 (N = 2140).

	Unstandardized β	Standardized β	95% CI	P-value
Knowledge				
Level of education (graduate vs undergraduate)	0.349	0.084	0.165-0.533	< 0.0001*
Age	0.032	0.081	0.014-0.049	< 0.0001*
Gender (male versus female)	-0.281	0.076	-0.435--0.126	< 0.0001*
Practice				
Knowledge score	0.172	0.214	0.138-0.205	< 0.0001*
Gender (male vs female)	-0.280	-0.095	-0.402--0.159	< 0.0001*
Age	0.014	0.047	0.002-0.027	< 0.0001*

* p-value < 0.05 is considered significant, 95% CI 95% confidence Interval.

the behavior of university students towards COVID-19 during quarantine. To the best of our knowledge, this is the first cross-sectional survey conducted in Lebanon. Our results showed that the majority of the university students had good knowledge about the disease, and more than half of the participants had good practice regarding COVID-19. The main common information source was the television. Our results also showed that graduate students were more knowledgeable compared to undergraduate students. However, male students had a negative impact on good practice.

Our findings of good level of knowledge is in line with a study conducted in Iran by Taghrir et al., who reported that appropriate knowledge was acquired by 86.96 % of medical university students [11]. This could be explained by the seriousness of the disease and the importance of media to increase the public's adherence to the safety measures to combat the spread of COVID-19, in addition to the effectiveness of different awareness campaigns conducted in Lebanon especially after the declaration of COVID-19 as a pandemic by the WHO [9].

We also found that students used TV 63.3% and social media 53.9% as sources of information. Although these platforms provide an easy way to get the information, they can also be a source of fake news. Thus, it is highly recommended to deliver effective health education campaign by the ministry of public health through TV and social media to improve the knowledge and the preventive measures of the students against COVID-19 epidemic in Lebanon. Moreover, reliable health information on local news media and public health messages should be disseminated to the Lebanese community to increase COVID-19 knowledge and disease prevention strategies.

With respect to practice, more than two third of the respondents 78.6% practiced appropriate protective measures in their daily life. However, putting on a mask when going out had the lowest score, highlighting the importance of governmental intervention to implement daily mask use.

Regarding the behavior, near half of the students reported that their food intake has increased and agreed to cook their own food to minimize the risk to contract the infection during the quarantine. it might be a reflection of the large amount of information circulated in the community and perceived by them, which necessitate for further awareness campaigns in order to minimize the

panic aroused among the population. Our results showed also that 82.5% of the students didn't practice sport during the quarantine. Physical activity and relaxation techniques can be valuable tools to help students remain calm and continue to protect their health during this time. We recommend online exercise classes. Many of these are free and can be found on YouTube to reduce sedentary behavior while at home in self-quarantine.

One of the most interesting finding is that the females in this study were more aware of the importance of COVID-19. Our result is similar with a study conducted in Bangladesh which found the female students were superior to man in terms of knowledge and practice [12]. Another Chinese study supports the finding Chinese women residents have appropriate practices towards COVID-19 [13].

LIMITATIONS

Our study had some limitations. Our sample was not based on a random selection and it is only from the Lebanese University which is a public university in Lebanon. Thus, the findings did not reflect the whole picture of all students enrolled in private and public universities in Lebanon. We should also mention the information bias; some participants might have provided socially desirable responses rather than their actual opinions. Finally, the cross-sectional nature of the study can only demonstrate association and not a cause-effect relationship.

Conclusions

Most Lebanese university students study revealed a good knowledge and possessed a good practice towards COVID-19. As the global threat of COVID-19 continues to emerge, findings support continued education and reinforcement of COVID-19 known facts to address the abundance of misinformation available online and on social media sites.

Acknowledgements

Conflict of interest statement

The authors have no potential conflicts of interest to declare.

Authors' contributions

LAA and ZN developed the project idea. AS, YJ and OI formulated the questionnaire. LAA and ZN organized and analyzed the survey. LAA, ZN, and RD drafted and critically reviewed the paper. YF reviewed the manuscript for important intellectual content. All authors read and agreed on the final version.

References

[1] Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, Zhao X, Huang B, Shi W, Lu R, Niu P, Zhan F, Ma X, Wang D, Xu W, Wu G, Gao GF, Tan W; China Novel coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727-733. https://doi.org/10.1056/NEJMoa2001017

[2] World Health Organization (WHO). Novel Coronavirus (2019-nCoV): situation report, 11. 2020 2020-01-31; Available from: https://apps.who.int/iris/handle/10665/330776

[3] Ministry of Public health (MOPH). Epidemiological surveillance program. Surveillance of COVID-19 in Lebanon. October 23, 2020.

[4] Disaster risk management (DRM). Daily-situation-report-04-Nov. November 5, 2020; Available from: http://drm.pcm.gov.lb/Media/News/Daily-situation-report-04-Nov-FINAL.pdf

[5] Jin YH, Cai L, Cheng ZS, Cheng H, Deng T, Fan YP, Fang C, Huang D, Huang LQ, Huang Q, Han Y, Hu B, Hu F, Li BH, Li YR, Liang K, Lin LK, Luo LS, Ma J, Ma LL, Peng ZY, Pan YB, Pan ZY, Ren XQ, Sun HM, Wang Y, Wang YY, Weng H, Wei CJ, Wu DF, Xia J, Xiong Y, Xu HB, Yao XM, Yuan YF, Ye TS, Zhang XC, Zhang YW, Zhang YG, Zhang HM, Zhao Y, Zhao MJ, Zi H, Zeng XT, Wang YY, Wang XH; for the Zhongnan Hospital of Wuhan University Novel Coronavirus Management and Research Team, Evidence-Based Medicine Chapter of China International Exchange and Promotive Association for Medical and Health Care (CPAM). A rapid advice guideline for the diagnosis and treatment of 2019 novel coronavirus (2019-nCoV) infected pneumonia (standard version). Mil Med Res 2020;7:4. https://doi.org/10.1186/s40779-020-0233-6

[6] Mo P, Xing Y, Xiao Y, Deng L, Zhao Q, Wang H, Xiong Y, Cheng Z, Gao S, Liang K, Luo M, Chen T, Song S, Ma Z, Chen X, Zheng R, Cao Q, Wang F, Zhang Y. Clinical characteristics of refractory coronavirus disease 2019 in Wuhan, China. Clin Infect Dis 2021;73:e4208-e4213. https://doi.org/10.1093/cid/ciaa270

[7] Chen N, Zhou M, Dong X, Qu J, Gong F, Han Y, Qiu Y, Wang J, Liu Y, Wei Y, Xia J, Yu T, Zhang X, Zhang L. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 2020;395:507-513. https://doi.org/10.1016/S0140-6736(20)30211-7

[8] Williams JR. The declaration of Helsinki and public health. Bull World Health Organ 2008;86:650-2. https://doi.org/10.2471/blt.08.050955

[9] Dauda Goni M, Hasan H, Naing NN, Wan-Arfah N, Zeiny Deris Z, Nor Arifin W, Abubakar Baaba A. Assessment of knowledge, attitude and practice towards prevention of respiratory tract infections among Hajj and Umrah Pilgrims from Malaysia in 2018. Int J Environ Res Public Health 2019;16:4569. https://doi.org/10.3390/ijerph16224569

[10] Akalu Y, Ayelign B, Molla MD. Knowledge, attitude and practice towards COVID-19 among chronic disease patients at Addis Zemen Hospital, Northwest Ethiopia. Infect Drug Resist 2020;13:1949-60. https://doi.org/10.2147/IDR.S258736

[11] Taghrir MH, Borazjani R, Shiraly R. COVID-19 and Iranian Medical Students; A Survey on their related-knowledge, preventive behaviors and risk perception. Arch Iran Med 2020;23:249-254. https://doi.org/10.34172/aim.2020.06

[12] Ferdous MZ, Islam MS, Sikder MT, Mosaddek ASM, Zegarra-Valdivia JA, Gozal D. Knowledge, attitude, and practice regarding COVID-19 outbreak in Bangladesh: An online-based cross-sectional study. PLoS One 2020;15:e0239254. https://doi.org/10.1371/journal.pone.0239254

[13] Zhong BL, Luo W, Li HM, Zhang QQ, Liu XG, Li WT, Li Y. Knowledge, attitudes, and practices towards COVID-19 among Chinese residents during the rapid rise period of the COVID-19 outbreak: a quick online cross-sectional survey. Int J Biol Sci 2020;16:1745-52. https://doi.org/10.7150/ijbs.45221

COVID-19 vaccination intention and hesitancy: Mistrust on COVID-19 vaccine benefit a major driver for vaccine hesitancy among healthcare workers; a cross-sectional study in North India

SINU JOSE[1], MANEESHA C. CYRIAC[2], MANJU DHANDAPANI[3], JULEE JOSEPH[4]

[1] MSc Nursing, Public health Nursing, PGIMER, Chandigarh; [2] BSc Nursing, Bel-Air College of Nursing Panchgani;
[3] PhD, Lecturer, National Institute of Nursing Education, PGIMER, Chandigarh;
[4] PhD, Professor, Government College of Nursing, Kottayam

Summary

Background. *The advent of an effective novel COVID-19 vaccine could extinguish the current devastating pandemic but the vaccine hesitancy is a hurdle for the public health system, so this study estimated the COVID-19 vaccination intention and hesitancy among the healthcare workers, the priority target group for the COVID-19 vaccination in India.*
Methods. *A web-based cross-sectional survey was conducted among the healthcare workers in Chandigarh, a union territory in North India, using a Snowball sampling technique. A total of 403 healthcare workers participated in the study between 2nd and 25th January 2021. The primary data collected were the intention to get vaccinated against the available COVID-19 vaccine and the concerns regarding the new vaccines. The attitude towards novel COVID-19 vaccine was assessed using developed Vaccine attitude examination scale. These questionnaire, which were delivered via WhatsApp, was filled by the participants over Google forms.*
Results. *Among the 403 respondents surveyed, the majority*

(54.6%) reported they were definitely intended to get vaccinated against COVID-19, however, 7% expressed a resistance for inoculation with COVID-19 vaccination. The perceived susceptibility (aOR = 0.511, CI 0.265-0.987) and severity of COVID-19 infection (aOR = 0.551 CI 0.196-0.704) and not being concerned about the efficacy of new COVID-19 vaccines (aOR = 0.702 CI 1.109-26.55) were found to have the highest significant odds of intention to take the COVID-19 vaccine. The majority (62%) were concerned about the safety of the vaccine, in terms of side-effects, quality control, and doubted efficacy of the vaccine. The mistrust of the benefits of the vaccine is a significant predictor for vaccine hesitancy among the healthcare workers (aOR = 5.205 CI 3.106-8.723).
Conclusion. *Therefore, strategic communication and vaccine-acceptance programs should be formulated in order to combat the prevailing mistrust on the vaccine safety and efficacy and attain effective coverage to gain herd immunity.*

Introduction

The severe acute respiratory syndrome corona virus-2 (COVID-19) pandemic had infected over 83 million people globally (affected more than 200 countries or territories) and reported about 1.8 million deaths since the start of the pandemic [1], and in India its estimated approximately 8.6 million cases and a 130000 deaths. Approximately 1.4 billion population in India are at risk of acquiring this infection with many are at risk for developing severe form of the infection. Hence this pandemic poses a significant threat to the public health system and for health care providers in India [2]. The widespread use of the effective SARS-CoV-2 vaccine could prevent the morbidity and mortality associated with COVID-19 infection and mitigate the other catastrophic impacts on the global economy and psycho-social well-being of the citizens with the enforcement of non-pharmacological strategies, such as testing, quarantine, lockdown, social distancing measures [3-10].
So the development of an effective and safe vaccines

against COVID-19 infection is the most effective strategy for limiting the spread of this disease by establishing a higher level of herd immunity and preventing repeated or continuous epidemic curves [3, 10]. The intensified international efforts resulted in the development of the safe and effective COVID-19 vaccines at an unprecedented speed and are made available for the public use [11, 12]. Therefore, almost all the health care workers and general population are eagerly waiting for the COVID-19 vaccine.
But many healthcare workers are anxious and afraid of the safety and efficiency of the vaccines, its adverse health outcomes, therefore, vaccine hesitancy among them is really worrisome and it might percolate down to the general population. So in this present situation, for the containment of this pandemic vaccine hesitancy will have a negative impact and forms a big barrier to overcome. For this it's necessary to address the factors behind this hesitancy and why the people are skeptical. Vaccine hesitancy is highly prevalent among those vaccines which had shown their efficiency through

years of accumulative scientific evidences, therefore, the acceptance of the novel vaccine which is being developed over a short span of time for the COVID-19 remains uncertain [5, 13, 14]. The experiences from previous pandemics reports that the acceptance of vaccines for H1N1 and H7N9 shown unsatisfying results with an acceptance rate varying from 8 to 67% in many developed countries [15-17]. Even among the health care workers in China during domestic H1N1 outbreak, only 25% received the vaccination, when the vaccine was provided for free [18].

So, vaccine hesitancy is a complex public health issue, as the intention to vaccination is the important factor in the success of vaccination program in an epidemic. There are multiple factors affecting the vaccine hesitancy, when a new vaccine is introduced. These includes varying social, cultural and political differences across the nation, public concern about vaccine safety and efficacy, adverse health outcomes, misconceptions about the need for vaccination, lack of trust in the health system, cost of vaccine, attitude and previous uptake history of influenza vaccination, perceived risk of infection, the severity of the event, personal consequences, history of previous vaccination etc. [15, 16, 19-22].

The equitable vaccination coverage across the population is essential for the containment of the COVID-19 pandemic, as the severity of the infection and burden caused to the nation are huge, compared with previous influenza pandemics. But, in order to flatten the epidemic curves higher vaccine coverage is required. The vaccine hesitancy affects not only the individual who are not willing to take the vaccine, but the whole community is affected, by not reaching the threshold to confer herd immunity. So, the vaccine hesitancy by the population undermines the public health benefits of the COVID -19 vaccination program and efforts.

Understanding individual's concerns regarding COVID-19 vaccine safety and efficacy should be assessed at the earliest for formulating strategic communication programs as this will strongly influence their intention to get vaccinated. The willingness of health workers to get vaccinated and a positive response towards vaccination are motivating factors to enhance the vaccination rate not only in the health workers, but also among general public. Due to the high risk of exposure to the virus, a high vaccination rate among the healthcare workers is mandatory to curb the rate of virus transmission. So far, we could not find any literature on COVID vaccination acceptance among health workers in India. Hence, this study was conducted for urgent understanding to assess the willingness of the health care workers in taking the COVID-19 vaccine in a union territory in North India, in order to formulate effective promotion strategies. The health care workers, they are of first to receive this novel vaccine, they will have diverse views on vaccination ranging from advocating for vaccination or demanding through to those who reject them and even a small group with anti-vaccine attitude.

Materials and methods

STUDY DESIGN AND SETTING

We conducted a cross-sectional study among the Nurses working in the COVID-19 units of two tertiary care hospitals in Chandigarh, a Union territory in North India. The study was conducted in January 2021, when the country was planning for the immunization against COVID-19 using COVAXIN and COVISHIELD.

STUDY SAMPLE

The researchers calculated the sample size using OpenEpi.com. The study by Lin et al. [22] showed a acceptance for COVID-19 vaccination as 46.8% in China, hence, the estimated sample size was 383 with a confidence interval of 95%. The researchers distributed the questionnaires among 500 nurses working in the COVID-19 units of selected tertiary care centers, we excluded persons with specific contraindications for the COVID-19 vaccine. We got 403 (80.6%) valid responses with repeated reminders. Incomplete questionnaires were excluded from the sample and were not analyzed.

TOOLS AND TECHNIQUES

The survey consisted of a validated self-administered electronic questionnaire, designed and developed by the investigators after a thorough literature review based on the objectives of the study. The research experts in the field of public health were reviewed the questionnaire and the content validity of the tools were established. The questionnaire was drafted and distributed in English language. The tool was designed as short, simple, and concise statements, easy to comprehend and quick to complete. The validity of the tool was obtained from the research experts in the field of public health and nursing. The final questionnaire consisted of:

Perception of healthcare workers regarding COVID-19 infection and COVID-19 vaccines: health belief model derived items under the headings of perceived susceptibility to COVID-19 (3 items), perceived severity of COVID-19(3 items), perceived benefits of COVID-19 vaccine (2 items), perceived barriers for the uptake of COVID-19 vaccine (5 items) and cues to action (2 items) were used to assess the respondents perception on a four point Likert scale ranging from strongly agree to strongly disagree [22-24].

Intention to receive a COVID-19 vaccine and vaccine preference, the intention for getting Vaccine against COVID-19 was assessed using a single four point scale (definitely no to definitely yes) question. The participants preference for domestically made and imported vaccine was assessed, and their level of confidence in these vaccines on a 4 point scale (completely confident to completely not confident) were assessed [3, 22-26].

Concerns for vaccinating against COVID-19: the participants were asked for the potential barriers/ concerns regarding COVID-19 vaccine using a multiple response question [26, 27].

COVID-19 vaccination attitude examination

scale: A specific attitude towards COVID-19 vaccine were examined using an 8-item Vaccination attitude examination scale (VAX) developed by the research team based on the literature [28, 29]. The participants were asked to focus specifically on the COVID-19 vaccine and were free to respond on a five point scale from strongly agree to strongly disagree under three specific subscales, viz 1) Mistrust on the COVID-19 vaccines benefits, 2) Safety concerns on the COVID-19 vaccination, and 3) preference for natural immunity over COVID-19 vaccination. Internal consistency of this tool in the current study was found to be good ($\alpha = 0.78$).

Data collection

The data collection started after obtaining permission from the Institutional Ethics Committee. A self-administered questionnaire was made using Google forms and distributed among the nurses through WhatsApp. At the beginning of the questionnaire, the participants were briefly informed about the objectives of the study, and informed consent was obtained within the introductory web page before the survey enrollment. The data collected were stored in Google drive and protected by username and password.

Ethical consideration

The study was conducted after getting approval from the Institutional Ethics Committee. This study was an online survey conducted among the health care workers, the identification details of the participants were not collected in this study. Informed consent was collected in the introductory page of the Google form and informed that the participation in the study is voluntary and non-commercial.

Statistical analysis

Collected data were analyzed using Google form and SPSS version 20. Descriptive statistics including frequencies and percentage were used to present the demographic data, Chi-square test was used to assess the significance of the association between COVID-19 vaccine acceptance and demographic variables and perception regarding COVID-19 vaccine. Logistic regression analysis was used to identify the predicting variables of vaccine acceptance.

Results

We got completely filled survey forms from 403 participants through a snowball sampling technique from various health care workers from the Government tertiary care centers in Chandigarh, a Union territory in North India.
Demographic and other characteristics of the participants In the present study, the participants were the health care professionals working in the government tertiary care center in Chandigarh, a Union territory in North India. Among the participants around half of the participants were in the age group of 28-35 (47%) with a mean age

of 30.12 ± 6.93 range from 21-53, 68.7% were females and married consisted of 253 (62.8%) participants. About 82% of the participants were living with family consisting of more than 3 members and 50% were having children up to the age of 18years. More than half of the respondents (54.6%) were planning to get vaccinated immediately whenever it is made available.

Table I shows that majority (69%) of the participants were had a degree level of education, In total, 74.2% thought that their health status was good or very good 85% of the participants reported perceived overall health condition as very good/good and 65% perceived themselves at the risk of COVID-19 infection because of occupational exposure. Type of the exposure with the patients showed that 46.4% were working with direct contact with the COVID-19 sick patients in isolation ward and 15.4% reported that they had a COVID-19 infection in any of the family members from the start of the pandemic.

Most of the participants (69.5%) revealed that they had not vaccinated against influenza in the previous years, and the intention to vaccinate against COVID-19 infection shows that overall, three in five participants (54.6%) would definitely get the vaccine, 38.5% had low levels of hesitancy, 6.5% had high levels of hesitancy, and only 2 were resistant (they expressed they were definitely not going to get the vaccine).

Majority (60%) of the participants expressed a preference for the foreign-made/imported vaccines, when they expressed 32% complete confidence on those vaccines. Among the participants, 64% expressed a confidence on the domestically made vaccine, while 94% for the imported vaccines.

Concerns/barriers regarding COVID-19 vaccine uptake among the healthcare workers

The major concerns about the COVID-19 vaccines among the healthcare workers were assessed using multiple response question, with the various aspects of major concerns on efficacy, safety and the perceived severity of the infection were considered. Only 5.9% of the responders mentioned no concerns on the vaccines, while majority concerned about the complications and adverse events following the immunization (62%), and 33.33% lacked confidence in the efficacy of the vaccines. The quality control of the vaccine was doubted by 22%, and 17.8% were planned to wait until tested by others in the community and confirm the safety and efficacy of the vaccines, whereas 11.6% were expressed a belief in the natural immunity over vaccination.

Health beliefs regarding COVID-19 infection and COVID vaccination

The participants perceptions regarding the COVID-19 infection and the COVID-19 vaccine were assessed based on the HBM construct, the participants expressed a high level of perceived susceptibility for COVID-19 infection with a mean percentage score of 78.41% (SD = 1.600) and perceived barriers, the mistrust in

Tab. I. Socio-demographic characteristics and the COVID-19 vaccination intention and preference and confidence on the COVID-19 vaccines (n = 403).

Variables	Frequency (%)
Age	
20-27	147 (36.5%)
28-35	190 (47.1%)
36-42	30 (7.4%)
> 43	36 (9%)
Gender	
Female	277 (68.7%)
Male	126 (31.3%)
Marital status	
Unmarried	150 (37.2%)
Married	253 (62.8%)
Educational status	
Diploma	28 (6.9%)
Degree	278 (69%)
Postgraduate and above	97 (24.1%)
Number of members in household	
Alone	24 (6%)
2	47 (11.7%)
3-4	208 (51.6%)
> 5	124 (30.8%)
Having children up to age 18 years	
Yes	202 (50.1%)
No	201 (49.9%)
Ever diagnosed with chronic diseases	
Yes	62 (15.4%)
No	341 (84.6%)
Perceived overall health	
Very good	103 (25.6%)
Good	240 (59.6%)
Fair/Poor	60 (14.8%)
Self-perception, at risk of severe illness from COVID-19	
Yes	262 (65%)
No	141 (35%)
Have you or anyone in the family got sick with COVID-19 since the start of pandemic	
Yes	62 (15.40%)
No	341 (84.60%)
How would you describe your exposure to COVID-19 sick patients while at work?	187 (46.4%)
Direct interaction with verified sick patients	86 (21.30%)
Direct interaction with non-verified patients	29 (7.2%)
No direct interactions	
No known interactions with COVID-19 patients	56 (13.9%)
Students	45 (11.2%)
Trust on the Government in addressing unexpected health threats to our nation, including COVID-19 epidemic	
Yes	272 (67.5%)
No	131 (32.5%)
Have you been vaccinated against the flu in the last year?	
Yes	123 (30.50%)
No	280 (69.50%)
Refused a recommended vaccine in the past	
Yes	50 (12.4%)
No	353 (87.6%)

▶

Variables	Frequency (%)
COVID-19 vaccination intention	
Definitely Yes	220 (54.6%)
Probably Yes	155 (38.5%)
Probably No	26 (6.4%)
Definitely No	2 (0.50%)
Preference for COVID-19 vaccine	
Domestically-made vaccine	161 (40%)
Foreign made vaccine	242 (60%)
Confidence in domestically made vaccine	
Completely confident	36 (8.9%)
Confident	222 (55.2%)
Not confident	109 (27%)
Completely not confident	36 (8.9%)
Confidence in foreign-made made vaccine	
Completely confident	129 (32%)
Confident	250 (62%)
Not confident	12 (3%)
Completely not confident	12 (3%)

the efficacy of the vaccine and worrying about the adverse effects of the vaccination for COVID-19 was expressed a score of 75.2% (SD = 1.52). The mean percentage score for perceived benefits of the COVID-19 vaccination and cues to action were 61.74% (SD = 1.02) and 64% (SD = 1.1).

Table II shows that the participants in the present study expressed a significant level of susceptibility of COVID-19 infection, more than 80% of the respondents were agreed that there is a great chance of getting COVID-19, and are worried about the complications. The participants had a high perception of the severity of COVID-19; 89% agreed that complications of COVID-19 are serious but only 55% were worried about becoming sick by COVID-19 infection. A higher proportion reported a higher confident on the perceived benefits of the COVID-19 vaccination in the prevention of the illness and its complications. Concerns about the safety and efficacy of the vaccines were expressed and found to be higher among the participants. Most of the participants (94%) reported they would take the vaccine when they are provided with adequate information and some (76%) reported they will take only when they got sufficient evidence from others taken.

ATTITUDE OF HEALTHCARE WORKERS REGARDING COVID-19 VACCINATION

The total mean percentage scores for the attitude of healthcare workers towards COVID-19 vaccines in mistrust on the vaccine benefits, safety concerns on the vaccination, and preference for natural immunity were 52.09% (7.814 out of 15, SD = 1.743), 72.47% (10.87 out of 15, SD = 2.152), and 12.25% (1.225 out of 10, SD = 0.35) respectively. This data clearly shows that the healthcare workers were concerns about the safety of the COVID-19 vaccines, the main driver of hesitancy or reluctance.

Tab. II. Health belief and perceptions of healthcare workers regarding COVID-19 infection and COVID-19 vaccination. (n = 403).

Health believes and perceptions	Strongly agree	Agree	Disagree	Strongly disagree
Perceived susceptibility				
Chance of getting COVID-19 for me and my family is still high	121 (30)	212 (52.6%)	67 (16.6%)	3 (0.7%)
Worry about the likelihood of getting COVID-19	75 (18.6%)	258 (64%)	64 (15.9%)	6 (1.5%)
COVID-19 pandemic had a severe impact on daily life	156 (38.7%)	209 (51.9%)	38 (9.4%)	0
Perceived severity				
Complications from COVID-19 are serious	115 (28.5%)	245 (60.8%)	41 (10.2%)	2 (0.5%)
I will be very sick if I get COVID-19	48 (11.9%)	177 (43.9%)	163 (40.4%)	15 (3.7%)
Perceived benefits				
Vaccination is a good idea because it makes me feel less worried about catching COVID-19	104 (25.8%)	260 (64.5%)	39 (9.7%)	0
Vaccination decreases my chance of getting COVID-19 or its complications	73 (18.1%)	265 (65.8%)	62 (15.4%)	3 (0.7%)
Perceived barriers				
Worry the possible side effects of COVID-19 vaccination would interfere with my usual activities	64 (15.9%)	214 (53.1%)	116 (28.8%)	9 (2.2%)
Concern about the efficacy of the COVID-19 vaccination	75 (18.6%)	289 (71.7%)	33 (8.2%)	6 (1.5%)
Concern about the safety of the COVID-19 vaccination	90 (22.3%)	278 (69%)	29 (7.2%)	6 (1.5%)
Cues to action				
I will only take the COVID-19 Vaccine if I was given adequate information about it	169 (41.8%)	210 (52%)	24 (5.9%)	0
I will only take the COVID-19 Vaccine if the vaccine is taken by many in the public and found effective	115 (28.5%)	194 (48%)	91 (22.5%)	3 (0.7%)

Figure 2 shows that majority (44.9%) among the respondents expressing a concern on the safety of the COVID-19 vaccines available. So adequate measures to combat this concern is the prime focus of the vaccination process. Only 18.3% were believing on a natural immunity over vaccination, and 3% expressing a severe negative attitude regarding the efficacy/benefits of up taking this novel vaccine. But these concerns should be addressed at the earliest to spread among the vast majority and the general public encounter with these healthcare workers in the professional and personal life.

Fig. 1. Concerns expressed by the Health care workers regarding COVID-19 vaccination (n = 403).
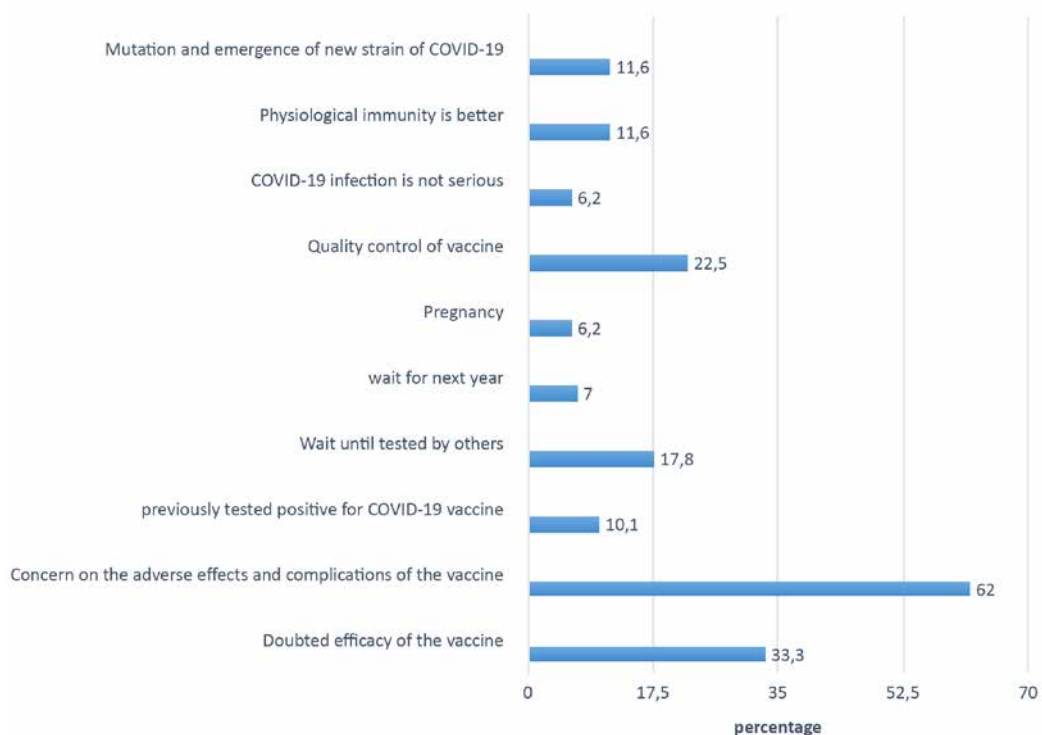
Fig. 2. Attitude of healthcare workers towards COVID-19 (n = 403).
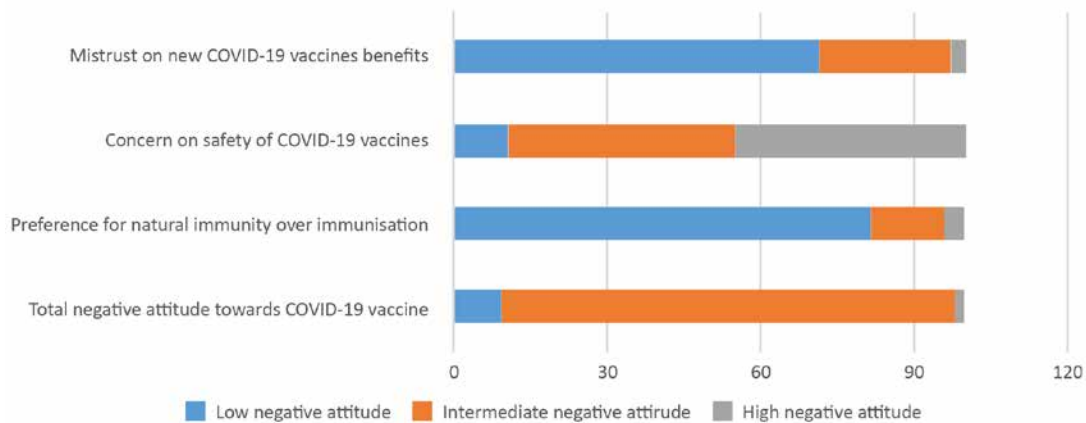
PREDICTORS OF WILLINGNESS OF THE HEALTHCARE WORKERS TO VACCINATE AGAINST COVID-19

Since the majority of the participants expressed an acceptance for COVID-19 vaccine, binomial regression was performed between those who definitely accept vaccine immediately and delay the uptake the vaccine to determine the predictive factors of COVID-19 vaccination acceptance. The comparison of the baseline characteristics of the two groups of vaccine acceptance was done using chi-square test.

Binary logistic regression analyses showed that as the age increases, significantly higher proportion of participants expressed a definite intention to vaccinate. Those who are educated diploma showed a lower vaccine acceptance (2.23%) whereas 4.72% where hesitant, with people with lower levels of education more likely to be unwilling. Those who had children less than 18 years expressed an increased intention to get vaccinated (30%); however the association was not found significant in the logistic analysis. Those healthcare workers who perceived an increased risk of COVID-19 infection shown a definite intention to get vaccinated (38.96%) while only 26% were delay the vaccine, the binary logistic analysis revealed that perceived risk for COVID-19 infection (aOR = 0.540, 95% CI 0.357-.817) and those who had trust on the government in addressing this pandemic (aOR = 0.582, 95% CI 0.343-.805) were strong significant association of having definite intention to vaccinated against COVID-19. Participants who had refused any of the recommended vaccine previously shown a strong correlation with denial or delaying the vaccine for COVID-19 (50.12%, aOR = 4.026, 95% CI 1.880-4.959).

Table III shows, in binary logic regression analysis, perceived susceptibility of COVID-19 infection for self and family, those who perceived that this pandemic will severely affects the daily life if not contained effectively, and worrying about the severity of the infection were showing a significant association with the vaccine acceptance. Perceived benefits of the vaccination against COVID-19 and more cues to action through appropriate communication strategies were found to be significant predictive factors for the adequate coverage of the vaccination program; whilst perceived concern on the efficacy of the vaccine is a negative factor associated with the acceptance. Mistrust on the benefits of the COVID-19 vaccination is found to be a significant predictor for the vaccine hesitancy among the health care workers.

Discussion

Vaccination is considered as a greatest public health achievement of the mankind, since the vaccines and immunization programs had resulted in the prevention and control of many life-threatening epidemics. However, many are reluctant or refuse recommended vaccination or delay some vaccines, because of the concerns about the vaccine safety and its regulations. So vaccine hesitancy is an unacceptable behavior caused by lack of confidence or trust in vaccines or provider, lack of perceived benefits or the need for vaccination, and inconvenience or unavailability (affordability) of vaccines [30]. So the next hurdle in the containment of the present COVID-19 pandemic is the adequate coverage of the vaccination, only by which we could substantially reduce the morbidity and mortality rates and thereby decreases the strain on the health care system and economy of the nation.

This study assessing intention to get vaccinated against COVID-19 among health care workers in Chandigarh, majority (54.6%) respondents reported they will definitely accept the vaccine against COVID-19 immediately although 45% expressed a vaccine hesitant behavior. This result of the study is especially striking as there is no reduction in the mortality and morbidity associated with the COVID-19 as in the initial stages, the acceptance rate for COVID-19 vaccine among health care workers in the present study is far lower than the

Tab. III. Binary Logic regression of factors associated with intention to vaccinate against COVID-19 (n = 403).

Variables	Intention to vaccinate against COVID-19		Chi square	p	aOR	SE	Sig	95% CI	
	Definitely Yes	No						Lower	Upper
Age groups									
20-27	75 (18.61)	72 (17.86)	12.694**	0.005	0.480	0.390	0.060	.223	1.031
28-35	111 (27.54)	79 (19.60)			0.356**	0.383	0.007	.168	0.754
36-42	22 (5.46)	8 (1.96)			0.182**	0.544	0.002	0.063	0.528
> 43	12 (2.98)	24 (5.96)			Reference				
Gender									
Female	145 (35.98)	75 (18.61)	1.800	0.180	1.339	0.218	0.180	0.874	2.051
Male	132 (32.75)	51 (12.66)			Reference				
Marital status									
Unmarried	78 (19.35)	72 (17.87)	0.647	0.421	0.910	0.424	0.824	0.397	2.088
Married	142 (35.23)	111 (27.54)							
Educational attainment									
High school/Diploma	9 (2.23)	19 (4.72)	11.096**	0.004	8.611	0.600***	<0.001	2.658	27.893
Degree/equivalent	147 (36.48)	131 (32.50)			1.591	0.407	0.722	0.520	2.570
Post-graduation and above	64 (15.88)	33 (8.2)			Reference				
Having children									
Yes	121 (30)	81 (20.1)	4.607*	0.032	1.156	0.407	0.722	0.520	2.570
No	99 (24.57)	102 (25.31)			Reference				
Self-perception, at risk of severe illness from COVID-19									
Yes	157 (38.96)	105 (26)	8.592**	0.003	0.540**	0.211	0.004	0.357	0.817
No	63 (15.63)	78 (19.35)			Reference				
Have you or anyone in the family got sick with COVID-19 since the start of pandemic									
Yes	30 (7.44)	190 (47.15)	1.137	0.286	0.748	0.433	0.530	0.320	1.748
No	32 (7.94)	151 (37.47)			Reference				
Job nature of exposure to COVID-19 sick patients while at work.									
Direct interaction with verified sick patients	106 (26.30)	81 (20)	6.764	0.149	1.064	0.504	0.903	0.396	2.859
Direct interaction with non-verified patients	54 (13.40)	32 (7.94)			0.796	0.580	0.694	0.255	2.480
No direct interactions	12 (2.98)	17 (4.22)			1.620	0.691	0.485	0.418	6.279
No known interactions with COVID-19 patients	27 (6.7)	29 (7.2)			2.105	0.646	0.250	0.593	7.474
Students	2 1 (5.21)	25 (6.20)			Reference				
Trust on the Government in addressing unexpected health threats to our nation, including COVID-19 epidemic									
Yes	162 (40.20)	110 (27.30)	8.332**	0.004	0.582**	0.217	0.003	0.343	0.805
No	58 (14.40)	73 (18.11)			Reference				
Perceived overall health									
Good	193 (47.89)	27 (6.7)	14.588	0.106	0.636	0.281	0.108	0.366	1.104
Poor	150 (37.22)	33 (8.2)			Reference				
Refused a recommended vaccine in the past									
Yes	18 (4.47)	202 (50.12)	7.958**	0.005	4.026**	0.477	0.004	1.880	4.959
No	32 (7.94)	151 (37.47)			Reference				
Preference for COVID-19 vaccine									
Domestic	81 (20)	139 (34.5)	1.981	0.159	1.293	0.361	0.476	0.637	2.625
Foreign-made	80 (19.85)	103 (25.55)			Reference				
Confidence in domestically made vaccine									
Confident	69 (17.12)	76 (18.86)	4.483*	0.034	1.555	0.210*	0.035	1.031	2.345
Not confident	151 (37.47)	107 (26.55)							
Confidence in foreign-made vaccine									
Confident	9 (2.23)	211 (52.36)	3.007	0.083	2.095	0.436	0.090	0.891	4.929
Not confident	15 (3.72)	168 (41.69)							

▶

Variables	Intention to vaccinate against COVID-19		Chi square	p	aOR	SE	Sig	95% CI	
	Definitely Yes	No						Lower	Upper
Health beliefs regarding COVID-19 infection and vaccines									
Perceived susceptibility Chance of getting COVID-19 for me and my family is still high									
Strongly agree/agree Strongly	193 (47.89)	140 (34.74)	8.769**	0.003	0.511*	0.335	0.046	0.265	0.987
disagree/disagree	27 (6.7)	43 (10.67)			Reference				
Worry about the likelihood of getting COVID-19									
Strongly agree/agree	187 (46.40)	146 (36.23)	1.896	0.169	1.186	0.344	6.19	0.389	2.630
Strongly disagree/ disagree	33 (8.2)	37 (9.2)			Reference				
COVID-19 pandemic had a severe impact on daily life									
Strongly agree/agree	208 (51.62)	157 (38.95)	8.962**	0.003	0.341*	0.450	0.017	0.072	0.858
Strongly disagree/ disagree	12 (2.98)	26 (6.45)			Reference				
Perceived severity Complications from COVID-19 are serious									
Strongly agree/agree	199 (49.38)	161 (40)	0.643	0.423	1.417	0.382	0.362	0.385	3.049
Strongly disagree/ disagree	21 (5.21)	22 (5.46)			Reference				
I will be very sick if I get COVID-19									
Strongly agree/agree	136 (33.75)	89 (22)	7.042**	0.008	0.551*	0.243	0.014	0.196	0.704
Strongly disagree/ disagree	84 (20.84)	94 (23.33)			Reference				
Perceived benefits Vaccination is a good idea because it makes me feel less worried about catching COVID-19									
Strongly agree/agree	205 (50.87)	159 (39.45)	4.531*	0.033	0.757	0.470	0.555	0.383	2.063
Strongly disagree/ disagree	15 (3.72)	24 (6)			Reference				
Vaccination decreases my chance of getting COVID-19 or its complications									
Strongly agree/agree	193 (48)	145 (36)	5.326**	0.021	0.638	0.341	0.187	0.383	2.063
Strongly disagree/ disagree	27 (6.7)	38 (9.42)			Reference				
Perceived barriers Worry the possible side effects of COVID-19 vaccination would interfere with my usual activities									
Strongly agree/agree	147 (36.48)	131 (32.50)	1.061	0.303	1.276	0.259	0.347	0.752	2.933
Strongly disagree/ disagree	73 (18.11)	52 (12.90)			Reference				
Concern about the efficacy of the COVID-19 vaccination									
Strongly agree/agree	193 (48)	171 (42.43)	3.733	0.063	3.979*	0.702	0.049	1.109	26.55
Strongly disagree/ disagree	27 (6.7)	12 (2.98)			Reference				
Concern about the safety of the COVID-19 vaccination									
Strongly agree/agree	199 (49.38)	169 (41.94)	0.452	0.501	0.397	0.734	0.209	0.089	2.828
Strongly disagree/ disagree	21 (5.21)	14 (3.47)			Reference				
Cues to action									
I will only take the COVID-19 Vaccine if I was given adequate information about it									
Strongly agree/agree	211 (52.36)	168 (42)	3.007	0.094	2.661*	0.295	0.05	0.077	1.026
Strongly disagree/ disagree	9 (2.23)	15 (3.72)							
I will only take the COVID-19 Vaccine if the vaccine is taken by many in the public and found effective.									
Strongly agree/agree	159 (39.5)	150 (37.22)	5.256	0.022	3.488***	0.747	0.001	1.389	5.747
Strongly disagree/ disagree	61 (15.14)	33 (9)							

▶

Variables	Intention to vaccinate against COVID-19		Chi square	p	aOR	SE	Sig	95% CI	
	Definitely Yes	No						Lower	Upper
Attitude towards COVID-19 vaccines									
Mistrust on benefits of COVID-19 vaccines									
Low negative attitude	188 (46.65)	26 (6.5)	45.159	<0.001	5.205	0.263	<0.001	3.106	8.723
Intermediate negative attitude	100 (24.8)	77 (19)			1.614	0.813	0.556	0.328	7.937
High negative attitude	6 (1.5)	6 (1.5)			Reference				
Safety concerns on COVID-19 vaccines									
Low negative attitude	24 (5.95)	100 (24.8)	0.354	0.838	0.726	0.533	0.541	0.256	2.064
Intermediate negative attitude	100 (24.8)	809 (19.85)			0.685	0.548	0.490	0.234	2.005
High negative attitude	96 (23.82)	180 (44.66)			Reference				
Preference for natural immunity									
Low negative attitude	188 (46.65)	141 (35)	6.412	0.041	1.376	0.311	0.305	0.748	2.534
Intermediate negative immunity	27 (6.7)	30 (7.44)			2.685	0.593	0.096	0.840	8.588
High negative attitude	5 (1.21)	12 (3)			Reference				

result of the study conducted during first epidemic curve in France [31]. But the findings of the national survey in China, Malaysia and United States, the definite intention to get vaccinated against COVID-19 among the general public was found only 54.8%, 48.2% and 57% respectively [32-34]. But the vaccine hesitancy among the health care workers in the present study is considerably worrying as this will threaten the adequate coverage, and could negatively impact the vaccination compliance among the general public. Among the healthcare workers the vaccine acceptance rates among the nurses for the influenza vaccines were often found less than other health workers, this is a concern as they had more and longer contacts with the patients in providing care, and were the most affected by SARS-CoV-2 among health care workers worldwide [27]. The adherence to the preventive measures and willingness to uptake COVID-19 vaccines may change according to the severity of the ongoing pandemic in terms of morbidity and mortality rates.

Since the vaccination is the only effective means to contain this pandemic, increasing vaccination rates confers a substantial achievement of expected benefits. The defined COVID -19 herd immunity can be achieved only when we reach a vaccination coverage of 70% in best-case scenario with efficient vaccine, using a pooled estimate of the R_0 of 3.32 [35, 36]. So a planned and coordinated programs should be organized at the earliest, in order to motivate a larger population to be vaccinated, otherwise those who are unsure about or resistant to being vaccinated will create a substantial gap in the number needed to be vaccinated to achieve herd immunity. The most significant concerns expressed by the responders regarding the novel COVID-19 vaccination program was the vaccines safety, the most frequently noted safety concerns were the efficacy, quality control and the occurrence of COVID-19 infection with the newly developed vaccine, consistent with studies on other vaccines [27, 37, 38]. Similarly in a survey the study participants expressed an acceptance of the vaccine if they receive adequate assurance about the safety of the vaccine, since the vaccine was manufactured in an unprecedented speed and the production of a large quantity of the vaccines in order to protect the entire global community makes them concern about the effective vaccine approach in clinical trials [39]. Hence these findings suggest that the vaccine safety should be addressed effectively through appropriate strategic communication to promote the COVID-19 vaccine compliance rates in the entire population.

In the study we observed that intention to get vaccinated against COVID-19 exceed the influenza vaccine rates in the previous season, but the health care workers are accepting COVID-19 vaccine irrespective of the previous influenza vaccination behavior, similar findings was found in a study among general population in US [34].

In this study, self-perception of increased susceptibility of COVID-19 infection for self and family and those who perceived COVID-19 pandemic if still persist will affect their daily life were significantly found associated with COVID-19 vaccine acceptance. So the perceived susceptibility to and seriousness of the COVID-19 are recognized as a significant predictors of vaccine acceptance, similarly in France where health care staff involved in the care of COVID-19 patients and those individuals who perceived at risk of severe diseases were reported a higher chance of acquiescence of vaccination against COVID-19 [31, 38]. But a concern on the efficacy of the new COVID-19 vaccine may contribute to the low vaccine acceptance, so everyone probably needed a highly effective COVID-19 vaccine, however due to the fast generation of the vaccine, inadequate clinical trial, have limited effectiveness, which could lead to mistrust. Doubted safety, efficacy and effectiveness about COVID-19 were the main perceived barriers among the health care workers to uptake COVID-19 vaccine [38-40].

The study participants expressed a high confidence in the foreign made/imported COVID-19 vaccine and a higher preference was given to the foreign made COVID-19 vaccines. As the efficacy for prevention of COVID-19 after administration of 2 doses of Pfizer BNT162b2 was found 95% in the phase 3 clinical trial, so majority developed a trust in that vaccine [41].

The perceived benefits of obtaining a vaccination against COVID-19 was also found significantly found associated with definite intention for COVID-19 vaccination, however no predictive effects were not identified. External cues to action were found to be significant in the intention for getting vaccinated immediately, imparting adequate information through effective communication strategies and provision of transparent evidence of safety and efficacy of the vaccine from field trials will definitely improve the coverage of vaccination. In this study 75% reported they would more likely to accept the vaccine when the vaccine is taken by many in the public. So these findings imply that advertorials and testimonials of healthcare workers and significant persons in the society may serve as a cues to action to get adequate coverage for the vaccination.

Healthcare workers plays a key role in the vaccination behavior of the general public through the consultation, role modelling and providers of substantial information, that are contributing the decision to be vaccinated or not. Therefore, the low intention to inoculate COVID-19 vaccine among the participants is significantly threatening, should be addressed immediately through effective communication strategies to solve the concerns and to improve the awareness, thereby we can ensure an adequate coverage among the population.

In this study the researchers specifically assessed the factors that predict the uncertainty or unwillingness to get vaccinated against COVID-19, so that specific interventions could be programmed among the target groups at the earliest. In this study the uncertain group consist of 38% which was a larger than the unwilling group (8%). This echoes findings from the national surveys in European and UK studies among the general public, so there is no significant difference found between the healthcare workers and general population [38, 42]. Notably, our research identified certain factors predict the unwillingness and uncertainty such as the age group 28-43, lower educational status, lack of trust on the government in addressing the pandemic, refusal of a recommended vaccine in the past. In this study gender was not regarded as a contributing factor for the vaccine hesitancy, but males were more likely to accept the Vaccine in Israel [27]. Having younger children indicated a negative association with accepting the COVID-19 vaccine.

So this means that appropriate public health campaign should be initiated to increasing the COVID-19 vaccine uptake, mainly focusing on the education and increasing trust on the efficacy and safety of the vaccination. Thus motivational communication campaigns targeted towards population at risk of vaccine hesitancy need to be urgently developed to combat mistrust in the vaccination and to improve the inoculation rates.

Limitations

Though we followed strict protocols to ensure the validity of the responses, the credibility of an online survey needs to be considered. In this study majority of the respondents were nurses, so the results could not be generalized to the other categories like hospital and sanitary assistants. Reaching to the large participants of different categories through social media and over a short period is difficult and the study was a cross-sectional in nature, so limiting inference for long term. In fact the sample in the study was not a representative nor certain specific sub groups within the population of health care workers. So a future intervention programs and its effectiveness should be addressed at the earliest on a priority basis. Compliance with second dose of vaccine needed to be addressed, many well-intentioned individual may be influenced by several factors and behaviors that prevent the recommended second stage.

Conclusion

The low COVID-19 vaccination acceptance rates among the healthcare workers is a concern, this should be addressed immediately without any fail as this could threaten the adequate coverage of the vaccination among the general public too. When the communication inadequate, it can negatively influence the vaccination uptake, results in vaccine hesitancy. So developing a trust among the population through appropriate communication strategies are beneficial to decrease the decreased inoculation rates.

Acknowledgements

Conflict of interest statement

Authors declare no competing interests.

Funding sources

Authors' contributions

SJ, MCC and MD developed the research concepts and design; SJ and MCC collected data and analysed. MDand SJ involved in the interpretation of results and drafting manuscript. JJ overall supervision of the research and manuscript reviewing. All authors reviewed and approved the final manuscript.

References

[1] WHO. Weekly epidemiological update - 5 January 2021. Emergency Situational Updates. 5 January 2021. Available from https://www.who.int/publications/m/item/weekly-epidemiological-update---5-january-2021

[2] Foy BH, Wahl B, Mehta K, Shet A, Menon GI, Britto C. Comparing COVID-19 vaccine allocation strategies in India: A mathematical modelling study. Int J Infect Dis 2020;103:431-8. https://doi.org/10.1016/j.ijid.2020.12.075

[3] Al-Mohaithef M, Padhi BK. Determinants of COVID-19 Vaccine Acceptance in Saudi Arabia: A Web-Based National Survey. J Multidiscip Healthc 2020;13:1657-63. https://doi.org/10.2147/JMDH.S276771

[4] Chakraborty C, Sharma AR, Sharma G, Bhattacharya M, Saha RP, Lee -S-S. Extensive partnership, collaboration, and teamwork is required to stop the COVID-19 outbreak. Arch Med Res 2020;51:728-30. https://doi.org/10.1016/j.arcmed.2020.05.021

[5] Nguyen LH, Drew DA, Graham MS, Joshi AD, Guo CG, Ma W, Mehta RS, Warner ET, Sikavi DR, Lo CH, Kwon S, Song M, Mucci LA, Stampfer MJ, Willett WC, Eliassen AH, Hart JE, Chavarro JE, Rich-Edwards JW, Davies R, Capdevila J, Lee KA, Lochlainn MN, Varsavsky T, Sudre CH, Cardoso MJ, Wolf J, Spector TD, Ourselin S, Steves CJ, Chan AT; COronavirus Pandemic Epidemiology Consortium. Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. Lancet Public Health 2020;5:e475-83. https://doi.org/10.1016/S2468-2667(20)30164-X

[6] Jose S, Dhandapani M, Cyriac MC. Burnout and Resilience among Frontline Nurses during COVID-19 Pandemic: A Cross-sectional Study in the Emergency Department of a Tertiary Care Center, North India. Indian J Crit Care Med 2020;24:1081-8. https://doi.org/10.5005/jp-journals-10071-23667

[7] Jose S, Cyriac MC, Dhandapani M. Health Problems and Skin Damages Caused by Personal Protective Equipment: Experience of Frontline Nurses Caring for Critical COVID-19 Patients in Intensive Care Units. Health Problems and Skin Damages Caused by Personal Protective Equipment: Experience of Frontline Nurses Caring for Critical COVID-19 Patients in Intensive Care Units. Indian J Crit Care Med 2021;24. Available from https://www. ijccm.org/doi/IJCCM/pdf/10.5005/jp-journals-10071-23713

[8] Gupta M, Mohanta SS, Rao A, Parameswaran GG, Agarwal M, Arora M, Mazumder A, Lohiya A, Behera P, Bansal A, Kumar R, Meena VP, Tiwari P, Mohan A, Bhatnagar S. Transmission dynamics of the COVID-19 epidemic in India and modeling optimal lockdown exit strategies. Int J Infect Dis 2020;103:579-89. https://doi.org/10.1016/j.ijid.2020.11.206

[9] Jose S, Cyriac MC, Dhandapani M, Mehra A, Sharma N. Mental Health Outcomes of Perceived Stress, Anxiety, Fear and Insomnia, and the Resilience among Frontline Nurses Caring for Critical COVID-19 Patients in Intensive Care Units. Indian J Crit Care Med 2022;26:174-8. https://doi.org/10.5005/jp-journals-10071-24119

[10] Foy BH, Wahl B, Mehta K, Shet A, Menon GI, Britto C. Comparing COVID-19 vaccine allocation strategies in India: A mathematical modelling study. Int J Infect Dis 2020;103:431-8. https://doi.org/10.1016/j.ijid.2020.12.075

[11] Randolph HE, Barreiro LB. Herd Immunity: Understanding COVID-19. Immunity 2020;52:737-41. https://doi.org/10.1016/j.immuni.2020.04.012

[12] Graham BS. Rapid COVID-19 vaccine development. Science 2020;368:945-6. https://doi.org/10.1126/science.abb892

[13] MacDonald NE, Butler R, Dubé E. Addressing barriers to vaccine acceptance: an overview. Hum Vaccin Immunother 2018;14:218-24. https://doi.org/10.1080/21645515.2017.1394533

[14] Hodgson SH, Mansatta K, Mallett G, Harris V, Emary KRW, Pollard AJ. What defines an efficacious COVID-19 vaccine? A review of the challenges assessing the clinical efficacy of vaccines against SARS-CoV-2. Lancet Infect Dis 2020;21:e26-35. https://doi.org/10.1016/S1473-3099(20)30773-8

[15] Seale H, Heywood AE, McLaws ML, Ward KF, Lowbridge CP, Van D, MacIntyre CR. Why do I need it? I am not at risk! Public perceptions towards the pandemic (H1N1) 2009 vaccine. BMC Infect Dis 2010;10:99. https://doi.org/10.1186/1471-2334-10-99

[16] Rubin GJ, Potts HW, Michie S. The impact of communications about swine flu (influenza A H1N1v) on public responses to the outbreak: results from 36 national telephone surveys in the UK. HTA 2010;14:183-266. https://doi.org/10.3310/hta14340-03

[17] Eastwood K, Durrheim DN, Jones A, Butler M. Acceptance of pandemic (H1N1) 2009 influenza vaccination by the Australian public. Med J Aust 2010;192:33-6. https://doi.org/10.5694/j.1326-5377.2010.tb03399.x

[18] Wang Q, Yue N, Zheng M, Wang D, Duan C, Yu X, Zhang X, Bao C, Jin, H. Influenza vaccination coverage of population and the factors influencing influenza vaccination in mainland China: A meta-analysis. Vaccine 2018;36:7262-9. https://doi.org/10.1016/j.vaccine.2018.10.045

[19] Dubé, E, MacDonald NE. Vaccine Acceptance: Barriers, Perceived Risks, Benefits, and Irrational Beliefs. In: Bloom BR, Lambert P, eds. The Vaccine Book. 2nd ed. Cambridge, MA, USA: Academic Press 2016, pp. 507-28.

[20] Larson HJ, Jarrett C, Eckersberger E, Smith DMD, Paterson P. Understanding vaccine hesitancy around vaccines and vaccination from a global perspective: A systematic review of published literature. Vaccine 2014;32:2150-9. https://doi.org/10.1016/j.vaccine.2014.01.081

[21] Henrich N, Holmes B. The public's acceptance of novel vaccines during a pandemic: A focus group study and its application to influenza H1N1. Emerg Health Threat J 2009;2:e8. https://doi.org/10.3134/ehtj.09.008

[22] Lin Y, Hu Z, Zhao Q, Alias H, Danaee M, Wong LP. Understanding COVID-19 vaccine demand and hesitancy: A nationwide online survey in China. PLoS Negl Trop Dis 2020;14:e0008961. https://doi.org/10.1371/journal.pntd.0008961

[23] Champion VL, Skinner CS. The health belief model In: Glanz K, Rimer BK, Viswanath K, eds. Health behavior and health education: Theory, research, and practice. Jossey-Bass 2008, pp. 45-65.

[24] Wong MCS, Wong ELY, Huang J, Cheung AWL, Law K, Chong MKC, Ng RWY, Lai CKC, Boon SS, Lau JTF, Chen Z, Chan PKS. Acceptance of the COVID-19 vaccine based on the health belief model: A population-based survey in Hong Kong. Vaccine 2021:S0264-410X(20)31695-9. https://doi.org/10.1016/j.vaccine.2020.12.083

[25] Lazarus JV, Ratzan SC, Palayew A, Gostin LO, Larson HJ, Rabin K, Kimball S, El-Mohandes A. A global survey of potential acceptance of a COVID-19 vaccine. Nat Med 2020;27:225-8. https://doi.org/10.1038/s41591-020-1124-9.

[26] Larson HJ, Jarrett C, Schulz WS, Chaudhuri M, Zhou Y, Dube E, Schuster M, MacDonald NE, Wilson R; SAGE Working Group on Vaccine Hesitancy. Measuring vaccine hesitancy: The development of a survey tool. Vaccine 2015;33:4165-75. https://doi.org/10.1016/j.vaccine.2015.04.037

[27] Dror AA, Eisenbach N, Taiber S, Morozov NG, Mizrachi M, Zigron A, Srouji S, Sela E. Vaccine hesitancy: the next challenge in the fight against COVID-19. Eur J Epidemiol 2020;35:775-9. https://doi.org/10.1007/s10654-020-00671-y

[28] Shapiro GK, Tatar O, Dube E, Amsel R, Knauper B, Naz A, Perez S, Rosberger Z. The vaccine hesitancy scale: Psychometric properties and validation. Vaccine 2018;36:660-7. https://doi.org/10.1016/j.vaccine.2017.12.043

[29] Martin LR, Petrie KJ. Understanding the Dimensions of Anti-Vaccination Attitudes: the Vaccination Attitudes Examination (VAX) Scale. Ann Behav Med 2017;51:652-60. https://doi.org/10.1007/s12160-017-9888-y

[30] MacDonald NE. SAGE Working Group on Vaccine Hesitancy. Vaccine hesitancy: Definition, scope and determinants. Vaccine 2015;33:4161-4. https://doi.org/10.1016/j.vaccine.2015.04.036

[31] Gagneux-Brunon A, Detoc M, Bruel S, Tardy B, Rozaire O, Frappe P, Botelho-Nevers E. Intention to get vaccinations against COVID-19 in French healthcare workers during the first pandemic wave: a cross-sectional survey. J Hosp Infect 2021;108:168-73. https://doi.org/10.1016/j.jhin.2020.11.020

[32] Lin Y, Hu Z, Zhao Q, Alias H, Danaee M, Wong LP. Understanding COVID-19 vaccine demand and hesitancy: A nationwide online survey in China. PLoS Negl Trop Dis 2020;14:e0008961. https://doi.org/10.1371/journal.pntd.0008961

[33] Wong LP, Alias H, Wong PF, Lee HY, AbuBakar S. The use of the health belief model to assess predictors of intent to receive the COVID-19 vaccine and willingness to pay. Hum Vaccin Immunother 2020;16:2204-14. https://doi.org/10.1080/21645515.2020.1790279

[34] Fisher KA, Bloomstone SJ, Walder J, Crawford S, Fouayzi H, Mazor KM. Attitudes Toward a Potential SARS-CoV-2 Vaccine: A Survey of U.S. Adults. Ann Intern Med 2020;173:964-73. https://doi.org/10.7326/M20-3569

[35] Fine P, Eames K, Heymann DL. "Herd immunity": a rough guide. Clin Infect Dis 2011;52:911-6. https://doi.org/10.1093/cid/cir007

[36] Alimohamadi Y, Taghdir M, Sepandi M. Estimate of the basic reproduction number for COVID-19: A systematic review and meta-analysis. J Prev Med Public Health 2020;53:151-7. https://doi.org/10.3961/jpmph.20.076

[37] Dubé E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. Hum Vaccin Immunother 2013;9:1763-73. https://doi.org/10.4161/hv.24657

[38] Neumann-Böhme S, Varghese NE, Sabat I, Barros PP, Brouwer W, van Exel J, Schreyögg J, Stargardt T. Once we have it, will we use it? A European survey on willingness to be vaccinated against COVID-19. Eur J Health Econ 2020;21:977-82. https://doi.org/10.1007/s10198-020-01208-6. PMID: 32591957; PMCID: PMC7317261

[39] Torreele E. The rush to create a covid-19 vaccine may do more harm than good. BMJ 2020;370:m3209. https://doi.org/10.1136/bmj.m3209

[40] Corey BL, Mascola JR, Fauci AS, Collins FS. A strategic approach to COVID-19 vaccine R&D. Science 2020;368:948-50. https://doi.org/10.1126/science.abc5312

[41] Polack FP, Thomas SJ, Kitchin N, Absalon J, Gurtman A, Lockhart S, Perez JL, Pérez Marc G, Moreira ED, Zerbini C, Bailey R, Swanson KA, Roychoudhury S, Koury K, Li P, Kalina WV, Cooper D, Frenck RW Jr, Hammitt LL, Türeci Ö, Nell H, Schaefer A, Ünal S, Tresnan DB, Mather S, Dormitzer PR, Şahin U, Jansen KU, Gruber WC; C4591001 Clinical Trial Group. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. N Engl J Med 2020;383:2603-15. https://doi.org/10.1056/NEJMoa2034577

[42] Sherman SM, Smith LE, Sim J, Amlôt R, Cutts M, Dasch H, Rubin GJ, Sevdalis N. COVID-19 vaccination intention in the UK: results from the COVID-19 vaccination acceptability study (CoVAccS), a nationally representative cross-sectional survey. Hum Vaccin Immunother 2021;17:1612-21. https://doi.org/10.1080/21645515.2020.1846397

Correspondence: Sinu Jose, Public Health Nursing Officer, Department of Community Medicine and School of Public Health, Postgraduate Institute of Medical Education and Research, Chandigarh, 160012. E-mail: sinujosekudilil87@gmail.com

Oral Hygiene practices and Oral Health Related Quality of Life observed in patients reporting to Dental Institution in North India during COVID-19 Pandemic

AVIJIT AVASTHI[1], TARUN KALRA[2], BALJEET SINGH[3]
[1] Department of Public Health Dentistry, Bhojia Dental College & Hospital, (H.P.), India;
[2] Department of Prosthodontics), Bhojia Dental College & Hospital, (H.P.), India;
[3] Department of Periodontology & Implantology), Bhojia Dental College & Hospital, (H.P.), India

Summary

Objective. *The purpose of the study was to ascertain Oral Health Related Quality of Life (OHRQOL) and evaluate oralhygiene practices in patients visiting a dental institution during COVID-19 time.*
Materials and methods. *Face-to face interviews were conducted using a semi-structured close-ended questionnaire,assessing oral hygiene practices and self-reported oral problems perceived in last 6 months, using both Hindi and English version of Oral Health Impact Profile (OHIP-14) Questionnaire. Frequency distribution of oral hygiene practices were obtained, and Descriptive statistics computed the scores of OHIP-14. Kruskal-wallis test and Independent t-test were used to match the association of OHIP-14 with demographic variables. Multiple linear regression*

analysis was utilized to compute the association of OHIP-14 with independent variables, age and gender.
Results. *Subjective evaluation of OHRQOL (Oral Health Related Quality of Life) using OHIP-14 Porforma resulted in high score for physical pain and psychological discomfort but subjects expressed less discomfort in connection to functional limitation, physical disability, psychological discomfort, social disability and handicap domains of OHIP-14. With progressive increase in age OHRQOL worsened. Females had poor OHRQOL, with significant difference as compared to males. Gender and marital status observed variance in OHIP-14 with statistically significant difference (P <0.000).*
Conclusion. *More than two-third subjects preferred cleaning their teeth using toothbrush and toothpaste. Therefore, COVID-19 consequently impacted OHRQOL of the general population.*

Introduction

Coronavirus disease (COVID-19) constituted unparalleled challenge to the humanity. WHO asserted COVID-19 as a public health emergency of international concern on 30th January 2020 and on 11th March 2020 it was announced pandemic. The pandemic has left an ineradicable mark impacting people's life physically, mentally, socially and economically [1]. To break the chain of transmission people were commanded to stay at home by dictating a countrywide lockdown on 24th March 2020 which lasted for more than 8 weeks [2]. The lockdown prohibited people from moving out of their dwellings. Work from home culture was adopted and nearly all educational institutions were closed. Few reports dawned on ramifications of COVID-19 on oral health [3].
The fright of succumbing to COVID-19 heightened during pandemic and as a result many people might have delayed their routine dental care. The medications and therapies used for treating coronavirus disease might have affected oral health resulting in xerostomia, stomatitis and mouth ulcers because of impaired immune system [3]. Since COVID-19 restricted physical movement this evolved in accumulation of dental problems for instance dental sensitivity, pain, bleeding from gums, onset of oral ulcers, salty sensation in mouth, oral malador, need for restoration, need of

artificial prosthesis and need for removal of teeth [4]. Those affected with COVID-19 could be at danger of contracting oral lesions such as white-hairy tongue, necrotic lesions, reddish macules and haemorrhagic ulcerations. Further poor compromised oral hygiene may cause aspiration of bacteria in oral cavity leading in inflammation of respiratory tract [5]. The earlier notion of Health defined by WHO 'Health being a state of complete physical, mental and social well being and not merely absence of disease or infirmity' [6] has changed over the course of time, now health is intermingledwith general health and people's quality of life (QOL) [7]. Now a robust approach has been conceived called Oral Health Related Quality of Life (OHRQOL) that estimates accordingly oral conditions influencing individual's attitude and social functioning [6].
US Department of Health and Human Services defines OHRQOL as a multidimensional constructwhich ponders upon people's comfort when eating, sleeping and engaging in social interaction; their pride; and their contentment with respect to their oral health. OHRQOL also deals with functional factors, psychological factors, social factors, and experience of pain [8, 9] Dental disturbances profoundly influence our social quality of life affecting mentally, emotionally and physically [10-13] An estimated 3.5 billion people are believed to be disturbed due to oral disease. Untreated

Tab. I. Distribution of Oral Hygiene Practices of OPD participants from North India (N = 391).

Type of Aid Used	N (%)
Toothbrush	361 (92.3%)
Finger	17 (4.4%)
Treestick	11 (2.8%)
Interdental Brush	2 (0.5%)
Type of Material Used	
Toothpaste	373 (95.4%)
Toothpowder	18 (4.6%)
Type of Toothpaste Used	
Fluoridated	14 (3.6%)
Non- Fluoridated	1 (0.3%)
Donot know	376 (96.1%)
Material Used for Tongue Cleaning	
Tongue Cleaner	257 (65.7%)
Toothbrush	93 (23.8%)
Finger	9 (2.3%)
Do not Clean	32 (8.2%)
Tongue Cleaning Duration	
Daily	323 (82.6%)
Once a week	17 (4.3%)
Two times in a week	12 (3.1%)
Once a month	8 (2%)
Do not Clean	31 (7.9%)
Frequency of Brushing	
Once a day	310 (79.3%)
Twice a day	80 (20.5%)
Greater than two times	1 (0.3%)
Cleaning of teeth during Day	
Before Meals	310 (79.3%)
Before and after every meal	80 (20.5%)
After meals	1 (0.3%)
Brand and type of Toothpaste used	
Fluoridated-(Colgate, Close-up)	261 (66.7%)
Non-fluoridated	81 (21%)
Desensitizing Toothpastes	31 (8.3%)
Unable to Recall	18 (4%)

* Fluoridated-(Colgate, Close-up); ** Non- Fluoridated-(Dabur Lal, Dant-kantipatanjali, Vestige); *** Desensitizing Toothpastes-(Sensodyne &Sensodent).

Tab. II. Mean response to sub-scales of Oral Health Impact Profile-(OHIP-14) in OPD participants from North India.

OHIP Variables	Mean (SD)
Functional Limitation	0.13 (0.75)
Physical Pain	3.53 (2.26)
Psychological Discomfort	1.21 (2.03)
Physical Disability	0.77 (1.75)
Psychological Disability	0.65 (1.63)
Social disability	0.85 (1.81)
Handicap	0.09 (0.70)
Total OHIP	7.41 (4.56)

2.11.2020 to conduct the cross-sectional study. The participants were interviewed face-to-face for OHRQOL, using Oral Health Impact Profile-14 questionnaire (OHIP-14) and oral hygiene practices were evaluated using a semi-structured questionnaire. OHIP-14 is based on theoretical model developed by the World Health Organization (WHO) and calculates social impact of oral disorders.

OHIP-14 focuses on 7 dimensions which consist of functional limitation, physical pain, psychological discomfort, physical disability, psychological disability, social disability and handicap. It gives more prominence to behavioural and psychological impact and is preferred in identifying psychological impact among individuals. The Responses were obtained using 5-point likert scale. Scores ranged from 0 to 56 and were obtained by adding the ordinal values for the 14 items. Higher OHIP-14 scores coincides to poor OHRQOL and lesser scores predict better OHRQOL. For an expected population size of 29,911, the sample size of 391 was determined using online sample size calculator [15] with confidence level set at 0.95 and margin of error at 5%. Thus, 391 subjects reporting to OPD were enquired for OHRQOL and oral hygiene practices using close-ended questionnaire. The respondents were interviewed, how often they felt oral problems over past 6 months using a validated English and Hindi version of OHIP-14. Reliability of OHIP scale was assessed before commencement with cronbach's alpha value $\acute{a} = 0.67$ considered acceptable. Subjects who had at least 20 functional teeth were evaluated and completely edentulous subjects were excluded.

STATISTICAL ANALYSIS

The data obtained was subjected to statistical analysis using SPSS Version 21.0 Armonk,NY:IBM Corp [16]. Descriptive statistics were computed for demographic variables and oral hygiene practices. Comparison of OHIP-14 in relation to age, gender and marital status was done using Kruskal-Wallis Test and Independent-t test. Chi-square test observed the association of oral hygiene practices with gender. Multiple linear regression analysis was conducted to substantiate the association between independent variables, such as gender and marital status with dependent variable (OHIP-14).

Oral disease induces pain, discomfort supplemented with severe periodontal disease [6]. The in-built reluctance to seek dental care due to COVID-19 scare and physical restrictions would have certainly influenced the OHRQOL [14]. Despite previous voluminous research done assessing OHRQOL in patients affected with dental disorders still fewer studies might have been initiated to assess the effect of COVID-19 pandemic on OHRQOL. Thus, the motive of this study was to explore Oral Health Related Quality of Life and observance of oral hygiene practices in patients visiting dental OPD during COVID-19.

Materials and methods

Ethical clearance was obtained from Institutional Ethical Committee bearing protocol number (BDC/3110) dated

Tab. III. Distribution of Responses to Oral Health Impact Profile (OHIP-14) among OPD Participants from North India (N = 391).

Items	Responses					Mean (SD)
	Never	Hardly Ever	Occasionally	Fairly Often	Very Often	
Have you had trouble pronouncing any words because of problems with your teeth/mouth	385 (98.4%)	3 (0.7%)	1 (0.3%)	1 (0.3%)	1 (0.3%)	0.03 (0.28)
Have you felt that your sense of taste has worsened because of problems with your teeth/mouth	371 (94.9%)	1 (0.3%)	16 (4.1%)	3 (0.7%)	0 (0%)	0.10 (0.47)
Have you had painful aching in your mouth because of problems with your teeth/mouth	89 (22.7%)	2 (0.5%)	180 (46.1%)	115 (29.4%)	5 (1.3%)	1.85 (1.11)
Have you found it uncomfortable to eat any food because of problems with your teeth/mouth	110 (28.2%)	3 (0.7%)	184 (47.1%)	88 (22.5%)	6 (1.5%)	1.68 (1.15)
Have you been self-conscious because of your teeth/mouth	270 (69.1%)	3 (0.7%)	88 (22.5%)	29 (7.4)	1 (0.3%)	0.69 (1.06)
Have you felt tense because of problems with your teeth/mouth	299 (76.5%)	2 (0.5%)	69 (17.6%)	20 (5.1%)	1 (0.3%)	0.52 (0.97)
Has your diet been unsatisfactory because of problems with your teeth/mouth	333 (85.2%)	2 (0.5%)	44 (11.3%)	9 (2.3%)	3 (0.7%)	0.32 (0.82)
Have you had to interrupt meals because of problems with your teeth/mouth	312 (79.8%)	1 (0.3%)	60 (15.4%)	15 (3.8%)	3 (0.7%)	0.45 (0.93)
Have you found it difficult to relax because of problems with your teeth/mouth	326 (83.3%)	0 (0%)	44 (11.3%)	21 (5.4%)	0 (0%)	0.38 (0.88)
Have you been a bit embarrassed because of problems with your teeth/mouth	343 (87.7%)	0 (0%)	37 (9.5%)	10 (2.5%)	1 (0.3%)	0.27 (0.75)
Have you been a bit irritable because of problems with your teeth/ mouth	273 (69.8%)	1 (0.3%)	90 (23%)	25 (6.4%)	2 (0.5%)	0.67 (1.06)
Have you had difficulty doing your usual job because of problems with your teeth/mouth	340 (87%)	0 (0%)	41 (10.4%)	10 (2.6%)	0 (0%)	0.28 (0.75)
Have you that life in general was less satisfying because of problems with your teeth/mouth	378 (96.8%)	2 (0.5%)	8 (2%)	3 (0.7%)	0 (0%)	0.06 (0.38)
Have you been totally unable to function because of problems with your teeth/mouth	386 (98.7%)	1 (0.3%)	2 (0.5%)	0 (0%)	2 (0.5%)	0.03 (0.32)

Results

Total of 391 subjects reporting in OPD were evaluated for oral hygiene practices and OHRQOL. The mean age was 35.13 ± 2.49 years out of which 63.7% (249) were males and 36.3% (142) were females. More than two-third were in the habit of cleaning their teeth using toothbrush and toothpaste. Nevertheless, a small proportion of subjects used finger (4.4%), treestick (2.8%) and interdental brush (0.5%) for cleaning. Four-fifth of the participants were unable to comprehend between fluoridated and non-fluoridated toothpaste. 82.6% maintained daily cleaning of their tongue and 79.3% practiced brushing their teeth before intake of meals. Practice of cleaning teeth, twice a day was observed in only 20.5% subjects. About a quarter of study subjects (29.3%) reported the use of desensitizing toothpaste and non-fluoridated toothpaste and greater than two-third of subjects (66.7%) trusted

Colgate toothpaste for cleaning their teeth (Tab. I). Out of the seven dimensions of OHIP-14 the subjects rated higher mean score for physical pain (3.53 ± 2.26) and psychological discomfort (1.21 ± 2.03) (Tab. II). However, less discomfort was perceived in relation to functional limitation, physical disability, psychological disability, social disability and handicap (Tab. III). The total OHIP-14 score ranged between 0 to 29. Females had higher mean OHIP-14 score (8.96 ± 5.57) in comparison with males (6.52 ± 3.60).

Females perceived more discomfort in OHRQOL when compared to males with significant differences seen in domains of psychological discomfort, physical disability, social disability and handicap. Similarly females beingmore conscious for their oral health, felt more tense because of problems with their teeth (P < 0.001).

Inter-group comparisongender wise observed significant difference in context to unsatisfactory diet and inability to consume meals. (Tab. IV).

Tab. IV. Gender association with Oral Health Impact Profile (OHIP-14) in OPD Participants from North India using Independent T Test.

Sr. No.	OHIP-14	Male Mean (SD)	Female Mean (SD)	T-value	P-value
1	Have you had trouble pronouncing any words because of problems with your teeth/mouth	0.03 (0.25)	0.02 (0.33)	0.13	0.81
2	Have you felt that your sense of taste has worsened because of problems with your teeth/mouth	0.10 (0.44)	0.10 (0.51)	0.05	0.95
3	Have you had painful aching in your mouth because of problems with your teeth/mouth	1.80 (1.08)	1.95 (1.17)	-1.31	0.39
4.	Have you found it uncomfortable to eat any food because of problems with your teeth/mouth	1.59 (1.13)	1.85 (1.16)	-2.17	0.22
5.	Have you been self-conscious because of your teeth, mouth	0.64 (1.05)	0.77 (1.09)	-1.176	**0.09**
6.	Have you felt tense because of problems with your teeth, mouth	0.37 (0.82)	0.78 (1.14)	-4.078	**< 0.001**
7.	Has your diet been unsatisfactory because of problems with your teeth, mouth	0.21 (0.63)	0.53 (1.05)	-3.802	**< 0.001**
8.	Have you had to interrupt meals because of problems with your teeth/mouth	0.37 (0.85)	0.59 (1.09)	-2.181	**< 0.001**
9.	Have you found it difficult to relax because of problems with your teeth/mouth	0.30 (0.78)	0.53 (1.02)	-2.527	**< 0.001**
10.	Have you been a bit embarrassed because of problems with your teeth/mouth	0.27 (0.75)	0.28 (0.76)	-0.018	0.85
11.	Have you been a bit irritable because of problems with your teeth/ mouth	0.49 (0.94)	0.99 (1.18)	-4.582	**< 0.001**
12.	Have you had difficulty doing your usual job because of problems with your teeth/ mouth	0.25 (0.70)	0.33 (0.83)	-1.021	**0.03**
13.	Have you that life in general was less satisfying because of problems with your teeth/ mouth	0.03 (0.23)	0.13 (0.56)	-2.500	**< 0.001**
14.	Have you been totally unable to function because of problems with your teeth/ mouth	0.16 (0.25)	0.06 (0.41)	-1.397	**< 0.001**
Total	Total OHIP-14	6.52 (3.60)	8.96 (5.57)	-5.247	**< 0.001**

Tab. V. Distribution of Oral Hygiene Practices of OPD participants from North India according to Gender using Chi-square test.

Type of Aid Used	Male (N = 249)	Female (N = 142)	P-value
Toothbrush	233 (93.6%)	128 (90.2%)	
Finger	5 (2%)	11 (7.7%)	
Treestick	1 (0.4%)	0 (0%)	0.08
Toothbrush + Treestick	8 (3.2%)	2 (1.4%)	
Toothbrush + Finger	1 (0.4%)	0 (0%)	
Toothbrush + Interdental Brush	1 (0.4%)	1 (0.7%)	
Type of Material Used	**Male (N = 249)**	**Female (N = 142)**	
Toothpaste	239 (95.9%)	134 (94.4%)	0.46
Toothpowder	10 (4.1%)	8 (5.6%)	
Content of Toothpaste Used	**Male (N = 249)**	**Female (N =1 42)**	
Do not Know	242 (97.2%)	134 (95%)	
Fluoridated	6 (2.4%)	8 (5%)	0.19
Non-Fluoridated	1 (0.4%)	0 (0%)	

Tab. VI. Age-wise Comparison of Oral Health Impact Profile-14 (OHIP-14) in OPD participants from North India using Kruskal-Wallis Test.

OHIP-14	Age Groups	Mean Rank	Mean (SD)	P-value
Have you had trouble pronouncing any words because of problems with your teeth mouth	18-26 yrs	196.34	0.03 (0.28)	0.17
	27-34 yrs	195.23		
	35-44 yrs	193.00		
	45-54 yrs	195.85		
	55-64 yrs	205.38		
	65-74 yrs	209.33		
Have you felt that your sense of taste has worsened because of problems with your teeth mouth	18-26 yrs	201.04	0.10 (0.47)	0.23
	27-34 yrs	190.58		
	35-44 yrs	192.52		
	45-54 yrs	203.04		
	55-64 yrs	186.00		
	65-74 yrs	186.00		
Have you had painful aching in your mouth because of problems with your teeth mouth	18-26 yrs	149.18	1.85 (1.11)	0.00
	27-34 yrs	209.01		
	35-44 yrs	219.09		
	45-54 yrs	217.50		
	55-64 yrs	223.28		
	65-74 yrs	224.92		
Have you found it uncomfortable to eat any food because of problems with your teeth mouth	18-26 yrs	152.66	1.68 (1.15)	0.00
	27-34 yrs	201.05		
	35-44 yrs	207.53		
	45-54 yrs	218.69		
	55-64 yrs	293.44		
	65-74 yrs	236.00		
Have you beenself-conscious of teeth because of problems with your teeth mouth	18-26 yrs	242.24	0.69 (1.06)	0.00
	27-34 yrs	177.94		
	35-44 yrs	184.93		
	45-54 yrs	161.31		
	55-64 yrs	181.81		
	65-74 yrs	175.58		
Have you felt tense because of teeth because of problems with your teeth mouth	18-26 yrs	190.88	0.52 (0.97)	0.75
	27-34 yrs	199.08		
	35-44 yrs	205.50		
	45-54 yrs	189.74		
	55-64 yrs	182.66		
	65-74 yrs	204.79		
Has your diet been unsatisfactory because of problems with your teeth mouth	18-26 yrs	183.36	0.32 (0.82)	0.00
	27-34 yrs	187.01		
	35-44 yrs	194.90		
	45-54 yrs	216.18		
	55-64 yrs	228.56		
	65-74 yrs	234.92		
Have you had to interrupt meals because of problems with your teeth mouth	18-26 yrs	179.73	0.30 (0.81)	0.31
	27-34 yrs	206.37		
	35-44 yrs	201.81		
	45-54 yrs	199.40		
	55-64 yrs	203.25		
	65-74 yrs	206.38		
Have you found it difficult to relax because of teeth because of problems with your teeth mouth	18-26 yrs	186.47	0.38 (0.88)	0.30
	27-34 yrs	196.52		
	35-44 yrs	205.70		
	45-54 yrs	192.62		
	55-64 yrs	223.34		
	65-74 yrs	194.33		

▶

Have you been a bit embarrassed because of problems with your teeth mouth	18-26 yrs	217.70	0.27 (0.75)	**0.00**
	27-34 yrs	198.48		
	35-44 yrs	182.70		
	45-54 yrs	180.38		
	55-64 yrs	183.88		
	65-74 yrs	172.00		
Have you been a bit irritable because of problems with your teeth mouth	18-26 yrs	184.69	0.67 (1.06)	0.63
	27-34 yrs	199.86		
	35-44 yrs	198.99		
	45-54 yrs	207.65		
	55-64 yrs	186.22		
	65-74 yrs	202.63		
Have you had difficulty doing your usual job because of problems with your teeth mouth	18-26 yrs	196.99	0.28 (0.75)	0.67
	27-34 yrs	198.24		
	35-44 yrs	200.65		
	45-54 yrs	192.91		
	55-64 yrs	182.41		
	65-74 yrs	170.50		
Have you felt life in general less satisfying because of problems with your teeth mouth	18-26 yrs	192.83	0.69 (0.38)	0.12
	27-34 yrs	193.93		
	35-44 yrs	200.34		
	45-54 yrs	192.29		
	55-64 yrs	213.88		
	65-74 yrs	206.21		
Have you been totally unable to function because of problems with your teeth mouth	18-26 yrs	193.50	0.03 (0.32)	**0.06**
	27-34 yrs	193.50		
	35-44 yrs	199.93		
	45-54 yrs	196.37		
	55-64 yrs	193.50		
	65-74 yrs	209.92		

Gender wise non-significant association was obtained in comparing usage of oral hygiene materials. However, males showed significant difference in relation to oral cleanliness aids used for cleaning their teeth (P < 0.08) (Tab. V).

Significant differences were drawn, age-wise in connection to physical pain and psychological discomfort (Tab. VI).

Symbolic association was reported in married subjects, when compared with unmarried subjects in relation to domains of physical pain (P < 0.001) and physical disability. Yet, unmarried subjects were more self-conscious and uncomfortable for their oral problems (Tab. VII).

On conducting multiple regression analysis both gender and marital status predicted OHIP-14 in a statistically significant manner $F_{(2,388)} = 18.164$, $P < 0.001$ $R^2 = 0.081$ (Tab. VIII).

Discussion

The overall mean OHIP-14 Score 7.41 ± 4.56 was much lower in comparison to earlier studies measuring OHRQOL [10, 17-20] which could be associated with better awareness about oral health.Females under prioritized their oral health which could be because of more involvement in household work, dependence on spouses and laid back attitude towards seeking immediate treatment which was in disagreement with previous studies where females utilized oral care services [10, 18]. Similarly, females subjects in this studyreported poor OHRQL which could be linked with rural background, hormonal imbalances and systemic illnesses such as diabetes and heart disease which are known to affect oral health [21].

Almost 90% of subjects reported the use of toothpaste and toothbrush and this observation was in agreement with previous studies [22, 23], still 7.8% subjects relied on traditional practices such as tree stick and finger. One-third (8.3%) revealed the use of desensitizing toothpastes which was higher when compared to earlier evidence [22, 24] and the probable reason could be readily available OTC toothpastes and media promotion of desensitizing toothpastes. Only 4.6% study subjects were accustomed to cleaning their teeth using toothpowder which differed with earlier study [23] however, similar observation was noted in a study from central India [22]. Only 20.5% of subjects reported cleaning of their teeth twice a day and this low proportion was comparable to previous studies [22, 23].

High mean scores for physical pain and psychological discomfort were reported with consistent findings from earlier research [10, 19, 25] and gender based differences were in concordance with a study done in

Tab. VII. Relationship of Marital status with Oral Health Impact Profile (OHIP-14) in OPD participants from North India using Independent T Test.

Sr. No.	OHIP-14	Married[a] n = 256 (65.5%) Mean (SD)	Single[b] n = 135 (34.5%) Mean (SD)	T-value	P-value
1	Have you had trouble pronouncing any words because of problems with your teeth/mouth	0.03 (0.29)	0.02 (0.27)	0.05	0.95
2	Have you felt that your sense of Taste has Worsened because of problems with your teeth mouth	0.08 (0.43)	0.14 (0.53)	-1.010	0.31
3	Have you had painful aching in your mouth because of problems with your teeth/mouth	2.12 (0.95)	1.34 (1.22)	6.970	**< 0.001**
4.	Have you found it uncomfortable to eat any food because of problems with your teeth/mouth	1.96 (1.04)	1.16 (1.16)	6.899	**< 0.001**
5.	Have you been self-conscious because of problems with your teeth/mouth	0.42 (0.89)	1.20 (1.18)	-7.287	**< 0.001**
6.	Have you felt tense because of problems with your teeth/mouth	0.57 (1.02)	0.41 (0.84)	1.585	0.11
7.	Has your diet been unsatisfactory because of problems with your teeth/mouth	0.42 (0.91)	0.15 (0.58)	3.073	**< 0.001**
8.	Have you had to interrupt meals because of problems with your teeth/ ,mouth	0.52 (0.98)	0.31 (0.83)	2.103	**0.03**
9.	Have you found it difficult to relax because of problems with your teeth/mouth	0.42 (0.94)	0.30 (0.76)	1.337	0.18
10.	Have you been a bit embarrassed because of problems with your teeth/mouth	0.13 (0.53)	0.54 (1.00)	-5.173	0.30
11.	Have you been a bit irritable because of problems with your teeth/mouth	0.76 (1.11)	0.51 (0.94)	2.230	**0.02**
12.	Have you had difficulty doing your usual job because of problems with your teeth/mouth	0.31 (0.78)	0.23 (0.68)	0.940	0.34
13.	Have you that life in general was less satisfying because of problems with your teeth/ mouth	0.08 (0.43)	0.04 (0.29)	0.907	0.36
14.	Have you been totally unable to function because of problems with your teeth/mouth	0.05 (0.39)	0.00 (0.00)	1.483	0.13
Total	Total OHIP-14	7.92 (4.77)	6.42 (3.98)	3.122	**< 0.001**

[b] Single (unmarried, widowed and divorced).

Tab. VIII. Multiple Linear Regression Analysis of Oral Health Impact Profile (OHIP-14) with marital status and gender in OPD participants from North India.

Parameters	Coefficients(SE)	t	Sig.	95% CI
Constant	5.857 (.906)	6.463	< .001	4.075-7.639
Gender	2.412 (.461)	5.236	< .001	1.506-3.317
Marital Status	-1.269 (.441)	-2.878	.004	-2.135-.402

* Standard Error (SE).

similar setting [18] but contradictory findings were seen in a study done on occupational workers [25]. Less than one-third of study subjects very often felt pain and discomfort on eating food, however, more than one-third subjects occasionally had pain in their mouth because of difficulty with their teeth/ mouth and this finding matched with previous studies [18, 26]. Majority of the respondents never experienced their diet to be unsatisfactory. The subjects were very often less self-conscious about their oral problems and this observation was similar to previous studies [18, 20] but in disagreement with earlier research [17].

In spite of pandemic, very few subjects felt irritable, observed difficulty in doing their daily routine work and sensed life in general less satisfying which differed from observations drawn from earlier studies [10, 12, 20]. Nearly half of the subjects occasionally were unable to eat food because of difficulty with their teeth which could be associated with nutritional imbalance [12].
The advancing age increased the severity of OHRQOL as shown by increased scores more so in patients affected with systemic and co morbid conditions [17, 18, 25-27]. Elderly witnessed increased suffering associated with physical pain and psychological discomfort which

attributed to anxiety in undergoing dental treatment and fear for overall wellbeing during COVID-19 [20]. Notably the marital status influenced the OHRQOL which is line with earlier explorations [17, 19]. Gender and marital status observed significant variance in OHIP-14 and a similar association was predicted in a study done on occupational workers [23]. The inference that can be drawn from these points is that married people in general ignore their oral health and need to prioritize this aspect of their life.

Although patients oral problems accumulated during COVID-19 time but the extent and severity of their oral problems was not as much when compared with earlier studies assessing the OHRQOL [10, 17, 19, 26].

LIMITATIONS

Cross-sectional pattern of this study had certain constraints, such as the subjects might have experienced difficulty in recalling oral problems and this resulted in underestimation of oral problems. No correlation was conducted between OHRQOL and clinical parameters, for instance dental caries and periodontal disease. Social desirability bias could also be one of the contributing factor yielding low scores of OHIP-14, because the participants might have shown inhibition in discussing their oral health during COVID-19. We did not estimate the OHRQOL in subjects who were wearing artificial prosthesis and in those who were completely edentulous.

Conclusion

COVID-19 instilled fear among the general public resulting in delayed approach to seek dental treatment which was responsible for physical pain and psychological discomfort in context to oral problems perceived by the patients. Therefore COVID-19 pandemic may escalate oral health problems which if deferred may result in long-term implications on oral health of general population.

Acknowledgements

Conflict of interest statement

Authors must fully disclose any existing or potential conflicts of interest of a financial, personal or any other nature that could affect or bias their research. If applicable, authors are also requested to describe the role of the finding source(s) in the study design, data acquisition, analysis and interpretation, and writing of the manuscript. No potential conflicts of interest must also be explicitly stated.

The authors declare that they have no competing interest.

Authors' contributions

The individual contributions of authors to the manuscript should be specified in this section.

AA, TK, BS: Study conception and design, AA, BS: Acquistion of data, AA, TK: Analysis and interpretation of Data, AA, BS: Drafting of Manuscript, AA, TK, BS: Critical revision. All authors have read and approved the final manuscript.

References

[1] Algahtani FD, Hassan S-u-N, Alsaif B, Zrieq R. Assessment of quality of life during COVID-19 Pandemic: A Cross-Sectional Survey from the Kingdom of Saudi Arabia. Int J Environ Res Public Health 2021;18:847-59. https://doi.org/10.3390/ijerph18030847

[2] COVID-19 Pandemic india-Wikipedia-Available from: https://en.wikipedia.org/wiki/COVID-19-pandemic_in_India (Accessed on 11 September 2021).

[3] Dziedzic A, Wojtyczka R. The impact of coronavirus infectious disease 19 (COVID-19) on oral health Oral Dis 2020;27:703-6. https://doi.org/10.1111/odi.13359

[4] Singh S, Rana A, Jain V, Sybil D, Khatter H. Effect of COVID-19 lockdown on dental care of patients: A Survey Analysis. Int J Res Rev 2021;7:1-8. https://doi.org/10.4444/ijrr.1002/2371

[5] Cristina Rusu L, CosminaArdelean L, Victoria Tigmeanu C, Matichescu A,Sauciur L, Adrian Bratu E. COVID-19 and Its repercussions on oral health: A review. Medicina (Kaunas) 2021;57:1-21. https://doi.org/10.3390/medicina57111189

[6] Sartorius N. The meanings of health and its promotion. Croat Med J 2006;47:662-4.

[7] Oral health - World Health Organization. Available from: https://www.who.int/news-room/fact-sheets/detail/oral-health [Cited on 9th September 2020]

[8] Oral Health and Quality of Life. FDI World Dental Federation. https://www.fdiworlddental.org/resources/policy-statements-and-resolutions/oral-health-and-quality-of-life (Cited on 10th September 2020).

[9] Bennadi D, Reddy CVK. Oral health related quality of life. J Int Soc Prev Community Dent 2013;3:1-6. https://doi.org/10.4103/2231-0762.115700.

[10] Fotedar S, Sharma KR, Fotedar V, Bhardwaj V, Chauhan A, Manchanda K. Relationship between oral health status and oral health related quality of life in adults attending H.P government dental college, Shimla, Himachal Pradesh-India. OHDM 2014;13:661-5.

[11] Manapoti JP, Chava VK, Ramesh Reddy BV. Evaluation of oral health related quality of life among professional students: A cross sectional study. J Indian Assoc Public Health Dent 2015;13:465-8. https://doi.org/10.4103/2319-5932.171174

[12] Bhalla A, Anup N, Bhalla AP, Singh SB, Gupta P, Bhalla S. Oral Health Related Quality of Life (OHRQOL) amongst head and neck cancer patients undergoing chemotherapy and radiotherapy at SawiMansingh Hospital Jaipur, India. Sch Acad J Biosci 2015;3:3-12.

[13] Vinita Mary A, Mahendra J, John J, Moses J, Rajesh Ebenezar AV, Kesavan R. Assessing Quality of Life using the Oral Health Impact Profile (OHIP-14) in subjects with and without orthodontic treatment need in Chennai, Tamil Nadu, India. J

Clin Diagnostic Res 2017;11:ZC78-81. https://doi.org/10.7860/JCDR/2017/27309.10442

[14] COVID-19 and Dentistry: Challenges and Opportunities for Providing Safe Care. Available from https://psnet.ahrq.gov/primer/covid-19-and-dentistry-challenges-and-opportunities-providing-safe-care

[15] Sample Size Calculator - The Survey System. Available from: https://www.surveysstem.com/sscale.htm#two (Cited on 12th September 2020).

[16] IBM Corp. Released 2012. IBM SPSS Statistics for Windows, Version 21.0. Armonk, NY: IBM Corp.

[17] Sagtani RA, Thapa S, Sagtani A. Smoking, general and oral health related quality of life - a comparative study from Nepal. Health Qual Life Outcomes 2020;18:1-7. https://doi.org/10.1186/s12955-020-01512-y

[18] Hajian-Tilaki A, Oliae F, Jenabian N, Hajian-Tilak K, Motallebnejad M. Oral health-related quality of life and periodontal and dental health status in Iranian hemodialysis patients. J Contemp Dent Pract 2014;15:482-90. https://doi.org/10.5005/jp-journals-10024-1566

[19] Bukhari OM. Dental caries experience and oral health related quality of life in working adults. Saudi Dent J 2020;32:382-389. https://doi.org/10.1016/j.sdentj.2019.11.003

[20] Ingle NA, Chaly PE, Zohara CK. Oral health related quality of life in adult population attending the outpatient department of a hospital in Chennai, India. J Int Oral Health 2010;4:45-56.

[21] Teixeira MFN, Martins AB, Celeste RK, Hugo FN, Hilgert JB. Association between resilience and quality of life related to oral health in the elderly. Rev Bras Epidemiol 2015;18:220-33. https://doi.org/10.1590/1980-5497201500010017

[22] Goryawala SN, Chavda P, Udhani S, Pathak NV, Pathak S, Ojha R. A survey on oral hygiene methods practiced by patients attending dentistry department at a tertiary care hospital from central gujarat. J Int Soc Prev Community Dent 2016;6:115-9. https://doi.org/10.4103/2231-0762.178750

[23] Avasthi A, Sogi GM, Veeresha KL. Oral health status and treatment needs of inpatients at a medical college hospital in Haryana. J Postgrad Med Education Res 2018;52:5-11. https://doi.org/10.5005/jp-journals-10028-1266

[24] Agrawal SK, Dahal S, Shrestha A, Bhagat TK. Assessment of Oral Health Impact Profile (OHIP-14) Among Villagers of Jyamirgadi vdc, Nepal: a Cross-Sectional Study. Eur J Biom Pharm Sci 2017;4:400-3.

[25] Guerra MJC, Greco RM, Leite ICG, Ferreira EF, Paula MVQ. Impact of oral health conditions on the quality of life of workers. Cien Saúde Colet 2014;19:4777-86. https://doi.org/10.1590/1413-812320141912.21352013

[26] Kahar P, Chapman C, Gupta J. Assessment of the effect of oral health on quality of life and oral-health indicators among ESRD patients in Southwest Florida: A pilot study. Int J Dentistry 2019;2019:1-9. https://doi.org/10.1155/2019/1608329

[27] Sadeghi R, Taleghani F, Farhadi S. Oral health related quality of life in diabetic patients. J Dent Res Dent Clin Dent Prospect 2014;8:230-4. https://doi.org/10.5681/joddd.2014.41

Correspondence: Avijit Avasthi, Department of Public Health Dentistry, Bhojia Dental College & Hospital, (H.P.), India. Tel.: 7837660552-E-mail:avijit123avasthi@gmail.com

Factors associated to acceptance and willingness to pay for COVID vaccine in Nepal

DEVARAJ ACHARYA[1], CHITRA BAHADUR BUDHATHOKI[2], SHANTI PRASAD KHANAL[2]
[1] Bhairahawa Multiple Campus, Tribhuvan University, Siddharthanagar, Rupandehi, Nepal;
[2] Central Department of Education, Tribhuvan University, Kathmandu, Nepal

Summary

Introduction. *Corona virus disease (COVID-19) remains pandemic globally. Vaccination is considered one of the best means to control both morbidity and mortality of COVID-19. The study aims to find out the people's acceptance and willingness to pay for it.*

Methods. *The study used cross-sectional survey design. Data were collected using a survey questionnaire from 1072 respondents (age 20-60 years) from 14 districts of Nepal. Socio-demographic characteristics of the respondents were independent and acceptance of vaccine was the dependent variable.*

Results. *The study found that 84% of the respondents accepted the COVID vaccine. Only one out of six did not accept the COVID vaccine while 16% of the respondents stated that they would like to pay for the COVID vaccination. The average willingness to pay (WTP) for vaccination was NRs. 1053 (US$ 9) while median and mode remained the same NRs. 500. The middle age groups*

(30-49 years), respondents belonged to Madhesi, business people in terms of occupation and the respondents who had completed school level education had a higher acceptance rate than other categories. It was observed that place of residence in terms of provinces or districts, age group, caste/ethnicity, and educational level of the respondents were significantly associated with the acceptance of the COVID vaccine. Moreover, respondents residing from Lumbini Province, age group of 30-39 years, and having secondary or higher education were noticed as more likely to accept the COVID vaccine than the respective compared groups.

Conclusion. *Appropriate information, education and communication needs to disseminate to minimize the misinformation about the COVID and lack of trust in vaccine that may lead to low acceptance and poor WTP for vaccine. These findings could be considered while making COVID and the COVID vaccine-related interventions.*

Introduction

Novel coronavirus disease (COVID-19) has become a serious public health problem globally. About 17 million people were infected and more the 3.5 million people lost their life due to COVID-19 [1]. Three main preventive measures: control the reservoir of infection, protect the susceptible host, and blocking the mode of transmission are the main keys to overcoming communicable diseases. The COVID-19 is noticed as a highly spreadable airborne disease and also appeared as out of control in many countries. Therefore, many states followed the protective measures as per the WHO's recommendations: social/physical distancing, masking, hygiene/sanitizing, isolation for infected cases and quarantine for suspected cases [1]. These measures are not enough to control the pandemic situation. On the other side, new variants of virus which have been identified in India and other countries makes the situation worst.

Nepal could not be an exception in this situation. The first case was detected in January 2020. With Nepali workers returning from India to their home town/village, the disease rapidly spread in all seven provinces and 77 districts of Nepal. By the end of May 2021, more than half a million people were recorded with COVID infection and more than seven thousand people lost their lives which accounts for 1.28 percent of the case fatality rate (CFR) [1]. Initially, the CFR was less than one percent but now it has appeared in an increasing trend which is making the government, public health experts and policymakers restless.

Observing such pandemic situation worldwide and as per the suggestion of WHO and public health experts, the Government of Nepal (GoN) imposed national level lockdown since 24th March 2020 and continued it 120 days up to 21st July 2020 [2, 3] 2019 (COVID-19). The second wave of COVID-19 pandemic in neighbouring countries is attributable to new variants of the virus, which are also responsible for the acceleration of the number of COVID cases in Nepal. With the rapid spread of the deadly virus in different parts of the country, the GoN imposed lockdown II on 28th April in almost all districts and was continued for a long time. The lockdown affected the daily routines of the people. Day to day life of country people adversely affected resulting in mental stress, suicidal tendencies, food insecurity, extreme poverty, inequality and difficulties in social services delivery system [4]. The government has been making its effort to inform and motivate people to follow protective measures such as physical distancing, improving hand

hygiene, wearing a facemask, avoiding crowded place, home quarantine and self-isolation through daily press meet and different mass media including radio and TV. People's unwillingness or hesitation to get vaccinated against COVID-19 may be due to misinformation and contagious [5]. Therefore, it needs time to time intervention for adequate and accurate information. The facts only cannot motivate people it needs mass campaigns to change or acceptance. Though vaccination could not be as a bullet to fight the COVID however vaccination and healthy behaviours, contact tracing with other combined efforts could eventually shrink the transmission of COVID [6].

Despite various efforts of the GoN and civil societies to curb the transmission of coronavirus infection, the situation could not be controlled. The situation not only affected the health of the people rather it affected the national economy, education and all other sectors. To date, no medicine is available to cure the diseases so preventive measures are key weapons to fight the disease pandemic. Therefore, only vaccination against COVID-19 is considered as a permanent solution to overcome the situation. However, there is much misinformation are also being spread. The misleading information could lead to mistrust, hesitancy, confusion and even rejection toward vaccination [7]. The trend showed that the GoN has been allocating nearly two to three percent of the total national budget on average for the health sector in the recent decade. The budget may not be enough to buy the COVID vaccine for all Nepalese people. In such instances, people participation would be compensated for health financing for buying the vaccine. However, we could not find any study regarding people's acceptance and willingness to pay for it in the context of Nepal. Therefore, the study aims to find out the people's acceptance and willingness to pay for the COVID vaccine.

Methods

RESEARCH DESIGN

The study used cross-sectional survey design.

STUDY SETTING AND PERIOD

The study covered all seven provinces of Nepal. We choose purposively two districts from each province. Therefore 14 districts were covered in this study. Sunsari and Dhankuta from Province one; Saptari and Parsa from Province two; Kathmandu and Chitwan from Bagmati; Baglung and Kaski from Gandaki; Rupandehi and Banke from Lumbini; Surkhet and Dailekh from Karnali; and Kailali and Bhajhang from Suderpaschim Province were purposively selected (Fig. 1). These districts were selected because the risk of COVID-19 was slightly higher compared to other districts in respective provinces. Fieldwork was started on 1st March 2021 and stopped on 27th April due to lockdown imposed by the GoN and local authorities.

Study population

People aged between 20-60 years living in the selected districts was the study population.
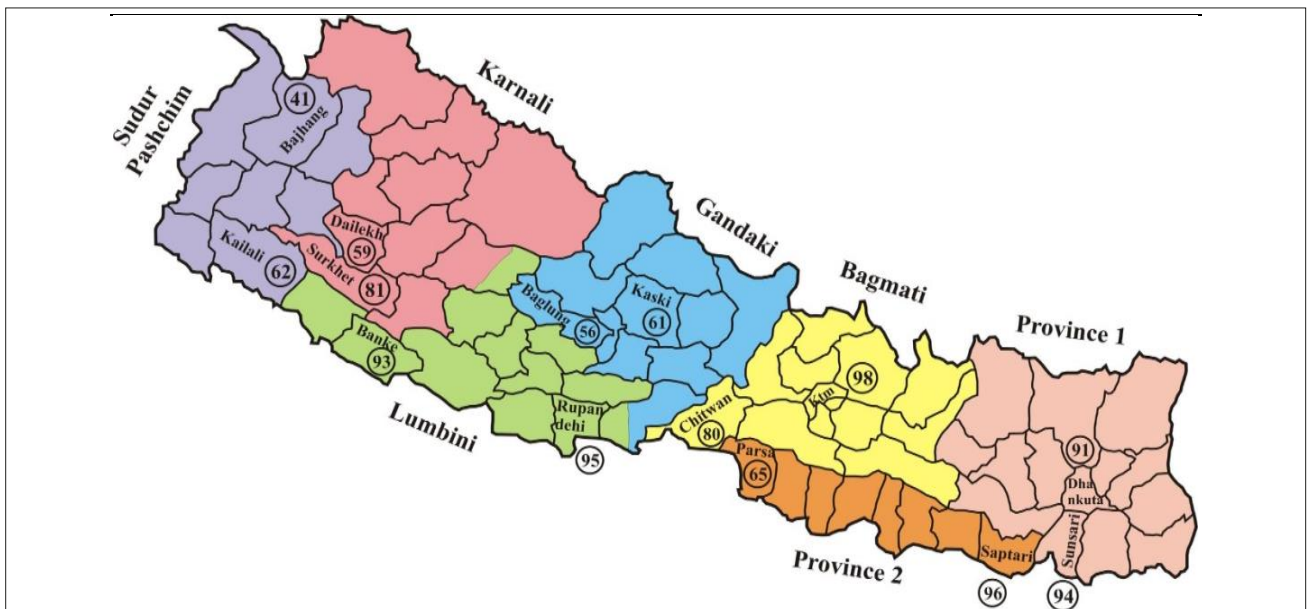
Sampling unit

Individuals of the household were the sampling unit. The ward of Rural Municipality (*Gaupalika*) and Urban Municipality (*Nagarpalika*) were the primary sampling unit (PSU) for the study.

Sample size

The required sample size was calculated using the formula [8].

$$n = \frac{t^2(p.q)}{d^2}.Def$$

Fig. 1. Sampling districts and sample size.

Tab. I. Background characteristics of the respondents.

Variables	Category	%	N
Province	Province 1	17.3	185
	Province 2	15.0	161
	Bagmati	16.6	178
	Gandaki	10.9	117
	Lumbini	17.5	188
	Karnali	13.1	140
	Sudur Pashchim	9.6	103
District	Sunsari	8.8	94
	Dhankuta	8.5	91
	Saptari	9.0	96
	Parsa	6.1	65
	Kathmandu	9.1	98
	Chitwan	7.5	80
	Baglung	5.2	56
	Kaski	5.7	61
	Rupandehi	8.9	95
	Banke	8.7	93
	Surkhet	7.6	81
	Dailekh	5.5	59
	Kailali	5.8	62
	Bajhang	3.8	41
Place of residence	Urban/Town	29.5	316
	Semi Urban/Small Town	26.3	282
	Rural Areas	44.2	474
Age group	20-29 yrs	42.9	460
	30-39 yrs	25.5	273
	40-49 yrs	17.6	189
	50 or more	14.0	150
Sex	Male	47.9	513
	Female	51.7	554
	Others	.5	5
Caste/Ethnicity	Brahman/Chhetri/Thakuri/Sanyasi	44.3	475
	Advantaged Janajatis	6.3	68
	Disadvantaged Janajatis	12.4	133
	Madhesi	23.2	249
	Muslim	3.1	33
	Dalit	10.2	109
	Others	.5	5
Main occupation	Subsistence Agriculture	25.3	271
	Cash crops/farming	7.9	85
	Business	8.9	95
	Service	26.5	284
	Foreign Employment	3.2	34
	Wage labour	8.5	91
	Housewife	10.9	117
	Other	8.9	95
Educational level	No education	8.7	93
	Basic education	15.2	163
	Secondary Education	40.4	433
	Higher education	35.7	383
Size of the family	Up to 5 members	48.1	516
	6 to 10 members	45.3	486
	11 or more members	6.5	70
Type of family	Nuclear	58.5	627
	Joint	41.5	445
Religion	Hindu	84.7	908
	Buddhist	6.2	66
	Islam	4.4	47
	Christianity	2.5	27
	Others	2.2	24
Chronic illness	No	77.1	827
	Yes	22.9	245

Where, n = size required; t = 95% confidence interval for cluster sampling (2.045) instead of (z = 1.96); p = estimated proportion of the variables = 0.5; $q = 1-p$, d = the degree of accuracy (d = 0.05), and Def = design effect = 3. The total sample accounted for 1255. After adjusting the non-response rate of 10 percent, then the sample size accounted for 1394 for 14 districts (99.9~100 for each district), therefore, the required sample size reached 14*100 = 1400.

Sampling Technique

The multistage sampling technique was used in the process of selecting sampling units. In the first stage, 14 districts from 7 provinces were purposively selected. In the second stage, one rural municipality and one municipality were selected purposively as applicable. In the third stage, two primary sampling units (two clusters/wards) were randomly selected from each of selected rural/municipalities. A list of the adult population [20-60 years] who were available at the cluster were listed. In the fourth stage, 25 households from each cluster/PSU were randomly selected.

Criteria for sample selection

Persons aged 20-60 years living in households of PSU were eligible for sample selection. Those persons who were willing to participate in the COVID survey were selected for the structured interview. Age less than 20 or more than 60, and an individual who did not want to participate and the guests who came from other than sample districts were excluded.

DATA COLLECTION TOLL

The survey questionnaire was the tool for data collection.

VALIDITY AND RELIABILITY OF THE TOOL

The research tool was pretested in Kathmandu, Chitwan, Rupandehi, and Surkhet districts of Nepal. The final set of questionnaires was tested among 40 persons living in rural and urban areas which were not included in PSU. Cronbach's alpha was calculated and found 0.754 which was eligible to administrate [9]. A webinar-based discussion was conducted to revise the study tool. After conducting the pre-testing, we also consulted with statisticians then some questions are removed as well as added as per the field experience.

DATA COLLECTION TECHNIQUES

After selecting the sample, filed enumerators stated about the objective of the study, voluntary participation, right to reject any time, data confidentiality and anonymity to the respondents. Consent was taken prior to the interview and then collected the data from the respondents at their home or the place where they felt comfort response such as field, workplace. Data were collected by using mobile technology through application software KoBo Toolbox. Though estimated the sample size was 1400 but the GoN imposed lockdown since 28th April 2021 in many districts. Then, we could not be able to collect the all

data as per the plan after the date. Altogether, responses from 1072 samples were recorded. So, the study yielded 77 (actual 85%: 1072/1255) percent of response rate due to lockdown and COVID-19 pandemic situation.

VARIABLES AND MEASURES

Socio-demographic characteristics of the respondents were independent, and acceptance and willingness to pay for the COVID vaccine were the dependent variables. Descriptive in terms of frequency and percentage, central tendency, and bivariate (chi-square test) analysis was performed to find out the association between the variables. For the statistical analysis, IBM SPSS statistics 20 was used.

POTENTIAL BIASES

This was a quantitative survey, there might be selection bias of respondents and recall bias of information. There might be confirmation bias from the researcher side in order to favour particular assumptions. The field enumerators were oriented about these biases and the ways of minimizing these biases during the orientation and training. Moreover, they were oriented about probing techniques to minimize recall and other biases.

ETHICAL CONSIDERATION

The study proposal was reviewed and approved by Nepal Health Research Council (NHRC) on 26th January 2021 (# 649/2020). The study followed all research ethics guidelines made by NHRC.

Results

CHARACTERISTICS OF THE RESPONDENTS

Though it was planned that a total of 200 respondents from each province. But due to the pandemic situation and the GoN and local authorities imposed lockdown we could not be able to collect the data after 28th April 2021. However, about 85 percent of the actual sample has been collected. Data were collected more than three-fourth of the total target sample. Of the total respondents, 44 percent were from rural areas and 30 percent from urban areas. The mean age of the respondent was 35 ± 11.29 years and 43 percent of the total samples were from 20 to 29 years of age. The majority (52%) of the respondents were female and 44 percent were from Brahmin, Chhetri, Dasnami and Thakuri. One-third of the respondents were involved in subsistence agriculture as the main occupation whereas 27 percent as in service. One out of ten (9%) of the respondents were illiterate but 36 percent had higher education degrees. Near to half (48%) of the respondents had up to five members in their family and 59 percent of the respondent were from nuclear families.

A vast majority (85%) of the respondent were Hindu and 23 percent of the respondents had some kind of chronic disease within family members.

ACCEPTANCE OF THE COVID VACCINE

A majority (84%) of the respondent expressed that they would accept the COVID-19 vaccine. Nearly half (46%, n = 495) of the respondents indicated that they would accept vaccines if the vaccine was available at free of cost and only about 16 percent (n = 167) of the respondents stated that they would accept vaccines even if they have to pay. One fifth (21%, n = 228) of the respondents indicated that they will decide how much they want to pay after the vaccine is available.

WILLINGNESS TO PAY FOR COVID VACCINE

Of the total respondents, only one out of six (16%) respondents wanted to pay for the COVID vaccine. The mean willingness to pay (WTP) for the COVID vaccine was Nepali Rupees (NRs.) 1053 (US$ 9), median and mode of the WTP for the COVID vaccine was NRs. 500 each where minimum NRs. 50 to maximum NRs. 10,000. The WTP of the respondents for COVID vaccine was asymmetry nature.

ASSOCIATION OF SOCIO-DEMOGRAPHIC CHARACTERISTICS AND ACCEPTANCE OF COVID VACCINE

Almost all (97%) of the respondents from Lumbini province expressed that they would accept the COVID vaccine followed by 90 percent from Province One, 88 percent from Province Two, and only 69 percent of the respondents from Bagmati province would accept the vaccine which was the lowest acceptance among all provinces ($p < 0.001$). In the same way, the cent percent of the respondents from Rupandehi district accepted the COVID vaccine what was the highest acceptance whereas 59 percent of the respondents from Dailekh district stated that they would accept the COVID vaccine which was the lowest acceptance rate among the districts ($p < 0.001$).

The acceptance rate of the vaccine was higher in the semi-urban areas (87%) compared to rural (85%) and urban (81%) areas. That means respondents from urban areas had a low acceptance rate for the COVID vaccine. Interestingly middle age group (30-49 years) had more acceptance rate which accounted for 88 to 89 percent compared to other age groups (80-83%) ($p < 0.01$). In the same way, female respondents had a comparatively low acceptance rate (84%) compared to other (85%). The respondents who were Madhesi had a higher acceptance rate (91%) of COVID vaccine compared to other caste groups ($p < 0.001$). Only 82 percent of the respondents from Muslim expressed that they would accept the COVID vaccine. Similarly, the respondents who were involved in business had a higher acceptance rate for vaccines which accounted for 92 percent whereas the respondents who were housewives had a low acceptance rate (73%) ($p < 0.01$).

Ninety percent of the respondents who completed secondary level of education had a higher acceptance rate which accounted for 90 percent compared to the respondents who had no formal education (76%) and higher education (79%) ($p < 0.001$). Data showed that the

higher the number of family size higher the acceptance for the COVID vaccine. It was observed that there was no difference of the acceptance rate of vaccines between nuclear and joint families. In the same way, there were no significant differences for the COVID vaccine acceptance rate among the religious groups and the family of the respondents having the chronic disease(s) within the family member(s) or not.

MULTIVARIATE ANALYSIS ON SOCIO-DEMOGRAPHIC CHARACTERISTICS AND ACCEPTANCE OF COVID VACCINE

Variables, that were found significant differences in bivariate analysis, were further analysed in the multivariate analysis except for districts. Before adjusting the variables in multivariate analysis some attributes were merged such as caste and occupation. In Model I, we presented the province and acceptance of the COVID vaccine, in Model II we adjusted age group and caste, and in Model III we adjusted occupation and education along with other variables. Nearly the same result was noticed in the tables but after adjusting the occupation and educational level of the respondent, the odds ratio of caste appeared in a fluctuated way.

It was noticed that the respondents from Bagmati province appeared 72% less likely to accept the COVID vaccine compared to the respondents from Province one (OR = 0.28, 95% CI: 0.15-0.52). In the same way, the respondents from Karnali Province noticed 59% less likely to accept the COVID vaccine compared to the respondents from Province one (OR = 0.41, 95% CI: 0.21-0.77). But, the respondents from Lumbini Province were observed almost 5.2 times more likely to accept the COVID vaccine compared to the respondents from Province one (OR = 5.20, 95%CI: 1.84-14.70).

The middle age group (30-39 years and 40-49 years) appeared 1.8 to 2.0 times more likely to accept the COVID vaccine compared to the age group of 20-29 years respectively (OR = 2.03, 95% CI: 1.26-3.27, and OR = 1.84, 95% CI: 1.04-3.25). In the same way, the respondents having secondary and higher education were noticed as more likely to accept the COVID vaccine compared to the respondents who had no education respectively (OR = 3.64, 95% CI: 1.78-7.42, and OR = 2.34, 95% CI: 1.14-4.89).

Discussion

The study found that a vast majority of the respondents accepted the COVID vaccine. Only one out of six did not accept the COVID vaccine while the same percentage of the respondents would like to pay for COVID vaccination. The average WTP for vaccination was NRs. 1053 (US$ 9) and median and mode of WTP remained the same NRs. 500. However, the range of WTP was NRs. 50-10,000. A high acceptance rate was found in Lumbini and a low acceptance rate was observed in Bagmati province. In the same way, a high acceptance rate was recorded in Rupandehi and a low in Dailekh

district. The middle age groups (30-49 years of age) had a higher acceptance rate of vaccination. Respondents who belonged to Madhesi and business people in terms of occupation had a higher acceptance rate than other related groups. The respondents who had completed school level education had a higher acceptance rate than others categories. The study revealed that place of residence in terms of provinces or districts, age group, caste/ethnicity, and educational level of the respondents were significantly associated with the acceptance of the COVID vaccine. Similarly, respondents from the Lumbini Province, the middle year of age 30-49 years, and secondary or higher education were noticed as more likely to accept the COVID vaccine compared to their respective attributes.

An e-survey conducted in Turkey showed that near to half (49.7%) of the respondents stated that they would be vaccinated [10] which was similar (42% acceptance rate) to the study from Russia [11]. Another study from France showed 77 percent of the respondents who were health workers would like to accept the COVID vaccination [12] which was lower than this study. The study further showed that gender, age and type of occupation were significantly associated with the acceptance of the COVID vaccine that was somehow similar result with the study [12]. In the initial days for the COVID vaccine, there was mistrust and hesitation to accept or be willing to participate in the vaccine trial. Nearly two-third (64-69%) of the respondents from China accepted for willingness for COVID vaccine trial [13,14] this paper aimed to describe the prevalence and correlates of willingness to participate in COVID-19 vaccine trials among university students in China. A cross-sectional survey with 1912 Chinese university students was conducted during March and April 2020. Bivariate and multivariate analyses were performed to identify variables associated with willingness to participate. The majority of participants (64.01%] similar to the study from Japan [15]. Nearly the same result was observed in the United States (US). Socio-demographic variables such as age, sex, ethnicity, education and income status were significantly associated with the intention to accept the COVID vaccine [16]. However, a systematic review showed that sex (female), age (younger), low social status (low economic and educational level), and caste (ethnic minority) were significantly associated with less likely to accept the CoViD vaccine [17].

The acceptance rate of the COVID vaccine was noticed to vary within a time interval. A longitudinal study conducted in the US showed that there was 71 percent vaccine acceptance rate was observed in April while it was declined to 54 percent in October 2020 [18]. So, the acceptance rate might be influenced not only by socio-demographic characteristics but also by the time interval. A prior study conducted in United Kingdoms showed that low socio-economic status, women and ethnic minorities appeared less likely to accept the COVID vaccine. Near to two-third (63.5%) of the respondents would like to accept the vaccine whereas about one fourth (22.5%) were unsure and 14 percent would like to reject

Tab. II. Acceptance of CoViD-19 vaccine.

Variable	Category	N	%
Acceptance of vaccine	No	169	15.8
	Yes	903	84.2
Accepted if (n = 903)	Available at free of cost	495	54.8
	Would pay if available	167	18.5
	Will decide after vaccine available	228	25.2
	Others	13	1.4

the vaccine [19]. A similar observation was found in Philadelphia that showed acceptance rate was 74 percent, 26 percent were unsure and 10 percent did not plan to the vaccine [20]. The prior study from France supports that gender, age and low education level were associated with the acceptance of the COVID vaccine [21]. The majority (64%) of the respondents from China expressed they would accept vaccines however lower socio-economic status and females were more likely to accept the COVID vaccine [22] which was somehow different from this study.

Surprisingly, near to half (46%) of the respondents from Egypt had hesitancy towards the COVID vaccine. Moreover, six percent each form respondents would like to accept as well as a reject [23]. Two-third (66%) and 14 percent of the respondents from the US would like to accept and reject the COVID vaccine respectively [24] which was near to similar with the study. More than half (56%) had a vaccine acceptance rate whereas the upper-income category(rich) had a higher chance to accept and health workers were appeared less likely to accept vaccines in the Democratic Republic of Congo [25]. Acceptance of COVID vaccine varies in time and place overall vaccine hesitancy rate appeared 9 to 43 percent in France [26]. A systematic reviews showed that the acceptance rate was varied from 28 to 78 percent in 33 different countries [27].

LIMITATIONS

We selected the districts purposively as per the magnitude of the problem so there may be selection bias. Similarly, response and recall biases may persist since we collected the data from the respondents in a single and first visit. Moreover, the cross-sectional study might not show the cause and effect relationship among the variables. Therefore, a mixed or multi-methods approach with wider perspectives would be better to study for acceptance and WTP for the COVID vaccine in near future.

Conclusion

A vast majority (8 out of 10) of the respondents accepted the COVID vaccine however only one out of six will pay for vaccination. Of the respondents, 16 percent did not accept the vaccine. Moreover, the average willingness to pay for the COVID vaccine was NRs. 1053 (US$ 9). These findings show that people do not want to pay but they would like to be vaccinated free of cost. Since the vaccination is in the initial phase globally. People may have misinformation and a lack of trust in it. Generally, negative information can spread faster than a positive message. Socio-demographic characteristics such as place of residence in terms of province and districts, age group of people, caste/ethnicity, occupation, educational level are significantly associated with the acceptance of the COVID vaccine. But, residence setting (in terms of Province and districts), age group, and educational status of the respondents were significant predictors for the acceptance of the COVID vaccine. The policymakers and stakeholders should take these findings into account while making COVID vaccine-related planning and intervention. Proper dissemination is required to minimize the COVID related misinformation and lack of trust in the COVID vaccine that would lead to higher acceptance and WTP for the vaccine.

Acknowledgements

Conflict of interest statement

The authors declare that they have no conflict of interest with this study.

Authors' contribution

DA: Design of the study, analysis of data, interpretation of data, drafting and approved the final version of the manuscript. CBB: Conception of the study, interpretation of data, revised the manuscript critically, approved the final version of the manuscript. SPK: Design of the study, acquisition of data, revised the manuscript critically, and approved the final version.

Tab. III. Willingness to pay for COVID vaccine.

Amount in NRs.	N	%	Mean	Median	Mode	SD	Minimum	Maximum	Range
Up to 500	105	63							
501 to 1000	30	18	1053	500	500	1761	50	10000	9950
More than 1000	32	19							
Total	167	100							

NRs: Nepalese Rupee [NRs 117.04 = 1 US$].

Tab. IV. Association of socio-demographic characteristics and acceptance of COVID vaccine.

Variables	Category	Acceptance of COVID-19 vaccine				χ^2	ρ
		No		Yes			
		N	%	N	%		
Province	Province 1	19	10.3	166	89.7	74.470	< 0.001
	Province 2	20	12.4	141	87.6		
	Bagmati	55	30.9	123	69.1		
	Gandaki	17	14.5	100	85.5		
	Lumbini	5	2.7	183	97.3		
	Karnali	38	27.1	102	72.9		
	Sudur Pashchim	15	14.6	88	85.4		
District	Sunsari	5	5.3	89	94.7	107.339	< 0.001
	Dhankuta	14	15.4	77	84.6		
	Saptari	13	13.5	83	86.5		
	Parsa	7	10.8	58	89.2		
	Kathmandu	28	28.6	70	71.4		
	Chitwan	27	33.8	53	66.3		
	Baglung	1	1.8	55	98.2		
	Kaski	16	26.2	45	73.8		
	Rupandehi			95	100.0		
	Banke	5	5.4	88	94.6		
	Surkhet	14	17.3	67	82.7		
	Dailekh	24	40.7	35	59.3		
	Kailali	9	14.5	53	85.5		
	Bajhang	6	14.6	35	85.4		
Place of residence	Urban/Town	61	19.3	255	80.7	4.686	0.096
	Semi Urban/Small Town	37	13.1	245	86.9		
	Rural Areas	71	15.0	403	85.0		
Age group	20-29 yrs	90	19.6	370	80.4	11.699	0.008
	30-39 yrs	31	11.4	242	88.6		
	40-49 yrs	22	11.6	167	88.4		
	50 or more	26	17.3	124	82.7		
Sex	Female	90	16.2	464	83.8	0.199	0.655
	Others	79	15.3	439	84.7		
Caste	Brahman/Chhetri/Thakuri/Sanyasi	97	20.4	378	79.6	21.799	0.001
	Advantaged Janajatis	10	14.7	58	85.3		
	Disadvantaged Janajatis	13	9.8	120	90.2		
	Madhesi	23	9.2	226	90.8		
	Muslim	6	18.2	27	81.8		
	Dalit	18	16.5	91	83.5		
	Others	2	40.0	3	60.0		
Main occupation	Subsistence Agriculture	43	15.9	228	84.1	18.890	0.009
	Cash crops/farming	14	16.5	71	83.5		
	Business	8	8.4	87	91.6		
	Service	36	12.7	248	87.3		
	Foreign Employment	7	20.6	27	79.4		
	Wage labour	16	17.6	75	82.4		
	Housewife	32	27.4	85	72.6		
	Other	13	13.7	82	86.3		
Educational level	No education	22	23.7	71	76.3	21.972	< 0.001
	Basic education	22	13.5	141	86.5		
	Secondary Education	45	10.4	388	89.6		
	Higher education	80	20.9	303	79.1		
Size of the family	Up to 5 members	84	16.3	432	83.7	0.554	0.758
	6 to 10 members	76	15.6	410	84.4		
	11 or more members	9	12.9	61	87.1		
Type of family	Nuclear	98	15.6	529	84.4	0.021	0.886
	Joint	71	16.0	374	84.0		
Religion	Hindu	135	14.9	773	85.1	4.573	0.334
	Buddhist	14	21.2	52	78.8		
	Islam	11	23.4	36	76.6		
	Christianity	4	14.8	23	85.2		
	Others	5	20.8	19	79.2		
Chronic illness	No	128	15.5	699	84.5	0.225	0.635
	Yes	41	16.7	204	83.3		

Note: Bold face of p-value indicates statistically significant.

Tab. V. Multivariate analysis on socio-demographic characteristics and acceptance of CoViD vaccine.

Variables	Category	Model I			Model II			Model III		
		OR	95% CI		OR	95% CI		OR	95% CI	
			Lower	Upper		Lower	Upper		Lower	Upper
Province	Province 1 (Ref.)	1.00						1.00		
	Province 2	.807	.414	1.572				0.871	0.400	1.897
	Bagmati	**.256**	**.145**	**.453**				**0.280**	**0.151**	**0.518**
	Gandaki	.673	.334	1.356				0.801	0.388	1.655
	Lumbini	**4.189**	**1.530**	**11.470**				**5.195**	**1.835**	**14.704**
	Karnali	**.307**	**.168**	**.562**				**0.405**	**0.214**	**0.768**
	Sudur Pashchim	.671	.325	1.386				0.899	0.418	1.932
Age group	20-29 yrs (Ref.)				1.00			1.00		
	30-39 yrs				**1.882**	**1.210**	**2.927**	**2.025**	**1.256**	**3.267**
	40-49 yrs				**1.723**	**1.040**	**2.855**	**1.841**	**1.043**	**3.248**
	50 or more				1.059	.650	1.726	1.283	0.686	2.398
Caste	Brahmin/Chhhetri/Thakuri/Dashanami (Ref.)				1.00			1.00		
	Janajatis				**1.964**	**1.202**	**3.209**	1.345	0.780	2.319
	Others				**1.796**	**1.231**	**2.622**	1.067	0.627	1.813
Occupation	Agriculture, business (Ref.)							1.00		
	Service, wage, foreign job							0.849	0.573	1.258
	Others							1.649	0.819	3.324
Educational level	No education (Ref.)							1.00		
	Basic education							1.902	0.923	3.919
	Secondary Education							**3.635**	**1.781**	**7.417**
	Higher education							**2.336**	**1.115**	**4.894**

References

[1] World Health Organization. WHO Coronavirus (COVID-19) Dashboard [Internet]. Situation by Region, Country, Territory & Area. 2021. Available at: https://covid19.who.int/table (Accessed on 29/05/2021).

[2] Khanal N, Singh AK. Knowledge, attitude and practice regarding COVID-19 and its impact on dentistry: A cross-sectional survey among Nepalese dentists. Kathmandu Univ Med J 2020;18:3-9. https://doi.org/10.3126/kumj.v18i2.32937

[3] Pathak KP, Gaire T, Acharya D. Novel coronavirus disease (Covid-19): Social distancing, isolation and quarantine are key success factors of Nepal's public health practices or something else? Kathmandu Univ Med J 2020;18:68-74. https://doi.org/10.3126/kumj.v18i2.33034

[4] Singh DR, Sunuwar DR, Karki K, Ghimire S, Shrestha N. Knowledge and perception towards universal safety precautions during early phase of the COVID-19 outbreak in Nepal. J Community Health 2020;45:1116-22. https://doi.org/10.1007/s10900-020-00839-3

[5] Wiysonge CS, Ndwandwe D, Ryan J, Jaca A, Batouré O, Anya BPM, Cooper S. Vaccine hesitancy in the era of COVID-19: could lessons from the past help in divining the future? Hum Vaccines Immunother 2022;18:1-3. https://doi.org/10.1080/21645515.2021.1893062

[6] Tibbetts JH. Will a covid vaccine be accepted? Bioscience 2021;71:11-7. https://doi.org/10.1093/biosci/biab046

[7] Lockyer B, Islam S, Rahman A, Dickerson J, Pickett K, Sheldon T, Wright J, McEachan R, Sheard L, on behalf of the Bradford Institute for Health Research Covid-19 Scientific Advisory Group. Understanding COVID-19 misinformation and vaccine hesitancy in context: Findings from a qualitative study involving citizens in Bradford, UK. Heal Expect. 2021;(00):1-10. https://doi.org/10.1101/2020.12.22.20248259

[8] Getnet GT. Sample Size Determination in Food Security Survey Studies. J Food Nutr Popul Heal 2021;5:1-3. Available at: https://www.imedpub.com/articles/sample-size-determination-in-food-security-survey-studies.pdf

[9] Hair JF, Black WC, Babin BJ, Anderson RE. Multivariate Data Analysis. 7th ed. Harlow, London: Pearson Education Limited 2014.

[10] Akarsu B, Canbay Özdemir D, Ayhan Baser D, Aksoy H, Fidancı İ, Cankurtaran M. While studies on COVID-19 vaccine is ongoing, the public's thoughts and attitudes to the future COVID-19 vaccine. Int J Clin Pract 2021;75:1-10. https://doi.org/10.1111/ijcp.13891

[11] Tran VD, Pak TV., Gribkova EI, Galkina GA, Loskutova EE, Dorofeeva VV, Dewey RS, Nguyen KT, Pham DT. Determinants of COVID-19 vaccine acceptance in a high infection-rate country: A cross-sectional study in Russia. Pharm Pract (Granada) 2021;19:1-12. https://doi.org/10.18549/PharmPract.2021.1.2276

[12] Gagneux-Brunon A, Detoc M, Bruel S, Tardy B, Rozaire O, Frappe P, Botelho-Nevers E. Intention to get vaccinations against COVID-19 in French healthcare workers during the first pandemic wave: a cross-sectional survey. J Hosp Infect [Internet]. 2021;108:168-73. https://doi.org/10.1016/j.jhin.2020.11.020

[13] Sun S, Lin D, Operario D. Interest in COVID-19 vaccine trials participation among young adults in China: Willingness, reasons for hesitancy, and demographic and psychosocial determinants. Prev Med Reports 2021;22:1-5. https://doi.org/10.1016/j.pmedr.2021.101350

[14] Wang C, Han B, Zhao T, Liu H, Liu B, Chen L, Xie M, Liu J, Zheng H, Zhang S, Wang Y, Huang N, Du J, Liu YQ, Lu QB, Cui F. Vaccination willingness, vaccine hesitancy, and estimated coverage at the first round of COVID-19 vaccination in China: A national cross-sectional study. Vaccine [Internet] 2021;39:2833-42. https://doi.org/10.1016/j.vaccine.2021.04.020

[15] Machida M, Nakamura I, Kojima T, Saito R, Nakaya T, Hanibuchi T, Takamiya T, Odagiri Y, Fukushima N, Kikuchi H, Amagasa S, Watanabe H, Inoue S. Acceptance of a COVID-19 vaccine in japan during the COVID-19 pandemic. Vaccines 2021;9:1-11. https://doi.org/10.3390/vaccines9030210

[16] Chu H, Liu S. Integrating health behavior theories to predict American's intention to receive a COVID-19 vaccine. Patient Educ Couns. 2021;104:1878-86. https://doi.org/10.1016/j.pec.2021.02.031

[17] Robinson E, Jones A, Lesser I, Daly M. International estimates of intended uptake and refusal of COVID-19 vaccines: A rapid systematic review and meta-analysis of large nationally representative samples. Vaccine 2021;39:2024-34. https://doi.org/10.1016/j.vaccine.2021.02.005

[18] Daly M, Robinson E. Willingness to vaccinate against COVID-19 in the U.S.: Representative longitudinal evidence from April to October 2020. Am J Prev Med 2021;60:766-73. https://doi.org/10.1016/j.amepre.2021.01.008

[19] Paul E, Steptoe A, Fancourt D. Attitudes towards vaccines and intention to vaccinate against COVID-19: Implications for public health communications. Lancet Reg Heal - Eur 2021;1:1-10. https://doi.org/10.1016/j.lanepe.2020.100012

[20] Kuter BJ, Browne S, Momplaisir FM, Feemster KA, Shen AK, Green-McKenzie J, Faig W, Offit PA. Perspectives on the receipt of a COVID-19 vaccine: A survey of employees in two large hospitals in Philadelphia. Vaccine 2021;39:1693-700. https://doi.org/10.1016/j.vaccine.2021.02.029

[21] Schwarzinger M, Watson V, Arwidson P, Alla F, Luchini S. COVID-19 vaccine hesitancy in a representative working-age population in France: a survey experiment based on vaccine characteristics. Lancet Public Heal 2021;6:e210-21. https://doi.org/10.1016/S2468-2667(21)00012-8

[22] Sun S, Lin D, Operario D. Interest in COVID-19 vaccine trials participation among young adults in China: Willingness, reasons for hesitancy, and demographic and psychosocial determinants. Prev Med Reports 2021;22. https://doi.org/10.1016/j.pmedr.2021.101350

[23] Saied SM, Saied EM, Kabbash IA, Abdo SAEF. Vaccine hesitancy: Beliefs and barriers associated with COVID-19 vaccination among Egyptian medical students. J Med Virol 2021;19. https://doi.org/10.1002/jmv.26910

[24] Ehde DM, Roberts MK, Herring TE, Alschuler KN. Willingness to obtain COVID-19 vaccination in adults with multiple sclerosis in the United States. Mult Scler Relat Disord 2021;49:102788. https://doi.org/10.1016/j.msard.2021.102788

[25] Ditekemena JD, Nkamba DM, Mutwadi A, Mavoko HM, Fodjo JNS, Luhata C, Obimpeh M, Van Hees S, Nachega JB, Colebunders R. Covid-19 vaccine acceptance in the democratic republic of congo: A cross-sectional survey. Vaccines 2021;9:1-11. https://doi.org/10.3390/vaccines9020153

[26] Verger P, Peretti-Watel P. Understanding the determinants of acceptance of COVID-19 vaccines: a challenge in a fast-moving situation. Lancet Public Heal 2021;6:e195-6. https://doi.org/10.1016/S2468-2667(21)00029-3

[27] Sallam M. Covid-19 vaccine hesitancy worldwide: A concise systematic review of vaccine acceptance rates. Vaccines 2021;9:1-15. https://doi.org/10.3390/vaccines9020160

Appendix I

Questionnaire
COVID-19 Behavioural Survey 2020

Section I: Respondents' Background Information

Q101 Where do you live?
      1.Province
      2. Province
      3. Province
      4. Province
      5. Province
      6. Province
      7. Province

Q102 What is your district name
      1. Sunasari
      2. Dhankuta
      3. Saptari
      4. Parsa
      5. Kathmandu
      6. Chitwan
      7. Baglung
      8. Kaski
      9. Rupandehi
      10. Banke
      11. Surkhet
      12. Dailekh
      13. Kailali
      14. Bajhang

Q103 Where do you live?
      1. Urban/Town
      2. Semi Urban/Small Town
      3. Rural Areas

Q104 What is your age? .... Years

Q105 What is your sex?
      1. Male
      2. Female
      3. Others

Q106 What is your caste/ethnicity?
      1. Brahman/Chhetri/Thakuri/Sanyais
      2. Advantaged Janajati
      3. Disadvantaged Janajati
      4. Madhesi
      5. Muslim
      6. Dalit
      7. Others

Q107 What is your main occupation
      1. Subsistence Agriculture
      2. Cash crops/farming
      3. Retail shop/business/Hotel
      4. Teacher/Government/Non-Government/Private Company Employee
      5. Foreign Employment
      6. Wage labour
      7. Housewife
      8. Other...............

Q108 What is your level of education ....

Q109 How many people are there in your family? .... Persons

Q110 Type of your family?
      1. Nuclear
      2. Joint

Q111 Which religions do you follow?
      1.   Hindu
      2.   Buddhist
      3.   Islam
      4.   Christianity
      5.   Others

Q112 Do you have any family member with chronic diseases who needs to take regular medicine?
      1. Yes
      0. No

Q112.1 If yes which disease related? (Multiple Response)
      1. Cancer
      2. Heart related diseases
      3. COPD
      4. Arthritis/Joint Related
      5. Gastritis
      6. Diabetes
      7. Kidney related .
      8. Uric Acid
      9. Mental related
      10. Thyroid related
      11. Others………. Specify…..........

Q113 Has anyone of your family recently returned to home from India or foreign country or corona epidemic area?
      1 Yes
      0. No

Q114 Have you recently returned to home from foreign country or India?
      1. Yes
      0. No

Q115 If Yes, did you stay in quarantine?
      1. Yes, Quarantine center
      2. Yes, Home Quarantine
      3. No

Section II: COVID-19 Communication and Knowledge/Awareness

Q201 Have your heard of coronavirus disease (COVID-19)?
      1. Yes
      0. No

Q202 Have you heard or seen any messages related to coronavirus disease within a last month?
      1. Yes
      0. No

Q203 What is your sources of information/message about coronavirus disease?

		Always	**Often**	**Rarely**	**Never**
1	Radio/FM				
2	TV				
3	Facebook and social media				
4	Online media				
5	Telephone ringtone				
6	Daily newspaper, posters and other printed media				
7	Gov, Health Minister and NHEICC Website				
8	Doctor, Nurses and health service providers				
9	Teachers				
10	Local Leaders				
11	Social and Development Workers				
12	Family members and friends				
13	Police and Security Personnnel				

Q204 It is difficult to decide which information I receive about the coronavirus is real, fake, or just rumors
      1. Agree
      2. Disagree
      3. Unknown

Q205 What is your most trusted source of information about coronavirus disease?
      Radio
      TV
      Newspaper
      Poster Pamphlet/Display Board
      Teachers
      Doctor/Health Worker
      Political Leader
      FCHV
      Relative
      Neighbour
      Family Member
      Friends
      Social/Online Media
      Others

Q206 Based on your responses to COVID-19 communication and media, what do you think of the following statements?

SN	Statements	Agree	Disagree	Not sure/No idea
01	Different media have increased public awareness and concern over coronavirus disease			
02	The information in the media are adequate to motivate people to follow protective behaviour/government recommendations			
03	I am still in confusion about prevention and treatment of coronavirus diseases due to socio-culturally inappropriate language and terms used by media and government press meet			
04	Biased information of media has increased stigma and discrimination against people infected with coronavirus			
05	Media is helping us to fight against coronavirus disease by creating awareness			

Q207 How do you feel about coronavirus disease?
    1. Very Fearful
    2. Fearful
    3. Not fearful
    4. Fearful but optimistic

Q208 How much are you worried about getting coronavirus disease yourself?
    1. Very worried
    2. Moderately worried
    3. Not worried

Q209 How does coronavirus spread among people?
    1. Through air
    2. Through vegetables, fruits and other goods coming from epidemic area
    3. Contact or close contact with infected persons
    4. Respiratory droplets of infected persons
    5. While touching surfaces around infected persons and things used/touched by infected persons
    6. No/No responses

Q210 Can you tell me symptoms of coronavirus disease?
    1. Fever
    2. Headache
    3. Dry cough
    4. Running stuffy nose
    5. Sore throat
    6. Loss of smell and taste
    7. Tiredness
    8. Diarrhea
    9. Shortness of breath
    10. No symptoms
    11. No/ No responses

Q211 Perceived Invulnerability

SN		Strongly Disagree	Disagree	Not sure	Agree	Strongly Agree
1	I am less likely than most people to get COVID-19					
2	People like me don't get COVID-19					
3	My body could fight off COVID-19 infection					
4	There is little chance that I could get or spread COVID-19 from what I do in my everyday life					

Q212 Perceived Susceptibility

SN		Strongly Disagree	Disagree	Not sure	Agree	Strongly Agree
1	I am likely to be infected with corona virus					
2	My family members are likely to be infected with corona virus					
3	People coming from India or foreign and persons close contact with them are more likely to be infected with corona virus					
4	I will be infected with corona if I visit visit family members of infected persons					
5	Corona virus can easily transmit in crowded place					

Q213 Perceived Severity

SN	Statement	Strongly Disagree	Disagree	Not sure	Agree	Strongly Agree
1	I may die if get infected with coronavirus					
2	Corona is fetal and danger disease					
3	It makes serious illness only older, weak and already ill persons					
4	Young and healthy people are less likely to be ill even if they get infected					
5	If I were infected with corona virus, I will recovery without treatment					

Q214 Perceived Barriers

SN	Statement	Strongly Disagree	Disagree	Not sure	Agree	Strongly Agree
1	I cannot wash hand with soap frequently due to lack of hand washing facilities					
2	I cannot use hand sanitizer regularly					
3	I cannot use facemask properly and regularly					
4	My family cannot afford to buy sanitizer and facemask all family members					
5	I cannot maintain physical distance in market and work place					
6	Always forget about hand hygiene, physical distance and covering nose and mouth					

Q215 Perceived Benefits

SN	Statements	Strongly Disagree	Disagree	Not sure	Agree	Strongly Agree
1	Hand hygiene (frequent hand washing/frequent use of sanitizer) will protect me completely from coronavirus infection					
2	I feel safe from infection by cleaning hands and wearing mask					
3	Physical distancing protects from corona infection					
4	Feel safe from infection by applying societal spacing					

Q216 Perceived Self-Efficacy

SN	Statements	Strongly Disagree	Disagree	Not sure	Agree
1	I will eat healthy diet to prevent the coronavirus infection				
2	I can wash hand frequently to prevent the coronavirus infection				
3	I can prevent myself from coronavirus infection by applying protective measures/guidelines				
4	I will not go outside home/crowded area unless I have essential/urgent work				
5	I can use facemask properly while going to market/crowded area				
6	I will maintain physical distance while going to market/bank and workplace				

Perceive level of effectiveness

Q217 How effective do you think washing your hands more frequently would be in preventing the disease?
   0. Do not know
   2. Not at all effective
   3. A little effective
   4. Moderately effective
   5. Very effective

Q218 How effective do you think wearing a face mask would be in preventing disease?
   0. Do not know
   2. Not at all effective
   3. A little effective
   4. Moderately effective
   5. Very effective

Q219 How effective do you think isolating yourself from others/social distancing would be in preventing disease?
   0. Do not know
   2. Not at all effective
   3. A little effective
   4. Moderately effective
   5. Very effective

Q220 Perceptions on Quarantine

SN	Statement	Agree	Disagree	Not sure/No idea
1	Home quarantine/isolation for suspected case is essential to prevent spread of coronavirus			
2	Home isolation of infected cases/suspected cases can help to prevent the spread of the disease			
3	All the people coming from India/Abroad should be kept in quarantine for 14 days			
4	Existing quarantine center cannot control the spread of coronavirus infection due to poor management			

Q221 Intention to take precautionary action

SN	Statement	Strongly Disagree	Disagree	Not sure	Agree	Strongly Agree
1	I intend to practice social/physical distancing					
2	I intend to wash my hands frequently					
3	I intend to buy and wear a surgical mask					

Section III: Protective Behaviour

Q301 Do you wash hand with soap and water daily?
     1. Yes
     0. No

Q302 When do you wash hand with soap and water?
     1. Before meal
     2. After using toilet
     3. After touching surface, materials or public transportation touched or used by others
     4. After returning home from outside/market/workplace
     5. After touching animal/pets
     6. After caring sick persons or visiting clinic/hospital

Q303 How many times do you wash your hands with soap and water in a day?

Q304 Do you wash your hands more frequently than usual?
     1. Yes
     0. No

Q305 What problem are you facing to wash hand with soap frequently?
     1. Hand washing facilities are not available outside home/public place/workplace
     2. Soap is not always available at hand washing place
     2. Lack of money to buy soap
     3. No need to wash unless there is visible dirt on hands
     4. It is not convenient to wash hand frequently

Q306 How often do you use face mask while going outside home?
     1. Always
     2. Often
     3. Rarely
     4. Never

Q307 How often do you cover your nose and mouth while coughing and sneezing?
     1. Always
     2. Often
     3. Rarely
     4. Never

Q308 How often do you use hand sanitizer?
     1. Always
     2. Often
     3. Rarely
     4. Never

Q309 How often do you maintain physical distance of one meter in public and work place?
     1. Always
     2. Often
     3. Rarely
     4. Never

Q310 What measuring are you currently taking to protect yourself from coronavirus infection?
     1. Washing hands more frequently
     2. Using hand sanitizer
     3. Wearing face mask
     4. Avoiding touching eyes, nose and mouth with hand/fingers
     5. Using disinfectant to clean surface of house/room
     6. Giving more attention to cleanliness
     7. Avoiding crowed place/large gathering
     8. Maintaining physical distance
     9. Avoiding close contact with suspected persons or persons having flu like symptoms
     10. Avoiding/reducing travel by public transportation
     11. Eating balanced and healthy diets

12. Drinking hot water daily
13. Using herbal drinking

Q311 What will you do if you experience some symptoms of coronavirus disease in future?
1. Continue my work
2. Stay at home and isolate myself to protect others
3. Not tell anybody about it to avoid discrimination/stigma
4. Report my condition to the nearest healthcare provider/health facility
5. Drink hot water/turmeric water
6. Use herbal drink
7. Do not know

Q312 Had any of your family member suffered coronavirus disease?
1. Yes, conformed by test
2. Yes, suspected
3. No

Q313 Have you ever infected with coronavirus disease??
1. Yes, conformed by test
2. Yes, suspected
3. No

Section IV: Intention towards vaccine

Q314 Do you want to use/inject vaccine if available?
1. Yes
2. No

Q315 If yes, in which condition would you take vaccine?
1. if available at free of cost
2. I would pay if available
3. I will decide after vaccine available
4. Others…

Q316 How much rupees do you want to pay for vaccine against COVID-19? Amount in (Nepali Rupee per individual)
…….
Name of Enumerator ………….

HEALTH PROMOTION

Political views and science literacy as indicators of vaccine confidence and COVID-19 concern

ALESSANDRO SIANI, ISABELLE CARTER, FLORENCE MOULTON
School of Biological Sciences, University of Portsmouth, Portsmouth, UK

Keywords

Vaccine hesitancy • Science literacy • Political views • COVID-19 • Pandemic concern

Summary

Introduction. *The distrust, delay and refusal of vaccinations represent serious threats to global public health. As demonstrated by the dramatic worldwide impact of the COVID-19 pandemic, adequate vaccine coverage against infectious diseases is essential towards the preservation and function of virtually every aspect of our society. While the determinants of vaccine hesitancy and pandemic concern have been widely investigated, conflicting evidence exists with regards to their association with education levels and political views.*

Methods. *This study aimed to investigate whether science literacy levels and standpoint on social and economic matters are associated with different levels of vaccine confidence and COVID-19 concern. An online survey was circulated amongst participants recruited via convenience sampling, and data were analysed using non-parametric statistical tests.*

Results. *The survey (n = 389) highlighted that participants who studied Science at General Certificate of Secondary Education level have a lower vaccine confidence than those with both lower and higher levels of science education. Participants with neutral/centrist political views expressed lower confidence than those with a libertarian social stance or a left-wing economic stance. A higher concern with the COVID-19 pandemic was associated with lower levels of science education, libertarian social views, and left-wing economic views.*

Conclusions. *The present study provides novel insight on the educational and political factors associated with vaccine hesitancy and pandemic concern within a British population sample.*

Introduction

Vaccine hesitancy: definition, causes and consequences Vaccine hesitancy, defined as the delay, refusal, or distrust of vaccinations, had been classified by the World Health Organization (WHO) as one of the top ten threats to global health even before the COVID-19 pandemic brought the subject of immunisation to the frontpage of worldwide news outlets [1]. Far from being a recent phenomenon, scepticism and hostility have accompanied the practice of artificial immunisation even prior to the administration of the first vaccine in 1796 by Edward Jenner [2]. It is worth noting that vaccine hesitancy rarely presents itself as a dichotomy between full acceptance and full refusal. In most cases, hesitancy represents a continuum whereby hesitant individuals do not oppose all vaccinations unconditionally, but rather accept some vaccinations while refusing or delaying others [3]. The multifaceted nature of vaccine hesitancy is underpinned by an equally complex combination of causative factors. Understanding why individuals hesitate or refuse to vaccinate themselves and their children is crucial towards helping policymakers and healthcare workers (HCW) deploy mitigation strategies [4]. Towards this endeavour, the WHO Strategic Advisory Group of Experts (SAGE) developed two keystone theoretical frameworks, namely the Complacency, Convenience and Confidence ("3Cs") model and the Determinants

of Vaccine Hesitancy Matrix [5]. In the 3Cs model, confidence is defined as trust in the effectiveness and safety of the vaccines, as well as the healthcare system and personnel that promote and deliver them. Complacency refers to the risks posed by specific vaccine-preventable diseases (VPD) being perceived as low and therefore not worth the risk/hassle associated with the vaccination. Convenience encompasses the factors relating to the availability, affordability, and accessibility of vaccinations. The Determinants of Vaccine Hesitancy Matrix provides a more complex framework to categorise the factors and influences that lead to vaccine hesitancy, arranging them into three broad categories: contextual influences, individual and group influences, and vaccine-specific issues. As high levels of vaccine coverage are crucial in maintaining herd immunity within a population, vaccine hesitancy and refusal have been linked to the re-emergence and diffusion of vaccine-preventable diseases (VPD). Historically, events leading to a decrease in vaccine confidence and uptake have resulted in VPD outbreaks in the following period. For example, a case report published in 1974 suggested a causative link between the DPT (diphtheria, pertussis, tetanus) vaccine and the onset of neurological damage in 36 children [6]. Although those findings were subsequently disproved due to inadequate experimental design and small sample size of the report, the controversy led to a decrease in DPT vaccination

uptake in several countries [7]. In the UK, DPT vaccine coverage decreased from 81% to 31% in the aftermath of the scandal, causing frequent pertussis outbreaks until vaccine uptake was restored to levels close to the herd immunity threshold [8]. Analysis of epidemiological data show that the incidence of pertussis was unaffected by the DPT controversy in countries where vaccine hesitancy was low and uptake high [9]. In comparison, pertussis incidence was 10-100 times higher in countries where the immunisation campaigns were disrupted by anti-vaccination movements. Similarly, the allegations of a causative link between the MMR (measles, mumps, rubella) vaccine and the onset of gastrointestinal and neurological symptoms proposed in 1998 by Andrew Wakefield in The Lancet led to a dramatic decrease in MMR coverage over the following years [10]. Despite the retraction of Wakefield's paper and his removal from the British medical register due to several counts of scientific malpractice and unethical conduct, the MMR controversy had a global detrimental impact on vaccine confidence, the consequences of which are still felt to this day [11]. Over the last decade, the affirmation of anti-vaccination movements in the aftermath of the MMR controversy has led to the re-emergence of measles outbreaks in several developed countries in which the disease had been nearly eradicated prior to the publication of Wakefield's fraudulent paper [12].

Politics and vaccine hesitancy

The deployment of the COVID-19 vaccines has already had a significant impact on the number of cases, hospitalisations and fatalities, and the success of vaccination campaigns is crucial in the global efforts of overcoming the current pandemic. However, this endeavour will require vaccine coverage to reach sufficiently high levels: although the herd immunity threshold for SARS-CoV-2 has not been determined yet, it is clear that the circulation of the virus can only be stopped if the vast majority of the global population receives a complete immunisation course against it [13]. The acceptance of the COVID-19 vaccination campaigns depends heavily on the population's trust in their governing bodies, which is in turn a direct consequence of the popular perception of the government's handling of the current pandemic [14]. In the UK, the observation of eminent governmental figures such as Chief Adviser Dominic Cummings (and, more recently, Health Secretary Matt Hancock) caught breaching lockdown restrictions and social distancing that they had personally contributed to impose, had a detrimental effect on the public's confidence in the National Health Service (NHS) and on the vaccination campaigns they promote [15]. A survey carried out amongst the French population revealed that political views are a key determinant of people's attitudes towards COVID-19 vaccinations. Far-right and far-left voting individuals, as well as those who abstain from voting, are significantly more likely to refuse a vaccine than those holding more moderate or centrist views [16]. The research also indicated that criticism of the government by opposing political parties caused distrust and uncertainty around vaccine campaigns. The problems that arise when political entities attempt to convince the public of vaccine safety are connected to the difficulty in assuring that the recommendations given are determined by scientific information, and not motivated by politics. These findings reinforce previous observations that individuals on the political fringes, far right and far left, tend to overestimate their own knowledge and have misplaced certainty in their views. This can make them resistant to change their views and beliefs, even when provided with evidence to the contrary, a metacognitive feature which may explain why anti-vaccine sentiment is more common in those with more radical political beliefs [17]. The last decade has seen the consolidation of populist worldviews in the global political panorama. Independently from their political colour, populist parties present themselves as standing for 'the people' against 'the elite', defining both categories by different (albeit frequently nebulous) criteria depending on where they fall in the political spectrum [18]. Both political populism and vaccine hesitancy are underpinned by a similar distrust in authority, and often accompanied by conspiratorial, anti-establishment, and anti-intellectual worldviews. A recent analysis of national-level data revealed a strong association between votes for populist parties in the 2014 European Parliament elections and vaccine hesitancy in the same country, highlighting that "Vaccine hesitancy and political populism are driven by similar dynamics: a profound distrust in elites and experts" [19].

Educational levels, science literacy and vaccine hesitancy

The correlation between educational levels and vaccine hesitancy has been widely investigated, however there is contrasting evidence with regards to the nature, or arguably even existence, of any such correlation. For example, while higher levels of hesitancy were associated with lower education and income levels in the Canadian Childhood National Immunization Coverage Survey [20], the inverse trend had been found in a previous a review of U.S. medical records [21]. On the other hand, no association between vaccine hesitancy and education levels was observed in a multi-national study carried out across five low- or middle-income countries [22]. These observations indicate that the analysis of the relationship between education and vaccine hesitancy is likely to be affected by other confounding variables of social, economic, cultural or religious nature. Another key factor complicating the elucidation of a relationship between education and vaccine hesitancy is that both variables themselves are defined and quantified differently across different studies, which frequently use dissimilar strategies for population sampling, survey design, and data analysis. Moreover, the majority of

studies investigating the demographic determinants of vaccine hesitancy mainly focus on the qualification level of participants or communities without taking into account the subject studied at each level [23]. As hesitancy is often underpinned by inadequate or incorrect information on the composition, mechanism of action, and safety of vaccines, it is reasonable to speculate that higher levels of literacy in biomedical subjects may be associated with increased levels of vaccine confidence. A recent systematic review highlighted that while there is a positive association between health literacy and vaccine acceptance, this relationship is influenced by confounding variables related to both the individual (country, age) and the nature of the vaccine [24].

Aims

The primary aim of this study was to elucidate whether science literacy and political views are associated with vaccine confidence (or lack thereof) in a British population sample. The secondary aim was to investigate the association of the same two factors with different levels of concern about the COVID-19 pandemic.

Science literacy (as opposed to health literacy) was chosen as an independent variable to account for the observation that vaccine hesitancy is caused not only by a lack of understanding of the biological bases of vaccination, but in many instances by a lack of trust in scientists and in the scientific method itself. Regardless of the scientific discipline studied, individuals familiar with its rudiments are more likely to understand and accept its basic principles (replicability, falsifiability, difference between correlation and causality) and therefore less likely to reject empirical evidence and take on pseudo-scientific or anti-scientific views [25, 26].

To gain a broader understanding of the correlation between political views and vaccine confidence in the sample population, the participants' stances on social and economic matters were used as two distinct independent variables. This is a crucial distinction because, unlike the one-dimensional left/right political axis, it allows to decouple the participants' stance along the libertarian/authoritarian axis from their position with regards to economic issues [27].

Methods

ETHICAL APPROVAL

This study was carried out in accordance with the Helsinki declaration for research involving human subjects and with the University of Portsmouth Ethics Policy. Ethical approval (code BIOL-ETHICS #009-

Tab. I. Questionnaire used in the survey. Answers to the questions highlighted with an asterisk were used in the calculation of the Vaccine Confidence Score.

Section 1: about you
1.1 What is your age?
1.2 What gender do you identify as?
1.3 What is your annual income?
1.4 How many children do you have?
1.5 What is your highest academic qualification?
1.6 What academic levels have you studied science at? (Tick all that apply)
1.7 What is your ethnic group?
1.8 What is your religion/spiritual belief?
1.9 How would you describe your stance on social matters?
1.10 How would you describe your stance on economic matters?
Section 2: attitude on vaccinations
*2.1 Vaccines are safe.
*2.2 I think vaccines should be a compulsory practice.
*2.3 I believe that vaccine-preventable diseases (like measles and mumps) can be serious.
*2.4 My healthcare provider (for example my GP) has mine and/or my child's best interests at heart.
2.5 I believe the government has my best health interests at heart
*2.6 Vaccines are beneficial for our health and wellbeing.
2.7 Are you opposed to any vaccinations?
2.7.1 If YES, which vaccinations are you opposed to and why?
Section 3: COVID-19
3.1 Do you agree or disagree with the following statement: "I am concerned with the current pandemic"?
3.2 How likely are you to get vaccinated against COVID-19 when a vaccine becomes available?
3.3 How likely are you to vaccinate your child/children against COVID-19? (Please leave blank if you do not currently have children or don't plan to have any)
3.4 With the ongoing pandemic, have you considered getting vaccinated against the common flu this year?
3.4.1 If NO, is there any specific reason?
3.4.2 If YES, is there any specific reason?

2020) was obtained by the investigators prior to the distribution of the survey. A disclaimer, provided at the beginning of the survey, described its voluntary and anonymous nature. Participants were informed of their right to omit any questions they did not feel comfortable answering, as well as their right to withdraw at any point by not clicking the "submit" button. No information that would allow the identification of individual participants was collected in the survey. All data were processed and stored in accordance with the General Data Protection Regulation (GDPR).

Survey design and distribution

The questionnaire used in this study (Tab. I) was structured in three sections. Section 1, titled "About you", contained questions designed to determine the demographic features of the participants (age, gender, ethnicity, annual income, academic qualifications) as well as their religious beliefs and stance on social and economic matters. Section 2 was titled "Attitude on Vaccinations", and required participants to respond to statements about their perception of the safety and benefits of the practice of vaccination in general. Section 3, titled "COVID-19", included questions to gather the public's perspectives on the COVID-19 pandemic and intentions to get vaccinated against it. It is important to note that the survey was distributed before COVID-19 vaccinations were publicly available, but at a time when their development and upcoming administration were prevalent in national and international news. The questionnaire contained a mix of multiple choice (Likert-type, yes/no, and tick box questions) and open-ended questions designed to gather, respectively, quantitative and qualitative data on the public's perception on the practice of vaccination. Some of the questions in sections 2 and 3 were adapted from the World Health Organisation survey "Determinants of vaccine hesitancy: sample survey questions" [28], while the remaining sections and questions were developed by the investigators specifically for this study. The survey was developed using Google Forms and distributed online between the 9th of November and the 11th of December 2020. A

Tab. II. Demographic characteristics of the study population.

Age	Count	%	Highest academic qualification	Count	%
18-24	207	53.2	GCSE/O-LEVEL/equivalent	41	10.5
25-30	13	3.3	A-level/BTEC/equivalent	188	48.3
31-45	41	10.5	Bachelor's degree	98	25.2
46-60	96	24.7	Post-graduate degree	50	12.8
60+	32	8.2	Other	7	1.8
Income	**Count**	**%**	**Religion**	**Count**	**%**
Not currently in employment	129	33.3	Agnostic / Atheist	185	48.3
£0 - 20,000	113	29.2	Buddhist	4	1.0
£21,000 - 30,000	50	12.9	Christian	179	46.7
£31,000 - 40,000	39	10.1	Hindu	1	0.3
£41,000 - 50,000	20	5.2	Jewish	0	0.0
£51,000 - 60,000	10	2.6	Muslim	6	1.6
£61,000 - 70,000	13	3.4	Sikh	0	0.0
£71,000 or more	13	3.4	Other	7	1.8
Ethnicity	**Count**	**%**	**Number of children**	**Count**	**%**
Arab	3	0.8	0	239	61.4
Asian - Bangladeshi	0	0.0	1	12	3.0
Asian - Chinese	3	0.8	2	90	23.1
Asian - Indian	2	0.5	3	35	8.9
Asian - Other	3	0.8	4	9	2.3
Asian - Pakistani	2	0.5	5+	3	0.7
Black - African	0	0.0			
Black - Caribbean	2	0.5	**Gender**	**Count**	**%**
Black - Other	2	0.5	Female	286	73.5
Mixed - White and Asian	4	1.0	Male	103	26.5
Mixed - White and Black African	0	0.0			
Mixed - Other	7	1.8			
Mixed - White and Black Caribbean	5	1.3			
White - English/Welsh/Scottish/Northern Irish	305	78.8			
White - Irish	9	2.3			
White - Gypsy or traveller	0	0.0			
White - Other	38	9.8			
Other ethnicity	2	0.5			

convenience sampling strategy was used, whereby the survey link was distributed by the investigators using different social media platforms, namely Facebook, Instagram, and WhatsApp.

Data Analysis

Data were analysed using IBM SPSS Statistics 26. Given the ordinal nature of the data gathered in the survey, non-parametric tests were used to analyse the statistical significance of the findings. In particular, Kruskal-Wallis tests were used with a significance p-value cut-off of 0.05 to compare median answers between different groups of participants. When statistically significant differences were highlighted via Kruskal-Wallis tests, post-hoc pairwise Dunn's tests were carried out to pinpoint where the differences lay, and the significance threshold adjusted using Bonferroni corrections to minimise family-wise error rate. The Vaccine Confidence Score (VCS) was used as a dependent variable in this study to provide a quantitative indication of respondents' confidence in vaccinations [29]. In brief, the VCS is calculated as the sum of the scores obtained from five selected Likert-type questions (questions 2.1, 2.2, 2.3, 2.4, 2.6) after converting the answer to each question to a numerical value (from 1-Strongly Disagree to 5-Strongly Agree). Therefore, VCS values range from 5 (lowest vaccine confidence) to 25 (highest vaccine confidence). Participants' science literacy (question 1.6) and stance on social (question 1.9) and economic (question 1.10) matters were used as grouping variables.

Results

Study population

A total of 389 adult volunteers took part in the survey. The demographic distribution of the population by age, gender, income, parental status, academic qualification, ethnicity and religion is provided in Table II. Due to the convenience sampling strategy used in this study, young women from a white ethnic background were heavily represented amongst the population, reflecting the demographic characteristics of the investigators who distributed the survey. The distribution of participants according to their science education level, stance

Fig. 1. Distribution of the study participants according to their highest level of science education
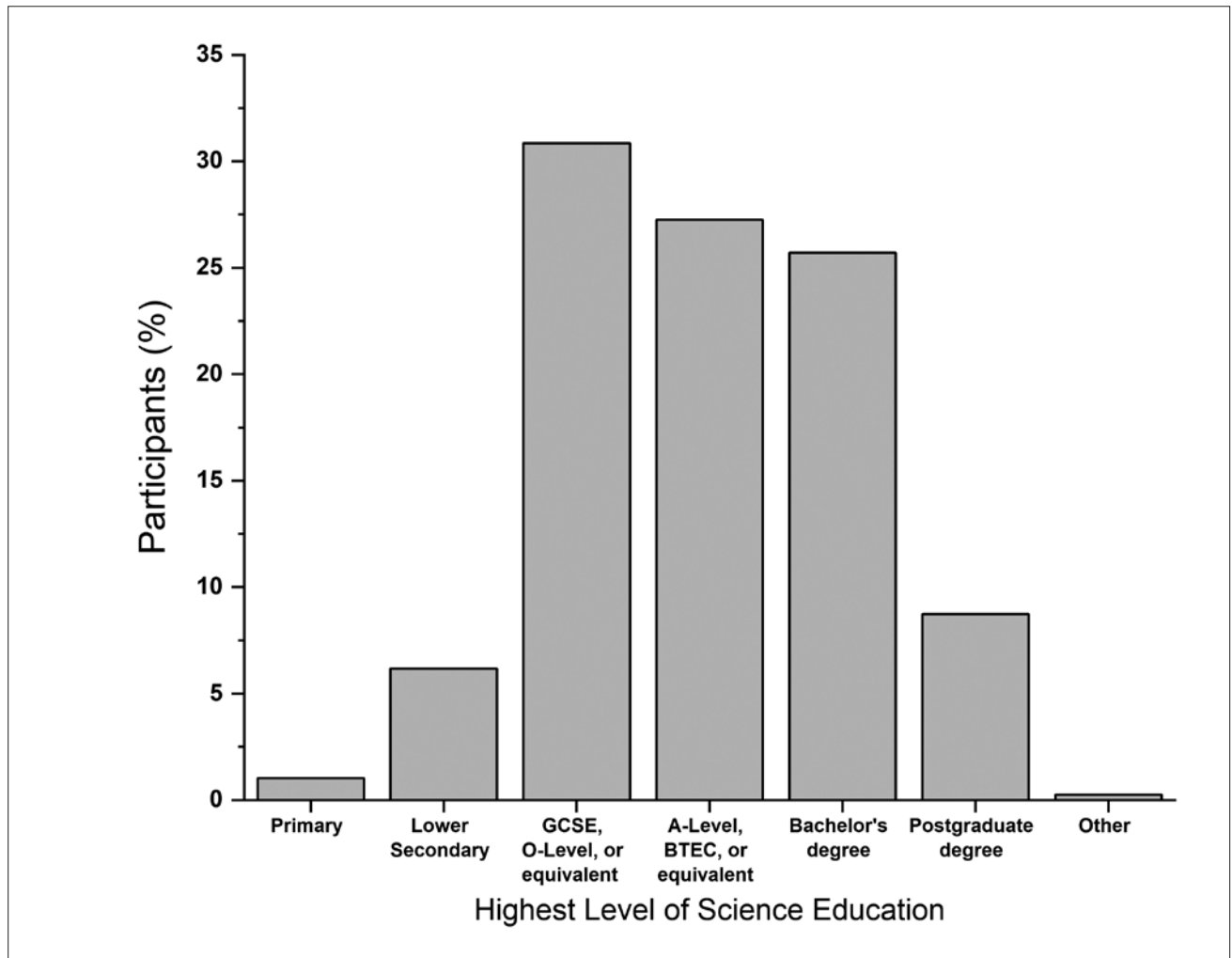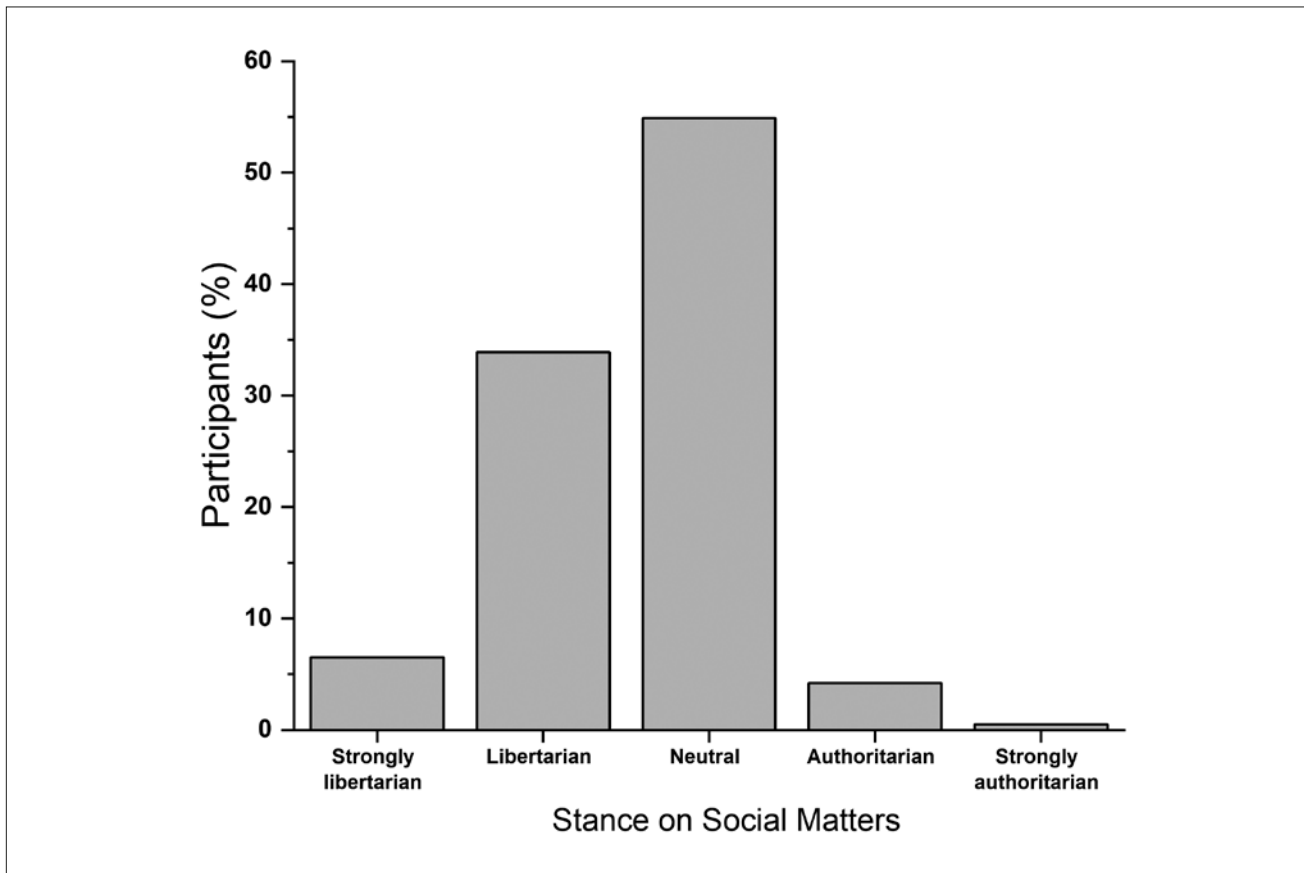
Fig. 2. Distribution of the study participants according to their stance on social matters.

on social matters and stance on economic matters is presented in Figure 1, 2, and 3 respectively. The majority of the population had a science education level between General Certificate of Secondary Education (GCSE) and Bachelor's degree, and neutral/centrist views on both social and economic matters.

SCIENCE LITERACY

The association between science literacy and vaccine confidence is shown in Figure 4. Due to the small numbers of participants whose highest level of science literacy was primary education, they were pooled with the lower secondary group and presented as "primary and lower secondary" for the following analysis. A Kruskal-Wallis test revealed the presence of statistically significant differences ($\chi^2 = 24.219$; df = 4; p = 0.000072) in median VCS between participants with different levels of science literacy. Post-hoc pairwise Dunn's tests identified that the p-value was below the 0.05 significance threshold when comparing participants who studied science at GCSE/O-level against those who studied it at A-level/BTEC (p = 0.0082), GCSE/O-level against primary/lower secondary (p = 0.049), GCSE/O-level against Bachelor's degree (p = 0.000001), postgraduate degree against Bachelor's degree (p = 0.048) and A-level/BTEC against Bachelor's degree (p = 0.028). However, when the significance threshold was adjusted via Bonferroni correction for multiple tests, a statistically significant

difference (p = 0.000011) was only observed between GCSE/O-level (median VCS = 20) and Bachelor's degree (median VCS = 22).

SOCIAL AND ECONOMIC STANCE

The association between vaccine confidence and stance on social and economic matters is presented in Figure 5 and 6 respectively. Due to the small number of respondents expressing extreme positions in terms of social and economic stance, participants belonging to fringe groups were pooled with their more moderate counterparts for the following analysis. A Kruskal-Wallis test revealed a significant difference ($\chi^2 = 11.985$; df = 2; p = 0.0024) in median VCS between participants with different social stances. Post-hoc tests revealed that participants with a neutral social stance were significantly less confident than those with libertarian views (p = 0.00073), but not those with authoritarian views. The significant difference in vaccine confidence between libertarian (median VCS = 21) and neutral (median VCS = 20) participants held true after adjusting the significance level using Bonferroni correction (p = 0.0022). A difference in VCS ($\chi^2 = 19.179$; df = 2; p = 0.00007) was also observed with respect to economic stance, whereby those with left wing views were significantly more vaccine-confident than those with centrist (p = 0.000012) and right wing (p = 0.050) views. However, after adjusting the significance levels

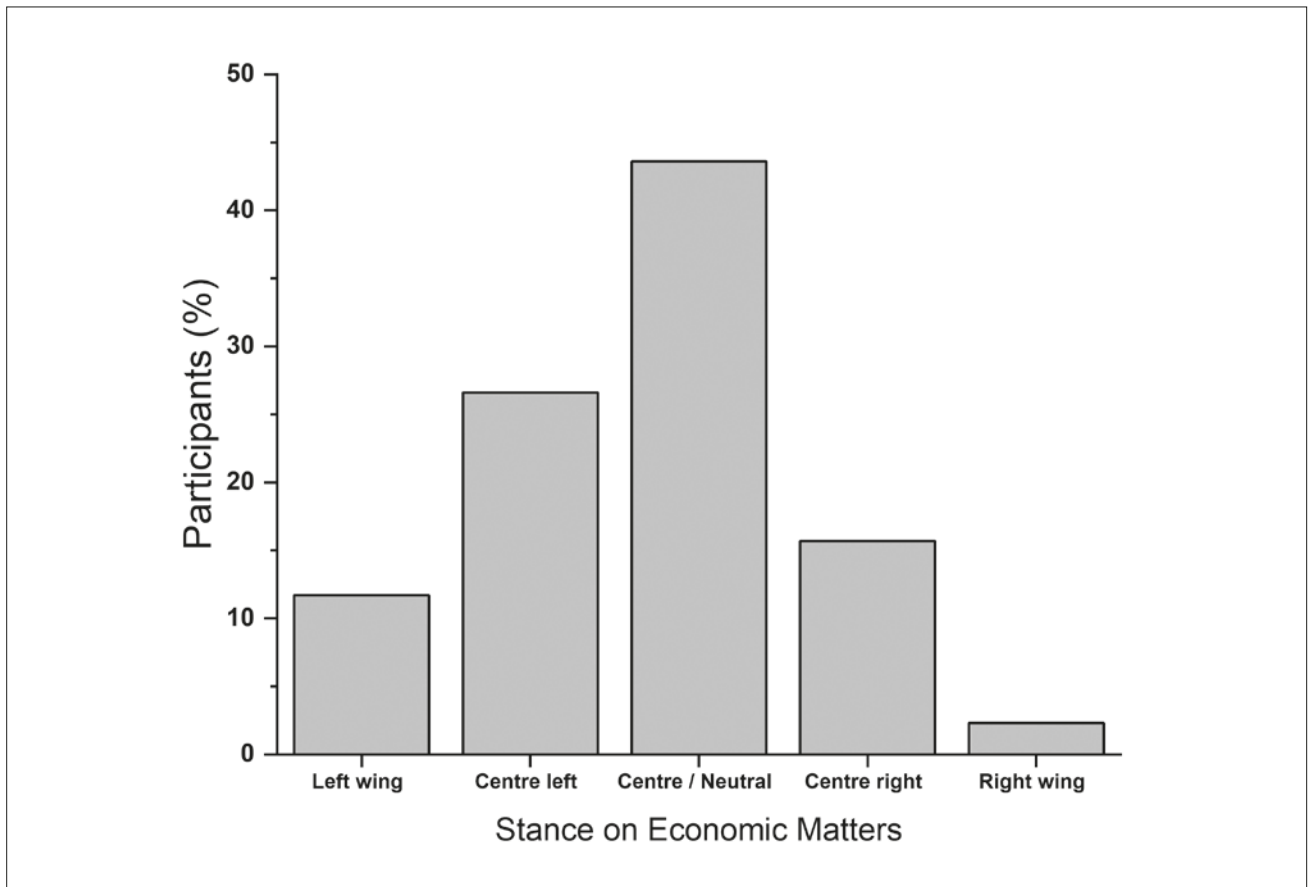**Fig. 3.** Distribution of the study participants according to their stance on economic matters.

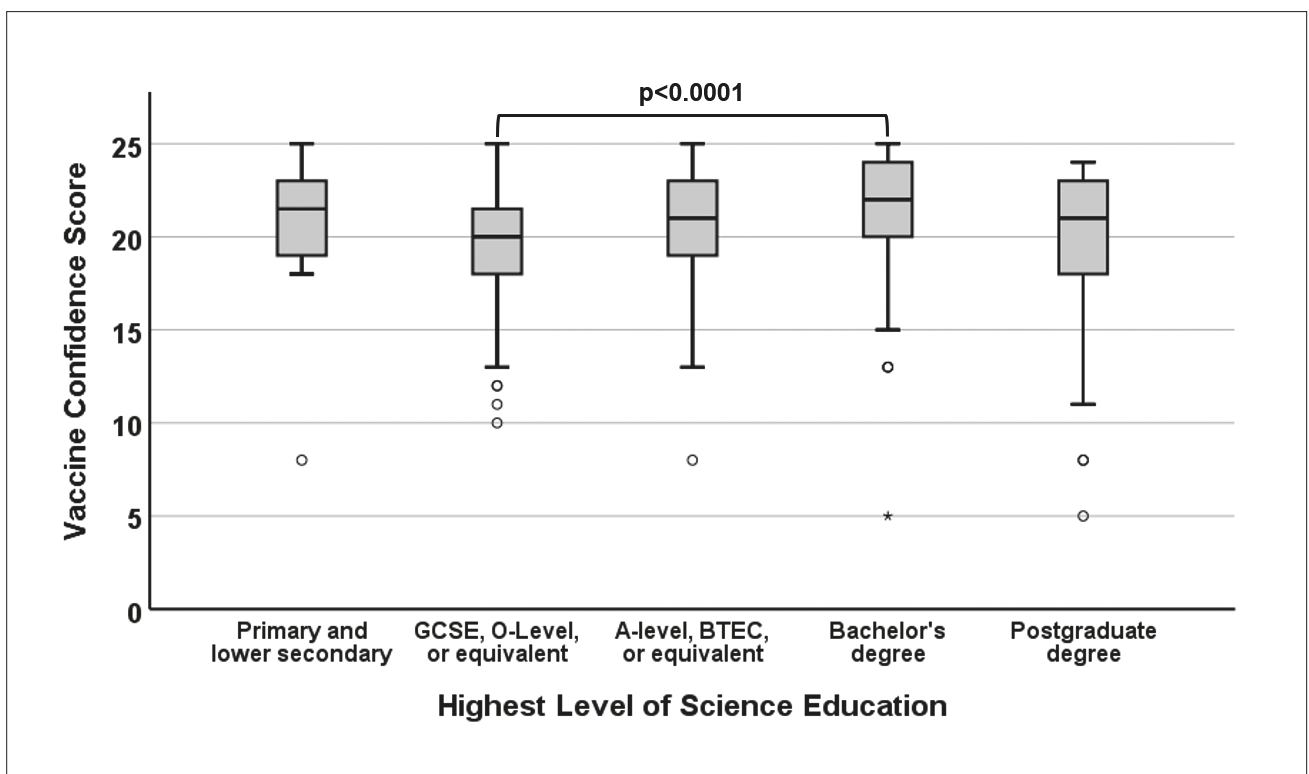**Fig. 4.** Association between participants' highest level of science education and their Vaccine Confidence Score.

Fig. 5. Association between participants' stance on social matters and their Vaccine Confidence Score.
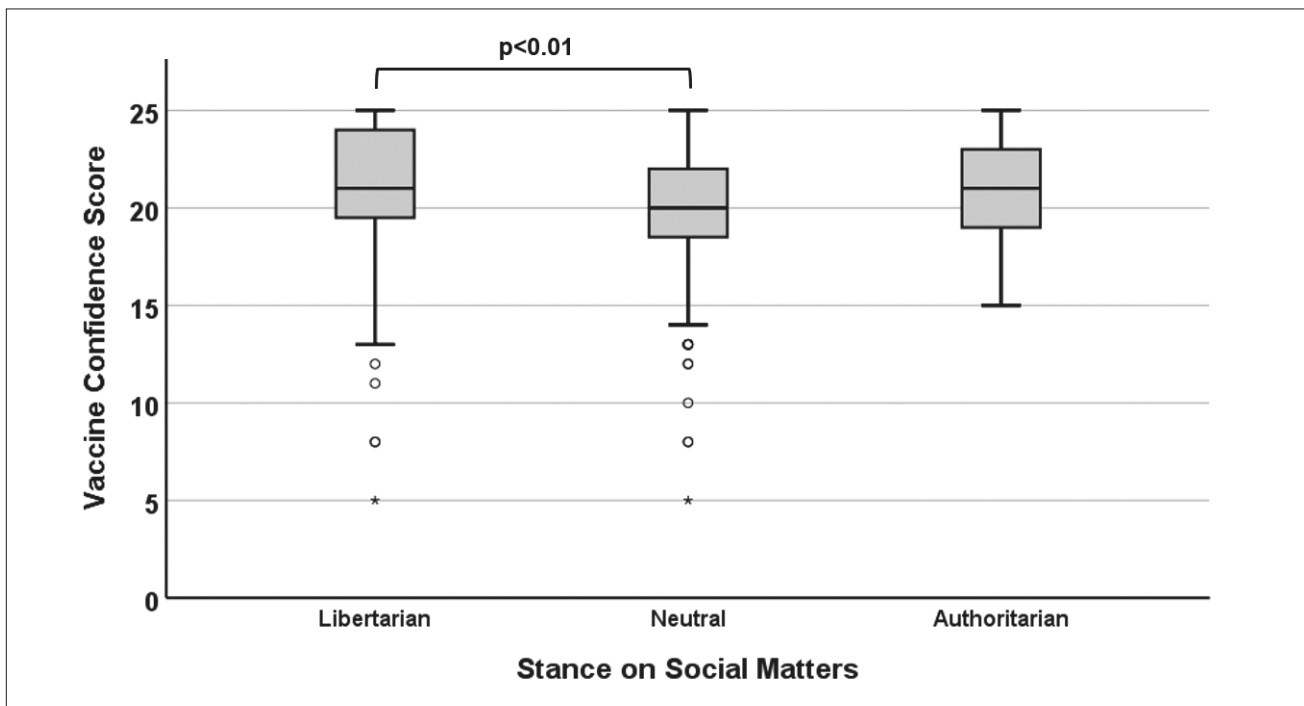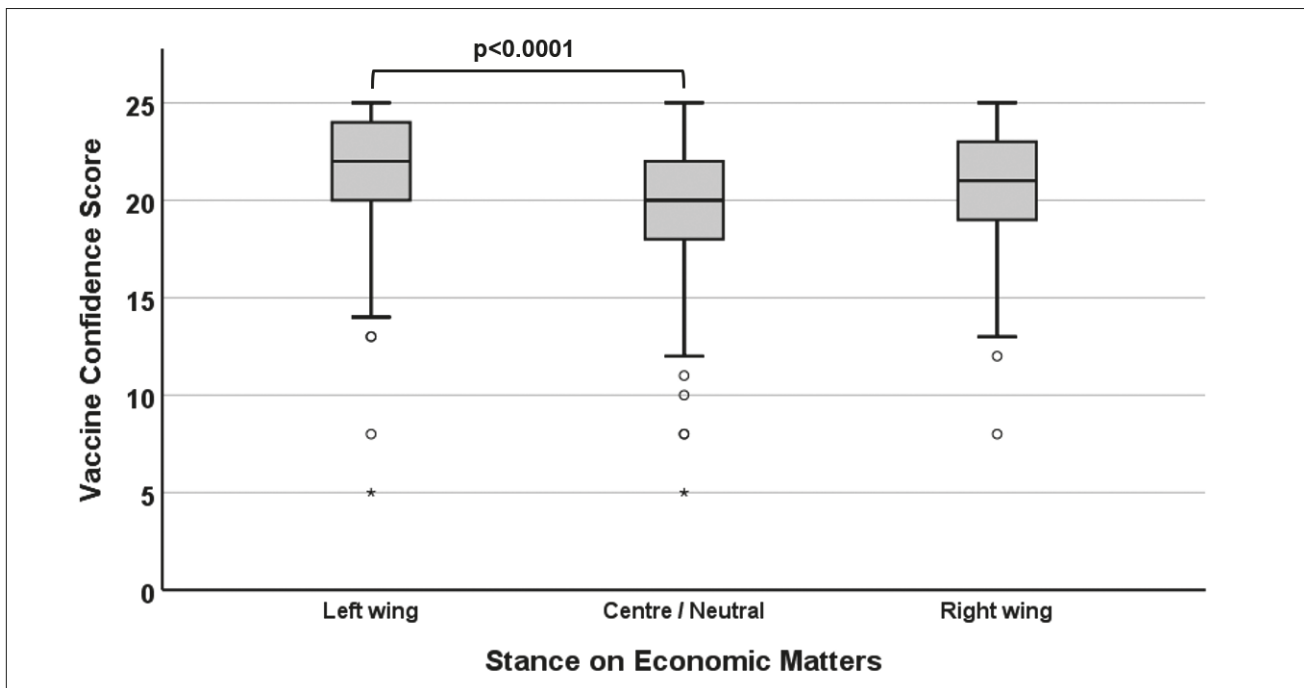

Fig. 6. Association between participants' stance on economic matters and their Vaccine Confidence Score.

for multiple comparisons, only the difference between left wingers (median VCS = 22) and centrists (median VCS = 20) remained significant (p = 0.00004)

LEVELS OF CONCERN ABOUT THE COVID-19 PANDEMIC

A statistically significant difference (χ^2 = 11.853; df = 4; p = 0.018) was observed in the levels of concern about the COVID-19 pandemic amongst participants with different levels of science education (Fig. 7). Participants who studied science at lower secondary level or below expressed the highest levels of concern, which was significantly higher than those at GCSE/O-level (p = 0.019), A-level/BTEC (p = 0.035), and bachelor's degree (p = 0.008). Participants who studied science at the postgraduate degree level showed the lowest

Fig. 7. Participants' agreement with the statement "I am concerned with the current pandemic" according to their highest level of science education.
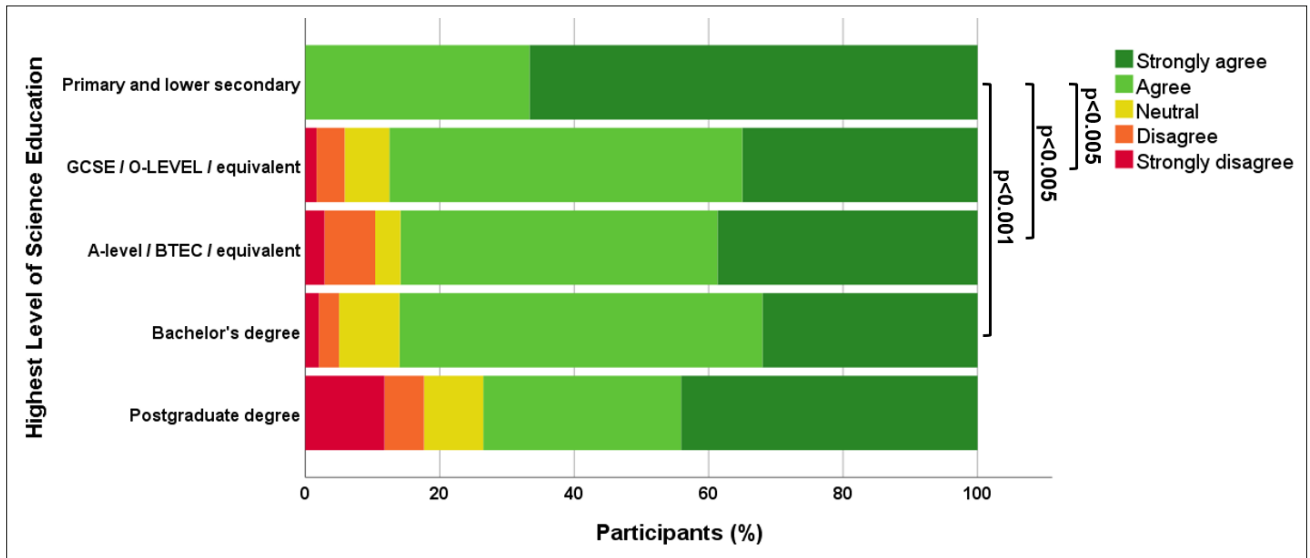

Fig. 8. Participants' agreement with the statement "I am concerned with the current pandemic" according to their stance on social matters.
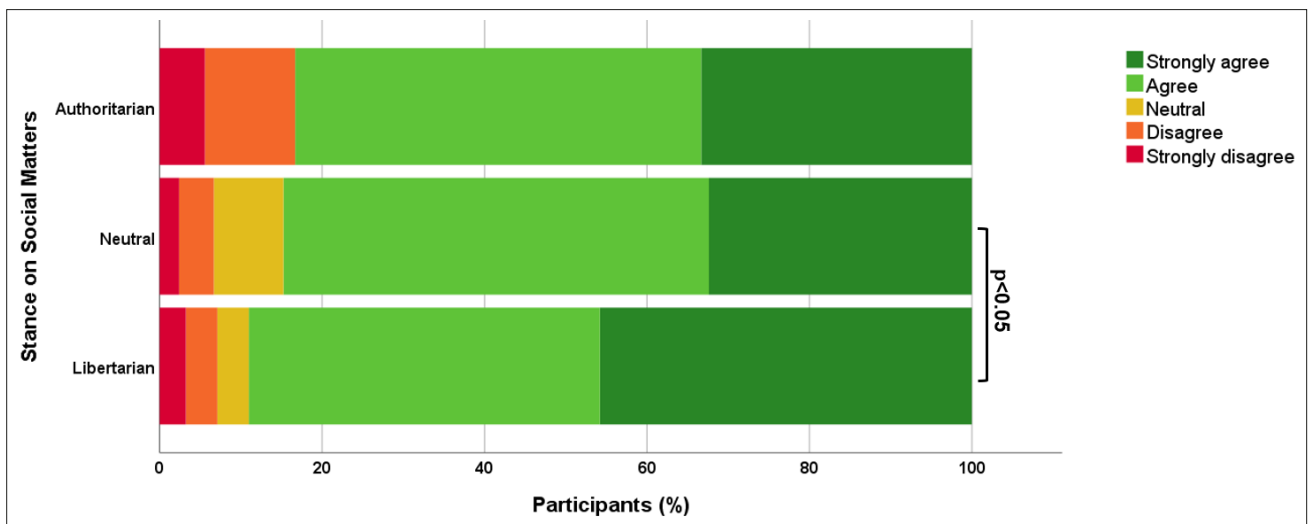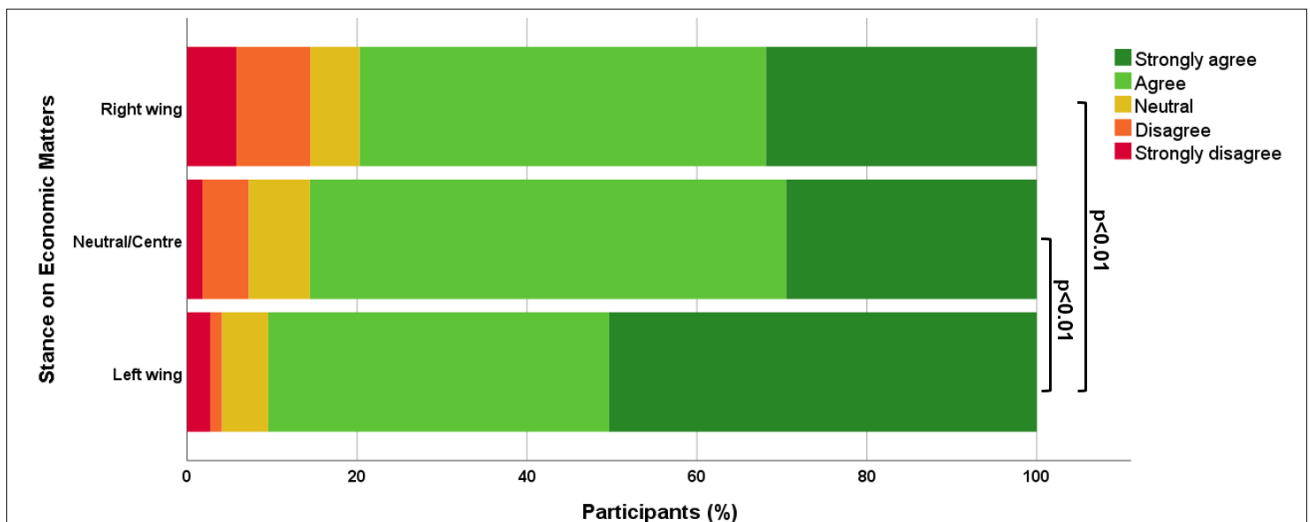

Fig. 9. Participants' agreement with the statement "I am concerned with the current pandemic" according to their stance on economic matters.

levels of concern. However, due to the small number of participants who studied science at the postgraduate level, none of the observed differences involving the postgraduate degree group were statistically significant after Bonferroni correction.

A significant difference (χ^2 = 6.453; df = 2; p = 0.039) in the levels of pandemic concern was observed between participants with different stances on social matters (Fig. 8). Participants with libertarian views expressed the highest concern about the COVID-19 pandemic, however the difference was only significant in comparison with those who expressed neutral (p = 0.039), but not authoritarian views.

Figure 9 shows statistically significant differences (χ^2 = 15.285; df = 2; p = 0.00048) in the level of COVID-19 concern between participants with different social stances along the left-right axis. Left-leaning participants showed higher concern than both right-leaning (p = 0.0077) and centrist (p = 0.0013) ones. The difference between centrist and right-leaning participants was not statistically significant.

Discussion

Vaccine hesitancy had already been identified as one of the top threats to global health prior to the onset of the COVID-19 pandemic, and the current circumstances reinforce the urgency to identify its root causes and deploy mitigation strategies. This study provides novel insight on the factors affecting vaccine confidence in a British population sample. A non-linear relationship was observed between vaccine confidence and science education levels, whereby participants who studied science up to GCSE level are more hesitant than those with both lower and higher science education levels. This difference was only statistically significant in comparison to participants who studied science at Bachelor's degree level, however the data indicate that the lack of statistical significance in the comparison with the other groups may represent a false negative caused by the use of Bonferroni correction. While this adjustment method for multiple comparisons is often regarded as exceedingly conservative and prone to type II errors, the loss of statistical power is offset by its high effectiveness in preventing type I errors [30]. The observation that individuals who studied science up to GCSE level are more vaccine-hesitant than those with both higher and lower levels of science education may be interpreted through the lens of the cognitive bias widely known as the Dunning-Kruger effect [31, 32]. Framing the present findings in the competence hierarchy model, it is conceivable that participants with the lowest level of science literacy may operate at the stage of unconscious incompetence with regards to the vaccination decision-making process, which may make them more likely to rely on expert advice on the matter [33, 34]. On the other hand, participants who have studied science up to secondary education levels may fall into what has been defined as "beginner's bubble", whereby they

overestimate their understanding of the topic and come to incorrect conclusions on it [35].

The results of the survey indicate that participants with libertarian social stances are significantly more vaccine-confident than those who expressed neutral views. This finding may at a first glance appear to conflict with the common claim that mandatory vaccination may infringe personal freedom and bodily autonomy. However, it has been theorised that not only libertarianism is compatible with vaccine acceptance, but also that government-enforced vaccination is morally justifiable within a libertarian political framework [36]. Within the study population, participants who expressed left-leaning stances on economic matters were significantly more vaccine-confident than those expressing centrist views. While there is no clear literature consensus as to the association between position on the left/right spectrum and vaccine confidence, our findings support previous observations that left-wing ideologies can be identified as predictors of vaccine confidence [37] and centrist worldviews are more likely to be associated with vaccine hesitancy [38]. Previous findings obtained amongst the French population that those holding moderate views are less vaccine hesitant than those with more radical stances were not confirmed in the present study [16]. Right-wing participants did not show any significant difference in vaccine confidence compared to the other groups. Vaccine confidence had previously been shown to be negatively associated with right-wing views amongst USA voters, however this was not the case amongst the UK electorate, compatibly with the findings of the present study [39]. These observations indicate that the association between political views and vaccine confidence may depend on other context-specific variables. Indeed, it has been suggested that an individual's vaccine attitude may not necessarily align with their left/right orientation, but rather with their political proximity with specific politicians or parties [40].

This study revealed that participants' levels of concern with the COVID-19 pandemic varied significantly with both their science education level and political views. 100% of participants with the lowest level of science education (primary or lower secondary) were in agreement with the statement "I am concerned with the current pandemic", whereas participants who studied science at the postgraduate level were the most likely to disagree with it. While several studies have investigated the determinants of concern, anxiety, and fear related to the COVID-19 pandemic, the present study is to the best of our knowledge the first to investigate the association between "coronaphobia" and science education levels [41-43].

Participants with libertarian views expressed higher pandemic concern than those with neutral and authoritarian views, however the difference was only statistically significant with the former group. While the present study did not evaluate the nature of the concern (*e.g.* whether it is based on health-related, economic, political or other reasons), the perceived loss of freedom

due to state-sanctioned restrictions and lockdowns has been identified as a reason for concern among libertarian individuals [44]. Left-wing participants expressed significantly higher levels of concern than those with centrist or right-wing views. To the best of our knowledge, this study is the first to correlate left-wing views and pandemic concern within the British population, confirming previous reports that left-wing views were associated with pandemic-induced stress in a Canadian population sample and with increased physical distancing amongst USA residents [45, 46].

Conclusions

At a time when many countries are still under the grip of the COVID-19 pandemic and limited vaccine uptake is hindering the global efforts to overcome the current crisis, this study provides novel insight into the factors underpinning vaccine confidence and pandemic concern. Considering that the majority of the population do not pursue further scientific studies after secondary education, the observation that participants who studied science up to GCSE level show the highest level of vaccine hesitancy should be a cause for concern. These findings highlight the urgency to ensure that topics of critical public health relevance are adequately covered in secondary school curricula, and that learners and educators are equipped with sufficient scientific and digital literacy to inform their vaccination decision-making process. Participants expressing neutral views on social and economic matters were significantly more vaccine-hesitant than, respectively, libertarian and left-wing participants. As political views intersect with numerous extrinsic and intrinsic factors (*e.g.* age, ethnicity, nationality, socio-economic status, current governing party, etc.), further studies would be advisable to investigate the context-dependency of their correlation with vaccine hesitancy. Within the study population, lower science education levels as well as libertarian and left-wing political views were found to be significantly associated with higher levels of concern regarding the COVID-19 pandemic. This study provides valuable quantitative insight into the educational and political factors associated with vaccine hesitancy and COVID-19 concern. A limitation of the study is represented by the non-random nature of the sample population caused by the use of convenience sampling. Further investigations employing stratified sampling strategies would be advisable to verify the applicability of the results to populations with different demographic makeups. Moreover, future studies employing qualitative methods such as interviews and focus groups would be beneficial to elucidate the specific nature of the concerns and of the causes underpinning vaccine hesitancy in different individuals and groups.

Funding

Conflict of interest statement

The authors declare that they have no conflict of interest.

Availability of data and materials

The dataset analysed in this study is available from the corresponding author on reasonable request.

Authors' contributions

AS designed the study, provided supervision for the co-authors, carried out statistical analysis and wrote the manuscript. IC and FM compiled and distributed the questionnaire, collected the data, contributed to part of the statistical analysis, figure and manuscript preparation, and provided feedback on the final version of the draft.

References

[1] World Health Organization. "Ten threats to global health in 2019." https://www.who.int/news-room/feature-stories/ten-threats-to-global-health-in-2019 (Accessed on: July 03, 2020).

[2] Schwartz JL. New media, old messages: themes in the history of vaccine hesitancy and refusal. Virtual Mentor 2012;14:50-5. https://doi.org/10.1001/virtualmentor.2012.14.1.mhst1-1201

[3] MacDonald NE; SAGE Working Group on Vaccine Hesitancy. Vaccine hesitancy: Definition, scope and determinants. Vaccine 2015;33:4161-4. https://doi.org/10.1016/j.vaccine.2015.04.036

[4] Butler AM, Grabinski VF, Boloker GD, Newland JG, Politi MC. A qualitative study examining pediatric clinicians' perceptions of delayed vaccine schedules. Vaccine 2020;38:4740-6. https://doi.org/10.1016/j.vaccine.2020.05.015

[5] World Health Organization. "Report of the SAGE Working Group on Vaccine Hesitancy." http://www.who.int/immunization/sage/meetings/2014/october/SAGE_working_group_revised_report_vaccine_hesitancy.pdf (Accessed on: June 06, 2020)

[6] Kulenkampff M, Schwartzman JS, Wilson J. Neurological complications of pertussis inoculation. Arch Dis Child 1974;4:46-9. https://doi.org/10.1136/adc.49.1.46

[7] Fenichel GM. The pertussis vaccine controversy. The danger of case reports. Arch Neurol 1983;40:193-4. https://doi.org/10.1001/archneur.1983.04050040023002

[8] Boulton J. The UK pertussis epidemic: implications for immunisation. Br J Nurs 2013;22:1046-50. https://doi.org/10.12968/bjon.2013.22.18.1046

[9] Gangarosa EJ, Galazka AM, Wolfe CR, Phillips LM, Gangarosa RE, Miller E, Chen RT. Impact of anti-vaccine movements on pertussis control: the untold story. Lancet 1998;351:356-61. https://doi.org/10.1016/s0140-6736(97)04334-1

[10] Wakefield AJ, Murch SH, Anthony A, Linnell J, Casson DM, Malik M, Berelowitz M, Dhillon AP, Thomson MA, Harvey P, Valentine A, Davies SE, Walker-Smith JA. Ileal-lymphoid-nodular hyperplasia, non-specific colitis, and pervasive developmental disorder in children. Lancet 1998;351:637-41. https://doi.org/10.1016/s0140-6736(97)11096-0. Retraction in: Lancet 2010;375:445. Erratum in: Lancet 2004;363:750.

[11] Gostin LO, Hodge JG Jr, Bloom BR, El-Mohandes A, Fielding J, Hotez P, Kurth A, Larson HJ, Orenstein WA,

Rabin K, Ratzan SC, Salmon D. The public health crisis of underimmunisation: a global plan of action. Lancet Infect Dis 2020;20:e11-e16. https://doi.org/10.1016/S1473-3099(19)30558-4

[12] Siani A. Measles outbreaks in Italy: A paradigm of the re-emergence of vaccine-preventable diseases in developed countries. Prev Med 2019;121:99-104. https://doi.org/10.1016/j.ypmed.2019.02.011

[13] Fontanet A, Cauchemez S. COVID-19 herd immunity: where are we? Nat Rev Immunol 2020;20:583-4. https://doi.org/10.1038/s41577-020-00451-5

[14] Mahase E. Covid-19: UK government's defence of senior aide has damaged public and NHS confidence, say experts. BMJ 2020;369:m2109. https://doi.org/10.1136/bmj.m2109

[15] Fancourt D, Steptoe A, Wright L. The Cummings effect: politics, trust, and behaviours during the COVID-19 pandemic. Lancet 2020;396:464-5. https://doi.org/10.1016/S0140-6736(20)31690-1

[16] COCONEL Group. A future vaccination campaign against COVID-19 at risk of vaccine hesitancy and politicisation. Lancet Infect Dis 2020;20:769-70. https://doi.org/10.1016/S1473-3099(20)30426-6

[17] Rollwage M, Dolan RJ, Fleming SM. Metacognitive failure as a feature of those holding radical beliefs. Curr Biol 2018;28:4014-21. https://doi.org/10.1016/j.cub.2018.10.053

[18] Van Kessel S. Populist parties in Europe: Agents of discontent? Springer 2015.

[19] Kennedy J. Populist politics and vaccine hesitancy in Western Europe: an analysis of national-level data. Eur J Public Health 2019;29:512-6. https://doi.org/10.1093/eurpub/ckz004

[20] Carpiano RM, Polonijo AN, Gilbert N, Cantin L, Dubé E. Socioeconomic status differences in parental immunization attitudes and child immunization in Canada: Findings from the 2013 Childhood National Immunization Coverage Survey (CNICS). Prev Med 2019;123:278-87. https://doi.org/10.1016/j.ypmed.2019.03.033

[21] Wei F, Mullooly JP, Goodman M, McCarty MC, Hanson AM, Crane B, Nordin JD. Identification and characteristics of vaccine refusers. BMC Pediatr 2009;9:18. https://doi.org/10.1186/1471-2431-9-18

[22] Wagner AL, Masters NB, Domek GJ, Mathew JL, Sun X, Asturias EJ, Ren J, Huang Z, Contreras-Roldan IL, Gebremeskel B, Boulton ML. Comparisons of vaccine hesitancy across five low- and middle-income countries. Vaccines 2019;7:155. https://doi.org/10.3390/vaccines7040155

[23] Bocquier A, Ward J, Raude J, Peretti-Watel P, Verger P. Socioeconomic differences in childhood vaccination in developed countries: a systematic review of quantitative studies. Expert Rev Vaccines 2017;16:1107-18. https://doi.org/10.1080/14760584.2017.1381020

[24] Lorini C, Santomauro F, Donzellini M, Capecchi L, Bechini A, Boccalini S, Bonanni P, Bonaccorsi G. Health literacy and vaccination: A systematic review. Hum Vaccin Immunother 2018;14:478-88. https://doi.org/10.1080/21645515.2017.1392423

[25] Fasce A, Picó A. Science as a Vaccine. Sci Educ 2019;28:109-25. https://doi.org/10.1007/s11191-018-00022-0

[26] Landrum AR, Olshansky A. The role of conspiracy mentality in denial of science and susceptibility to viral deception about science. Politics Life Sci 2019;38:193-209. https://doi.org/10.1017/pls.2019.9

[27] Evans G, Heath A, Lalljee M. Measuring left-right and libertarian-authoritarian values in the British electorate. Br J Sociol 1996;47:93-112. https://doi.org/10.2307/591118

[28] World Health Organization. "The determinants of vaccine hesitancy: Sample survey questions." https://www.who.int/immunization/sage/meetings/2013/april/4_survey_questionsRevised.pdf (Accessed on: July 20, 2020).

[29] Siani A, Driscoll M, Hurst TM, Coker T, Grantham AG, Bunet A. Investigating the determinants of vaccine hesitancy within undergraduate students' social sphere. Z Gesundh Wiss 2021:1-9. https://doi.org/10.1007/s10389-021-01538-6

[30] VanderWeele TJ, Mathur MB. Some desirable properties of the bonferroni correction: is the bonferroni correction really so bad? Am J Epidemiol 2019;188:617-8. https://doi.org/10.1093/aje/kwy250

[31] Kruger J, Dunning D. Unskilled and unaware of it: how difficulties in recognizing one's own incompetence lead to inflated self-assessments. J Pers Soc Psychol 1999;77:1121-34. https://doi.org/10.1037//0022-3514.77.6.1121

[32] Motta M, Callaghan T, Sylvester S. Knowing less but presuming more: Dunning-Kruger effects and the endorsement of anti-vaccine policy attitudes. Soc Sci Med 2018;211:274-81. https://doi.org/10.1016/j.socscimed.2018.06.032

[33] Hendriks F, Kienhues D. Science understanding between scientific literacy and trust: contributions from psychological and educational research. In: Leßmöllmann A, Dascal M, Gloning T, ed. Science Communication. Berlin, Boston: De Gruyter Mouton 2019, pp. 29-50. https://doi.org/10.1515/9783110255522-002

[34] Bromme R, Kienhues D, Porsch T. Who knows what and who can we believe? Epistemological beliefs are beliefs about knowledge (mostly) to be attained from others. In: Bendixen L F. Feucht L, eds. Personal Epistemology in the Classroom Theory, Research, and Implications for Practice. Cambridge University Press 2010, pp. 163-94. https://doi.org/10.1017/CBO9780511691904.006

[35] Sanchez C, Dunning D. Overconfidence among beginners: Is a little learning a dangerous thing? J Pers Soc Psychol 2018;114:10-28. https://doi.org/10.1037/pspa0000102

[36] Brennan J. A libertarian case for mandatory vaccination. J Med Ethics 2018;44:37-43. https://doi.org/10.1136/medethics-2016-103486

[37] Joslyn MR, Sylvester SM. The Determinants and Consequences of Accurate Beliefs About Childhood Vaccinations (in English). Am Politics Res 2019;47:628-49. https://doi.org/10.1177/1532673X17745342

[38] Lamot M, Krajnc M T, Kirbiš A. Demographic And Socioeconomic Characteristics, Health Status And Political Orientation As Predictors Of Covid-19 Vaccine Hesitancy Among The Slovenian Public. Druz Razr 2020;36:55-73.

[39] Allington D, McAndrew S, Moxham-Hall VL, Duffy B. Media usage predicts intention to be vaccinated against SARS-CoV-2 in the US and the UK. Vaccine 2021;39:2595-603. https://doi.org/10.1016/j.vaccine.2021.02.054

[40] Ward JK, Alleaume C, Peretti-Watel P; COCONEL Group. The French public's attitudes to a future COVID-19 vaccine: The politicization of a public health issue. Soc Sci Med 2020;265:113414. https://doi.org/10.1016/j.socscimed.2020.113414

[41] Arora A, Jha AK, Alat P, Das SS. Understanding coronaphobia. Asian J Psychiatr 2020;54:102384. https://doi.org/10.1016/j.ajp.2020.102384

[42] Coelho CM, Suttiwan P, Arato N, Zsido AN. On the nature of fear and anxiety triggered by COVID-19. Front Psychol 2020;11:581314. https://doi.org/10.3389/fpsyg.2020.581314

[43] Mertens G, Gerritsen L, Duijndam S, Salemink E, Engelhard IM. Fear of the coronavirus (COVID-19): Predictors in an online study conducted in March 2020. J Anxiety Disord 2020;74:102258. https://doi.org/10.1016/j.janxdis.2020.102258

[44] Delanty G. Six political philosophies in search of a virus: Critical perspectives on the coronavirus pandemic. LEQS Paper n. 156, 2020.

[45] Robillard R, Saad M, Edwards J, Solomonova E, Pennestri MH, Daros A, Veissière SPL, Quilty L, Dion K, Nixon A, Phillips J, Bhatla R, Spilg E, Godbout R, Yazji B, Rushton C, Gifford WA, Gautam M, Boafo A, Swartz R, Kendzerska T. Social, financial and psychological stress during an emerging pandemic: observations from a population survey in the acute phase of COVID-19. BMJ Open 2020;10:e043805. https://doi.org/10.1136/bmjopen-2020-043805

[46] Gollwitzer A, Martel C, Brady WJ, Pärnamets P, Freedman IG, Knowles ED, Van Bavel JJ. Partisan differences in physical distancing are linked to health outcomes during the COVID-19 pandemic. Nat Hum Behav 2020;4:1186-97. https://doi.org/10.1038/s41562-020-00977-7

Correspondence: Alessandro Siani, University of Portsmouth, King Henry Building, King Henry 1st Street, PO1 2DY Portsmouth (UK). Tel.: +44 2392842025 - E-mail: alessandro.siani@port.ac.uk

Knowledge, attitudes, and health status of childbearing age young women regarding preconception health - an Italian survey

DRIEDA ZAÇE[1], EMANUELE LA GATTA[1], ALESSIA ORFINO[2], ANNA MARIA VITERITTI[3], MARIA LUISA DI PIETRO[1]

[1] Sezione di Igiene, Dipartimento Universitario di Scienze della Vita e Sanità Pubblica, Università Cattolica del Sacro Cuore, Roma, Italia; [2] ASL Roma 2, Roma, Italia; [3] Fondazione Policlinico Universitario A. Gemelli IRCCS, Roma, Italia

Summary

Introduction. *Preconception health is a public health issue, concerning aspects that could have repercussions on pregnancy outcomes. Despite the importance, often there is a lack of knowledge, particularly among young women. This cross-sectional study aims to evaluate knowledge, attitudes and health status of young women regarding preconception health in the Italian context.*
Methods. *From July 2020 until April 2021 a validated questionnaire (systematic review, Delphi procedure and pilot study) was administered to a sample of 340 women aged 18 to 25 years, without previous pregnancy and not planning it, attending secondary grade schools and universities. It collected information on knowledge, physical, sexual and mental health. T-test and analysis of variance (ANOVA) were used to determine a significant difference in knowledge mean score (KMS) among different groups.*

Results. *KMS was 67.6% (SD = 18.1). Participants with Italian nationality, enrolled in a health-field university, with a full-time job, a family income higher than 35,000 €/year and teachers or health providers as information source, had a significantly higher KMS. Only 15.9% of women who saw a gynaecologist in the last year (47.7%) asked about preconception health. 56.5% knew that folic acid is effective in reducing the risk of neural tube defects, while 5.9% was taking it. 82.3% was living in stressing environment. Gender-based discrimination at work, school or family was felt by 25.1%, while 38.2% experienced at least one type of violence.*
Conclusions. *Promoting preconception health by improving knowledge, attitudes and behaviours may be an impactful possibility to improve women's, children's, and communities' health.*

Introduction

Preconception health refers to women's health before they become pregnant. From a public health perspective, the preconception period can relate to a sensitive phase in the life course, such as adolescence, when health behaviours are established, before the first pregnancy [1]. It has received higher attention in the last years [2, 3], considering the importance of knowing how health conditions and risk factors could affect women or their unborn children in the case of a future pregnancy [4, 5]. Preconception health is a very broad concept and embraces different topics, such as management of physical and genetic diseases, proper nutrition, body weight control, healthy lifestyles, mental/emotional and social health [6], all of which could be associated to poorer pregnancy outcomes and could influence offspring's health extending across two or more generations [7]. An optimal preconception health could be achieved through accurate preconception care, which is the provision of biomedical, behavioural and social health interventions (i.e., health promotion, screening, etc.) to women of reproductive age before conception occurs, in order to reduce risk factors [8] and improve woman's and child's health [9].

One of the crucial pillars of promoting preconception health is the knowledge of women, as well as healthcare providers, regarding this topic. In fact, lack of knowledge and awareness could act as barriers for preconception care use [10]. Nevertheless, to date, women's knowledge is not satisfying, and little is said in schools and in environments where health care is provided. According to the current state of the literature, women's knowledge about preconception health is poor, especially if they have never had a pregnancy, do not plan it and are not trying to get pregnant [6, 11].
Particular attention is paid to young women, who are more at risk for unintended pregnancies [12] and generally report a low and uneven level of knowledge on preconception health [13]. As some studies show, despite the information provided on preconception health, many young women have difficulty understanding some aspects. Due to lacking knowledge and education, young women tend to prolong their unhealthy behaviours over time [13]. As reported in literature preventive care for young women might promote some aspects of preconception health, but topics related specifically to pregnancy outcomes might be missed [14]. Hence, the need for targeted strategies to promote preconception health in this population group.
The data on preconception health, in the Italian context,

concern exclusively women planning a pregnancy [15]. Nevertheless, as mentioned above, these women have different needs, knowledge and attitudes regarding preconception health than those who are not planning a pregnancy [11, 16].

Considering the importance of preconception health for women and their offsprings, and the lack of data in the Italian context, the objective of this study is to evaluate the knowledge, attitudes and health status of young women regarding preconception health.

Methods

OBJECTIVES

The primary objective of this study was to assess the level of knowledge on the preconception health of childbearing age young women in Italy. Secondary objectives included studying factors associated to the level of knowledge, evaluating the amount of folic acid consumption, and assessing physical, sexual, mental, emotional, and social health of childbearing age young women.

RESEARCH DESIGN AND SETTING

This was a cross-sectional study, conducted among young women attending secondary grade schools and universities in Italy, from July 2020 until April 2021.

STUDY POPULATION

Young women of childbearing age from 18 to 25 years were included in the study. This age group was chosen as it represents women's most fertile period. In addition, such young women generally report a low and uneven level of knowledge on preconception health, being at higher risk for unintended pregnancies [6, 15, 17].

Pregnant women, those that were planning a pregnancy and women who already had a child were excluded. These categories generally have knowledge and behaviours influenced by the presence of a child already born or on the way, which are different from those of women who are not planning a pregnancy [11, 16].

QUESTIONNAIRE

The questionnaire used for data collection was structured and validated through a three-step methodology. First, a systematic review was conducted to determine the main topics that needed to be investigated within the questionnaire [18]. On this basis, the different sections of the questionnaire were structured including socio-demographic information, knowledge (evaluating knowledge on issues like preconception health definition; gynaecological visit best timing; neural tube defects; herbal supplements and teas safety; obesity, overweight, moderate exercise and alcohol impact; infectious diseases, including sexually transmitted; folic acid and vitamins consumption; family and genetic history; medications revision; malformations; endocrine disruptors), attitudes, physical health (sexual, mental,

emotional, social, vaccination status) and lifestyles (dietary behaviours, risky behaviours, physical activity; data reported elsewhere).

Subsequently, the questionnaire was validated through a two-round Delphi procedure. The 21 experts involved were asked to evaluate each item through a Likert scale ranging from 1 (Totally Disagree: the question is not relevant at all for the purpose of the questionnaire) to 5 (Strongly agree: the question is very relevant for the purpose of the questionnaire). After two rounds, the questionnaire presented a Content Validity Index of 0.93. The final validation step included a pilot study among 20 women who gave feedback on the questionnaire, reporting a Cronbach's alpha of 0.99.

SAMPLE RECRUITMENT

Sample recruitment took place online. The link to the questionnaire was disseminated and publicized through pages linked to schools and universities, subject to their authorization. The link was published on the community pages on the social networks (Facebook) of schools or universities.

SAMPLE SIZE

To calculate the needed sample size, we considered a type 1 error of 5%, an absolute error (accuracy) of 2.5%, and an expected percentage of preconception health knowledge among young women of 67% [19]. The number obtained was corrected considering an expected response rate of 70%, establishing the need to recruit 485 young women, to reach a final sample size of 340 young women.

STATISTICAL ANALYSIS

The data were analysed through descriptive statistical methods using frequencies and percentages (N, %) for all qualitative variables. Quantitative data were summarized by means and standard deviations (M, SD). Correct answers regarding knowledge questions (20) were coded as "1" and incorrect answers as "0". This allowed us to calculate a total knowledge score for each participant that sums all the scores for each answer. The correct total score was, then, divided by the maximum score (20) and multiplied by 100, to give the correct knowledge mean score (KMS) as a percentage. T-test and Analysis of Variance (ANOVA) were used to determine if there was a statistically significant difference between the KMS (continuous variable) and different variables concerning attitudes and behaviour, with Bonferroni post-hoc analysis. Associations with p-value < 0.05 were considered statistically significant. Statistical analysis was performed using the STATA 15 software.

ETHICAL AND ADMINISTRATIVE PROCEDURE

The study protocol was approved by the Ethics Committee of the Fondazione Policlinico Universitario "A. Gemelli" - Università Cattolica del Sacro Cuore, Rome, Italy.

The approval was emitted on 12/12/2019, number

50160/19 ID 2902.

Results

CHARACTERISTICS OF THE STUDY POPULATION

The studied population consisted of 340 young women, with a mean age of 21.9 (SD = 1.9) and with 98.2% being of Italian nationality. 83.5% of the participants was attending school/university, of which 48.4% were enrolled in a health sciences university, 42.2% in a non-health sciences university and the rest in high school. Among the participants, only 17.7% had a part time job and 13.5% had a full-time job. 34.7% of women was single, 59.1% was in a stable relationship, 3.8% had an occasional partner and 2.4% chose not to answer. Subjects lived in families composed by an average of 4 people (SD = 1.4). 35.9% of participants had a family income inferior to 35000 €/year, 18.2% higher than 35000 €/year and 45.9% preferred not to answer.

KNOWLEDGE REGARDING PRECONCEPTION HEALTH

Higher knowledge was identified on topics such as which group of women could benefit from preconception health (90.6%), the negative effects of alcohol on pregnancy (85.3%), the importance of weight control before pregnancy (83.5%), the most effective technique to prevent sexually transmitted diseases (93.8%), the impact of regular physical activity on the foetus (96.5%), the revision of medications with a healthcare provider before pregnancy (94.7%).

Women had a lower level of knowledge regarding the safety of using herbal supplements during pregnancy (25.9%), the diseases that can be contracted due to raw foods (34.1%), when should the use of vitamin supplements be started (29.1%), the effects of endocrine disruptors on reproduction (32.9%) (Tab. I).

The mean knowledge score concerning the 20 questions was 67.6% (SD = 18.1). Participants with Italian nationality, enrolled in a health-field university, who had a full-time job and with a family income higher than 35,000 €/year had a significantly higher mean knowledge score. The mean knowledge score was also higher among subjects who had teachers and healthcare professionals as information source and those who were using at least one contraceptive method (Tab. II).

ATTITUDES REGARDING PRECONCEPTION HEALTH

The vast majority of women (82.1%) had seen a general practitioner in the last year, while only 47.7% had seen a gynaecologist (Tab. III). The main reasons for not seeing a gynaecologist were not having any symptoms, because of shame/fear and not having had any sexual intercourse. Even when a gynaecologist visit took place, only in 15.9% of cases, women asked about preconception health. Only few women were currently taking folic acid (5.9%), while 23.2% was taking additional vitamins (Tab. III). Women who had had a gynaecological examination in the last year had higher mean knowledge score compared to those who did not have an examination or that had it more than one year before (Tab. II).

PHYSICAL AND SEXUAL HEALTH

Among the participants, 68.4% had a normal Body Mass Index (BMI), 13.9% was underweight and the rest was overweight (17.8%) (Tab. IV). 74.4% of women was not affected by any chronic disease. When a chronic disease was diagnosed, the most frequent were anaemia, asthma and autoimmune diseases and, in 15.9% of cases, a treatment was being followed. The most used therapies were Levothyroxine, the combination Iron + Folic acid and Antiasthmatics. 30% of women suffered from urinary infections, with an average of 2.2 (SD = 1.9; min-max 1-12) episodes in the last year, the majority of whom (88.6%) were treated. A genetic disease in the family was reported by 14.4% of women, among which the most common were diabetes (34.9%), thalassemia (9.3%), coagulopathies (7%), thyroid and cardio-vascular diseases (4.7%, respectively). As for family diseases linked to pregnancy and birth, 51.2% did not report one, while 32.4% did not know and the rest reported at least one disease, the most frequent of which were preterm birth (7.6%), recurrent miscarriage (7.4%) and gestational diabetes (4.4%). Homeopathic substances or natural medicines were being taken by 20.3%. Exposure to Bisphenol A, Pesticides, Solvents and Poly- and Perfluoroalchilic substances had a frequency of 1-4 exposures/month in 45.9%, 25.5%, 28.9% and 25.6% of cases, respectively. Young women reported being vaccinated against Varicella, Measles, Rubella, Mumps, Hepatitis A, Hepatitis B, Meningococcus, Tetanus, Diphtheria, Pertussis, Polio in 47%, 76.5%, 68.5%, 56.2%, 46.8%, 63.5%, 52.6%, 72.9%, 46.2%, 53.3%, 48% of cases, respectively. A vaccine against Human Papilloma Virus (HPV) was administered in 58.8% of cases. Vaccination status was unknown to 24.7% of young women in the sample.

A therapy to regulate the menstrual cycle was followed in 23.8% of cases, 96.7% of which used the estroprogestin pill (Tab. V). In 67.9% of cases women had sexual intercourses in the last year, using a contraceptive technique in 91.3% of cases. The most used contraceptive methods were Condom (64.6%), Contraceptive Pill (34.1%) and Coitus interruptus (23.6%). A genital tract infection was reported in 28.9% of cases, with an average of 2.1 (SD = 1.3) episodes in the last year, 86.4% of which were treated mainly with antibiotics (33.3%) and vaginal ovules (23.8%). A sexually transmitted disease was diagnosed in 6.3% of women, most frequently being HPV infection (40%), Genital HSV (herpes simplex virus) infection (20%), Chlamydiosis (13.3%), Candidiasis (13.3%), and treated in 86.7% of cases. 15.6% had a gynaecological disease, which was being treated in 57.6% of cases.

MENTAL AND EMOTIONAL HEALTH

Participants in the study reported the presence of stressing factors in the living environment in 82.3% of cases (Tab. VI). The main strategies to face these

Tab. I. Answers to the 20 questions regarding knowledge of young women on preconception health.

Question	Total	Correct answer, N (%)	Incorrect answers, N (%)
1. Preconception health refers only to women who are planning a pregnancy: Yes/No	340	308 (90.6)	32 (9.4)
2. Preconception health is only important for those who have health problems: Yes/No	340	330 (97.1)	10 (2.9)
3. What is the best time to have a gynaecological visit when thinking of getting pregnant?	340	278 (81.8)	62 (18.2)
4. Which of the following strategies has proven to be effective in reducing the risk of neural tube defects in the foetus such as, for example, spina bifida (birth defect in which there is an incomplete closure of the spine)? (Vitamin A; Folic acid; Calcium; Iron)	340	192 (56.5)	148 (43.5)
5. Are herbal supplements (a plant-based product that is considered useful for the treatment of diseases or for well-being) and herbal teas always safe to consume during pregnancy?: Yes/No	340	88 (25.9)	252 (75.1)
6. When you are pregnant, eating raw foods can increase the risk of contracting diseases such as Toxoplasmosis; Salmonella; Listeria: Yes/No	340	116 (34.1)	224 (65.9)
7. The consumption, even if on one occasion, of a high amount of alcohol, even before being aware of the pregnancy, can cause serious birth defects: Yes/No	340	290 (85.3)	50 (14.7)
8. Obese pregnant women, compared to pregnant women of normal weight, have a higher risk for all of the following clinical conditions, EXCEPT: (Low blood pressure during pregnancy; Gestational diabetes; Miscarriage; Having a baby with a birth defect) : Yes/No	340	201 (59.1)	139 (40.9)
9. Control of weight before pregnancy in overweight or underweight women reduces the risks during pregnancy: Yes/No	340	284 (83.5)	56 (16.5)
10. The most effective technique against sexually transmitted diseases is: (Condom; Estroprogestin pill; Vaginal ring)	340	319 (93.8)	21 (6.2)
11. If a pregnant woman has an active sexually transmitted disease, such as genital herpes or syphilis, can she transmit it to the baby?: Yes/No	340	192 (56.5)	148 (43.5)
12. Which of the following substances are NOT dangerous during pregnancy and have NOT been associated with birth defects or negative pregnancy outcomes (such as miscarriage, prematurity or low birth weight)? (Smoke; Alcohol; Cocaine; Folic acid; Marijuana)	340	225 (66.2)	115 (33.8)
13. ONLY pregnant women should consume folic acid: Yes/No	340	233 (68.5)	107 (31.5)
14. Before a pregnancy, it is advisable for the woman and her partner to retrace their family and genetic history with their doctor: Yes/No	340	295 (86.8)	45 (13.2)
15. Moderate regular exercise (for example, walking for an hour, 3 times a week) can harm the foetus: Yes/No	340	328 (96.5)	12 (3.5)
16. When looking for a pregnancy, the medications taken should be reviewed with the doctor: Yes/No	340	322 (94.7)	18 (5.3)
17. When should the use of vitamin supplements be started?	340	99 (29.1)	241 (70.9)
18. During which trimester of pregnancy the developing embryo/foetus is most at risk of malformations due to exposure to harmful substances	340	167 (49.1)	173 (50.9)
19. When pregnant it is risky to come into contact with animals such as the cat: Yes/No	340	207 (60.9)	133 (39.1)
20. What can endocrine disruptors (substances that alter the normal hormonal function of the endocrine system, such as the thyroid, ovary, pancreas.) cause	340	112 (32.9)	228 (67.1)
Mean Total Knowledge	67.6% ± 18.1%		

stressors emerged to be elaborating stressing factors to not let them become a problem (51.8%) and looking for relatives/friends' help (23.6%). Most participants (63.7%) had never consulted a mental health specialist in their life. In 16.7% of women a mental disorder was diagnosed, most frequently being anxiety and depression (10.3% and 2.9%, respectively). Only 23.7% of women with a mental disorder diagnosis was under treatment. 38.2% of women experienced, at least, one type of violence during their life, the most common being verbal (26.2%) and psychological (23.8%), for which they chose to talk mainly to their parents (43.2%) and friends (37.5%). Gender-based discrimination at work, school or family was felt by 25.1% of participants, according to which, men have more advantages at work (54.7%), and at school and work (19.4%). Women felt averagely fulfilled at home (3.9 ± 1.1), at school/university and in the social context they live in (3.5 ± 1.0, respectively), and less at work (2.9 ± 1.2).

Tab. II. Knowledge regarding preconception health and variables associated to it.

Variable	Total	Number of participants	Mean knowledge	SD	p-value
Nationality	340				0.006
Italian		334	67.9	17.9	
Other		6	49.2	22.7	
Attending school/university and field	267				< 0.001
High school		18	58.3	17.3	
Health field university		133	79.1	14.1	
Non health field university		116	57.5	14.6	
Not specified		8	65.6	18.9	
Employment	338				< 0.001
No		232	69.7	16.9	
Part time		60	57.8	18.0	
Full time		46	70.5	20.2	
Family income	340				< 0.001
< 35000 €/y		122	65.6	18.1	
> 35000 €/y		62	75.4	18.2	
Prefers not to answer		156	66.0	17.4	
Source of information of those who have heard of preconception health	180				< 0.001
Social network (Instagram, Facebook, etc.)		14	56.4	8.8	
Internet or medical websites		46	68.2	18.1	
Family		14	64.6	16.2	
Healthcare professionals (obstetricians, nurses, doctors...)		75	75.8	15.2	
Teachers		16	75.9	12.8	
Books or magazines		9	75.6	15.1	
Other		6	61.7	19.1	
Gynaecological examination	340				0.005
No		80	64.9	16.1	
Yes, in the last year		162	70.9	18.4	
Yes, more than one year ago		98	64.2	18.4	
BMI	339				0.001
Below 18.5		47	71.9	17.6	
18.5-24.9		233	67.9	17.4	
25.0-29.9		46	65.1	19.5	
30.0-34.9		6	50.0	13.4	
35.0-39.9		3	80.0	8.7	
Above 40		4	41.3	27.2	
Contraceptive technique used among those who have had sexual intercourse in the last year	229				< 0.001
At least one		209	70.4	17.2	
None		20	53.3	15.5	

Discussion

The present study aimed at assessing the knowledge, attitudes and health status of young women regarding preconception health, considering its importance for women and their offspring [9], the lack of data in the Italian context and the fact that information on knowledge and associated gaps could serve as starting point for any future intervention.

Participants in this study had higher knowledge on topics such as, which group of women could benefit from preconception health, the negative effects of alcohol on pregnancy, the importance of weight control before pregnancy, the most effective technique to prevent sexually transmitted diseases, the impact of regular physical activity on the foetus, the revision of medications with a healthcare provider before pregnancy. However, there are some topics that were less known to young women, such as the safety of using herbal supplements during pregnancy, diseases that can be contracted due to raw foods, when should the use of vitamin supplements be started, the effects of endocrine disruptors on reproduction, in line with the published literature [20]. In our sample the level of knowledge was significantly associated to Italian nationality, health-field university, job, yearly family income and information source. This

Tab. III. Attitudes of participants regarding preconception health.

Variable	Total	Number for each group	%
General practitioner examination in the last year	340		
No		61	17.9
Yes		279	82.1
Gynaecological examination	340		
No		80	23.5
Yes, in the last year		162	47.7
Yes, more than one year ago		98	28.8
If not, why?	46		
Did not need it		29	63.0
Because of shame/fear		5	10.9
Own mother never spoke about it		3	6.5
Never had intercourse		3	6.5
Tends to procrastinate		2	4.4
Not looking for pregnancy		1	2.2
Does not know		3	6.5
Asked a gynaecologist about preconception health	340		
No		286	84.1
Yes		54	15.9
Dental examination in the last year	340		
No		102	30.0
Yes		238	70.0
Folic acid consumption	340		
No		320	94.1
Yes		20	5.9
Additional vitamins	340		
No		261	76.8
Yes		79	23.2
Which vitamins	64		
D Vitamin		21	32.8
B12 Vitamin		5	7.8
C Vitamin		7	10.9
Iron		2	3.1
Multivitamin		28	43.8
A Vitamin		1	1.6

asserts the importance of socio-demographic variables on women's preconception health, as reported also by published literature, to increase health equity and provide the same possibilities also to disadvantaged population groups [11, 21, 22].

Less than half of the participants had seen a gynaecologist in the last year and only few of them had talked about preconception health. Healthcare professionals remain one of the most important sources of information, however a gynaecological visit is not always associated to better knowledge regarding preconception health. Therefore, there is a need to promote the importance of preconception care among health providers, since they play a crucial role in supporting young women and addressing health issues in clinical consultations [23, 24]. Only 5.9% of women in our sample were taking folic acid, even if 56.5% knew that folic acid has been shown to be effective in reducing the risk of neural tube defects in the foetus. The vast majority of participants (68.5%) thought that only pregnant women should take folic acid. Based on this, it should be noted that folic acid remains an issue to be addressed within preconception health and there is the need for more targeted interventions which should focus not only on increasing women's knowledge, but also changing their attitudes and behaviours, since not always higher knowledge translates into improved behaviours.

Several participants reported being diagnosed with chronic, genetic or sexually transmitted diseases. Lack of knowledge could perpetuate unhealthy behaviours, as for example, in our sample, a relatively high percentage of women were using coitus interruptus or contraceptive pill which exposes them to sexually transmitted diseases and unplanned pregnancies. Furthermore, almost 1/4 of the sample did not know their vaccination status. This highlights the importance of regularly checking with a healthcare professional to control the health status, and receive the right information not only before planning a

Tab. IV. Physical health of young women in childbearing age.

Variable	Total	Number for each group	%
BMI	339		
Underweight (Below 18.5)		47	13.9
Normal weight (18.5-24.9)		232	68.4
Pre-obesity (25.0-29.9)		46	13.6
Obesity class I (30.0-34.9)		6	1.8
Obesity class II (35.0-39.9)		3	0.9
Obesity class III (Above 40)		5	1.5
Chronic disease	327		
None		253	74.4
Anemia		22	6.5
Asthma		8	2.4
Autoimmune diseases		6	1.8
Other		27	8.0
Does not know		11	3.2
Drugs or treatments for chronic disease	293		
No		247	84.3
Yes		46	15.7
Urinary infections in the last year	340		
No		231	67.9
Yes		102	30.0
Does not know		4	1.2
Prefers not to answer		3	0.9
Treatments for urinary infections	105		
No		12	11.4
Yes		93	88.6
Genetic disease in family	340		
No		237	69.7
Yes		49	14.4
Does not know		51	15.0
Prefers not to answer		3	0.9
Homeopathic substances, integrators or natural medicines	340		
No		271	79.7
Yes		69	20.3
Exposure to Bisphenol A	283		
1-4 exposures/year		67	23.7
1-4 exposures/month		130	45.9
1-4 exposures/week		82	29.0
More than 4 exposures/week		4	1.4
Exposure to Pesticides	275		
1-4 exposures/year		73	26.6
1-4 exposures/month		70	25.5
1-4 exposures/week		94	34.2
More than 4 exposures/week		38	13.8
Exposure to Solvents	273		
1-4 exposures/year		44	16.1
1-4 exposures/month		79	28.9
1-4 exposures/week		110	40.3
More than 4 exposures/week		40	14.7
Exposure to Poly- and Perfluoroalchilic substances	289		
1-4 exposures/year		56	19.4
1-4 exposures/month		74	25.6
1-4 exposures/week		79	27.3
More than 4 exposures/week		80	27.7
Family history of disease linked to pregnancy and birth (multiple answers)	379		
Recurrent miscarriage		25	7.4
Preterm birth		26	7.6
Pregravidic or gestational diabetes		15	4.4
Gestational or chronic hypertension		8	2.4
Autoimmune diseases		5	1.5
Preeclampsia		5	1.5
Other		11	3.2
None		174	51.2
Does not know		110	32.4

Tab. V. Sexual health of childbearing age young women.

Variable	Number	%
Age first menstrual cycle (mean ± SD)	12.3 ± 1.5	
Drugs to regulate the menstrual cycle		
No	255	75.0
Yes	81	23.8
Does not know	1	0.3
Prefers not to answer	3	0.9
Sexual intercourses in the last year		
No	103	30.3
Yes	231	67.9
Prefers not to answer	6	1.8
Use of contraceptive methods		
No	20	8.7
Yes	209	91.3
Contraceptive method		
Condom	148	64.6
Contraceptive Pill	78	34.1
IUD	3	1.3
Sexual abstinence	6	2.6
Coitus interruptus	54	23.6
Other	8	3.5
Genital tract infections in the last year		
No	161	67.9
Yes	66	28.9
Does not know	8	3.4
Prefers not to answer	2	0.8
How many infection episodes		
1-3	37	86.0
> 3	6	14.0
Treatments for genital infections		
No	8	12.1
Yes	57	86.4
Prefers not to answer	1	1.5
Sexually Transmitted Diseases in the last year		
No	218	92.0
Genital HSV infection	3	1.3
HPV infection	6	2.5
Chlamydiosis	2	0.8
Candidiasis	2	0.8
Condyloma	1	0.4
Ureaplasma urealyticum infection	1	0.4
Does not know	3	1.3
Prefers not to answer	1	0.4
Treatment for STDs		
No	2	13.3
Yes	13	86.7
Gynaecological disease		
None	281	82.9
Endometriosis	3	0.9
Polycystic Ovary Syndrome (PCOS)	46	13.6
Uterine polyps	2	0.6
Myomas	2	0.6
Prefers not to answer	5	1.5
Treatments for gynaecological disease		
No	25	42.4
Yes	34	57.6

Tab. VI. Mental and emotional health of young women in childbearing age.

Variable	Number	%
Stressing factors present in the living environment		
No	60	17.7
Yes	280	82.3
Strategies to face stressing factors		
Ignoring them	12	4.4
Trying to elaborate them to not let them become a problem	143	51.8
Does not manage to face them and they become a problem	31	11.2
Looking for professional help	5	1.8
Looking for relatives/friends' help	65	23.6
Does not know how to behave	20	7.3
Consulting a specialist for mental health		
Never	216	63.7
Psychologist/Psychiatrist	109	32.2
General practitioner/Gynaecologist	4	1.2
Prefers not to answer	10	3.0
Mental disorder diagnosed		
No	280	82.4
Anxiety	35	10.3
Depression	10	2.9
Mood disorder	4	1.2
Other	8	2.4
Prefers not to answer	3	0.9
Treatments for mental disorder at the moment		
No	45	76.3
Yes	14	23.7
Violence suffered		
No	184	54.1
Physical	22	6.5
Psychological	81	23.8
Verbal	89	26.2
Sexual	17	5.0
Prefers not to answer	26	7.7
Ever talked with someone about violence		
No	224	66.5
Yes	113	33.5
With whom have talked about violence		
Parents	38	43.2
Siblings	5	5.7
Family	11	12.5
Friends	33	37.5
Partner	13	14.8
Professors	16	18.2
Psychologist	18	20.5
Gender based discrimination		
No	254	74.9
At school	49	14.5
At work	28	8.3
Within the family	31	9.1
More advantages for men		
No	80	23.5
At school	8	2.4
At school and at work	66	19.4
At work	186	54.7
Feeling fulfilled at school/university (mean ± SD; min-max 1-5)	3.5 ± 1.0	
Feeling fulfilled at work (mean ± SD; min-max 1-5)	2.9 ± 1.2	
Feeling fulfilled at home (mean ± SD; min-max 1-5)	3.9 ± 1.1	
Feeling fulfilled in social context (mean ± SD; min-max 1-5)	3.5 ± 1.0	
Life satisfaction (mean ± SD; min-max 1-5)	3.4 ± 0.9	

pregnancy, but anytime in women's lifespan [25].

An important role in the preconception care is played by mental health, which influences pregnancy outcomes, women's and children's health and should be addressed. More than 2/3 of women in our sample was living in a stressful environment, in most cases not knowing how to face this stress. Furthermore, more than 1/3 of women experienced at least one type of violence during their life, the most common being verbal and psychological, asking, more often, their parents and friends for support.

The results of this study are important since they refer to a particularly vulnerable population, with a higher risk for unhealthy behaviours and unintended pregnancies, and they could be a starting point to provide information for targeted interventions to increase the knowledge and improve attitudes and behaviours of young women concerning preconception health. From a public health point of view interventions implemented in such a young population group could have an even greater impact on preconception health [26] and would bring a long-lasting positive effect on women's and children's health [27]. Nevertheless, higher knowledge and awareness are not always associated to modified behaviours, which calls for personalized, targeted interventions, based on evidence and women's preferences, in order to have a greater impact [28]. In this context this study provides input and could act as impetus for future interventions, which should focus on disseminating knowledge on topics such as diseases that can be contracted due to raw foods, vitamin and herbal supplements be started, endocrine disruptors, the importance of talking to a healthcare provider about preconception health, taking folic acid, controlling health conditions and therapies. As previously reported by women themselves, interventions could include having access to reputable and easily accessible online sources of preconception health information, education at secondary schools and public health campaigns, considering women's personal preferences for accessible and tailored preconception health information and support at individual, interpersonal, community and organizational levels [29, 30].

As reported also by the Centers for Disease Control and Prevention (CDC) recommendations, the goal of preconception care and services should be to improve the knowledge, attitudes and behaviours of women related to preconception health, assure that all women of childbearing age receive preconception care services (i.e., evidence-based risk screening, health promotion, and interventions) that will enable them to enter pregnancy in optimal health and reduce the disparities in adverse pregnancy outcomes [8].

The results of this study should be interpreted in the light of some limitations. Firstly, the cross- sectional design does not permit to report causality, but only association between the level of knowledge and the different variables. The questionnaire was filled through an online link and only women more attentive to their health in general, and preconception health in particular, may have answered, which could have introduced a bias. Moreover, since all measures were self-reported and health is a sensitive issue, it is possible that there was a response bias.

However, this study has several strong points. To the best of our knowledge, it is the first to explore knowledge, attitudes, behaviours and health status of young Italian women. The sample size was calculated for the study to have the appropriate statistical power. The questionnaire used to collect the data was created based on a systematic literature review and validated through a two-round Delphi procedure followed by a pilot study. Hence, the questionnaire could be a useful tool, acting as an impetus for future research in the field, not only in Italy, but also in other countries.

Conclusions

Poor preconception health could create health disparities across the globe or attenuate already existing ones [31]. That is why promoting preconception care by improving knowledge, attitudes and behaviours is seen as an impactful possibility to reduce inequalities and improve women's, children's and communities' health. Women in our sample lacked knowledge in several issues regarding preconception health, had some unhealthy attitudes and behaviours and needed guide by their healthcare providers on this topic. Healthcare providers, including midwives, gynaecologists, general practitioners, nurses, etc., and teachers play an important role as the main sources of information regarding preconception health. Through information campaigns, it would be advisable to encourage young women to see their health professionals, to check their status health and improve their knowledge, not only before becoming pregnant, but in every moment of their fertile life, in order to avoid unhealthy behaviours. The consumption of folic acid before pregnancy remains an issue of preconception health, and it deserves particular attention in information campaigns. It is important to integrate preconception health promotion into the continuum of women's healthcare through raising awareness, providing information, improving clinical practice, and providing high quality research to inform policy makers and guidelines [32].

Acknowledgments

Conflict of interest statement

The Authors declare no conflicts of interest.

Authors' contributions

DZ and MLDP conceived the research hypothesis and designed the study. DZ, AO, AMV, MLDP contributed to build the questionnaire. DZ and ELG performed the statistical analysis. DZ, ELG, AO, AMV wrote a first draft of the manuscript and MLDP revised the work for important intellectual content. All authors gave the final approval of the version to be published, and agreed on all aspects of the work, especially concerning its accuracy and integrity.

References

[1] Moss JL, Harris KM. Impact of maternal and paternal preconception health on birth outcomes using prospective couples' data in Add Health. Arch Gynecol Obstet 2015;291:287-98. https://doi.org/10.1007/s00404-014-3521-0

[2] Lu MC. Recommendations for preconception care. Am Fam Physician 2007;76:397-400.

[3] American College of Obstetricians and Gynecologists. ACOG Committee Opinion #313: the importance of preconception care in the continuum of women' health care. Obstet Gynecol 2005;106:665-6. https://doi.org/10.1097/00006250-200509000-00052

[4] WHO. Preconception Care: maximizing the gains for maternal and child health. Published online 2013.

[5] Thompson EL, Vázquez-Otero C, Vamos CA, Marhefka SL, Kline NS, Daley EM. Rethinking preconception care: a critical, women's health perspective. Matern Child Health J 2017;21:1147-55. https://doi.org/10.1007/s10995-016-2213-8

[6] Xaverius PK, Tenkku LE, Salas J. Differences between women at higher and lower risk for an unintended pregnancy. Womens Health Issues 2009;19:306-12. https://doi.org/10.1016/j.whi.2009.06.002

[7] Stephenson J, Schoenaker D, Hinton W, Poston L, Barker M, Alwan N, Godfrey K, Hanson M, de Lusignan S. A wake-up call for preconception health: a clinical review. Br J Gen Pract 2021;71:233-6. https://doi.org/10.3399/bjgp21X715733

[8] Johnson K, Posner S, Biermann J, Cordero J, Atrash H, Parker C, Boulet S, Curtis MG, CDC/ATSDR Preconception Care Work Group, Select Panel on Preconception Care. Recommendations to improve preconception health and health care--United States. A report of the CDC/ATSDR Preconception Care Work Group and the Select Panel on Preconception Care. MMWR Recomm Rep 2006;55:1-23.

[9] Stephenson J, Heslehurst N, Hall J, Schoenaker D, Hutchinson J, Cade J, Poston L, Barrett G, Crozier S, Barker M, Kumaran K, Yajnik C, Baird J, Mishra G. Before the beginning: nutrition and lifestyle in the preconception period and its importance for future health. Lancet 2018;391:1830-41. https://doi.org/10.1016/S0140-6736(18)30311-8

[10] Poels M, Koster MPH, Boeije HR, Franx A, van Stel HF. Why do women not use preconception care? A systematic review on barriers and facilitators. Obstet Gynecol Surv 2016;71:603-12. https://doi.org/10.1097/OGX.0000000000000360

[11] Harelick L, Viola D, Tahara D. Preconception health of low socioeconomic status women: Assessing knowledge and behaviors. Womens Health Issues 2011;21:272-6. https://doi.org/10.1016/j.whi.2011.03.006

[12] Finer LB, Zolna MR. Unintended pregnancy in the United States: incidence and disparities, 2006. Contraception 2011;84:478-85. https://doi.org/10.1016/j.contraception.2011.07.013

[13] Ekstrand Ragnar M, Grandahl M, Stern J, Mattebo M. Important but far away: adolescents' beliefs, awareness and experiences of fertility and preconception health. Eur J Contracept Reprod Health Care 2018;23:265-73. https://doi.org/10.1080/13625187.2018.1481942

[14] Upadhya KK, Jalazo ER, Connor KA, Mistry KB, Cheng TL. Optimizing preconception health among young women: What are we missing? J Pediatr Adolesc Gynecol 2016;29:464-6. https://doi.org/10.1016/j.jpag.2016.02.010

[15] Mastroiacovo P, Nilsen R, Leoncini E, Gastaldi P, Allegri V, Boiani A, Faravelli F, Ferrazzoli F, Guala A, Madrigali V, Scarano G. Prevalence of maternal preconception risk factors: an Italian multicenter survey. Ital J Pediatr 2014;40:91. https://doi.org/10.1186/s13052-014-0091-5

[16] Naimi TS, Lipscomb LE, Brewer RD, Gilbert BC. Binge drinking in the preconception period and the risk of unintended pregnancy: implications for women and their children. Pediatrics 2003;111:1136-41. https://doi.org/10.1542/peds.111.S1.1136

[17] Richards J, Mosseau A. Community-based participatory research to improve preconception health among Northern Plains American Indian adolescent women. Am Indian Alask Native Ment Health Res 2012;19:154-85. https://doi.org/10.5820/aian.1901.2012.154

[18] Zaçe D, Orfino A, Viteritti AM, Versace V, Ricciardi W, di Pietro ML. A comprehensive assessment of preconception health needs and interventions regarding women of childbearing age: a systematic review . J Prev Med Hyg 2022;63:E174-99. https://doi.org/10.15167/2421-4248/jpmh2022.63.1.2391

[19] Delgado CEF. Undergraduate Student Awareness of Issues Related to Preconception Health and Pregnancy. Matern Child Health J 2008;12:774-82. https://doi.org/10.1007/s10995-007-0300-6

[20] Toivonen KI, Oinonen KA, Duchene KM. Preconception health behaviours: A scoping review. Prev Med 2017;96:1-15. https://doi.org/10.1016/j.ypmed.2016.11.022

[21] Denny CH, Floyd RL, Green PP, Hayes DK. Racial and ethnic disparities in preconception risk factors and preconception care. J Womens Health 2012;21:720-9. https://doi.org/10.1089/jwh.2011.3259

[22] Horner-Johnson W, Akobirshoev I, Amutah-Onukagha NN, Slaughter-Acey JC, Mitra M. Preconception Health Risks Among U.S. Women: Disparities at the Intersection of Disability and Race or Ethnicity. Womens Health Issues 2021;31:65-74. https://doi.org/10.1016/j.whi.2020.10.001

[23] Jacob C, Killeen S, McAuliffe F, Stephenson J, Hod M, Diaz Yamal I, Malhotra J, Mocanu E, McIntyre H, Kihara A, Ma R, Divakar H, Kapur A, Ferriani R, Ng E, Henry L, Van Der Spuy Z, Rosenwaks Z, Hanson M. Prevention of noncommunicable diseases by interventions in the preconception period: A FIGO position paper for action by healthcare practitioners. Int J Gynecol Obstet 2020;151(Suppl 1):6-15. https://doi.org/10.1002/ijgo.13331

[24] Frey KA, Files JA. Preconception healthcare: What women know and believe. Matern Child Health J 2006;10(Suppl 1):73-7. https://doi.org/10.1007/s10995-006-0110-2

[25] Dunlop AL, Logue KM, Thorne C, Badal HJ. Change in women's knowledge of general and personal preconception health risks following targeted brief counseling in publicly funded primary care settings. Am J Health Promot 2013;27(Suppl 3):S50-7. https://doi.org/10.4278/ajhp.120116-QUAN-39

[26] Barker M, Dombrowski S, Colbourn T, Fall C, Kriznik N, Lawrence W, Norris S, Ngaiza G, Patel D, Skordis-Worrall J, Sniehotta F, Steegers-Theunissen R, Vogel C, Woods-Townsend K, Stephenson J. Intervention strategies to improve nutrition and health behaviours before conception. Lancet 2018;391:1853-64. https://doi.org/10.1016/S0140-6736(18)30313-1

[27] Dean SV, Lassi ZS, Imam AM, Bhutta ZA. Preconception care: closing the gap in the continuum of care to accelerate improvements in maternal, newborn and child health. Reprod Health 2014;11(Suppl 3):S1. https://doi.org/10.1186/1742-4755-11-S3-1

[28] DeJoy SB. Pilot test of a preconception and midwifery care promotion program for college women. J Midwifery Womens Health 2014;59:523-7. https://doi.org/10.1111/jmwh.12106

[29] Walker R, Drakeley S, Boyle J. Preconception women's views of promoting preconception women's health in Australia. Health Promot J Austr 2021;32:22-8. https://doi.org/10.1002/hpja.402

[30] Batra P, Mangione C, Cheng E, Steers W, Nguyen T, Bell D, Kuo A, Gregory K. A Cluster randomized controlled trial of the myfamilyplan online preconception health education tool. Am J Health Promot 2018;32:897-905. https://doi.org/10.1177/0890117117700585

[31] Mumford SL, Michels KA, Salaria N, Valanzasca P, Belizán JM. Preconception care: it's never too early. Reprod Health 2014;11:73. https://doi.org/10.1186/1742-4755-11-73

[32] Lang A, Boyle J, Fitzgerald G, Teede H, Mazza D, Moran L, Harrison C. Optimizing preconception health in women of reproductive age. Minerva Gynecol 2018;70:99-119. https://doi.org/10.23736/S0026-4784.17.04140-5

Correspondence: Emanuele La Gatta, Sezione di Igiene, Dipartimento Universitario di Scienze della Vita e Sanità Pubblica, Università Cattolica del Sacro Cuore, Largo F. Vito 1, Roma, Italia. Tel.: +39 340 7074407 - E-mail: emanuele.lagatta01@icatt.it

Antimicrobial efficacy of Xylitol, Probiotic and Chlorhexidine mouth rinses among children and elderly population at high risk for dental caries – A Randomized Controlled Trial

NC KRUPA, HM THIPPESWAMY, BR CHANDRASHEKAR
Department of Public Health Dentistry, JSS Dental College & Hospital (Constituent College),
JSS Academy of Higher Education & Research, Mysuru, Karnataka, India

Summary

Introduction. *Chlorhexidine is considered the most potent chemotherapeutic agent against Streptococcus mutans. However, its side effects due to prolonged use, indicates need for alternatives. The study intended to assess and compare antimicrobial efficacies of probiotic, xylitol and chlorhexidine mouth rinses in children and elderly.*
Methods. *The study was a Double blind Randomized Controlled Trial conducted among residential school children aged 5-12 years and elderly greater than 60 years residing in old age homes. (ClinicalTrials.gov ID: NCT04399161). 30 participants each among children and elderly were chosen based on eligibility criterion (high risk for caries). They were further randomly divided into 3 groups with 10 participants in each group. Participants were asked to rinse with 15 ml of freshly prepared mouth rinses once daily for 2 minutes for 14 days. Antimicrobial efficacy was determined by assessing change in Streptococcus mutans levels in dental plaque.*
Results. *Significant reduction in Streptococcus mutans counts were observed in both children and elderly (Chlorhexidine: mean difference = 3.11 log10CFU/g, p = 0.022, Xylitol: mean difference = 0.93 log10CFU/g, p = 0.046, Probiotic: mean difference = 1.91 log10CFU/g, p = 0.023 in children); (Chlorhexidine: mean difference = 2.23 log10CFU/g, Xylitol: mean difference = 1.39 log10CFU/g, p = 0.009, Probiotic: mean difference = 1.61 log10CFU/g, p = 0.018 in elderly). Intergroup comparison showed no significant difference.*
Conclusions. *Antimicrobial efficacy of xylitol and probiotic mouth rinses were comparable to that of chlorhexidine in both children and elderly. Probiotics could potentially be more efficacious than xylitol among children.*

Introduction

WHO defines dental caries as a localized, post eruptive pathological process of extreme origin involving softening of the hard tooth tissue and proceeding to the formation of cavity. The process involves bacterial interactions in plaque accumulated on the surface of the teeth. *Streptococcus mutans* in plaque is the most commonly isolated organism amidst all other cariogens. It ferments sucrose and the resulting acid causes demineralization of tooth enamel [1].

While mechanical methods of plaque control can maintain adequate oral hygiene, such methods are not being used appropriately. This necessitates use of adjuncts to mechanical plaque control methods [2]. Chlorhexidine mouth rinse has been considered the most effective agent in inhibiting *Streptococcus mutans* [3]. However, adverse effects due to prolonged use such as staining of teeth, xerostomia, altered taste sensation, mouth/ throat irritation, antimicrobial resistance, etc. has necessitated research on other alternatives.

Xylitol used as an artificial sweetener in foods, cannot be metabolized by oral bacteria thereby contributing to caries prevention. Adverse effects, as reported in studies, are due to consumption in large quantities and its magnitude, as compared to that of chlorhexidine, is indistinct. Although studies have assessed effects of xylitol chewing gum on caries, there is less literature on its efficacy as a mouth rinse [4].

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. Probiotic products seem to have an effect on the oral health of individuals by prompting beneficial bacteria to defend teeth and gums against harmful ones. There have been no issues of antibiotic resistance, as they contains only commensal flora and there has been no proof of intoxication or allergies on consumption [5]. Research on their use as mouth rinses are scanty.

Antimicrobial efficacies of probiotics and xylitol mouth rinses have not been compared till date. Also their effects on young and elderly population have not been compared. Hence the study intended to assess and compare antimicrobial efficacies of xylitol, probiotic and chlorhexidine mouth rinses in children and elderly.

Methods

The research was a randomized, double blind, parallel, controlled trial (ClinicalTrials.gov ID: NCT04399161) conducted in full accordance with the World Medical Association Declaration of Helsinki. The study protocol was approved by the institution's ethics committee (No: JSSDCH/Ethical/05/2016-17). The study was conducted over a period of 10 months between February and December 2017.

The study was conducted among residential school children aged 5-12 years at high risk for caries chosen from a government residential school and elderly citizens (above 60 years) at high risk for caries residing in an old age home. The residential school and old age home were chosen by a convenience sampling method. Permission to conduct the study in the residential school and old age home was obtained from the concerned authorities. Details about the study were presented to the participants in the form of a study information sheet or communicated verbally in both English and in the local language. Only the eligible participants who provided written consent after they were briefed about the study procedure were included in the study. In case of children, written consent was obtained from the guardian. Eligibility criteria were as follows. Inclusion criteria: 1) Individuals with high risk for caries who were identified using a customized caries risk assessment tool. 2) Not under antimicrobial therapy or probiotic products for the past 1 month. Exclusion criteria: 1) Using mouth rinse routinely. 2) Undergoing any dental treatment during the study period. 3) Not able to brush their teeth and rinse on their own. Twelve participants were chosen per group. Sample size was based on previous literature with similar study objectives. With 3 products involved in each of the 2 population groups (children and elderly) the sample size was 36 child participants and 36 elderly participants.

The caries risk assessment tool comprised of information on socio-economic status, oral hygiene practices, fluoride exposure, caries experience amongst family members, symptoms of dry mouth, quantity and frequency of intake of sweetened food and caries experience in the past and present. Each item was scored as 0 or 1 and the total score was obtained by summing up the scores of all the items. Any participant with total score greater than 5 was considered to be at high risk for caries.

Antimicrobial efficacy of the mouth rinses was assessed by assessment of *Streptococcus mutans* levels in plaque. Participants were asked to refrain from brushing on the day of plaque collection. Plaque samples were collected from the buccal surface of a non-carious permanent maxillary first molar (adjacent tooth was considered if the index tooth was missing). Plaque collection was done using an autoclaved scaler under daylight. The collected plaque was then stored in a pre-weighed sterile eppendorf tube. The tubes were weighed again after plaque collection. The weight of the collected plaque (in grams) was determined by subtracting the weight of the empty eppendorf tube from the weight of the tube with the collected plaque. The samples were stored at -4°X and transported to a culture lab within an hour to avoid using transport media.

1 ml saline was added to the eppendorf tube and vortexed for even distribution of plaque. This mixture was used as stock solution for serial dilutions. From the stock solution, 100 µl was transferred to a sterile test tube containing 900 µl of saline and vortexed to arrive at 1:10 dilution. Similar dilutions were prepared to obtain 10^0, 10^{-1}, 10^{-2} and 10^{-3} dilutions. 50 µl from each of the dilutions was plated onto the selective medium (Mitis Salivarius Bacitracin Agar) by spread plate method. After plating, the MSB agar plates were placed in the anaerobic jar and incubated at 37°C for 72 hours.

Colonies of *Streptococcus mutans* were identified based on the following morphologic characteristics, a) 0.5 mm raised convex undulated colonies b) light blue color with rough margins c) granular frosted glass appearance [6]. The colonies were confirmed by a catalase test (negative catalase reaction) and gram staining (gram positive cocci). Bacterial colonies were counted manually. The standard formula used for determining Colony Forming Units (CFU) was CFU/g = [Number of colonies * Dilution factor] / [Volume plated (in ml) * Amount of plaque (in g)].

After data collection at baseline, the subjects were allocated into three groups, Group A, B and C, by simple random sampling (lottery method). Group A was given Chlorhexidine mouth rinse; Group B was given Xylitol mouth rinse and Group C Probiotic mouth rinse. The participants and the investigator were blinded from the allocation sequence. After 14 days of using the mouth rinses, the same procedures were repeated and comparisons were made with baseline values.

Xylitol mouth rinse at 10% concentration was used. Studies have observed that xylitol at concentrations as low as 1% inhibited *S. mutans* growth [7]. Hence a concentration of 10% was expected to inhibit S. mutans growth. The mouth rinse was prepared by dissolving 1.5 g of xylitol powder (Loba Chemie, code 06512) in 15 ml of water. Probiotic mouth rinse was prepared by using a commercially available probiotic product (Sporolac Plus powder-1 g sachet containing not less than 1.5 billion cells of *Lactobacillus acidophilus*-R 0052, *Lactobacillus rhamnosus*-R 0011, *Bifidobacterium longum*-R 00175, *Bacillus coagulans*-SNZ 1969, *Saccharomyces boulardii*). Each sachet was dissolved in 15 ml of water in a measuring cup and was used as a mouth rinse. A commercially available chlorhexidine mouth rinse (Hexidine-0.2% Chlorhexidine gluconate) containing 0.2% chlorhexidine gluconate per 10 ml was used. 7.5 ml of the concentrate was diluted with equal amounts of water to make 15 ml that was used for rinsing. The subjects were asked to rinse their mouth once daily (at night) for 2 minutes, using 15 ml of mouth rinse. The intervention was carried out for a period of 14 days. Mouth rinsing was supervised during the study period by an assistant. A record was maintained to document regular usage of the mouth rinse and also to record any adverse effects occurring during the intervention period.

Fig. 1. Flow of participants throughout the study.
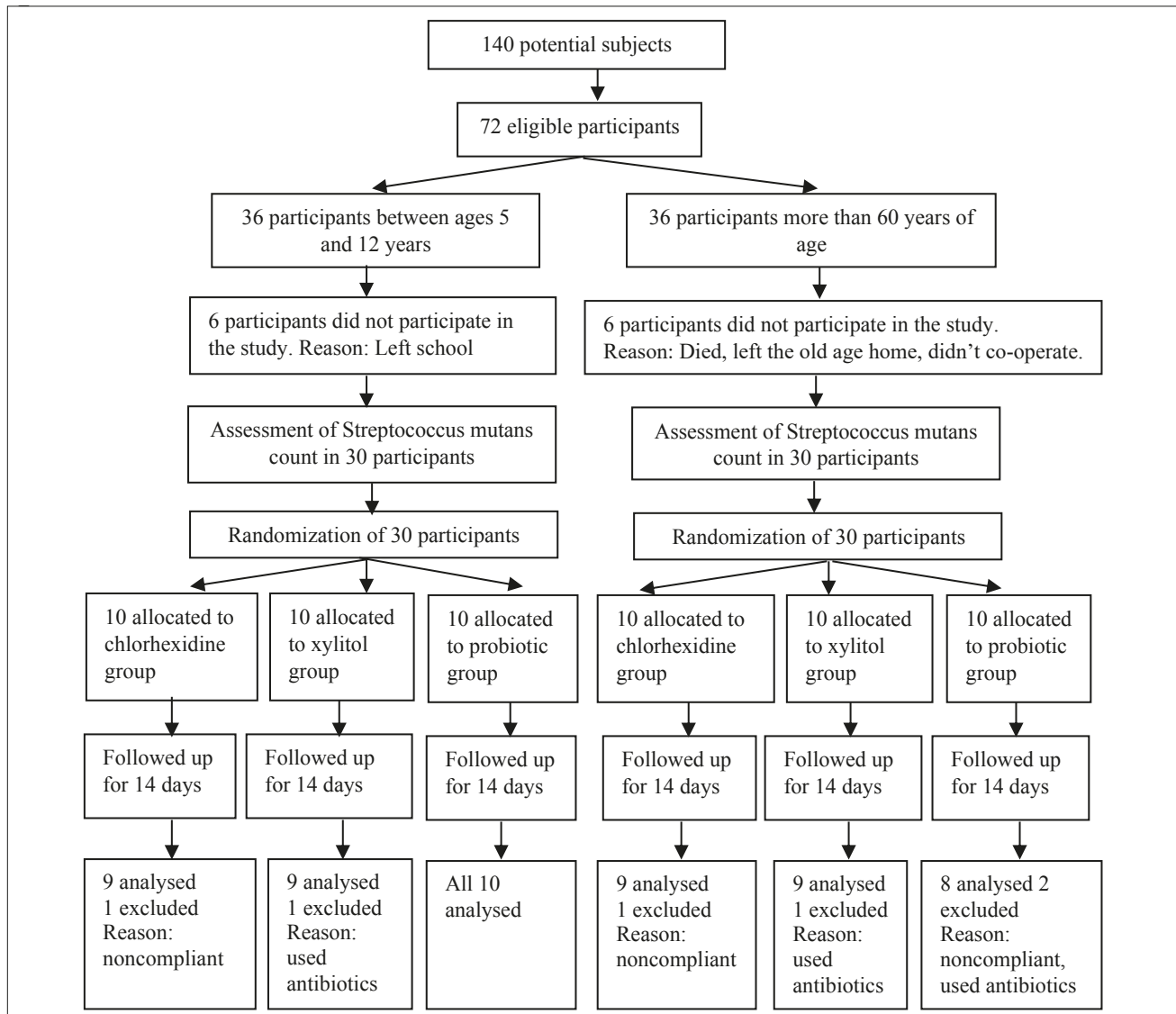
Data was analyzed using SPSS (Version 22.0; SPSS Inc., Chicago, IL, USA). Comparisons before and after interventions were done using Paired t Test. Comparisons between Chlorhexidine, probiotic and xylitol groups were done using ANOVA. Statistical significance was fixed at $p \leq 0.05$. Effect size estimates were obtained for pre and post intervention comparisons and also for comparison between groups.

Results

A total of 72 participants (36 children and 36 elderly) were recruited for the study of which 12 (6 children and 6 elderly) were excluded. The remaining (30 children and 30 elderly) were randomly divided into 3 groups with 10 participants per group. Amongst the participants chosen for the study 2 children and 4 elderly were lost to follow-up (Fig. 1).

Among children, significant reduction in *Streptococcus*

mutans counts were observed in all three groups (chlorhexidine: mean difference = 3.11 $\log_{10}$CFU/g; SD = 2.32; t = 3.28; p = 0.022); (xylitol: mean difference = 0.93 $\log_{10}$CFU/g; SD = 0.86; t = 2.64; p = 0.046); (probiotic: mean difference = 1.91 $\log_{10}$CFU/g; SD = 1.67; t = 3.02; p = 0.023). Likewise significant reduction in *Streptococcus mutans* counts were observed among elderly (chlorhexidine: mean difference = 2.23 $\log_{10}$CFU/g; SD = 1.08; t = 5.07; p = 0.004); (xylitol: mean difference = 1.39 $\log_{10}$CFU/g; SD = 0.81; t = 4.19; p = 0.009); (probiotic: mean difference = 1.61 $\log_{10}$CFU/g; SD = 0.92; t = 3.90; p = 0.018). The before and after comparisons also showed large effect sizes in all three groups in both children and elderly (Tabs. I, II).

There was no statistically significant difference in *Streptococcus mutans* count on comparing the 3 mouth rinses in children (F = 2.39; p = 0.123) and elderly (F = 1.26; p = 0.314). Medium effect size ($\omega^2 = 0.13$) was observed on comparing *Streptococcus mutans*

Tab. I. Comparison of Streptococcus mutans counts in children before and after using mouth rinses.

Mouth rinse used	Streptococcus mutans count in children log$_{10}$CFU/g (SD)			t	p-value	Hedges' g
	Before using mouth rinse	After using mouth rinse	Mean difference			
Chlorhexidine	6.43 (1.28)	3.33 (2.71)	3.11 (2.32)	3.28	0.022*	1.4
Xylitol	6.60 (0.95)	5.67 (1.12)	0.93 (0.86)	2.64	0.046*	0.8
Probiotic	6.88 (0.76)	4.97 (2.36)	1.91 (1.67)	3.02	0.023*	1.0

* Significant; SD: standard deviation; CFU/g: Colony Forming Units/ gram.

Tab. II. Comparison of Streptococcus mutans counts in elderly before and after using mouth rinses.

Mouth rinse used	Streptococcus mutans count in elderly log$_{10}$CFU/g (SD)			t	p-value	Hedges' g
	Before using mouth rinse	After using mouth rinse	Mean difference			
Chlorhexidine	7.13 (1.15)	4.91 (0.73)	2.23 (1.08)	5.07	0.004*	2.1
Xylitol	6.42 (1.10)	5.03 (0.47)	1.39 (0.81)	4.19	0.009*	1.5
Probiotic	7.16 (0.80)	5.55 (0.43)	1.61 (0.92)	3.90	0.018*	2.2

* Significant; SD: standard deviation; CFU/g: Colony Forming Units/ gram.

Tab. III. Comparison of mean reduction in Streptococcus mutans counts between three mouth rinses in children and elderly.

Study groups	Mouth rinse used		Mean difference in *Streptococcus mutans* reduction (I-J) log$_{10}$CFU/g	F	p-value	ω²
	(I)	(J)				
Children	Chlorhexidine	Xylitol	2.17	2.39	0.123	0.13
	Chlorhexidine	Probiotic	1.19			
	Xylitol	Probiotic	-0.98			
Elderly	Chlorhexidine	Xylitol	0.84	1.26	0.314	0.03
	Chlorhexidine	Probiotic	0.62			
	Xylitol	Probiotic	-0.22			

CFU/g: Colony Forming Units/ gram.

counts between the three mouth rinses among children while the effect size was small ($\omega^2 = 0.03$) on making similar comparisons among elderly (Tab. III).

Percentage reductions in *Streptococcus mutans* counts were greater with probiotic (28%) than xylitol (14%) among children while they were similar (probiotic: 23%, xylitol: 22%) among elderly (Fig. 2).

Discussion

The bisbiguanide chlorhexidine, which has been studied extensively for over 20 years, is currently the most potent chemotherapeutic agent against *Streptococcus mutans* and has been often used as a positive control for assessment of the anticariogenic potential of other agents [8]. Side effects reported with use of chlorhexidine provides opportunities to study the potency of other products in inhibiting *Streptococcus mutans* activity [4, 9-11]. In this background the study attempted to assess and compare the antimicrobial efficacies of chlorhexidine, xylitol and probiotic mouth rinses by assessment of *Streptococcus mutans* levels in plaque.

The methodology involved assessment of Streptococcus mutans levels in plaque among children and elderly who were at high risk for dental caries. Concentration of mouth rinses used were based on inhibitory concentrations as determined in previous studies [7, 12]. Plaque was used

as an alternative to saliva (due to variable secretion rates, duration of contact with the biofilm, etc.) as it has been proven to be a better indicator of microbial load in the oral cavity [13, 14]. The dropout rate in the study was around 7%. The main reason for dropout was systemic illnesses and antibiotic use.

We observed significant reduction in Streptococcus mutans counts after using the 3 mouth rinses for 14 days. The results were supported by studies conducted by Yousuf et al. [9], Jindal et al. [15], Priyadharshini et al. [10] and Laleman et al. [16] in case of probiotics and by El Salhy et al. [4] and Arunakul et al. [11] in case of xylitol. Large effect sizes were obtained in all the groups. Hence it may be inferred that use of any of the mouth rinses significantly reduces microbial load in plaque as compared to non-use.

Comparison of the mean reduction in *Streptococcus mutans* counts between groups gave insignificant results. Also the effect sizes observed between the different mouth rinses were trivial. Hence it may be inferred that the antimicrobial efficacy of three mouth rinses are comparable. Similar results were reported in another study [17] conducted among adults. Better compliance was however observed with probiotic and xylitol mouth rinses as compared to that of chlorhexidine mouth rinse (few complained of burning sensation on using chlorhexidine mouth rinse). Percentage reduction in *Streptococcus mutans* counts show that probiotics could be potentially more efficacious than xylitol among

Fig. 2. Percentage reduction in Streptococcus mutans counts in children and elderly after using the three mouth rinses.
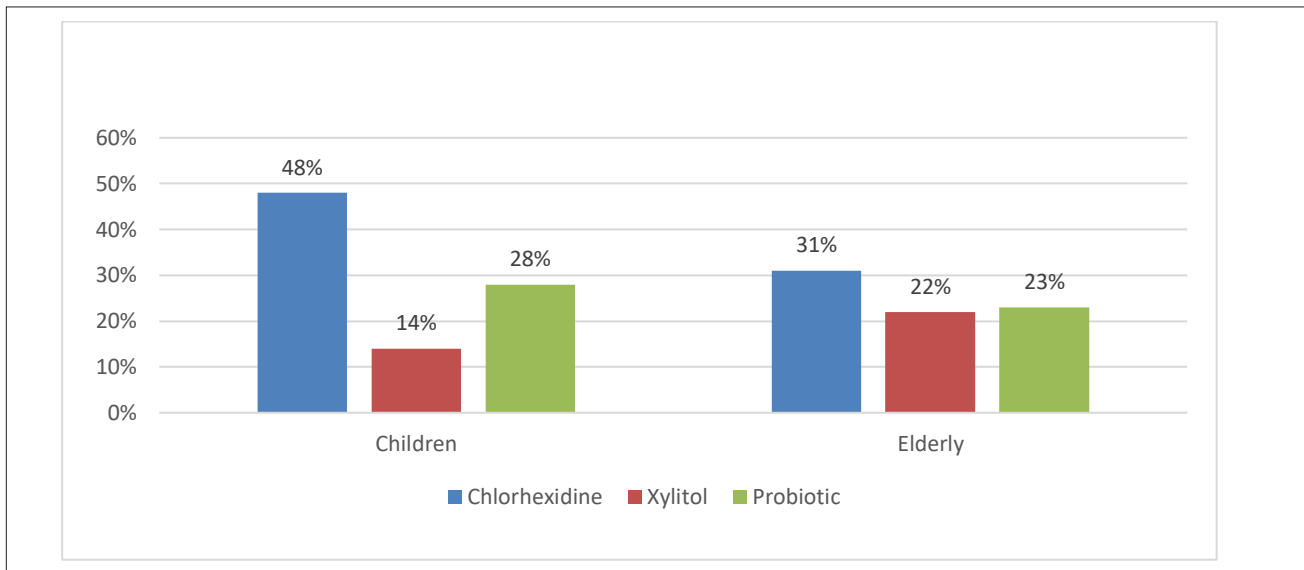
children while both had similar effects among elderly. There is scanty documenting of the effect of mouth rinses on compromised individuals (high caries risk) which may be considered a strength in our study. Antimicrobial efficacies of probiotics and xylitol mouth rinses especially among elderly population have not been compared till date. A major limitation was the small sample size. Also, the effect of the mouth rinses was tested on *Streptococcus mutans* alone. The fact that more than one microbe is involved in the caries process provides scope for further research.

Conclusion

Antimicrobial efficacy of xylitol and probiotic mouth rinses were comparable to that of chlorhexidine in both children and elderly. Probiotics could potentially be more efficacious than xylitol among children.

Acknowledgements

None.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

Concepts, design, definition of intellectual content: KNC, THM; Literature search, data acquisition, data analysis, manuscript preparation: KNC; Manuscript editing, manuscript review: THM, CBR.

References

[1] Prasanth M. Antimicrobial Efficacy of Different Toothpastes and Mouthrinses: An In Vitro Study. Dent Res J 2011;8:85-94.

[2] Barnett ML. The role of therapeutic antimicrobial mouthrinses in clinical practice: control of supragingival plaque and gingivitis. J Am Dent Assoc 2003;134:699-704. https://doi.org/10.14219/jada.archive.2003.0255

[3] van Rijkom HM, Truin GJ, van't Hof MA. A meta-analysis of clinical studies on the caries-inhibiting effect of chlorhexidine treatment. J Dent Res 1996;75:790-5. https://doi.org/10.1177/00220345960750020901

[4] ElSalhy M, Sayed Zahid I, Honkala E. Effects of xylitol mouthrinse on Streptococcus mutans. J Dent 2012;40:1151-4. https://doi.org/10.1016/j.jdent.2012.08.014

[5] Harini PM, Anegundi RT. Efficacy of a probiotic and chlorhexidine mouth rinses: A short-term clinical study. J Indian Soc Pedod Prev Dent 2010;28:179-82. https://doi.org/10.4103/0970-4388.73799

[6] Emilson CG. Prevalence of Streptococcus mutans with different colonial morphologies in human plaque and saliva. Scand J Dent Res 1983;91:26-32. https://doi.org/10.1111/j.1600-0722.1983.tb00771.x

[7] Söderling EM, Ekman TC, Taipale TJ. Growth inhibition of Streptococcus mutans with low xylitol concentrations. Curr Microbiol 2008;56:382-5. https://doi.org/10.1007/s00284-007-9076-6

[8] Emilson CG. Potential efficacy of chlorhexidine against mutans streptococci and human dental caries. J Dent Res 1994;73:682-91. https://doi.org/10.1177/00220345940730031401

[9] Yousuf A, Nagaraj A, Ganta S, Sidiq M, Pareek S, Vishnani P, Acharya S, Singh, K. Comparative evaluation of commercially available freeze dried powdered probiotics on mutans strepto-

cocci count: A randomized, double blind, clinical study. J Dent 2015;12:729-38.

[10] Priyadharshini VI, Ingle NA, Chaly PE, Reddy VC. Effectiveness of probiotic and chlorhexidine mouthrinses on reduction of plaque, gingivitis & mutans streptococci count in saliva-a clinical trial. J Indian Assoc Public Health Dent 2013;11:23-32.

[11] Arunakul M, Thaweboon B, Thaweboon S, Asvanund Y, Charoenchaikorn K. Efficacy of xylitol and fluoride mouthrinses on salivary Mutans streptococci. Asian Pac J Trop Biomed 2011;1:488-90. https://doi.org/10.1016/S2221-1691(11)60106-8

[12] Najafi MH, Taheri M, Mokhtari MR, Forouzanfar A, Farazi F, Mirzaee M, Ebrahiminik Z, Mehrara R. Comparative study of 0.2% and 0.12% digluconate chlorhexidine mouth rinses on the level of dental staining and gingival indices. Dent Res J 2012;9:305-8.

[13] Gibbons RJ, van Houte J. Dental caries. Annu Rev Med 1975;26:121-36. https://doi.org/10.1146/annurev.me.26.020175.001005

[14] Seki M, Karakama F, Terajima T, Ichikawa Y, Ozaki T, Yoshida S, Yamashita Y. Evaluation of mutans streptococci in plaque and saliva: correlation with caries development in preschool children. J Dent 2003;31:283-90. https://doi.org/10.1016/s0300-5712(03)00033-2

[15] Jindal G, Pandey RK, Agarwal J, Singh M. A comparative evaluation of probiotics on salivary mutans streptococci counts in Indian children. Eur Arch Paediatr Dent 2011;12:211-15. https://doi.org/10.1007/BF03262809

[16] Laleman I, Detailleur V, Slot DE, Slomka V, Quirynen M, Teughels W. Probiotics reduce mutans streptococci counts in humans: a systematic review and meta-analysis. Clin Oral Investig 2014;18:1539-52. https://doi.org/10.1007/s00784-014-1228-z

[17] Marya CM, Taneja P, Nagpal R, Marya V, Oberoi SS, Arora D. Efficacy of Chlorhexidine, Xylitol, and Chlorhexidine + Xylitol against Dental Plaque, Gingivitis, and Salivary Streptococcus mutans Load: A Randomised Controlled Trial. Oral Health Prev Dent 2017;15:529-36. https://doi.org/10.3290/j.ohpd.a39669

Correspondence: Krupa NC, Post Graduate Student, Department of Public Health Dentistry, JSS Dental College & Hospital (Constituent College), JSS Academy of Higher Education & Research, Sri Shivarathreeshwara Nagar, Mysuru- 570015, Karnataka, India. E-mail: kripa_555@yahoo.com

INFECTIOUS DISEASE

A surveillance for hepatitis C virus infection in northeastern, Thailand: a 10-year cohort

TANITA SUTTICHAIMONGKOL, CHITCHAI RATTANANUKROM, ARTHIT WONGSAENSOOK,
WATTANA SUKEEPAISARNJAROEN, KITTISAK SAWANYAWISUTH
Department of Medicine, Faculty of Medicine, Sleep Apnea Research Group, Khon Kaen University, Khon Kaen, Thailand

Summary

Introduction. *Hepatitis C virus (HCV) infection is an infection that may lead to cirrhosis and hepatocellular carcinoma. Most patients with HCV infection are asymptomatic. The previous study conducted in age group of 30-64 years and in two provinces. Additionally, most surveillance studies conducted in a point period; not longitudinally. This study aimed to evaluate HCV infection rate in all age groups in the northeastern, Thailand in a longitudinal fashion.*
Methods. *This was a surveillance study conducted in 20 provinces of northeastern, Thailand. The study period was between July 2010 and November 2019. During the surveillance, demographic data of participants were collected. HCV screening test was performed in each participant by using a rapid point-of-care assay. Rates of HCV infection in each province and in overall were calculated.*

Results. *During the surveillance period, there were 31,855 subjects who participated the project. Of those, 1,285 subjects (4.037%) were tested positive for HCV infection (Tab. 1). The HCV infection rate was highest in 2011 (8.98%): ranges 1.28 to 9.59%. The age group of over 50 years had 690 subjects with HCV infection (5.45%) out of 12,660 subjected tested in this age group. There was significant different among age groups (p < 0.001) and difference of age over 30 years and sex (p 0.043).*
Conclusions. *This longitudinal surveillance showed that HCV infection rates in northeastern, Thailand were varied across the provinces with the highest rate of 9.59%. The HCV infection should be aware in male with age over 30 years.*

Introduction

Hepatitis C virus (HCV) infection is an infection that may lead to cirrhosis and hepatocellular carcinoma. Its global prevalence was approximately 1.6% or 115 million persons [1]. HCV infection is much more common in adults compare with children (90%:10%) or 104 vs 11 million patients [1]. The prevalence rate of HCV infection is varied among countries with the highest rate in Egypt at 14.70%.

A serological surveillance in 310 Belgian forest workers showed seroprevalence of Lyme disease which determined the population at risk for those asymptomatic [2]. Patients with HCV infection are mostly asymptomatic. Therefore, community surveillance may be helpful to identify infected patients. In Thailand, endemic areas for HCV infection, found the prevalence of HCV infection was 6.9% reported in 2020 and previously reported to be 15.5% in 2017 [3, 4]. The previous study conducted in age group of 30-64 years and in two provinces [5]. Additionally, most surveillance studies conducted in a point period; not longitudinally. This study aimed to evaluate HCV infection rate in all age groups in the northeastern, Thailand in a longitudinal fashion.

Methods

This was a surveillance study conducted in 20 provinces of northeastern, Thailand. The study period was between July 2010 and November 2019. The surveillance was conducted in multiple areas in each province on a random basis. Each surveillance comprised of HCV screening and educational activities regarding HCV awareness by multidisciplinary health care team. The concept of awareness of HCV infection according to the world hepatitis alliance was implemented.

During the surveillance, demographic data of participants were collected. HCV screening test was performed in each participant by using a rapid point-of-care assay (One Step Rapid Test for HCV; HEALGEN, TX77401, USA). This rapid test has sensitivity and specificity for HCV infection of 98.1% and 98.9%, respectively. Those with test positive for HCV infection were referred for proper treatment. Rates of HCV infection in each province and in overall were calculated. Descriptive statistics were used to compute the differences by age group and sex. A p-value of less than 0.05 considered statistical significance.

The study protocol was approved by the ethic committee in human research, Khon Kaen University, Thailand (HE621134). An informed consent was not obtained due to retrospective data collection.

Results

During the surveillance period, there were 31,855 subjects who participated the project. Of those, 1,285 subjects

Tab. I. Details of hepatitis C virus (HCV) infection by the HCV surveillance project in northeastern, Thailand.

Year	Total tested for HCV (n)	Test positive for HCV (n)	Test positive for HCV (%)
2010	419	24	5.73
2011	846	76	8.98
2012	2,964	162	5.46
2013	4,761	253	5.31
2014	5,076	88	1.73
2015	3,139	66	2.10
2016	4,314	279	6.46
2017	4,811	255	5.30
2018	2,948	53	1.79
2019	2,577	29	1.12
Total	31,855	1,285	4.03

(4.037%) were tested positive for HCV infection (Tab. I). The HCV infection rate was highest in 2011 (8.98%). Among 20 provinces, Udonthani and Khon Kaen province were the top two provinces with the highest HCV infection rate at 9.59%, and 7.86% (Tab. II). The HCV infection ranged from 1.28 to 9.59%. The age group of over 50 years had 690 subjects with HCV infection (5.45%) out of 12,660 subjected tested in this age group (Tab. III). There was significant different among age groups ($p < 0.001$) and difference of age over 30 years and sex (p 0.043).

Discussion

As previously reported, estimation of disease is not enough for people who inject drugs [6]. HCV infection is estimated to be 52.3% of people with inject drug. This surveillance showed that average HCV infection rate in this 10-year cohort among 20 provinces. The highest rate of HCV infection was higher than the recent survey in 2020 (9.59% vs 6.9%) [3].

This study found similar findings with the previous study on HCV infection rate among age groups [4]. The seroprevalence was low at age group of under 35-40 years: ranges 0.0-3.5%. In this study, we found that the HCV infection rate was dramatically increasing from 0.0%-0.90% in age group below 30 years to 3.74% in age group of 31-40 years (Tab. III) which was also statistically significant ($p < 0.001$). However, this rising rate was not shown in both groups: only male sex (p = 0.043). The female group had quite steady rate from 0.0% to 0.77% (Tab. III). These findings may be explained from higher rate of people with inject drug in male patients. A study from northern, Thailand found that 81.8% out of 164 people with inject drug were male and 57.3% of subjects had first intravenous drug use at age below 24 years [7]. These finding may also explain why the HCV infection was significantly increased after age group of 30 years.

This study showed 10-year surveillance in almost provinces in the northeastern, Thailand. However, there are some limitations. First, participants in the project were those participated the world hepatitis alliance in that province. The total population tested for HCV infection was quite large at 31.855 persons though. And, the HCV test was the point of care test but it has a good sensitivity and specificity [8]. Some related conditions were not studied [9-16]. Finally, HCV genotypes were not evaluated.

Tab. II. Details of hepatitis C virus (HCV) infection by the HCV surveillance project in northeastern, Thailand categorized by province.

Provinces	Year tested	Total tested for HCV (n)	Test positive for HCV (n)	Test positive for HCV (%)
Beung kan	2017	603	25	6.51
Khon Kaen	2010-2019	4,913	386	7.86
Sakon Nakhon	2012-2014, 2017	981	26	2.65
Si sa ket	2014-2017	1,727	64	3.70
Burirum	2012-2016, 2018	1,647	58	3.52
Mukdaharn	2015, 2017	462	10	2.16
Amnat Chareon	2017	261	13	4.98
Maha Sarakam	2013, 2015-2017	1,459	56	3.84
Udonthani	2011-2017	1,365	131	9.59
Nong khai	2013-2019	4,332	118	2.72
Nakorn Panom	2015, 2017	766	22	2.87
Ubon Ratchathani	2013, 2014 2018	975	15	1.54
Nakorn Ratchasima	2012, 2014, 2016, 2019	1,571	43	2.74
Chaiyaphum	2013-2014, 2016, 2017	1,906	74	3.88
Surin	2011-2019	3,275	61	1.86
Kalasin	2013-2014, 2016-2019	2,151	114	5.29
Loei	2014, 2018	701	9	1.28
Roi-et	2012-2014, 2018	2,069	47	2.27
Yasothon	2018	304	7	2.30
Nong bua lumphu	2016, 2019	387	6	1.55
Total		31,855	1,285	4.03

Tab. III. Details of hepatitis B virus (HCV) infection by the HCV surveillance project in northeastern, Thailand categorized by age group and sex.

Age group	Total tested (n)	Test positive for HCV, n (%)	Test positive for HCV, n (%)	
			Male	Female
0-10	210	0	0	0
11-20	1,053	1 (0.9)	1 (0.09)	0 (0)
21-30	3,919	25 (0.65)	17 (0.43)	8 (0.2)
31-40	4,247	159 (3.74)	135 (3.18)	24 (0.56)
41-50	9,766	410 (4.19)	335 (3.43)	75 (0.77)
> 50-60	12,660	690 (5.45)	607 (4.79)	83 (0.66)
Total	31,855	1,285 (4.03)	1,095 (3.44)	190 (0.60)

Conclusions

This longitudinal surveillance showed that HCV infection rates in northeastern, Thailand were varied across the provinces with the highest rate of 9.59%. The HCV infection should be aware in male with age over 30 years.

Acknowledgements

None.

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

Tanita Suttichaimongkol: study design, data interpretation, writing a draft; Chitchai Rattananukrom: data interpretation, review a manuscript; Arthit Wongsaensook: data interpretation, review a manuscript; Wattana Sukeepaisarnjaroen: study design, data interpretation, review a manuscript; Kittisak Sawanyawisuth: study design, data interpretation, review a manuscript.

References

[1] Gower E, Estes C, Blach S, Razavi-Shearer K, Razavi H. Global epidemiology and genotype distribution of the hepatitis C virus infection. J Hepatol 2014;61(Supp 1):S45-57. https://doi.org/10.1016/j.jhep.2014.07.027

[2] De Keukeleire M, Robert A, Luyasu V, Kabamba B, Vanwambeke SO. Seroprevalence of Borrelia burgdorferi in Belgian forestry workers and associated risk factors. Parasit Vectors 2018;11:277. https://doi.org/10.1186/s13071-018-2860-2

[3] Wasitthankasem R, Pimsingh N, Treesun K, Posuwan N, Vichaiwattana P, Auphimai C, Thongpan I, Tongsima S, Vongpunsawad S, Poovorawan Y. Prevalence of Hepatitis C Virus in an endemic area of Thailand: burden assessment toward HCV elimination. Am J Trop Med Hyg 2020;103:175-82. https://doi.org/10.4269/ajtmh.19-0817

[4] Wasitthankasem R, Vichaiwattana P, Siripon N, Posuwan N, Auphimai C, Klinfueng S, Thanetkongtong N, Vuthitanachot V, Saiyatha S, Thongmai C, Sochoo S, Sukthong P, Poovorawan K, Tangkijvanich P, Poovorawan Y. Birth-cohort HCV screening target in Thailand to expand and optimize the national HCV screening for public health policy. PLoS One 2018;13:e0202991. https://doi.org/10.1371/journal.pone.0202991

[5] Wasitthankasem R, Vichaiwattana P, Siripon N, Posuwan N, Auphimai C, Klinfueng S, Thaneskongtong N, Vuthitanachot V, Saiyatha S, Thongmai C, Suwanpatoomlerd S, Sochoo S, Pongsuwan N, Poovorawan K, Tangkijvanich P, Vongpunsawad S, Poovorawan Y. Assessment of hepatitis C virus infection in two adjacent Thai provinces with drastically different seroprevalence. PLoS One 2017;12:e0177022. https://doi.org/10.1371/journal.pone.0177022

[6] Prins M, Bruneau J. Estimates are not enough: scaling-up interventions to improve the health of people who inject drugs. Lancet Glob Health 2017;5:e1162-3. https://doi.org/10.1016/S2214-109X(17)30430-8

[7] Prouté M, Le Coeur S, Tiv MH, Dub T, Jongpaijitsakul P, Ratnamhin A, Angkurawaranon C, Aramrattana A, Lallemant M. Risky injection practices and HCV awareness in Chiang Mai Province, Thailand: a respondent-driven sampling study of people who inject drugs. BMC Public Health 2020;20:1450. https://doi.org/10.1186/s12889-020-09549-w

[8] Charoentanyarak S, Sawunyavisuth B, Deepai S, Sawanyawisuth K. A point-of-care serum lactate level and mortality in adult sepsis patients: a community hospital setting. J Prim Care Community Health 2021;12:21501327211000233. https://doi.org/10.1177/21501327211000233

[9] Tongdee S, Sawunyavisuth B, Sukeepaisarnjaroen W, Boonsawat W, Khamsai S, Sawanyawisuth K. Clinical factors predictive of appropriate treatment in COPD: a community hospital setting. Drug Target Insights 2021;15:21-5. https://doi.org/10.33393/dti.2021.2291

[10] Martins EC, Silva MC, De Oliveira JA, Pereira R, Reis TM. Sleep disturbances in hepatitis C patients undergoing treatment: minisleep questionnaire as a screening tool. Minerva Gastroenterol Dietol 2015;61:125-30.

[11] Khamsai S, Chootrakool A, Limpawattana P, Chindaprasirt J, Sukeepaisarnjaroen W, Chotmongkol V, Silaruks S, Senthong V, Sittichanbuncha Y, Sawunyavisuth B, Sawanyawisuth K. Hypertensive crisis in patients with obstructive sleep apnea-induced hypertension. BMC Cardiovasc Disord 2021;21:310. https://doi.org/10.1186/s12872-021-02119-x

[12] Jeerasuwannakul B, Sawunyavisuth B, Khamsai S, Sawanyawisuth K. Prevalence and risk factors of proteinuria in patients with type 2 diabetes mellitus. Asia Pac J Sci Technol 2021;26:APST-26-04-02. https://doi.org/10.14456/apst.2021.32

[13] Soontornrungsun B, Khamsai S, Sawunyavisuth B, Limpawattana P, Chindaprasirt J, Senthong V, Chotmongkol V, Sawanyawisuth K. Obstructive sleep apnea in patients with diabetes less than 40 years of age. Diabetes Metab Syndr 2020;14:1859-63. https://doi.org/10.1016/j.dsx.2020.09.008

[14] Manasirisuk P, Chainirun N, Tiamkao S, Lertsinudom S, Phunikhom K, Sawunyavisuth B, Sawanyawisuth K. Efficacy of generic atorvastatin in a real-world setting. Clin Pharmacol 2021;13:45-51. https://doi.org/10.2147/CPAA.S285750

[15] Sawunyavisuth B. What are predictors for a continuous positive airway pressure machine purchasing in obstructive sleep apnea patients? Asia-Pac J Sci Technol 2018;23:APST-23-03-10. https://doi.org/10.14456/apst.2018.10

[16] Tomar A, Bhardwaj A, Choudhary A, Bhattacharyya D. Association of Obstructive Sleep Apnea with Nocturnal Hypoxemia in Metabolic-Associated Fatty Liver Disease Patients: A Cross-sectional Analysis of Record-based Data. J Family Med Prim Care 2021;10:3105-10. https://doi.org/10.4103/jfmpc.jfmpc_412_21

INFECTIOUS DISEASE

Decreased online hepatitis information seeking during the COVID-19 pandemic: an Infodemiology study

ERIC DAVID BICALDO ORNOS, OURLAD ALZEUS GADDI TANTENGCO
College of Medicine, University of the Philippines, Ermita, Manila, Philippines

Summary

Introduction. *Viral hepatitis remains a public health concern worldwide, mainly in developing countries. The public's awareness and interest in viral hepatitis information are essential in preventing and controlling this disease. Infodemiology has been used as a surrogate to assess the general understanding of disease and measure public awareness of health topics. However, this analysis has not been applied to viral hepatitis. Thus, this study investigated the online global search interest for viral hepatitis in the last decade, focusing on the period before and during the COVID-19 pandemic.*
Methods. *Global online search interest for hepatitis was measured using the Google Trends™ database. Spearman's rank-order correlation correlated country-specific characteristics and prevalence data with search volume index.*
Results. *There was a significant reduction in online search inter-est for hepatitis during the COVID-19 pandemic (2020). People searching for hepatitis are also interested in hepatitis vaccination. Search volume index is positively correlated with viral hepatitis and HIV prevalence and negatively correlated with GDP. This correlation mirrors the high burden of viral hepatitis in developing countries and their citizens' desire to be informed about this disease.*
Conclusions. *Our study found decreased global online interest in viral hepatitis during the pandemic. Moreover, higher online interest in hepatitis was observed in countries with a lower gross domestic product and high viral hepatitis and HIV prevalence. We demonstrated that global online interest toward viral hepatitis could be assessed through the infodemiologic approach using Google Trends™.*

Introduction

Viral hepatitis continues to be a significant public health problem. Five infectious disease agents cause most of viral hepatitis: hepatitis A virus (HAV), hepatitis B virus (HBV), hepatitis C virus (HCV), hepatitis D virus (HDV), and hepatitis E virus (HEV) [1]. It is estimated that around 2.3 billion people worldwide are infected by at least one of these viruses [2]. Viral hepatitis has caused about 1.34 million deaths annually due to chronic liver disease and primary liver cancer [2-4]. Moreover, while mortality from other infectious diseases such as tuberculosis and HIV decreases, deaths due to viral hepatitis increase over time [4]. Low rates of diagnosis, incomplete vaccination coverage and inaccessible drugs are some of the challenges of the efforts to eliminate viral hepatitis [5].
The COVID-19 pandemic compounded these challenges in eliminating viral hepatitis. COVID-19 has infected around 255 million and has caused around five million deaths [6]. But effects of COVID-19 extend beyond its morbidity and mortality. Management and care of non-COVID disease have significantly been affected [7-9]. Significant reductions in visits to viral hepatitis clinics have been observed in several countries, with some regions recording as much as a 95% decline [10, 11]. Indeed, concerns have been raised regarding the impact of the COVID-19 pandemic in the prevention, control, management, and elimination of viral hepatitis [12].
The internet is an essential source of health information for the public, especially during this COVID-19 pandemic, as evidenced by the increase in online searches for health-related information [13, 14]. The field of infodemiology aims to characterize the distribution and determinants of this digital information [15, 16]. Infodemiology has been utilized to assess the general understanding of disease and measure public awareness and interest in health-related topics [17-20]. Infodemiology has evaluated other infectious diseases such as tuberculosis and influenza [21-23]. However, global infodemiological studies on viral hepatitis are lacking. Thus, this research characterized the online global search interest for viral hepatitis in the last decade, focusing on the period before and during the pandemic. Factors associated with online interest for viral hepatitis were also presented in this study.

Methods

Global online search interest for hepatitis was measured using the Google Trends™ database, which provides reports on search trends in the unit of search volume index (SVI). This number represents the search interest relative to the highest point on the chart for the given region and

Tab. I. Comparison of search volume indices for hepatitis search terms in 2019 (before the pandemic) *vs* 2020 (during the pandemic).

Search Term	Median Annual SVI		p-value
	2019	2020	
Hepatitis	86	65	< 0.0001
Hepatitis A	72	40.5	< 0.0001
Hepatitis B	94.5	71.5	< 0.0001
Hepatitis C	64.5	44.5	< 0.0001
Hepatitis D	71.5	62	0.015
Hepatitis E	68	51	0.0008

Tab. II. Top associated search terms also used by people searching for "Hepatitis" (2011 to 2021).

Search Query	Search Volume Index
Hepatitis vaccine	100
Hepatitis symptoms	95
La hepatitis	90
What is hepatitis	75
Hepatitis B vaccine	62
Hepatitis virus	60
Liver hepatitis	58
Liver	57
Hepatitis treatment	50
Hepatitis test	46
Hepatitis a vaccine	43
Symptoms of hepatitis	40
Hepatitis sintomas	40
Viral hepatitis	37
Hepatitis C symptoms	34
HIV	34

time. An SVI of 100 corresponds to the peak popularity for the search term. A value of 50 means that the term is half as popular. A score of 0 means that there was insufficient data for the search term. SVI has been shown in previous studies to provide insight into population health-seeking behavior and collective health trends.

Google Trends™ was accessed by visiting http://trends.google.com. "Hepatitis", "Hepatitis A", "Hepatitis B", "Hepatitis C", "Hepatitis D", and "Hepatitis E". We limited the results to 10 years from the Search Query (October 11, 2011 - November 11, 2021). SVI and related queries were obtained from Google Trends™. The information about GDP allocation (% GDP), HIV prevalence, hepatitis prevalence was obtained from the World Bank [24] and CDA Foundation's Polaris Observatory [25].

Correlation between country-specific characteristics and SVI was determined using Spearman's rank-order correlation. A Spearman's correlation coefficient (ρ) with a p-value of less than 0.05 was considered significant. This statistical analysis was done using GraphPad Prism software version 7 (GraphPad Software, San Diego, CA).

Results

The SVI for hepatitis search terms for 2011-2021 is shown in Figure 1. There has been a gradual increase in the online interest for hepatitis in the last decade until early 2020 where a global online drop of interest can be appreciated. The declaration of the World Health Organization of COVID-19 as a pandemic coincided with this decline in online interest for hepatitis.

To determine if COVID-19 has affected global online interest in hepatitis, we compared the average SVI between 2019 (pre-pandemic) and 2020 (pandemic season. The SVI for "Hepatitis" (p < 0.0001), "Hepatitis A" (p < 0.0001), Hepatitis B (p < 0.0001), "Hepatitis C" (p < 0.0001), "Hepatitis D" (p = 0.015), and "Hepatitis E" (p = 0.0008) significantly decreased during the pandemic compared to the pre-pandemic season (Tab. I). People searching for hepatitis have also searched for vaccines for hepatitis, for hepatitis B and hepatitis B (Tab. II). People are also interested in knowing symptoms of hepatitis, the definition of viral hepatitis, hepatitis test, and hepatitis treatment. We also noted that "hiv" is related to online interest for hepatitis.

We also identified the countries where hepatitis search terms were most popular for the past ten years. For "Hepatitis", we found that the top countries were Ghana, Nigeria, Uganda, Ethiopia, and Venezuela (Fig. 2A). For the search term "Hepatitis A", the top countries were Venezuela, Guatemala, Peru, Honduras, and Ghana (Fig. 2B). On the other hand, Ghana, Uganda, Nigeria, Ethiopia, and Cameroon have more searches for "Hepatitis B" (Fig. 2C). "Hepatitis C" was most popular in Pakistan, Puerto Rico, the United States, Dominican Republic, and Ghana (Fig. 2D). The search term "Hepatitis D" yielded more results in Nigeria, Nepal, Kyrgyzstan, Pakistan, Bolivia (Fig. 2E). Lastly, "Hepatitis E" was more popular in Nigeria, Nepal, Kyrgyzstan, Pakistan, Bolivia (Fig. 2F).

We found that online interest in hepatitis was positively correlated with the prevalence of hepatitis B (p = 0.86), hepatitis D (p = 0.36), and hepatitis E (p = 0.80) (Tab. III). Furthermore, there was also a positive correlation between hepatitis B prevalence and SVI for "hepatitis B" (p = 0.23), the prevalence of hepatitis C with SVI for "hepatitis C" (p = 0.55), and prevalence of hepatitis E with SVI for "hepatitis E" (p = 0.08). We also found that GDP had a negative correlation with the search terms "hepatitis" (p < 0.0001), hepatitis A (0.0005), hepatitis B (< 0.0001), hepatitis C (0.02), hepatitis D (0.009), and hepatitis E (p = 0.008).

Due to the propensity of hepatitis to have coinfection with HIV, we also checked the correlation of HIV prevalence with online interest in hepatitis. HIV

Fig. 1. Search volume indices for the terms "Hepatitis", "Hepatitis A", "Hepatitis B", "Hepatitis C", "Hepatitis D", and "Hepatitis E" in the year 2011 to 2021. SVIs were calculated separately for each search term such that SVIs are normalized within each term.
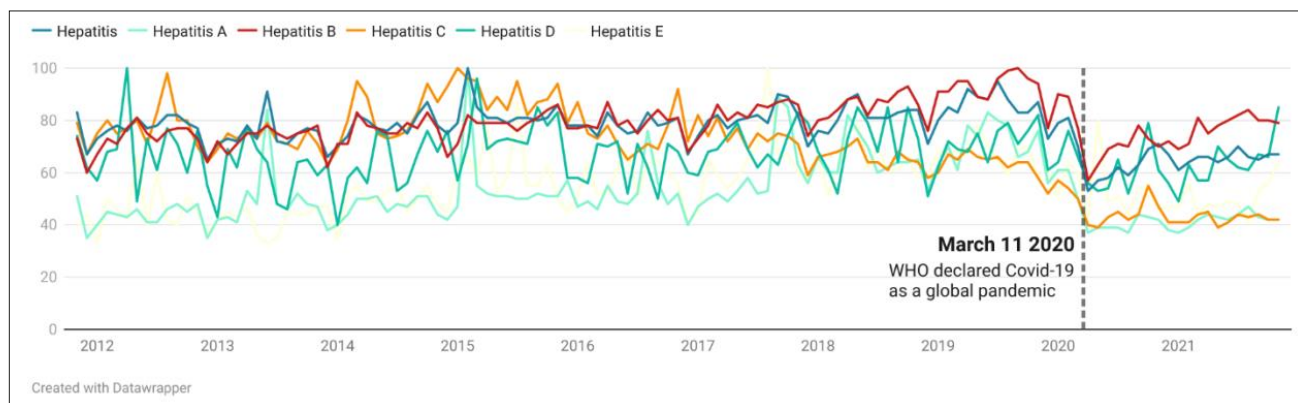

Fig. 2. Search frequencies for "Hepatitis" (A), "Hepatitis A" (B), "Hepatitis B" (C), "Hepatitis C" (D), "Hepatitis D" (E), and "Hepatitis E" (F) by country in the year 2011 to 2021. The color intensity represents the percentage of searches for the leading search term in a particular region. Search term popularity is relative to the total number of Google searches performed at a specific time, in a specific location.
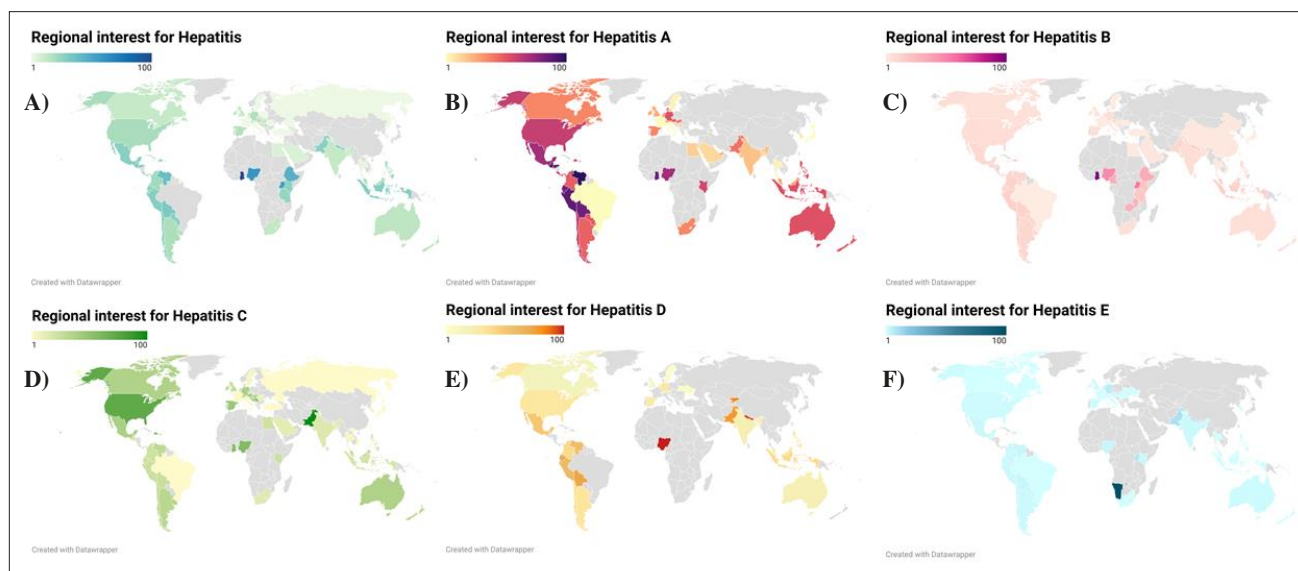
prevalence was positively correlated with the SVI for "hepatitis" (p = 0.007), hepatitis A (p = 0.0305), and hepatitis B (0.007).

Discussion

This study showed that the online interest in hepatitis has gradually increased in the last decade. However, we observed a significant decrease in the global online interest for hepatitis during the COVID-19 pandemic. The worldwide reduction of online interest in hepatitis parallels the decline of public interest in non-COVID diseases, including cancer, obesity, rheumatic, and ophthalmologic diseases during the pandemic [26-30]. Management of non-COVID diseases has been affected by COVID-19. Emergency department visits and hospital admissions of non-COVID illnesses have decreased during the early months of the pandemic. A decrease in the public interest for viral hepatitis is evident in online search behavior and decline in physical visits in the viral hepatitis clinics during the pandemic [10, 11]. This decrease in online interest might hinder efforts to curb the threat of viral hepatitis.

We noted that those searching for hepatitis also searched for hepatitis vaccines. This is good because the public is also aware of the availability of vaccines to prevent hepatitis. Vaccination is part of WHO's core interventions to eliminate hepatitis in 2030 [4]. Global coverage of the hepatitis B vaccine has steadily increased since the 1990s and has reached 85% coverage in 2019. A slight dip was noted in 2020, with 83% coverage for the Hep B vaccine [31]. Overall global basic vaccination coverage significantly dropped in 2020 [31, 32]. Reduced vaccination has been affected by vaccine supply, vaccine hesitancy, and change in health-seeking behavior [32, 33]. Our results showing decreased online interest in hepatitis is consistent with decreased health-

Tab. III. Correlations between SVIs for hepatitis search terms and country specific characteristics.

Country-specific characteristics	Search Terms	r	P-value
Hepatitis B prevalence	"Hepatitis"	0.023	0.859
	"Hepatitis B"	0.149	0.235
Hepatitis C prevalence	"Hepatitis"	-0.116	0.393
	"Hepatitis C"	0.088	0.548
Hepatitis D prevalence	"Hepatitis"	0.250	0.364
	"Hepatitis D"	-0.100	0.950
Hepatitis E prevalence	"Hepatitis"	0.040	0.800
	"Hepatitis E"	0.320	0.085
GDP (current US$)	"Hepatitis"	-0.525	< 0.0001
	"Hepatitis A"	-0.459	< 0.001
	"Hepatitis B"	-0.540	< 0.0001
	"Hepatitis C"	-0.302	0.021
	"Hepatitis D"	-0.482	0.009
	"Hepatitis E"	-0.370	0.008
Prevalence HIV	"Hepatitis"	0.383	0.007
	"Hepatitis A"	0.343	0.031
	"Hepatitis B"	0.460	< 0.001
	"Hepatitis C"	0.035	0.829
	"Hepatitis D"	0.084	0.709
	"Hepatitis E"	0.250	0.130

seeking behavior for hepatitis. Reduced vaccination coverage might increase the global burden of chronic hepatitis and hinder the progress towards hepatitis elimination [32].

Several developing countries are represented in the top countries searching for hepatitis online. Furthermore, our results showed that GDP is negatively correlated with the online search interest for hepatitis. The high online interest for hepatitis among developing countries might be due to the high prevalence of hepatitis in these countries [2, 4]. This was confirmed in our correlation analysis, which showed that online interest in global hepatitis was positively correlated with the prevalence of viral hepatitis. This is consistent with the positive relationship between online search interest via Google Trends and the prevalence of infectious diseases [34]. Moreover, in developing countries with high hepatitis prevalence, numerous public health programs, and health education campaigns are conducted by several NGOs [35]. These campaigns might have increased the public's awareness of the disease and might have affected their online health-seeking behavior.

Our results also showed that people searching for viral hepatitis are also interested in HIV. We also found that HIV prevalence is positively correlated with online interest for hepatitis search terms. This reflects the close relationship between hepatitis and HIV infection. Hepatitis B and hepatitis C share similar modes of transmission with HIV [36]. Furthermore, viral hepatitis and HIV have a propensity for coinfection, which results in significant morbidity and mortality [36, 37].

This study has several limitations. Although the most popular search tool, Google is not the sole web search engine available, and its penetration to different countries may vary. Also, the data is subjected to the inherent nonrepresentative sampling bias in Google search trends. The data used in this study was collected from people with internet access. This might have excluded lower-income groups and areas with issues on freedom of speech. We have limited our search to the English language. Moreover, this might have omitted searches using other languages used in other parts of the world. Despite these limitations, this study still analyzed the pattern and geographical distribution of global online interest in viral hepatitis.

Conclusion

Our study, which utilized Google Trend analysis, showed a significant drop in the online interest for hepatitis during the COVID-19 pandemic. The decrease in online interest is consistent with the decreased health-seeking behavior for hepatitis disease during the pandemic. We noted that people searching for hepatitis are also interested in the hepatitis vaccine, a cornerstone for hepatitis control, prevention, and elimination. However, vaccination efforts have been hampered during the COVID-19 pandemic. Decreased health-seeking behavior for hepatitis might be one of the factors for reduced vaccination. Search volume index is positively correlated with viral hepatitis and HIV prevalence and is negatively correlated with GDP. This mirrors the high burden of viral hepatitis and HIV disease in developing countries and the desire of their citizens to know more about these diseases. Overall, our study has shown that infodemiologic approach through Google Trends™ can be used as a tool to assess the online interest of people toward viral hepatitis.

Acknowledgements

Funding

Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author's contribution

Conceptualization: EDBO, OAGT. Data Processing: EDBO. Data Analysis: EDBO, OAGT. Writing original draft: EDBO. Writing-review and editing: OAGT.

References

[1] Castaneda D, Gonzalez AJ, Alomari M, Tandon K, Zervos XB. From hepatitis A to E: A critical review of viral hepatitis. World J Gastroenterol 2021;27:1691-715. https://doi.org/10.3748/wjg.v27.i16.1691

[2] Jefferies M, Rauff B, Rashid H, Lam T, Rafiq S. Update on global epidemiology of viral hepatitis and preventive strategies. World J Clin Cases 2018;6:589-99. https://doi.org/10.12998/wjcc.v6.i13.589

[3] Stanaway JD, Flaxman AD, Naghavi M, Fitzmaurice C, Vos T, Abubakar I, Abu-Raddad LJ, Assadi R, Bhala N, Cowie B, Forouzanfour MH, Groeger J, Hanafiah KM, Jacobsen KH, James SL, MacLachlan J, Malekzadeh R, Martin NK, Mokdad AA, Mokdad AH, Murray CJL, Plass D, Rana S, Rein DB, Richardus JH, Sanabria J, Saylan M, Shahraz S, So S, Vlassov V v., Weiderpass E, Wiersma ST, Younis M, Yu C, el Sayed Zaki M, Cooke GS. The global burden of viral hepatitis from 1990 to 2013: findings from the Global Burden of Disease Study 2013. Lancet 2016;388:1081-8. https://doi.org/10.1016/S0140-6736(16)30579-7

[4] World Health Organization. Global hepatitis report 2017. Geneva: World Health Organization; 2017. Available at: https://apps.who.int/iris/bitstream/handle/10665/255016/9789?sequence=1 (Accessed on: January 27, 2022).

[5] Waheed Y, Siddiq M, Jamil Z, Najmi MH. Hepatitis elimination by 2030: Progress and challenges. World J Gastroenterol 2018;24:4959-61. https://doi.org/10.3748/wjg.v24.i44.4959

[6] Dong E, Du H, Gardner L. An interactive web-based dashboard to track COVID-19 in real time. Lancet Infect Dis 2020;20:533-4. https://doi.org/10.1016/S1473-3099(20)30120-1

[7] Barach P, Fisher SD, Adams MJ, Burstein GR, Brophy PD, Kuo DZ, Lipshultz SE. Disruption of healthcare: Will the COVID pandemic worsen non-COVID outcomes and disease outbreaks? Prog PediatR Cardiol 2020;59. https://doi.org/10.1016/j.ppedcard.2020.101254

[8] Christey G, Amey J, Campbell A, Smith A. Variation in volumes and characteristics of trauma patients admitted to a level one trauma centre during national level 4 lockdown for COVID-19 in New Zealand. NZMJ. 2020;133:1513. Available from: https://journal.nzma.org.nz/journal-articles/variation-in-volumes-and-characteristics-of-trauma-patients-admitted-to-a-level-one-trauma-centre-during-national-level-4-lockdown-for-covid-19-in-new-zealand (Accessed on: January 25, 2022).

[9] June M, Hartnett KP, Kite-Powell A, Devies J, Coletta MA, Boehmer TK, Adjemian J, Gundlapalli AY, National; Surveillance S. Impact of the COVID-19 Pandemic on Emergency Department Visits - United States, January 1, 2019-May 30, 2020. 2019;69. Available from: https://www.hhs.gov/about/agencies/iea/regional-offices/index.html (Accessed on: January 28, 2022).

[10] Mustafa ZU, Kow CS, Hasan SS. Effect of COVID-19 on viral hepatitis services in Pakistan. Lancet Gastroenterol Hepatol 2021;6:163-4. https://doi.org/10.1016/S2468-1253(21)00006-6

[11] Uwishema O, Adanur I, Babatunde AO, Hasan MM, Elmahi OKO, Olajumoke KB, Aborode AT, Emmanuella N, Costa AC dos S, Ahmad S, Essar MY. Viral infections amidst COVID-19 in Africa: Implications and recommendations. J Med Virol 2021;93:6798-802. https://doi.org/10.1002/jmv.27211

[12] Wingrove C, Ferrier L, James C, Wang S. The impact of COVID-19 on hepatitis elimination. Lancet Gastroenterol Hepatol 2020;5:792-4. https://doi.org/10.1016/S2468-1253(20)30238-7

[13] Du H, Yang J, King RB, Yang L, Chi P. COVID-19 Increases Online Searches for Emotional and Health-Related Terms. Appl Psychol: Health Well-Being 2020;12:1039-53. https://doi.org/10.1111/aphw.12237

[14] Starcevic V, Schimmenti A, Billieux J, Berle D. Cyberchondria in the time of the COVID-19 pandemic. Hum Behav Emerg Technol 2021;3:53-62. https://doi.org/10.1002/hbe2.233

[15] Eysenbach G. Infodemiology and infoveillance: Framework for an emerging set of public health informatics methods to analyze search, communication and publication behavior on the internet. J Med Internet Res 2009;11. https://doi.org/10.2196/jmir.1157

[16] Mavragani A. Infodemiology and infoveillance: Scoping review. J Med Internet Res 2020;22:e16206. https://doi.org/10.2196/16206

[17] Schootman M, Toor A, Cavazos-Rehg P, Jeffe DB, McQueen A, Eberth J, Davidson NO. The utility of Google Trends data to examine interest in cancer screening. BMJ Open 2015;5:e006678. https://doi.org/10.1136/bmjopen-2014-006678

[18] Foroughi F, Lam AKY, Lim MSC, Saremi N, Ahmadvand A. "googling" for cancer: An infodemiological assessment of online search interests in Australia, Canada, New Zealand, the United Kingdom, and the United States. JMIR Cancer 2016;2. https://doi.org/10.2196/cancer.5212

[19] Berlinberg EJ, Deiner MS, Porco TC, Acharya NR. Monitoring interest in herpes zoster vaccination: Analysis of google search data. JMIR Public Health Surveill 2018;4. https://doi.org/10.2196/10180

[20] Krishnan N, Anand S, Sandlas G. Evaluating the impact of COVID-19 pandemic on public interest in minimally invasive surgery: An infodemiology study using Google Trends. Cureus 2021;13. https://doi.org/10.7759/cureus.18848

[21] Ginsberg J, Mohebbi MH, Patel RS, Brammer L, Smolinski MS, Brilliant L. Detecting influenza epidemics using search engine query data. Nature 2009;457:1012-4. https://doi.org/10.1038/nature07634

[22] Fudholi DH, Fikri K. Towards an effective tuberculosis surveillance in Indonesia through Google Trends. Kinetik 2020;5:299-308. https://doi.org/10.22219/kinetik.v5i4.1114

[23] Frauenfeld L, Nann D, Sulyok Z, Feng YS, Sulyok M. Forecasting tuberculosis using diabetes-related Google Trends data. Pathog Globa Health 2020;114:236-41. https://doi.org/10.1080/20477724.2020.1767854

[24] The World Bank. World Bank Open Data. 2020. Available at: https://data.worldbank.org/. (Accessed on January 15, 2022).

[25] CDA Foundation. CDA Foundation's Polaris Observatory. 2021. Available at: https://cdafound.org/polaris-countries-dashboard/ (Accessed on January 15, 2022).

[26] Adelhoefer S, Berning P, Solomon SB, Maybody M, Whelton SP, Blaha MJ, Dzaye O. Decreased public pursuit of cancer-related information during the COVID-19 pandemic in the United States. Cancer Causes Control 2021;32:577-85. https://doi.org/10.1007/s10552-021-01409-1

[27] Snyder A, Jang S, Nazari IS, Som A, Flores EJ, Succi MD, Little BP. Google search volume trends for cancer screening terms during the COVID-19 pandemic. J Med Screen 2021;28:210-2. https://doi.org/10.1177/0969141321999426

[28] Kardeş S, Kuzu AS, Raiker R, Pakhchanian H, Karagülle M. Public interest in rheumatic diseases and rheumatologist in the United States during the COVID-19 pandemic: evidence from Google Trends. Rheumatol Int 2021;41:329-34. https://doi.org/10.1007/s00296-020-04728-9

[29] Gupta R, Pakhchanian H, Raiker R, Asahi M, Raparla N, Belyea D. Public Interest in Refractive Diseases and Treatments During the COVID-19 Pandemic: A Google Trends Analysis. Cureus 2021;13:e17207. https://doi.org/10.7759/cureus.17207

[30] Tantengco OAG. Decreased global online interest in obesity from 2004 to 2021: An infodemiology study. Obes Med 2022;30:e100389. https://doi.org/10.1016/j.obmed.2022.100389

[31] World Health Organization. Hepatitis B vaccination coverage. Available at: https://www.who.int/data/gho/indicator-metadata-registry/imr-details/95 (Accessed on January 17, 2022).

[32] Pley CM, McNaughton AL, Matthews PC, Lourenço J. The global impact of the COVID-19 pandemic on the prevention, diagnosis and treatment of hepatitis B virus (HBV) infection. BMJ Global Health 2021;6. https://doi.org/10.1136/bmjgh-2020-004275

[33] Gupta N, Desalegn H, Ocama P, Lacombe K, Njouom R, Afihene M, Cunha L, Spearman CW, Sonderup MW, Kateera F. Converging pandemics: implications of COVID-19 for the viral hepatitis response in sub-Saharan Africa. Lancet Gastroenterol Hepatol 2020;5:634-6. https://doi.org/10.1016/S2468-1253(20)30155-2

[34] Mavragani A, Ochoa G. Infoveillance of infectious diseases in USA: STDs, tuberculosis, and hepatitis. J Big Data 2018;5. https://doi.org/10.1186/s40537-018-0140-9

[35] Eze Anugwom E. Introductory chapter: public health afflictions and challenges in the developing world. In: Public Health in Developing Countries - Challenges and Opportunities. IntechOpen 2020. https://doi.org/10.5772/intechopen.93145

[36] Lacombe K, Rockstroh J. HIV and viral hepatitis coinfections: Advances and challenges. Gut 2012;61:i47-58. https://doi.org/10.1136/gutjnl-2012-302062

[37] Matthews PC, Geretti AM, Goulder PJR, Klenerman P. Epidemiology and impact of HIV coinfection with Hepatitis B and Hepatitis C viruses in Sub-Saharan Africa. J Clin Virol 2014,61:20-33. https://doi.org/10.1016/j.jcv.2014.05.018

Prediction the survival of patients with breast cancer using random survival forests for competing risks

ROYA NAJAFI-VOSOUGH[1], JAVAD FARADMAL[1,2], LEILI TAPAK[1,2], BEHNAZ ALAFCHI[1], KHADIJEH NAJAFI-GHOBADI[1], TAYEB MOHAMMADI[1]

[1] Department of Biostatistics and Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran; [2] Modeling of Noncommunicable Diseases Research Center, Hamadan University of Medical Sciences, Hamadan, Iran

Summary

Objectives. *Breast cancer (BC) is the most common cause of cancer death in Iranian women. Sometimes death from other causes precludes the event of interest and makes the analysis complicated. The purpose of this study was to identify important prognostic factors associated with survival duration among patients with BC using random survival forests (RSF) model in presence of competing risks. Also, its performance was compared with cause-specific hazard model.*

Methods. *This retrospective cohort study assessed 222 patients with BC who were admitted to Ayatollah Khansari hospital in Arak, a major industrial city and the capital of Markazi province in Iran. The cause-specific Cox proportional hazards and RSF models were employed to determine the important risk factors for survival of the patients.*

Results. *The mean and median survival duration of the patients were 90.71 (95%CI: 83.8-97.6) and 100.73 (95%CI: 89.2-121.5) months, respectively. The cause-specific model indicated that type of surgery and HER2 had statistically significant effects on the risk of death of BC. Moreover, the RSF model identified that HER2 was the most important variable for the event of interest.*

Conclusion. *According to the results of this study, the performance of the RSF model was better than the cause-specific hazard model. Moreover, HER2 was the most important variable for death of BC in both of the models.*

Introduction

Cancer is known as the most leading and the second cause of death in developed and developing countries, respectively. Annually, 7.6 million deaths occur due to cancer, worldwide. Among women, breast cancer (BC) is the most frequent cancer. It is estimated that BC accounts for about 23% of all new cases of cancer [1, 2]. About 27.2% of all new cancer diagnosed cases and about 19% of all deaths due to cancer among Asian women are related to BC. In Iran as a developing country, BC was showed an increasing trend during 1965-2000, and the rank of its prevalence changed from the second most to the first most frequent malignancy [1]. Annually, about 8090 new cases were diagnosed and more than 1300 of them died because of BC. Hence, it is an important public health problem in Iran. Some type of surgery to remove the tumor is the main treatment for women with BC. According to previous studies, the number of involved lymph nodes and tumor size are the most important prognostic factors in BC [3].

Survival analysis is used to analyze the time-to-event data. Cox proportional hazards (PH) regression model is the most common model to analyze survival data. The basic assumption of this model is the proportionality of hazards which is determinative. In practice, the explanatory variables may not satisfy the PH assumption or they may be correlated [4]. Moreover, when data typically has a high rate of censoring, the performance of traditional models such as the Cox PH regression model will not be reliable [5]. In some studies, all covariates are measured at the baseline and none of them are time-varying covariates, but their effects may change over time. So, more flexible models are needed. Moreover, in some situations, a patient only can experience one of the different types of possible events over the follow-up. The probabilities of these events are referred to as competing risks and the competing risks models are the best choice to analyze such data. The random survival forest (RSF) is appropriate to analyze right-censored survival data and also is free of model assumptions. The most important feature of a random forest is its good performance in determining the importance of each variable in predicting the response variable [6]. The aim of this study was to identify important prognostic factors associated with survival among patients with BC using RSF in the presence of competing events and compare its performance with the cause-specific hazard regression model.

Materials and methods

DATA COLLECTION

The data of this study are related to patients with BC who were admitted to Ayatollah Khansari hospital in Arak, a major industrial city and the capital of Markazi

province in Iran, during 2012-2015. Due to the lack of electronic medical records, data are extracted from the paper-based medical records into the pre-prepared checklist. The study entrance criteria were female patients with diagnosed BC that had more than 18 years old. Also, patients who had many missing data in their clinical and demographic records were excluded. The gathered data included age at diagnosis, type of surgery (Radical mastectomy, Segmental mastectomy, Simple mastectomy), number of involved lymph nodes (less than 2, 3-6, and more than 7), estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) status, family history of BC, stage of the tumor, type of tumor (Ductal, Lobular, Medullar), and tumor size (less than 2, 2-5, and greater than 5 cm), based on the American Joint Committee on Cancer classification [7].

Survival time was calculated as the number of months from diagnosis until death due to BC, other causes, or the end of the study. The event of interest was death due to BC and death due to other causes were the competing event. Patients who withdrew, lost-to-follow-up, or did not die up to the end of the study were considered censored.

STATISTICAL ANALYSIS

Describing survival

When there are competing risks, the Kaplan-Meier (KM) may not be very informative to describe survival probability because it is based on an independent assumption about competing risks that cannot be verified. So, the cumulative incidence function that can be used for different causes of failure, was employed for the statistical description of survival [8].

Cause-specific hazard regression model

The cause-specific hazard regression model can be fit with Cox regression by treating failures from the cause of interest as events and failure from other causes as censored observation. The adjusted and unadjusted effects of risk factors on cause-specific hazards were estimated using the Cox PH regression model [4].

Random survival forests model for competing risks

RSF is a survival model based on the tree method for the analysis of right-censored survival data. To develop and validate the RSF, data were divided to learning (63% of data to develop the model) and test (37 of data to check the data validity) parts. Totally, 1000 bootstraps samples were constructed from the learning part. Then a competing risk tree for each bootstrap sample was grown. To split each node of a tree, a subset of p variables was selected randomly, and the node was split using the candidate variable that maximizes a competing risk splitting rule. The tree is grown to full size under the constraint that a terminal node should have no less than unique cases. Then we calculate cumulative incidence functions and cumulative cause-specific hazards for all events (Death of BC, Death of other causes) for each

tree. Eventually, take the average of each estimator over all trees to obtain its ensemble [9]. In RSF, variables can be selected by filtering on the basis of their variable importance (VIMP). The VIMP for x, a risk factor, is the prediction error for the original ensemble subtracted from the prediction error for the new ensemble obtained using randomizing x assignments [9, 10]. A large positive VIMP indicates a potentially predictive variable whereas zero or negative values identify non-predictive variables to be filtered [9].

Comparison and computational software

We used the integrated Brier score (IBS) to compare the efficiency of the RSF for competing risks and the cause-specific hazard regression model [11].

Statistical analysis was performed using R packages' "randomForestSRC" [12], "riskRegression" [13], "cmprsk" [14] and "pec" [11], version 3.3.3 (The R Foundation for Statistical Computing, Vienna, Austria; http://www.r-project.org).

ETHICS STATEMENT

This study was approved by the Research Ethics Committee of Hamadan University (No. IR.UMSHA. REC. 1396.738). We received informed written consentfrom all participants and for illiterate people and participants under the age of 16 from legally authorized parents/representatives.

Results

The study involved 222 patients with BC. Approximately 26% (n = 58) of patients experienced death due to BC, 13% (n = 29) experienced death due to other causes and the remaining were right censored. The mean and median survival time of the patients were 90.71 (95% CI: 83.82-97.60) and 100.73 (95% CI: 89.16-121.46) months, respectively. The mean (SD) age at diagnosis was 46.53 (10.21) years. The baseline characteristics of patients with BC are given in Table I.

Figure 1 shows that non-parametric estimates of cumulative incidence functions (CIF) for death due to BC and other causes. As can be seen in this figure, cumulative incidence probability for death of BC is higher than the competing event of death.

The results of cause-specific model are shown in Table II. According to the results, type of surgery (Segmental Mastectomy) and HER2 were statistically significant for the event of interest (death due to BC) (P < 0.05). So, the risk of death for a patient who has segmental mastectomy was 2.98 times larger compared with a patient with radical mastectomy. Moreover, the risk of death in patients with HER2 positive was higher than patients with HER2 negative.

Results from the event-specific variable importance (VIMP) for all used variables in RSF are given in Table III. The event-specific VIMP were obtained using log-rank splitting. An important variable is known if the value of its VIMP be more than 0.002 [15]. According to Table

Tab. I. Baseline characteristics of patients with breast cancer.

Variables	Death of BC N (%)	Death of other causes N (%)	Censored N (%)	Total N (%)
Type of surgery				
Radical Mastectomy	49 (84.5)	26 (89.7)	109 (80.7)	184 (82.9)
Segmental Mastectomy	5 (8.6)	1 (3.4)	9 (6.7)	15 (6.8)
Simple Mastectomy	4 (6.9)	2 (6.9)	17 (12.6)	23 (10.4)
Number of involved lymph nodes				
≤ 2	34 (58.6)	13 (44.8)	80 (59.3)	127 (57.2)
3-6	14 (24.1)	7 (24.1)	5 (3.7)	33 (14.9)
≥ 7	10 (17.2)	9 (31.0)	28 (20.7)	47 (21.2)
ER				
Positive	26 (44.8)	15 (51.7)	66 (48.9)	107 (48.2)
Negative	32 (55.2)	14 (48.3)	69 (51.1)	115 (51.8)
PR				
Positive	23 (39.7)	14 (48.3)	57 (42.2)	94 (42.3)
Negative	35 (60.3)	15 (51.7)	78 (51.1)	128 (57.7)
HER2				
Positive	44 (75.9)	17 (58.6)	68 (50.4)	129 (58.1)
Negative	14 (24.1)	12 (41.4)	67 (49.6)	93 (41.9)
Family history of BC				
No	6 (10.3)	2 (6.9)	8 (5.9)	16 (7.2)
Yes	52 (89.7)	27 (93.1)	127 (94.1)	206 (92.8)
Stage of disease				
I	30 (51.7)	11 (39.7)	79 (58.5)	120 (54.1)
II	13 (22.4)	8 (27.6)	20 (14.8)	41 (18.5)
III	15 (25.9)	10 (34.5)	36 (26.7)	61 (27.5)
Type of tumor				
Ductal	50 (86.2)	26 (89.7)	115 (85.2)	191 (86.0)
Lobular	4 (6.9)	2 (6.9)	12 (8.9)	18 (8.1)
Medullar	4 (6.9)	1 (3.4)	8 (5.9)	13 (5.9)
Tumor size (cm)				
≤ 2	35 (60.3)	16 (55.2)	101 (74.8)	152 (68.5)
2-5	21 (36.2)	12 (41.4)	33 (24.4)	66 (29.7)
> 5	2 (3.4)	1 (3.4)	1 (0.7)	4 (1.8)

Fig 1. CIF for death due to breast cancer and other causes in patients with breast cancer.
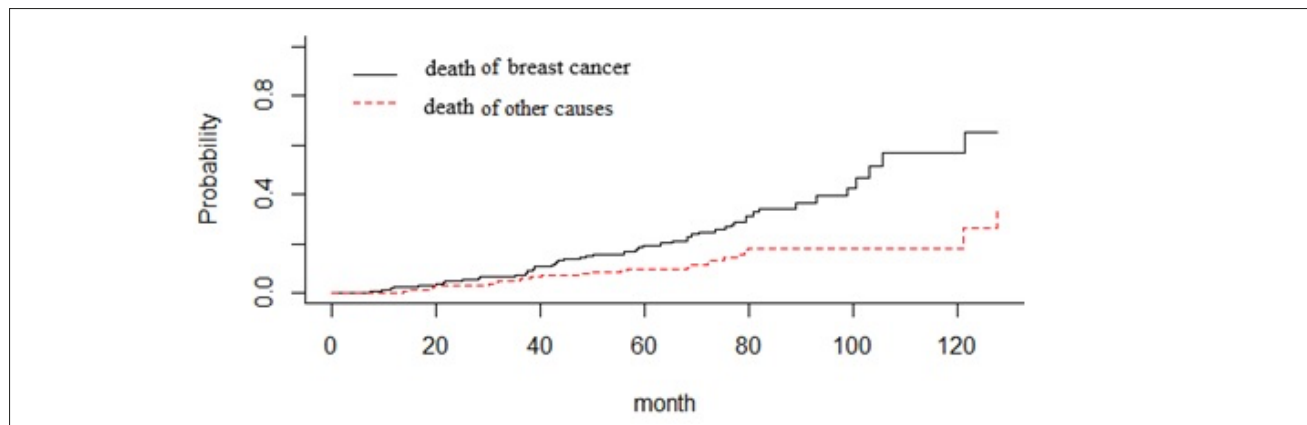
III, HER2, number of involved lymph nodes and age at diagnosis are the top three variables for death due to BC. In order to compare the efficiency of RSF with cause-specific model, the integrated Brier score (IBS) criterion was used. The smaller value of this criterion shows better performance. Values of this criterion for RSF and cause-specific model were reported in Table IV. The IBS score of the RSF was 0.132 for death due to BC, which was smaller than the one for the cause-specific hazard regression model.

Tab. II. Results of cause specific models for BC progression and death competing events.

Variables	Death of BC	Death of other causes
	HR (95% CI)	HR (95% CI)
Age at diagnosis	0.99 (0.97, 1.02)	0.99 (0.96, 1.03)
Type of surgery		
Radical Mastectomy	1.00	1.00
Segmental Mastectomy	2.98 (1.07, 8.28)*	1.05 (0.12, 8.69)
Simple Mastectomy	1.13 (0.38, 3.35)	1.20 (0.25, 5.63)
Number of involved lymph nodes		
≤ 2	1.00	1.00
3-6	1.18 (0.54, 2.58)	1.39 (0.47, 4.11)
≥ 7	0.31 (0.08, 1.23)	2.31 (0.34, 15.69)
ER		
Negative	1.00	1.00
Positive	0.98 (0.43, 2.27)	0.87 (0.24, 3.13)
PR		
Negative	1.00	1.00
Positive	0.92 (0.40, 2.14)	1.57 (0.44, 5.56)
HER2		
Negative	1.00	1.00
Positive	3.08 (1.58, 6.01)*	1.28 (0.56, 2.92)
Family history of BC		
Yes	1.00	1.00
No	0.63 (0.26, 1.55)	1.09 (0.24, 4.83)
Stage of disease		
I	1.00	1.00
II	0.66 (0.21, 2.03)	1.57 (0.37, 6.50)
III	1.82 (0.50, 6.63)	0.99 (0.14, 6.71)
Type of tumor		
Ductal	1.00	1.00
Lobular	1.19 (0.41, 3.42)	0.94 (0.21, 4.17)
Medullar	0.65 (0.21, 2.05)	0.61 (0.07, 4.85)
Tumor size (cm)		
≤ 2	1.00	1.00
2-5	1.55 (0.59, 4.08)	1.12 (0.35, 3.57)
> 5	0.84 (0.13, 5.35)	1.03 (0.09, 10.98)
* Significant (p-value < 0.05); BC: breast cancer.		

Discussion

In the analysis of survival data, it is possible that subjects be at risk of more than one event in a way that the occurrence of one, prevents the others. In this situation, there are several methods for analyzing survival data. We focused on modeling with RSF for competing risks. This method is an assumption-free model that is very efficient for the analysis of data with high-correlation predictor variables, nonlinear effects, and high-level interactions [9, 10].

Several studies have been done to determine the importance of risk factors in the survival of BC patients using RSF. In these studies, in which only one death event was considered, factors such as progesterone receptor, number of involved lymph nodes, stage of disease, and so on were recognized as important variables [10, 16, 17].

According to the results of the RSF model in this study, HER2, number of involved lymph nodes, and age at diagnosis as three important prognostic factors of survival in BC patients who died due to BC. This result is similar to the result of the study done by Safe et al. [16]. HER2 was also, statistically significant cause specific of death using traditional competing risks model. As the results of this model showed, the risk of death in patients with HER2 positive was higher than patients with the HER2 negative. However, the other important variables not significant in cause-specific hazards model. This finding was very similar to the results of the study by Poorolajal et al. [18] and Karimi et al. [19].

For the competing event, metastasis status was the most important variable for RSF. For the competing event, the Family history of BC was the most important variable for RSF. However, using classical models, no variable was significant in the cause-specific hazards model.

In order to compare the performance of the cause-specific hazard regression model and RSF were compared were used the integrated Brier score criterion. Based on the results of the IBS criterion, the performance of RSF was better than the cause-specific hazard regression model. This result was consistent with the studies done by Ishwaran et al. [10] and Hamidi et al. [15]. This may be because the nonlinear effects and interactions between variables are considered in the RSF model [10, 15].

The main limitation of this study was the small number of deaths and the high rate of censoring. Despite this limitation, the current study reveals the important prognosis factors for survival in patients with BC.

Conclusion

According to the results of this study, the performance of the RSF model was better than the cause-specific hazard model. Also, HER2 was the most important variable for death of BC in both models.

Acknowledgements

Tab. III. The event-specific VIMP for risk factors from BC analysis for the two events.

Variables	VIMP			
	Death of BC	Variables' Rank	Death of other causes	Variables' Rank
Age at diagnosis	0.014	3	-0.002	5
Type of surgery	0.010	4	-0.006	6
Number of involved lymph nodes	0.019	2	0.018	4
ER	0.002	7	-0.015	10
PR	-0.003	10	-0.010	8
HER2	0.079	1	-0.007	7
Family history of BC	0.004	6	0.024	1
Stage of disease	-0.002	9	0.018	3
Type of tumor	0.005	5	-0.015	9
Tumor size (cm)	-0.002	8	0.020	2

Tab. IV. Overview of the IBS criterion.

Models	IBS	
	Death due to BC	Death of other causes
RSF*	0.132	0.154
Cause-specific hazard regression model	0.165	0.179

* Related to RSFs using generalized log-rank splitting rule.

Conflict of interest statement

The authors declare that they have no conflicts of interest.

Funding

Author' contributions

RNV and JF contributed to the study design, analysis, and interpretation of data. LT participated in data collection, data analysis. BA, TM and KhNGh participated in the interpretations and drafting of the manuscript. All authors read and approved the final manuscript.

References

[1] Jafari-Koshki T, Schmid VJ, Mahaki B. Trends of breast cancer incidence in Iran during 2004-2008: A Bayesian space-time model. Asian Pac J Cancer Prev 2014;15:1557-61. http://doi.org/10.7314/APJCP.2014.15.4.1557

[2] DeSantis C, Ma J, Bryan L, Jemal A. Breast cancer statistics, 2013. CA: Cancer J Clin 2014;64:52-62. http://doi.org/10.3322/caac.21203

[3] Akbari ME, Mozaffar M, Heidari A, Zirakzadeh H, Akbari A, Akbari M, Hosseinizadegan Shirazi F.. Recurrence and survival effect in breast conserving surgery: What are the predictive and/or prognostic factors? Iran J Cancer Prev 2011;4:49-54.

[4] Kleinbaum DG, Klein M. Survival analysis. Springer 2010.

[5] Hsich E, Gorodeski EZ, Blackstone EH, Ishwaran H, Lauer MS. Identifying important risk factors for survival in patient with systolic heart failure using random survival forests. Circ Cardiovasc Qual Outcomes 2011;4:39-45. http://'doi.org/10.1161/CIRCOUTCOMES.110.939371

[6] Breiman L. Random Forests. Machine Learning 2001;45:5-32.

[7] Egner JR. AJCC cancer staging manual. JAMA 2010;304:1726-7. http://doi.org/10.1001/jama.2010.1525

[8] Pintilie M. Competing risks: a practical perspective. John Wiley & Sons 2006.

[9] Ishwaran H, Gerds TA, Kogalur UB, Moore RD, Gange SJ, Lau BM. Random survival forests for competing risks. Biostatistics 2014;15:757-73. http://doi.org/10.1093/biostatistics/kxu010

[10] Ishwaran H, Kogalur UB, Blackstone EH, Lauer MS. Random survival forests. Ann Appl Stat 2008;2:841-60. http://doi.org/10.1214/08-AOAS169

[11] Mogensen UB, Ishwaran H, Gerds TA. Evaluating random forests for survival analysis using prediction error curves. J Stat Softw 2012;50:1. http://doi.org/10.18637/jss.v050.i11

[12] Ishwaran H, Kogalur UB. Random forests for survival, regression, and classification (RF-SRC), R package version 2.5.1. (2017).

[13] Gerds TA, Scheike TH, Blanche P, Ozenne B. riskRegression: risk regression models and prediction scores for survival analysis with competing risks. R package version 1.3.7. (2017).

[14] Gray B. cmprsk: subdistribution analysis of competing risks. R package version 2.2-7 (2014).

[15] Hamidi O, Tapak M, Poorolajal J, Amini P, Tapak L. Application of random survival forest for competing risks in prediction of cumulative incidence function for progression to AIDS. Epidemiol Biostat Public Health 2017;14. https://doi.org/10.2427/12663

[16] Safe M, Mahjub H, Faradmal J. A comparative study for modelling the survival of breast cancer patients in the west of Iran. Glob J Health Sci 2016;9:215. https://doi.org/10.5539/gjhs.v9n2p215

[17] Omurlu IK, Ture M, Tokatli F. The comparisons of random survival forests and Cox regression analysis with simulation and an application related to breast cancer. Expert Syst with Appl 2009;36:8582-8. https://doi.org/10.1016/j.eswa.2008.10.023

[18] Jalal Poorolajal NN, Akbari ME, Mahjub H, Esmailnasab N. Breast cancer survival analysis based on immunohistochemis-

try subtypes (ER/PR/HER2): a retrospective cohort study. Arch Iran Med 2016;19:680-6.

[19] Karimi A, Delpisheh A, Sayehmiri K, Saboori H, Rahimi E. Predictive factors of survival time of breast cancer in kurdis-tan province of Iran between 2006-2014: a cox regression approach. Asian Pac J Cancer Prev 2014;15:8483-8. http://doi.org/10.7314/APJCP.2014.15.19.8483

Correspondence: Javad Faradmal, Associate Professor, Modeling of Noncommunicable Diseases Research Center & Department of Biostatistics and Epidemiology, School of Public Health, Hamadan University of Medical Sciences, Hamadan, Iran. Tel.: +988138380398 - Fax: +988138380509 - E-mail: javad.faradmal@umsha.ac.ir

Predicting Healthcare-associated Infections: are Point of Prevalence Surveys data useful?

MARCO GOLFERA[1], FABRIZIO TOSCANO[1], GABRIELE CEVENINI[2], MARIA F. DE MARCO[3], BARBARA R. PORCHIA[3], ANDREA SERAFINI[1,4], EMMA CERIALE[5], DANIELE LENZI[3], GABRIELE MESSINA[6]
[1] Post Graduate School of Public Health, University of Siena, Italy; [2] Department of Medical Biotechnologies, University of Siena, Italy; [3] Medical Management, "Le Scotte" Teaching Hospital, Siena, Italy; [4] Medical Management, "Misericordia" Hospital, AUSL Sud-Est Grosseto, Italy; [5] Public Hygiene and Nutrition, "Ruffolo" Hospital, Siena, Italy; [6] Department of Molecular and Developmental Medicine, University of Siena, Italy

Summary

Introduction. *Since 2012, the European Centre for Disease Prevention and Control (ECDC) promotes a point prevalence survey (PPS) of HAIs in European acute care hospitals. Through a retrospective analysis of 2012, 2015 and 2017 PPS of HAIs performed in a tertiary academic hospital in Italy, we developed a model to predict the risk of HAI.*
Methods. *Following ECDC protocol we surveyed 1382 patients across three years. Bivariate logistic regression analyses were conducted to assess the relationship between HAI and several variables. Those statistically significant were included in a stepwise multiple regression model. The goodness of fit of the latter model was*

assessed with the Hosmer-Lemeshow test, ultimately constructing a probability curve to estimate the risk of developing HAIs.
Results. *Three variables resulted statistically significant in the stepwise logistic regression model: length of stay (OR 1.03; 95% CI: 1.02-1.05), devices breaking the skin (i.e. peripheral or central vascular catheter, OR 4.38; 95% CI: 1.52-12.63), urinary catheter (OR 4.71; 95% CI: 2.78-7.98).*
Conclusion. *PPSs are a convenient and reliable source of data to develop HAIs prediction models. The differences found between our results and previously published studies suggest the need of developing hospital-specific databases and predictive models for HAIs.*

Introduction

Healthcare-associated infections (HAIs) are a Public Health threat worldwide, with a significant impact on patients' mortality, morbidity, hospital length of stay and cost [1, 2]. HAIs surveillance is listed by the European Center for Disease Control (ECDC) as a critical measure of prevention. Since 2011-2012, the ECDC promotes and coordinates a point prevalence survey (PPS) of HAIs in acute care hospitals. The report published thereafter estimated the prevalence of HAIs in more than 1100 European acute care hospitals was 6.0% over 273 753 patients [3]. It concluded that, thanks to infection prevention and control programmes – including surveillance of HAIs –, at least 20% of these healthcare-associated infections can be prevented [3].

Hospital-wide continuous incidence surveillance is very resource demanding, and consensus has been reached that repeated PPS is a more efficient approach to address this challenge [3]. Even if PPS may show limitations regarding the accuracy of data collected, it is a more scalable, less time consuming and less expensive alternative [4, 5].

Data collected through PPS of HAIs is meant to be used as part of a multicenter initiative, but may become a valuable source of information also at local level (e.g. hospital, local health agency, etc.) [3]. These data in fact, can be analyzed to better identify those patients

presenting with risk factors that increase the chances of developing HAIs during their hospital stay.

We performed a retrospective analysis of 2012, 2015 and 2017 PPS of HAIs conducted in a tertiary academic hospital in Italy. The aim of this research is to explore the usability of data collected through PPS of HAIs to develop hospital-specific models to predict HAIs.

Methods

DATA SOURCE

Three PPS have been conducted in an Italian tertiary academic hospital since the first ECDC PPS: in November 2012, in February 2015 and in April 2017. At the moment of the survey, the patients' files analyzed were 467 in 2012, 468 in 2015 and 447 in 2017. All the PPS of HAIs included in this study followed the ECDC protocol version 4.2 [6], firstly distributed to Member States in early May 2011. Information regarding definition of HAI, patients' inclusion and exclusion criteria, remained constant throughout the different surveys [3].

The surveys were conducted by small teams of two trained professionals, selected among infection control specialists, resident physicians and nurses in the weeks before the survey.

During every survey, when necessary, the teams were assisted by house staff of the ward they were visiting.

After each PPS, data were entered in the software HelicsWin.net, a software application developed for the manual entry of data of the ECDC HAI-Net surveillance of healthcare-associated infections [7], and also analyzed for internal purposes.

In May 2017, after the third PPS of HAIs was conducted in our hospital, data have been aggregated in a single dataset. We checked the database for patients occurring in two or more surveys, to assure independent entries.

Patients' attribution to wards has been checked, since the hospital went through several wards' reorganizations after 2012 (i.e. wards aggregated or divided, wards renamed, etc.). Therefore, to allow comparability between the different editions of the survey, we relied on the specialty of the consulting physician. Eventually, for statistical analysis purposes, all wards have been grouped under six different categories suggested by the ECDC: Intensive Care Units (ICU), Medical (MED), Surgical (SUR), Pediatric (PED), Obstetrics/Gynecology (OB/GYN), Psychiatric (PSY) [6].

Among several information collected, we also assigned the McCabe score to each patient. This score reports the prognosis of the patient, based on his underlying medical conditions. It allows to classify patients in several categories: non-fatal, ultimately fatal or rapidly fatal, if their prognosis is respectively above 5 years, between 1 and 5 years or below 1 year at the moment of the survey. The info entered in the dataset were based on the ECDC standard patient form ("Form A" of protocol version 4.2). Ultimately, we extracted the following information from the forms: age (in years), sex, ward category, length of hospital stay (LOS), surgery since admission, McCabe score, urinary catheter (UC), central vascular catheter (CC), peripheral vascular catheter (PC), intubation (INT), presence of active HAI.

"Surgery since admission" reports if the patient has undergone surgery during the hospitalization, providing details about the type of surgery, if minimally invasive or not, according to Centers for Disease Control and Prevention (CDC) definition of NHSN (National Heathcare Safety Network) operative procedure [8].

Several professionals involved in the PPSs complained about the difficulties detecting the McCabe. In fact, we found that this data has the highest share of unknown entry in our DB (Tab. I). In order to assess if this data has been recorded with statistically significant differences from one year to the other one, we performed a Chi-squared test. Statistically significant differences were found when comparing the year 2015 and 2017 and the year 2012 with 2017.

A research conducted in 20 European hospitals in 2016 shows that the reliability of the McCabe score using in PPS of HAIs is low. The authors conclude that training data collector seems necessary to reduce variability in the attribution of this score [9].

Unable to determine from the available data whether this difference is due to a change of the hospital case-mix or to professionals' different interpretation of the score, and relying on current literature on this topic, we decided to still include this variable in the analysis.

Statistical Analysis

Firstly, we conducted several bivariate logistic regressions to assess the relationship between the dependent variable, presence of HAI, and the aforementioned independent variables.

Given the strong relationship between invasive devices and the development of HAIs [10], we decided to create a new dichotomic variable named DBS, i.e. "devices breaking the skin". This variable is an indicator of presence of a central and/or a peripheral vascular catheter. These devices in fact, as opposed to urinary catheter and intubation, both interrupt the continuity of the skin, instead of exploiting an anatomical way to access the body.

Secondly, a forward stepwise multivariate logistic regression has been conducted using the Hosmer-Lemeshow method. Starting from the latter model, we defined the probability of developing HAIs according to the following formula:

$$P\left(\frac{HAI}{X}\right) = \frac{e^{BX^T + c}}{1 + e^{BX^T + c}}$$

Where B (B_1, B_2, B_3) indicates the logistic coefficient regression of the i-esim variables, while X (X_1, X_2, X_3) defines the vector of independent variables relative for each subject and T indicates the transposition operator. Figure I footnote reports the final version of the formula. The Hosmer-Lemeshow test allowed us to verify the goodness-of-fit of our predictive model. Relying on the expected proportion between the observed and the expected HAIs, we constructed a probability curve and measured the area underneath (AUC).

The statistical analysis was performed using STATA v14.1 (Stata Corp., College Station, TX), except for the forward stepwise multivariate logistic regression, performed with SPSS v24 (IBM, Armonk, NY).

Results

A total of 1382 patients were observed across the three surveys (Tab. I). The mean patient's age was 59 years (DS ± 24.7) and 51.2% were females. The average LOS was 10.0 days (DS ± 14.1), however a progressive reduction was observed from 2012 (10.3 days, DS ± 14.1) to 2017 (9.5 days, DS ± 13.3). The hospital ward category with the longest average length of hospitalization was the ICU, with 16.4 days (DS ± 20.7), followed by MED with 10.5 days (DS ± 12.0) and PED with 8.6 days (DS ± 23.9).

The overall prevalence of HAIs was estimated to be 6.7% (95% CI: 5.4%-8.1%), 92 patients across three surveys. More than 90% of patients (83/92) had one HAI, almost 9% (8/92) had two infections at same time and only one patient had three simultaneous HAIs, making up to a total of 102 nosocomial infections detected. These were mostly located in MED wards (42.2%), secondly in ICU wards (33.3%), thirdly in SUR wards (23.5%).

The prevalence of patients with at least one HAI ranged from 6.0% in 2012 (28/467 patients, 95% CI: 4.0-8.6) to 7.8% in 2017 (35/447, 95% CI: 5.5-10.7).

Of the 92 patients with HAIs, 78 (84.8%) originated in

Tab. I. Characteristics of the surveyed population.

	Total Patients (n = 1382)	Patients with HAIs (n = 92)	p
Mean age (SD)*			
Female	59.00 (24.80)	67.57 (19.00)	0.032
Male	61.13 (24.68)	63.24 (22.53)	0.37
Gender**			
Female	707	45	< 0.0001
Male	673	47	
UNK	2	-	-
Ward category**			
General medicine	630	40	< 0.0001
Intensive care unit	148	32	
Paediatrics	110	1	
Surgery	439	19	
Psychiatric	38	0	-
Gynaecology/ obstetrics	17	0	-
Lenght of Stay (SD)*			
General medicine	10.46 (12.00)	27.50 (24.65)	< 0,0001
Intensive care unit	16.43 (20.72)	28.22 (27.40)	< 0,0001
Paediatrics	8.65 (23.92)	8.00 (0.0)	0,28
Surgery	8.25 (10.55)	18.01 (14.58)	< 0,0001
Psychiatric	3.76 (3.83)	-(-)	-
Gynaecology/ obstetrics	2.94 (1.34)	-(-)	-
Surgery**			
None	905	48	< 0.0001
Invasive	262	26	
Minimally Invasive	202	18	
UNK	13	-	-
McCabe **			
Non Fatal (> 5 years)	855	44	< 0.0001
Rapidly Fatal (< 1 years)	140	14	
Ultimatily Fata (1-5 years)	279	30	
UNK	108	4	-
Device**			
Devices Breaking Skin			
Absent	442	1	< 0.0001
Present	940	91	
Urinary Catheter			
Absent	980	29	< 0.0001
Present	393	62	
UNK	9	1	-
Intubation			
Absent	1307	76	< 0.0001
Present	52	15	
UNK	23	1	-

HAI: Healthcare-associated Infection; SD: Standard Deviation; UNK: Unknown. * Wilcoxon-Mann-Whitney test was used. ** Chi-squared test.

the current hospital, while 14 (15.2%) cases originated from a different hospital or healthcare facility (e.g. nursing home, private hospital, etc.).

Slightly more than 34% of patients included in the analysis had undergone surgery since their admission at the moment of the PPS (Tab. I). In particular, 54.9% had an invasive surgery/NHSN, while 42.4% had a minimally invasive surgery/Non-NHSN (2.73% were unknow). When focusing on the 92 patients with HAIs, 47.8% had surgery, of which 59.1% had an invasive procedure/NHSN and 40.9% had a minimally invasive surgery/Non-NHSN. Patients have been stratified for severity of their underlying medical conditions using the McCabe Score (Tab. I). More than half of patients observed (61.9%) had a non-fatal condition (i.e. life expectancy over 5 years at the moment of the PPS), 20.2% had a prognosis of 1-5 years, and ultimately 10.1% had a prognosis inferior to 1 year (7.81% patients had an unknown McCabe score). Considering patients with HAI only, 47.8% had a non-fatal condition, 32.6% had a prognosis of 1-5 years, and ultimately 15.2% had a prognosis inferior to 1 year (4.4% of patients with HAI had unknown McCabe score).

Slightly more than half of total patients (69.0%) had at least one device, i.e. UC, DBS or INT (Tab. I). Among patients with HAIs instead, 97.8% had at least one device. The device with the highest prevalence was the DBS, present in 66.9% of patients, and in 98.9% of patients with HAI.

The risk factors mostly associated with HAIs resulted from the bivariate analysis (Tab. II) were: age (OR 1.01; 95% CI: 1.00-1.02), ward category (ICU, OR 3.98; 95% CI: 2.38-6.66-PED, OR 0.13; 95% CI: 0.01-0.97), LOS (OR 1.04; 95% CI: 1.03-1.06), surgery since admission (invasive/NHSN, OR 1.86; 95% CI: 1.13-3.05), McCabe Score (Ultimately Fatal, OR 2.12; 95% CI: 1.31-3.45; Rapidly Fatal, OR 2.1; 95% CI: 1.13-3.89), DBS (OR 11.92; 95% CI: 4.29-33.13), UC (OR 6.23; 95% CI: 3.91-9.93), INT (OR 6.40; 95% CI: 3.33-12.31). Sex was the only variable not associated with developing HAIs at the bivariate analysis.

Of the previously listed variables, only three resulted statistically significant in the stepwise logistic regression model: LOS (OR 1.03; 95% CI: 1.02-1.05), the DBS (OR 4.38; 95% CI: 1.52-12.63) and UC (OR 4.71; 95% CI: 2.78-7.98). Figure 1 displays the probability over time of developing HAI when such devices are involved. The discriminatory accuracy of the predictive model was assessed using receiver operating characteristic (ROC) analysis which showed an AUC of 0.85 (95% CI: 0.82-0.89).

Discussion

The ECDC report estimated a 6.3% HAIs prevalence on any given day in acute care hospitals in Italy (95% CI 5.4-7.4), consistent with the European mean (5.7%, 95% CI: 4.5-7.4) [3]. Therefore, our results (6.7%) are comparable both with the Italian and the European estimates of HAIs.

However, considering each survey included in this analysis, a growing trend can be seen, although without statistically significant differences. This could be explained by the increased awareness towards HAIs in our hospital after the first PPS promoted by the ECDC. The correlation between HAIs and the use of devices is well known in literature. Several studies found the

Tab. II. Risk factors for healthcare-associated infection (HAI), results of bivariate and multivariate analysis.

	Unadjusted			Adjusted		
	OR	(95%CI)	p	OR	(95%CI)	p
Gender (n = 1364, missing = 18)						
Female	1	-	-	-	-	-
Male	1.13	0.75-1.72	0.56	-	-	-
Age	1.01	1.001-1.022	0.02*	-	-	-
Ward category (n = 1382)						
General medicine	1	-	-	-	-	-
Intensive care unit	3.98	2.38-6.66	< 0.0001	-	-	-
Paediatrics	0.13	0.01-0.97	0.019	-	-	-
Surgery	0.72	0.42-1.24	0.23	-	-	-
Psychiatric	-	-	-	-	-	-
Gynaecology/obstetrics	-	-	-	-	-	-
Length Of Stay	1.04	1.03-1.06	< 0.001*	1.03	1.02-1.05	< 0.001
Surgery (n = 1369, missing = 13)						
None	1	-	-	-	-	-
Invasive	1.86	1.13-3.05	0.01	-	-	-
Minimally Invasive	1.62	0.92-2.83	0.09	-	-	-
McCabe Score (n = 1274, missing = 108)						
Non Fatal (> 5years)	1	-	-	-	-	-
Rapidly Fatal (< 1 years)	2.10	1.13-3.45	0.002	-	-	-
Ultimately Fata (1-5 years)	2.13	1.14-3.89	0.015	-	-	-
Device						
Devices Breaking Skin (n = 1382)						
Absent	1	-	-	1	-	-
Present	11.92	4.29-33.13	< 0.0001	4.38	1.52-12.63	0,006
Urinary Catheter (n=1373, missing = 9)						
Absent	1	-	-	1	-	-
Present	6.23	3.91-9.93	< 0.0001	4.71	2.78-7.98	< 0.001
Intubation (n = 1359, missing = 23)						
Absent	1	-	-	-	-	-
Present	6.40	3.33-12.31	< 0.0001	-	-	-

OR: Odds Ratio; 95%CI: 95% Confidence Interval.

association between the UC and the development of HAIs [11, 12]. Moreover, they suggest the implementation of education and training on urinary catheter insertion technique, as well as of strategies to early remove this device that can easily convey an infection [4, 13, 14]. In our database, a UC was present in 28.4% of the patients, a similar value found in the ECDC report. However, among patients with at least one HAI, UC had a prevalence of 67.4%, much higher than reported by the ECDC and other studies [10, 14].

This result suggests the need of improving the management of UC in our hospital, which could potentially lead to a reduction in hospital- acquired UTI. The 102 HAIs found in our database were mostly infections of the urinary tract (UTI), 33.3% (34/102), followed by pneumonia 21.6% (22/102), and infections of the surgical site (SSI) and the gastrointestinal system, both at 7.8% (8/102). The data from the ECDC PPS of HAIs report about Italy shows the following types of HAIs as the most common: pneumonia (26.1%), UTI (20.8%), SSI (16.2%), and bloodstream infections (15.8%). These numbers differ from those we found but are similar to those reported by studies conducted in Italy in contexts comparable to that one of our hospital [4, 15]. These differences highlight the need for each hospital to

strictly monitor HAIs, as their prevalence may differ for epidemiological reasons or for matters strictly related to the hospital itself (e.g. complexity of care provided, multidrug resistant bacteria, professionals' habits, hygiene standards, etc.).

Several studies tried to determine which variables could predict the development of HAIs in hospital admitted patients relying on point-prevalence surveys. A study conducted in a tertiary hospital in China found that age older than 85 years, male sex, being hospitalized in the ICU, and the presence of a UC or INT, are all factors predisposing to the development of an HAI [11]. On the other hand, a study conducted in 2001 on national level data in Slovenia, found that undergoing surgery in the seven days before the survey, or having an high McCabe score predisposed to HAIs [10]. Finally, the ECDC report found that age, male sex, LOS, McCabe Score and number of invasive devices are directly correlated with the risk of developing an HAI [16]. Despite different results, all these studies provided valuable information, either for clinicians or policy makers, depending on the level of analysis.

The findings of our study agree – to some extent – with previously published data. However, the differences found support the need of monitoring HAIs in every hospital, as well as developing and updating a facility-

Fig. 1. HAI probability by devices. The four graphs above show the probability of developing HAI if are present both devices (A) , one of them (B,C) or no devices (D) according to the following formula.

$$P(HAI/X) = \frac{e^{B1*X1+B2*X2+B3*X3+C}}{1+e^{B1*X1+B2*X2+B3*X3+C}}$$

The coefficient value so identified were B1= 0,033 (length of stay), B2 = 1,550 (urinary catheter), B3 = 1,477 (devices breaking the skin); C indicates regression constant (C = -5,057); X defines the vector of independent variables relatives for each subject, in detail X1 for length of stay, X2 for presence/absence of urinary catheter and X3 for devices breaking the skin.
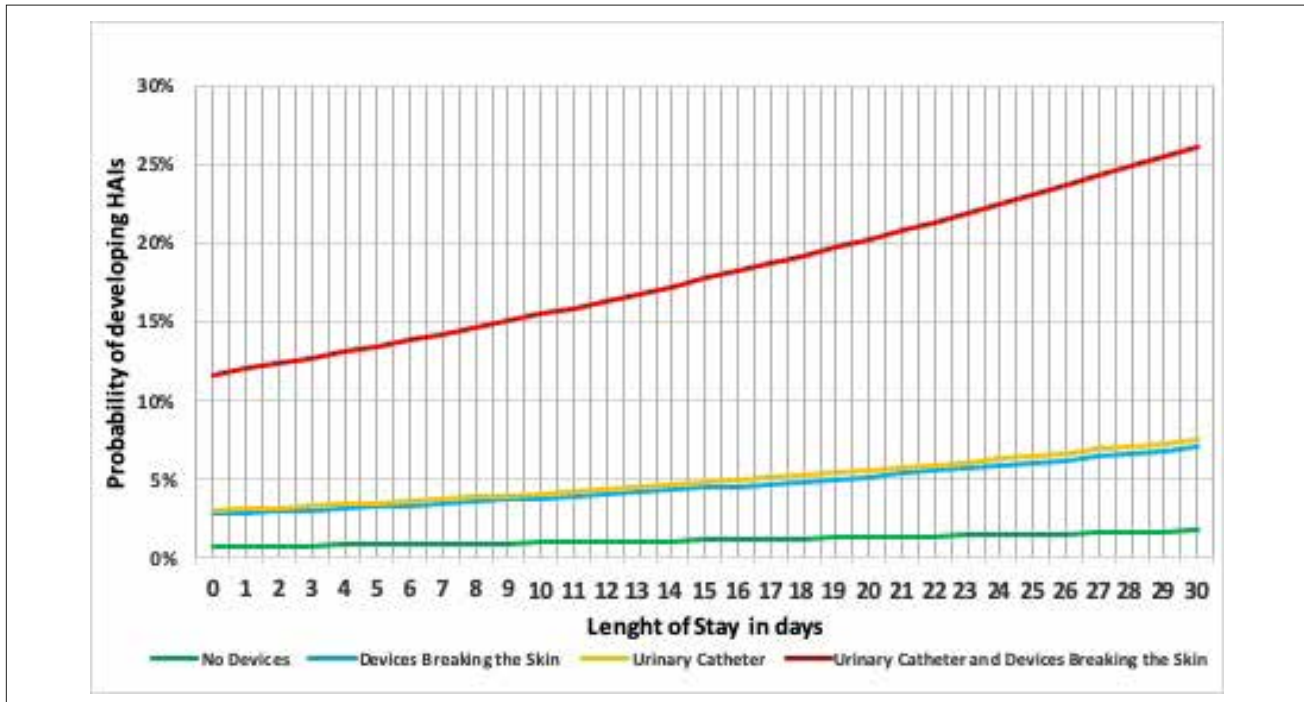
specific database of HAIs. This would ease the identification of risk factors specific to the hospital, profiling patients at risk of developing HAIs, and ultimately helping professionals in making decisions.

The source of this data could be point-prevalence surveys, instead of the more resource-intensive continuous incidence surveillance. Since the methodology to conduct this type of survey has already been implemented into most European hospitals – thanks to the ECDC –, this should simplify the use of such data to develop hospital-based database of HAIs.

This study has two limitation. Firstly, it's a retrospective study of data collected during PPSs of HAIs conducted in three different years. Despite following the same protocol, different professionals were involved in the process in different moments, while the awareness towards the problem of HAIs could have been different. Secondly, the hospital went through several changes during the study period. Relying on the available data, we were unable to determine if this somehow affected the developing of HAIs.

Conclusion

PPSs are a convenient and reliable source of data to develop hospital-specific HAIs prediction models. They represent a less time consuming and less expensive alternative to continuous surveillance of HAIs, especially when paired with the development of a predictive model. In the near future, the rapid spread of Electronic Health Record (EHR) will make collecting relevant information about patients easier and easier. Predictive models with data automatically collected from EHR would generate alerts for physicians to draw their attention to those devices in place for long time, therefore at higher risk of housing an infection in a certain patient [17]. This would allow to timely address that 20% of HAIs identified by the ECDC as avoidable, as well as exceed that goal and sensibly reduce healthcare-associated infections [4].

Acknowledgements

Conflict of interest statement

None to declare

Authors' contributions

FT conceived the study. AS, EC, BRP, MFDM, collected

the data. FT and MG reviewed the relevant literature. FT, MG and GC drafted the manuscript. GM, DL and MFDM revised the manuscript. All the authors critically revised the manuscript and approved the final version.

References

[1] World Health Organization (WHO). Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. WHO, 2018. Available at: https://www.who.int/publications/i/item/9789241549929 (Accessed on: November 01, 2018).

[2] Ferreira E, Pina E, Sousa-Uva M, Sousa-Uva A. Risk factors for health care-associated infections: From better knowledge to better prevention. Am J Infect Control 2017;45:e103-7. https://doi.org/10.1016/j.ajic.2017.03.036

[3] Suetens C, Hopkins S, Kolman J, Diaz Högberg L. Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals Point prevalence survey of healthcare- associated infections and antimicrobial use in European acute care hospitals 2011. Available at: https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/healthcare-associated-infections-antimicrobial-use-PPS.pdf (Accessed on July 8, 2022).

[4] Antonioli P, Manzalini MC, Stefanati A, Bonato B, Verzola A, Formaglio A, Gabutti G. Temporal trends of healthcare associated infections and antimicrobial use in 2011-2013, observed with annual point prevalence surveys in Ferrara University Hospital, Italy. J Prev Med Hyg 2016;57:E135-41. https://doi.org/10.15167/2421-4248/jpmh2016.57.3.620

[5] Nair V, Sharma D, Sahni AK, Grover N, Shankar S, Jaiswal SS, Dalal SS, Basannar DR, Phutane VS, Kotwal A, Gopal Rao G, Batura D, Venkatesh MD, Sinha T, Kumar S, Joshi DP. Antimicrobial use and antimicrobial resistance in nosocomial pathogens at a tertiary care hospital in Pune. Med J Armed Forces India 2015;71:112-9. https://doi.org/10.1016/j.mjafi.2014.12.024

[6] European Centre for Disease Prevention and Control (ECDC). Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals. Protocol version 4.2., 2011. Available at: https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/0419-TED-PPS-HAI-antimicrobial-use-protocol.pdf (Accessed on March 20, 2020), updated to 4.3 available at: https://www.ecdc.europa.eu/sites/default/files/media/en/publications/Publications/0512-TED-PPS-HAI-antimicrobial-use-protocol.pdf (Accessed on July 08, 2022).

[7] "HelicsWin.Net (HWN). Available at: https://ecdc.europa.eu/en/publications-data/helicswinnet-hwn (Accessed on September 26, 2018).

[8] Center for Disease Control and Prevention (CDC). Oid, Ncezid, DHQP. 9 Surgical Site Infection (SSI) Event,2018. Available at: https://www.cdc.gov/nhsn/psc/ssi/index.html (Accessed on: October 10, 2018).

[9] Reilly JS, Coignard B, Price L, Godwin J, Cairns S, Hopkins S, Lyytikäinen O, Hansen S, Malcolm W, Hughes GJ. The reliability of the McCabe score as a marker of co-morbidity in healthcare-associated infection point prevalence studies. J Infect Prev 2016;17:127-9. https://doi.org/10.1177/1757177415617245

[10] Klavs I, Bufon Lužnik T, Škerl M, Grgič-Vitek M, Lejko Zupanc T, Dolinšek M, Prodan V, Vegnuti M, Kraigher A, Arnež Z. Prevalance of and risk factors for hospital-acquired infections in Slovenia-results of the first national survey, 2001. J Hosp Infect 2003;54:149-57. https://doi.org/10.1016/S0195-6701(03)00112-9

[11] Zhang Y, Zhang J, Wei D, Yang Z, Wang Y, Yao Z. Annual surveys for point-prevalence of healthcare-associated infection in a tertiary hospital in Beijing, China, 2012-2014. BMC Infect Dis 2016;16:161. https://doi.org/10.1186/s12879-016-1504-4

[12] Saint S, Kaufman SR, Rogers MAM, Baker PD, Boyko EJ, Lipsky BS. Risk factors for nosocomial urinary tract–related bacteremia: A case-control study. Am J Infect Control 2006;34:401-7. https://doi.org/10.1016/J.AJIC.2006.03.001

[13] Meddings J, Rogers MAM, Krein SL, Fakih MG, Olmsted RN, Saint S. Reducing unnecessary urinary catheter use and other strategies to prevent catheter-associated urinary tract infection: an integrative review. BMJ Qual Saf 2014;23:277-89. https://doi.org/10.1136/bmjqs-2012-001774

[14] Segagni Lusignani L, Blacky A, Starzengruber P, Diab-Elschahawi M, Wrba T, Presterl E. A national point prevalence study on healthcare-associated infections and antimicrobial use in Austria. Wien Klin Wochenschr 2016;128:89-94. https://doi.org/10.1007/s00508-015-0947-8

[15] Sticchi C, Alberti M, Artioli S, Assensi M, Baldelli I, Battistini A, Boni S, Cassola G, Castagnola E, Cattaneo M, Cenderello N, Cristina ML, De Mite AM, Fabbri P, Federa F, Giacobbe DR, La Masa D, Lorusso C, Marioni K, Masi VM, Mentore B, Montoro S, Orsi A, Raiteri D, Riente R, Samengo I, C. Viscoli C, Carloni R, Alicino C, Barberis I, Faccio V, Grammatico F, Magnasco L, Paganino C, Saffioti C, Sarteschi G, Ungaro R, Bellina D, Daturi V, Di Bella AM, Guglielmi B, Icardi G, Morando A, Talamini A, Tomei M, Crisalli MP, Sansone P, Santini M. Regional point prevalence study of healthcare-associated infections and antimicrobial use in acute care hospitals in Liguria, Italy. J Hosp Infect 2018;99:8-16. https://doi.org/10.1016/j.jhin.2017.12.008

[16] Zarb P, Coignard B, Griskeviciene J, Muller A, Vankerckhoven V, Weist K, Goossens MM, Vaerenberg S, Hopkins S, Catry B, Monnet DL, Goossens H, Suetens C; National Contact Points for the ECDC pilot point prevalence survey; Hospital Contact Points for the ECDC pilot point prevalence survey. The European Centre for Disease Prevention and Control (ECDC) pilot point prevalence survey of healthcare-associated infections and antimicrobial use. Euro Surveill 2012;17:20316. https://doi.org/10.2807/ese.17.46.20316-en

[17] Paxton C, Niculescu-Mizil A, Saria S. Developing predictive models using electronic medical records: challenges and pitfalls. AMIA Annu Symp Proc 2013;2013:1109-15.

Foodborne zoonotic trematode infections in Yen Bai, Vietnam: a situational analysis on knowledge, attitude, and practice (KAP) and risk behaviors

NGAN THI THUY PHI[1], THAO THI BICH NGUYEN[2], TRANG THI HUYEN LE[3], DUNG TRUNG DO[4], MARC LENAERTS[5],
BERTRAND LOSSON[6], OLIVIER VANDENBERG[2], PIERRE DORNY[7], MINNA VAN GERVEN[8], MAGDA BOERE-BOONKAMP[9],
DUNG THI BUI[10,11]

[1] Faculty of Science and Technology, University of Twente, Enschede, The Netherlands; [2] School of Public Health,
Université Libre de Bruxelles, Bruxelles, Belgium; [3] International Livestock Research Institute, Hanoi, Vietnam;
[4] Department of Parasitology, National Institute of Malariology, Parasitology and Entomology, Ha Noi, Vietnam;
[5] Laboratory of Anthropology of Contemporary Worlds, Université Libre de Bruxelles, Bruxelles, Belgium;
[6] Laboratory of Parasitology and Parasitic Diseases, Faculty of Veterinary Medicine, Université de Liège, Liège, Belgium;
[7] Department of Biomedical Science, Institute of Tropical Medicine, Antwerp, Belgium; [8] Faculty of Social Sciences,
University of Helsinki, Finland; [9] Faculty of Behavioural, Management and Social Sciences, University of Twente, Enschede,
The Netherlands; [10] Department of Parasitology, Institute of Ecology and Biological Resources, Viet Nam Academy of Science
and Technology, Ha Noi, Vietnam; [11] Graduate University of Science and Technology, Viet Nam Academy of Science and Technology,
Ha Noi, Vietnam

Summary

Introduction. *Foodborne Zoonotic Trematode Infections (FZTi) are neglected tropical diseases of public health concern in Vietnam. The transmission of FZTi is linked to human behavior patterns. The aims to investigate the knowledge, attitude, and practices regarding FZTi among local people.*

Methods. *A cross-sectional study was conducted using a mixed method, which included a baseline survey and in-depth interviews. 375 participants were interviewed face-to-face in the survey, and 27 participants had the in-depth interviews.*

Results. *The results showed that 36.3% passed the knowledge assessment, 86.7% passed the attitude assessment, and 24% passed the practical assessment. There were differences in average knowledge scores among gender (men higher than women,*

p = 0.006), ethnicities (Kinh higher than Dao and Tay, p < 0.001), and educational level (higher education, higher knowledge score, p < 0.001). There were differences in the frequency of eating raw fish between men and women (men higher than women, p < 0.001), and in the average practice score between men and women (women higher than men, p = 0.028). Eating raw fish and/or undercooked fish, raw vegetables, and drinking untreated water from Thac Ba lake in Yen Bai province were identified as FZTi risk behaviors. The occurrence of these risky habits can be explained by the lack of knowledge on FZTi, poor economic conditions and typical social features of local people.

Conclusion. *The current knowledge of local people in regard to safe eating practices is poor. They keep performing unsafe practices, which lead to infection with FZTi; therefore, an integrated control of FZTi is essential.*

Introduction

Foodborne Zoonotic Trematode infections (FZTi) are important public health concerns, particularly in South East Asia, and are on the World Health Organization (WHO) list of neglected tropical diseases. FZTi comprises a group of parasitic infections caused by trematodes that are acquired through ingestion of food contaminated with the larval stages of a parasite [1-3]. According to the WHO, it is estimated that 200,000 illnesses and more than 7,000 deaths are caused annually by FZTi, which leads to a disease burden of over two million disability-adjusted life-years (DALYs) globally [4].

Vietnam is particularly susceptible to the development and transmission of FZTi including the following: small liver fluke infections (*Clonorchiasis/Opisthorchiasis*), small intestinal fluke infections (caused by *Haplorchis* spp., *Echinostoma* spp., *Centrocestus* spp., *Echinochasmus* spp.), large liver fluke infections (*Fascioliasis*), and lung fluke infections (*Paragonimiasis*) [5, 6]. Indeed, in this

tropical country, the life cycle of these parasites is maintained by the use of human stools for fertilizing vegetable gardens and fish ponds, and by traditional eating of raw or undercooked fish and/or vegetables. Human cases of small liver fluke infection were reported in at least 21 provinces in North and Central Vietnam [7-9], with prevalent figures ranging from 15-37% [10,11]. While small liver fluke infections are caused by *Clonorchis sinensis* in most Northern provinces, *Opisthorchis viverrini* is the common species in Central provinces of Vietnam [11]. Large liver fluke infections caused by *Fasciola gigantica* occur in 47 provinces and cities, with the highest prevalence in provinces in Central Vietnam, Central Highlands [12]. A total of 11,240 fascioliasis cases were recorded from 2006 to 2009, mainly from Central Vietnam [13]. Infections with small and large liver flukes cause inflammation of the liver, gall bladder, and pancreas, and impaired absorption of nutrients [14]. Additionally, small liver flukes are highly associated with the occurrence of cholangiocarcinoma

(CCA), a fatal cancer of the bile duct [15]. Liver flukes have complex life cycles and epidemiology, in which they exist in different stages and pass through different intermediate hosts such as snails and fishes before they are ingested by humans. The transmission is linked to human behavioral patterns that are related to methods of producing, processing, and preparing foods, particularly, habits or traditional customs of eating raw or undercooked fish and raw vegetables. In order to stop FZTi, changing the behaviors/habits of individuals and communities is important and can be achieved through health education programs. However, before any health education intervention in communities can be developed and implemented, understanding knowledge, attitude and practice regarding disease prevention among a specific community is essential.

Thac Ba Lake, one of the biggest lakes in Vietnam, is the main source of fish in Yen Bai province. It has been reported that the local population has the habit of eating raw or undercooked fish and vegetables, putting them at high risk of suffering from FZTi, particularly *C. sinensis* [16]. The present study aims to answer two research questions: (1) What are the Knowledge, Attitude, and Practice (KAP) regarding to liver fluke infection (including small and large liver flukes) of local people in Yen Bai province?, and (2) Why do people in this province show risk behaviors regarding liver fluke infection?

Methods

STUDY SITES

This study was conducted in two communes (Vu Linh and Phuc An) in Yen Bai, which is a Northern mountainous province in Vietnam (Fig. 1). The study area was selected because of the reported habit of eating raw fish, which was 86.95% (40/46 interviewees) [17]. Vu Linh and Phuc An have a population of approximately 9,400 people that cover 2,059 households, 10 ethnic groups and 21 villages. In 2017, according to the reports of Commune Health Stations, an estimated 10-15% and 10-20% of the populations of Phuc An and Vu Linh communes, respectively, had small liver fluke infections.

STUDY DESIGN

This study was conducted from February to July 2018 and was designed as a cross-sectional study using mixed methods, including both a baseline survey and in-depth interviews.

We first performed a quantitative survey on the Knowledge, Attitude, and Practice (KAP survey) of liver fluke among people in Vu Linh and Phuc An, Yen Bai, aged between 15 and 65. This survey aimed to answer the first research question. In this part, participants were invited randomly to be interviewed face-to-face by researchers with the use of a structured questionnaire.

We then performed a qualitative investigation about risk behaviors leading to getting liver fluke infection. In this part, participants were invited to an in-depth interview to provide more detailed information about eating raw fish and raw vegetables and their reasons to explain why they conducted those risk behaviors.

KNOWLEDGE, ATTITUDE, AND PRACTICE (KAP) SURVEY

A KAP survey is a quantitative approach that enables the researcher to study the Knowledge (K), Attitude (A), and

Fig. 1. A. Map of Vietnam with indication of Yen Bai province; B. Map of Yen Bai province with indications of study sites: Vu Linh and Phuc An communes in Yen Binh district.
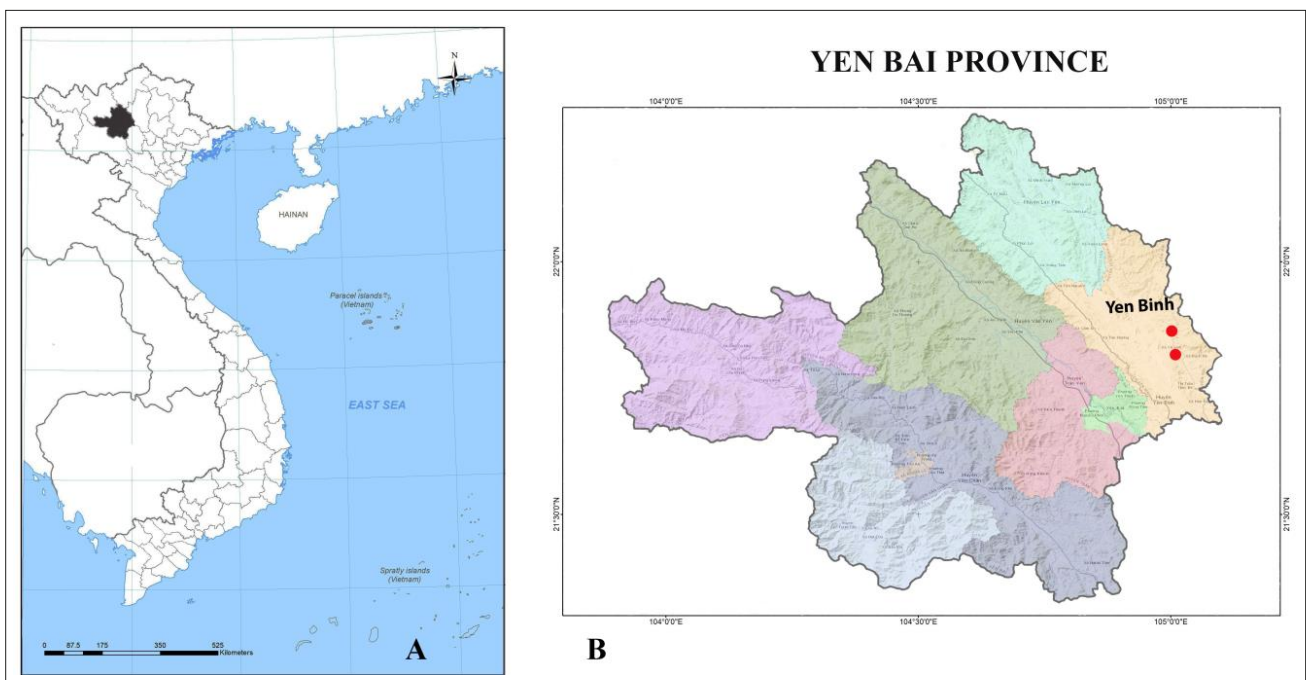
Practice (P) of the target population. It is the first step to establish baseline data to be used in further assessments such as, selecting the most suitable intervention or assessing the changes after an intervention [18, 19]. The KAP survey in this study is a part of the "Foodborne Zoonotic Trematode Infections and Integrated Control in Vietnam project" (FOODTINC). The survey design needed to fit with other components of the project; therefore, the sample size of the KAP survey was all people selected for the parasitological part of the study [20]. The estimated sample size required for each commune, Vu Linh and Phuc An, was calculated using the following formula with 95% confidence interval, acceptable margin of error d = 0.05, and estimated prevalence rate of liver fluke infection p = 0.15 according to the annual report of 2017 of the Health Station at Phuc An commune:

$$N = \frac{z^2_{1 - \alpha/2} \times p \times (1 - p)}{d^2}$$

As a result, among 392 participants randomly selected in the parasitology part, 375 participants at the age of 15 to 65 years were invited to the KAP survey. Participants were invited to be face-to-face interviewed in order to obtain personal data and to determine their knowledge, attitudes and practices regarding prevention methods and risk behaviors related to the disease. The interview lasted for around 15 minutes by using the designed questionnaire on a tablet or a mobile phone. The identification numbers and answers were saved on the electrical devices when the interview ended. In order to measure the knowledge, there were three questions on general awareness, one question on causes to get a liver fluke infection, six questions on basic knowledge including, transmission, symptoms, treatment, re-infection and prevention. In order to measure the attitude of the participants, there was one question on perception of seriousness, one question on concerns, four questions on attitude towards specific habits, and two questions on attitudes towards prevention events and medication programs. In order to measure the practice of the participants, there were three questions on eating raw fish, two questions on eating raw vegetables, one question on drinking untreated water, one question on defecation hygiene (using hygienic toilets), and two questions on diagnosis and treatment.

Data were entered and managed by Kobo ToolBox software (https://www.kobotoolbox.org/), processed and analyzed by SPSS 16.0. By giving a score of 1 for each correct answer, the maximum scores for the Knowledge, Attitude, and Practice were 10, 8 and 6, respectively. Each individual obtained a KAP score based on their answers. We used Bloom's cut-off point of 60% [21] to establish sufficient knowledge, positive attitude, and good practices. In other words, each participant might pass the knowledge section if his/her knowledge score was greater than 6, pass the attitude assessment if his/her attitude score was greater than 4, and pass the practice assessment if his/her practice score was greater than 3. Descriptive statistics were conducted through estimating mean, median, standard deviation (for numeric variables) and frequencies, rates (for categorical variables). The relationship between demographic characteristics and the KAP score of individuals were tested using correlation test (between two numeric variables), Chi-square test (comparing counts of categorical responses between two independent groups), independent-samples t test (comparing means of two independent groups), and One-way ANOVA/post hoc test (comparing means of many independent groups). A p-value < 0.05 was considered to be significant.

RISK BEHAVIOR INVESTIGATION

In the Risk Behavior Investigation, in-depth interviews were organized to provide more information on characteristics of the risk behaviors including eating raw fish and/or raw vegetable and drinking untreated water from lakes/ rivers and on reasons why people show these behaviors. We used two methods to select the participants. During the KAP survey, the researchers identified people who were at risk of infection and demonstrated a risky behaviors of eating raw fish, and individuals with an existing liver fluke infection based on their fecal/blood test result performed by the another group of the FOODTINC project were invited to the in-depth interview. The second method was snowball sampling. After each in-depth interview ended, the interviewee was asked to introduce or refer to other individuals who were showing risk behaviors. Data were collected using an in depth interview guideline. The topics of the in-depth interviews were about the habits of eating raw fish, raw vegetable, and drinking untreated water from rivers/lakes, reasons, frequency and locations. Participants who reported eating raw fish were also asked about the fish species, the preparation procedure and occasions or seasons when they ate raw fish. Forty-five-minute face-to-face interviews were conducted when researchers visited participants' house. Each interviewee was given an ID-number and his/her name was saved in a different file to ensure the confidentiality of the data. All the interviews were recorded and transcribed. In this part, the data were coded by deductive approach, which means data were analyzed based on the topics and questions given in the interview. The transcription was re-read at least three times by the researcher. A matrix including rows and columns was created in Excel Microsoft. Each row was one record of one interviewee, and each column was one label of information which was in line with interview topics/questions. Each interview record was filled in the matrix and synthesized according to topics.

RESEARCH ETHICS

The activities in the current study were under the "Foodborne Zoonotic Trematode Infections and Integrated Control in Vietnam" (FOODTINC) project, which was approved by The Science, Technology and Ethics committee at the National Institute of Malariology, Parasitology and Entomology (Decision number 113/ QĐ-VSR, January 25th, 2018). The study was also approved by the Ethics Committee of the Faculty of

Behavioral, Management and Social sciences (BMS) of the University of Twente (Request number 18299). Before the field trip, the Provincial and District Health Office were informed and asked for a permission to work in the selected communes. Participants who took part in the study were informed and explained sufficiently about the aims and the contents of the research by documents that included two forms: 1) Rights and Responsibilities, and 2) Consent Form. All collected data were processed anonymously.

Results

KNOWLEDGE, ATTITUDE, PRACTICE (KAP) SURVEY

Demographic information

Among the 375 participants, 59.2% (n = 222) were female; 53.6% of participants were between 31 and 50 years old, 61.9% belonged to a minority ethnic group (Dao, Tay, Cao Lan, Nung, Muong, Pati), with Dao being more predominant (48.3%). In terms of education, 77.6% of participants were under the level of secondary school with 10.9% people not having attended school at all (n = 41). Only 2.7% of the participants had a bachelor degree (n = 10). The main occupation of participants was farmer (60.8%), and only 6.9% were government officers.

Knowledge on FZTi

Of all participants, 88.5% had heard about liver fluke (n = 332), but only 1% could name at least one type of liver fluke (small or large liver fluke) (Tabb. I, II). When it comes to the way of transmission, less than half of participants gave the correct answer (49.1%, n = 184), 15.2% of all participants stated they did not know the way liver flukes are transmitted, and 24.3% of all participants had a wrong understanding on the transmission of liver fluke infections (n = 91), they believed that liver flukes can be transmitted from human to human. With regards to the symptoms of liver fluke infection, an open question was asked. A total of 44% of participants did not know the symptoms of liver fluke. Weight loss and jaundice were the two commonest symptoms that participants had listed, followed by the symptoms of decreased appetite, itch, and dyspepsia.

Of all participants, 36.3% passed the knowledge assessment by answering more than 6/10 correctly (n = 136). The correlation between the age of participants and their knowledge score was explored using correlation analysis. Results indicated that the higher the age of the participant, the lower the knowledge score he/she had. Old people highly likely had a low knowledge about liver fluke infection. There was a weak but significant negative correlation between participants' age and their knowledge score (r = -0.165, p = 0.001). There were significant differences in the average knowledge between males and females (p = 0.006), between ethnic groups (p < 0.001), and between education levels (p < 0.001) (Tab. I).

Attitude on FZTi

Of all the participants, 84.3% believed that being infected with liver fluke is a moderate or very serious condition (n = 316), but only 54.4% were really concerned about liver fluke infection (n = 204). The distributions of participants' attitude toward the risky and healthy behaviors of preventing liver fluke infection are presented in Table III. It is noted that only people who had heard about liver fluke infection (n = 332) were asked to give their reaction on statements regarding behaviors in avoiding liver fluke. Although 43 people (11.5%) had never heard about liver fluke infection, they were willing to take part in the communication and treatment program. A total of 99.5% of all participants were willing to take part in communication events on liver fluke infection, and they would be willing to take part in a free diagnosis program and willing to be treated if they got the disease (n = 373).

Of all participants, 86.7% passed the attitude assessment with an attitude score of more than 4 (n = 325). There was no correlation between participants' age and their attitude score (p = 0.592). The attitude average scores were also not associated with demographic characteristics (Tab. II).

Practice on FZTi prevention

Of all 375 participants, 54.9% reported to have eaten raw fish at least once in their life (n = 206), among which 48.1% drank alcohol while consuming raw fish (n = 99). Regarding vegetables, 91.2% of all participants reported to have eaten raw vegetables at least once in their lifetime (n = 342), and 10.4% admitted to have drunk untreated water from lakes/rivers in the last three months (n = 39). Regarding to defecation hygiene, only 71.1% of participants used hygienic toilets (n = 269). The rest of the participants did not use hygienic toilets, and 8.3% of all participants did not even have a toilet in their house (n = 31), they discharged faeces freely in the environment. Regarding diagnosis and treatment, 29.3% had their faeces examined for liver fluke infections (n = 110), and 19.2% had received a fluke treatment (n = 73).

The frequencies of eating raw fish/raw vegetable are presented in Figure 2. Many people explained that they ate raw fish because it was delicious (20.5%, n = 77). Only 1.6% of participants thought it was cool and tonic for their body, and 1.6% confirmed it was their habit (n = 6). 5.6% of respondents did not like eating raw fish, but they ate it with family and friends (n = 21).

The practice of eating raw fish was significantly higher among men than women, with percentages of 61.65% and 38.35%, respectively (p < 0.001). There was no association between age and ethnicity with the practice of eating raw fish. Of all participants, only 24% of participants had passed the practice assessment (n = 91). There was no correlation between the age of participants and their practice score. The average practice scores by demographic characteristics are presented in Table II. The average practice score (SD) of the female group was 2.85 (0.98), which was

Tab. I. Average score in Knowledge, Attitude, and Practice by demographic characteristics of 375 participants in Yen Bai province.

| Demographic characteristics	N	Knowledge score		Attitude score		Practice score	
		Mean (SD)	P-value	Mean (SD)	P-value	Mean (SD)	P-value
Total	375	4.48 (2.07)		6.55 (1.90)		2.75 (1.01)	
Gender							
Female	153	4.25 (2.13)	0.006	6.59 (2.05)	0.657	2.85 (0.98)	0.028
Male	222	4.84 (1.92)		6.50 (1.66)		2.61 (1.05)	
Ethnicity							
Kinh	143	4.96 (1.85)		6.71 (1.69)		2.88 (1.00)	
Dao	181	4.05 (2.18)		6.38 (2.08)		2.69 (1.08)	
Tay	24	3.88 (2.25)	< 0.001	6.17 (2.30)	0.143	2.58 (0.65)	0.379
Cao Lan	24	5.42 (1.32)		7.21 (0.78)		2.71 (0.81)	
Other	3	6.00 (1.00)		7.33 (0.58)		2.33 (0.58)	
Education							
No education	41	3.02 (2.17)		5.90 (2.44)		2.80 (0.95)	
Primary school	103	3.91 (2.14)		6.56 (2.12)		2.63 (1.17)	
Secondary school	147	4.73 (1.93)	< 0.001	6.63 (1.82)	0.209	2.74 (0.98)	0.401
High school	62	5.32 (1.59)		6.63 (1.44)		2.82 (0.88)	
Vocational School	12	5.75 (1.14)		7.33 (0.78)		3.08 (0.90)	
Bachelor	10	6.20 (1.03)		6.50 (1.18)		3.20 (0.79)	
Occupation							
Farmer	228	4.29 (2.08)		6.64 (1.98)		2.74 (1.04)	
Worker	9	4.44 (1.94)		6.22 (2.17)		2.56 (0.88)	
Student	5	6.20 (1.64)		6.20 (1.48)		2.60 (1.14)	
Government officer	26	5.54 (1.53)		6.54 (1.39)		3.19 (0.80)	
Freelance	60	4.48 (2.11)	0.098	6.32 (1.88)	0.685	2.73 (1.06)	0.356
Fish seller	5	7.00 (0)		8.00 (0)		4.00 (0)	
Fisherman	13	4.75 (1.48)		6.67 (0.98)		2.42 (1.08)	
Business	15	4.87 (1.77)		7.00 (1.60)		2.80 (0.86)	
Unemployed	14	4.36 (2.90)		5.64 (2.53)		2.86 (0.86)	

significantly higher than the average practice score (SD) of the male group with 2.61 (1.05) (p = 0.028). Other demographic characteristics had no association with the practice score.

There was a significantly positive correlation between the knowledge and the attitude scores (r = 0.699, p < 0.001). There was no correlation between the knowledge score and the practice score (r = 0.083, p = 0.109), or between the attitude score and the practice score (r = 0.081, p = 0.116).

Risk Behavior Investigation

A total of 27 people, aged between 25 and 64 years, took part in the in-depth interviews, in which 16 came from

Fig. 2. Distribution of raw fish and raw vegetable eating frequency of 375 respondents.
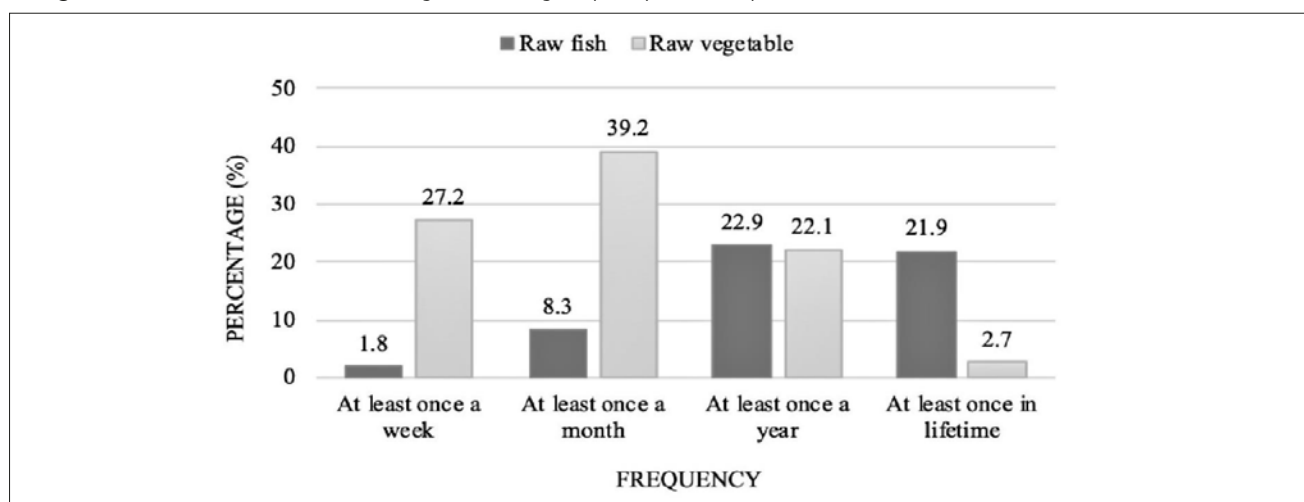
Tab. II. Main participants' responses to knowledge questions on liver flukes.

Question/Statements	Correct answer	
	n	%
General awareness		
Have you ever heard about live flukes?	332	88.5
What kinds of liver fluke do you know? (Participants were expected to name at least one type of liver fluke (small or large liver fluke))	4	1.06
Does liver fluke affect human health?	325	86.7
Causes		
How can people get liver fluke infection? By eating raw fish	275	73.3
By eating raw vegetables	158	42.1
Treatment		
Liver fluke infection can be treated by drugs	219	58.4
Liver fluke infection cannot be treated by drugs	74	19.7
Respondents did not know whether liver fluke infection can be treated by drugs or not	82	21.86
Re-infection		
After patients with liver fluke infection are successfully treated, they cannot get reinfected (Participants were expected to state that this sentence is wrong)	231	61.6
Eating infected fish always causes liver fluke infection, whether or not the fish is cooked (Participants were expected to state that this sentence is wrong)	121	32.3
Prevention		
Liver fluke cannot be prevented (Participants were expected to state that this sentence is wrong)	218	58.1
Symptoms		
What are the symptoms in people infected with liver fluke?	210	56.0

Vu Linh commune and 11 from Phuc An commune. Thirteen participants were selected from the KAP survey when they were showing the habit of eating raw fish and they were open to share their story of eating raw fish. The rest of the participants were introduced by the previous interviewee in the in-depth interviews or the village health workers.

"Gỏi cá" is a popular Vietnamese name of a raw fish dish eaten by local people in Vu Linh and Phuc An, Yen Bai. Three respondents reported that the practice of eating raw fish started in the 1970s when Thac Ba Lake was created, following the construction of the Thac Ba Hydropower dam. The other respondents declared that they had seen the practice of eating raw fish for decades. Many participants reported that they had eaten raw fish since they were young. The information of eating raw fish ("*Gỏi cá*") is summarized in Table IV. Interviewees reported that most fish consumed raw is caught in Thac Ba Lake. The local people consider fish from Thac Ba lake fresher, cleaner, and more delicious than fish originating from the few fishponds in the area. In addition, fishes in the lake are readily available, easy to catch and are free. Ditch fish (*Hemiculter leucisculus*) and Snake-head fish (*Channa* spp.) are the fish species that are most preferred in raw fish dishes because of their firm and tasty flesh. However, the Nile Tilapia (*Oreochromis niloticus*) was the most common fish species for making raw fish because of its availability in the lake. Some people reported that other fish species such as, Common carp (*Cyprinus carpio*), Grass carp (*Ctenopharyngodon idella*), Big-head carp (*Hypophthalmichthys nobilis*), Cyprinid carp (*Cultrichthys erythropterus*), Red-eyed carp (*Squaliobarbus curriculus*) were also used to prepare raw fish dishes. Most fishermen had the habit of sharing raw fish together. After returning from fishing, they usually gather to prepare "*Gỏi cá*" and drink alcohol. Some of their family members, including women and children may also join and enjoy raw fish.

It was reported that raw fish was consumed mainly in the summer and autumn (April to September) which is the rainy season in North Vietnam. Local people said that during this period, fish had finished the breeding season; therefore, the fishes were firm, fishes had finished the breeding season; therefore, their flesh were firm fat, and there were no eggs inside the female fishes, which led to a better taste. This period was also reported as the annual fishing time. However, some people admitted that they may eat raw fish anytime in the year, and they did not care about the season. Regarding the population who consume raw fish, people admitted that there were not any differences between age groups among adults who ate raw fish. However, it is highly likely that men consumed more raw fish than women because raw fish eating is often associated with drinking alcohol. Fishermen or people who lived by the lakeside were highly likely to have the habit of eating raw fish.

In the study sites, people usually grow herbs and vegetables in their garden and use water from wells or from the Thac Ba lake. Raw vegetables and herbs were used as ingredients to prepare raw fish dishes. Many fishermen reported that they drink untreated water directly from Thac Ba lake during the time they go fishing.

Tab. III. Distribution of participants' attitude toward risk and health behaviors, measured with four statements.

Statement	Attitude Scale		
	Disagree	Neither agree nor disagree	Agree
To prevent liver fluke infection, I do not eat raw fish or undercooked fish anymore	4 (1.1%)	7 (1.9%)	320 (85.3%)
To prevent liver fluke infection, I do not eat raw vegetables anymore	69 (18.4%)	27 (7.2%)	235 (62.7%)
To prevent liver fluke infection, I do not defecate in a public space	1 (0.3%)	2 (0.5%)	329 (87.7%)
To prevent liver fluke infection, I do not feed fish with fresh human or animal faeces	11 (2.9%)	15 (4.0%)	306 (81.6%)

Tab. IV. Summary of information on the habit of eating raw fish in Yen Bai Province.

Interview topic	Main answers
Origin of fish	Mostly from Thac Ba lake, rarely from fish ponds
Fish species	Mainly: Ditch fish, Snake-head fish, Tilapia Other: common carp, grass carp, silver carp, squaliobarbus, cyprinid fish
Preparation procedure	Fish is washed and cleaned, and then cut into thin slices (2-3 mm). After that, it is marinated with lime juice, salt and seasoning for 15 to 30 minutes. Finally, it is mixed with fried rice powder and herbs (or raw vegetables)
Location of eating raw fish	Home or friend's home
Occasion	No special occasions, usually after people catch fresh fishes and drink alcohol together
Seasons of eating	Mainly in summer, rainy season, from April to September. Some people reported that they eat raw fish year round

REASONS OF LOCAL PEOPLE PERFORMING RISK BEHAVIORS

Habit shaped by previous generations

Firstly, it was confirmed by local people that the habit of raw fish consumption (*Gỏi cá*) is not a traditional custom or culture. Indeed, 26/27 participants declared that raw fish eating was not a traditional custom, and a few of them said that raw fish is not served at traditional festivals or on special occasions. They believed that the habit of eating raw fish appeared many years ago and was passed between generations. Therefore, eating raw fish is a habit shaped since people were young.

Consequences of poor economic conditions and cultural factors

The habit of eating raw fish was the consequence of poor economic conditions. In fact, most people are farmers without a stable income, and they produce and consume agricultural products mainly for home consumption. Therefore, fishing is a way to earn more money and to improve their daily meal. Fish has become one of the main food sources. Numerous respondents reported that the poor economic conditions made them less concerned about their health. Sometimes, fish was the only food they had, and they prepared fish in ways to be easily eaten, such as, *Gỏi cá*. Social factors also affect the habit of eating raw fish. As mentioned above, fishermen declared to share and enjoy raw fish together, and this action enabled this habit to pass from person to person. At those meals or parties, people enjoyed consuming raw fish with alcohol, and it was seen as a way for people to socialize. Another culture in Yen Bai is that people often invite their friends to try strange or delicious dishes such as raw fish. Some people reported that they did not like or did not want to eat raw fish because of health risks, but they could not refuse the invitation from their hosts.

Lack of knowledge on liver fluke infection

One of the important reasons which leads to risk behaviors among local people is that they lack the knowledge on FZTi. Instead of knowing that eating raw fish is a bad habit, they believed that it is tonic and good for their health. Most interviewees (19/27) reported that they like eating raw fish because of the taste. Men confessed that they would still keep the habit of eating raw fish after knowing the risk of getting liver fluke infection, because they know that the disease can be treated well by drugs. While many participants were not aware of the risk of getting liver fluke infection when eating raw fish or raw vegetables, a few knew about the risks of raw fish consumption, but they kept this habit because of insufficient or wrong knowledge. As a consequence of lacking knowledge on liver fluke infection, many people underestimated its harmfulness and showed a bad attitude towards prevention.

Discussion

By applying both quantitative and qualitative research methods, we found that: (1) the knowledge regarding liver fluke infection among local people was low, with 11.5% of all participants having never heard of liver fluke, and only 36.3% passing the knowledge assessment; (2) the attitude regarding liver fluke infection and its prevention was quite positive, which was determined by 86.6% of all respondents passing the attitude assessment; and

despite the fact that many people had not heard about the disease, they were willing to join a communication or treatment program if applicable; (3) the proportion of people with good practice was low with only 24% of all participants passing the practice assessment; and (4) the habit of eating raw fish in Yen Bai was not only a consequence of a lack of knowledge but also related to economic and social factors.

The KAP scores of the participants in the current study were lower than those reported in Northeast Thailand by [22]. Although Thailand and Vietnam share many features including, the climate, the culture, and the practice of eating raw fish, overall the economic conditions are better in Thailand than in Vietnam. Thailand is one of the most developed countries in the region, with a GDP per capita of 7,806.96 USD compared to a GDP per capita of 3,416.23 USD in Vietnam (2019) [23]. Therefore, the participants in the Thai study might have had a higher education level than the participants in this study. Furthermore, differences of the study designs might also have caused differences in KAP results. For example, the knowledge of Thai participants was ranked as good if the score was above the median, which is different from the interpretation of the KAP scores in the current study [22].

We also found differences in the KAP results in people from Yen Bai and from other areas in Vietnam. The knowledge and practice results of residents in Yen Bai were lower than, in Thanh Hoa, in Central Vietnam, where 46.5% and 30.6% of the studied population passed the knowledge and practice assessments, respectively [24], and in Phu Yen, in South Vietnam, where 39.2% and 40.1% passed the knowledge and practice, respectively [25]. While only 33.3% of the studied population in Phu Yen ate raw fish, we found Yen Bai province was 54.9%. In contrast, the attitudes of people in Yen Bai were more positive than that in Thanh Hoa and Phu Yen, Indeed, most people in Yen Bai were willing to take part in communication and treatment programs. The differences among these studies may be explained by the study design and we could not confirm whether the differences among populations in the three provinces are statistically significant. Interestingly, the provinces in the three studies represent the three regions in Vietnam, *i.e.* the North, the Centre, and the South.

In the current study, the population was living in a rural mountainous area with a general low educational level. A high proportion of the population was farmer with the habit of going fishing in Thac Ba lake. The results in the risk behavior investigation showed that the practice of eating raw fish was affected by gender. Specifically, men were more likely to eat raw fish than women because men usually went fishing together, after which they would gather to drink alcohol and eat the raw fish. Women who ate raw fish mostly belonged to households in which the father, the husband or the son had a habit of eating raw fish. We also showed that men still ate raw fish even after knowing the risk of getting liver fluke infection because they know the disease may be treated with drugs. This result is in line with the findings

of a report in North Vietnam [7]. Additionally, living in villages where a tradition of sharing raw fish is common has then transmitted to a habit of eating raw fish, making this practice it more popular, which is consistent with the findings of fascioliasis in Thua Thien Hue, Vietnam [26]. The study also revealed that gender and age are factors affecting the knowledge. The average knowledge score among men was greater than that among women, and the score among younger people was greater than that among the older. This is understandable because young people are more likely to have higher education and it is much easier for them to access information via mobile phones or the internet. However, the risk behavior investigation revealed that eating raw fish was not associated with demographic characteristics such as age, ethnicity, and educational levels. This result was confirmed by the results in the KAP survey.

The findings showed that the better knowledge people have, the better attitude they display. Nevertheless, there was not enough evidence to confirm the relationship between the knowledge and the practice, and between the attitude and the practice of the population. This revealed that unsafe practices were not only caused by lack of knowledge and attitude factors, but also by other factors in the living environment. This was consistent with the results in the risk behavior investigation that showed that a habit of eating raw fish was a consequence of the poor economic conditions and social structures, which also determined a large aspect of local people's attitude.

The findings of the study contributed to filling the gap of knowledge regarding to liver fluke infection in Vietnam, and they confirmed the findings of the previous studies in different contexts. The results reflected the lack of knowledge and bad practice of residents not only in two studied communes but also all around Thac Ba lake. It is apparent that living near natural water bodies, specifically Thac Ba lake in Yen Bai, plays an important role in the context of eating raw fish and therefore getting infected with liver fluke. The lake is the origin of the raw fish eating habit, and it provides a huge source of fish, consequently it is easy for nearby residents to exploit and form habits of fishing and sharing raw fish. This study can be translated to other similar areas in which the residents live near high-density natural water bodies and eat raw fish.

Eating raw vegetables and drinking untreated water were identified as risk factors for large liver fluke infection in the Thac Ba area. This finding is similar to a fascioliasis KAP survey in Quang Nam province (Central Vietnam) [27], where all interviewees were eating raw vegetables and drinking untreated water. The attitude score for *Fasciola* prevention by not eating raw vegetable were 62.7%. This finding is surprising because Vietnamese people like to eat raw vegetables.

The results of this study must be interpreted taking into account both strengths and limitations. An important strength in the study is the use of an integrated approach with both quantitative (KAP) and qualitative methods, so the results in each part may support and complement each other. In the KAP survey, the respondents may give

different answers in different contexts although their KAP is constant. For example, respondents may have given socially desirable answers if they felt unsafe at the health station. However, the in-depth interview at home provided the participants with a comfortable and safe environment to answer the questions. The information from the qualitative part of the study can also explain the relationship among variables in the KAP. With regard to the limitations, the differences in knowledge, attitudes, and practice among different demographic characteristics that we observed were statistically significant, but the differences were small and the correlation did not show a strong relationship among variables. Moreover, the current knowledge, attitudes, and practices were described primarily through the scores, and these were given the same weight. It may be that results would be more accurate if the questions would have been given different weights in the KAP survey.

Conclusions

In conclusion, the residents in the two communes in Yen Bai, Vu Linh and Phuc An still have a poor knowledge and perform bad practices regarding to liver fluke infections. The findings suggest that the lack of knowledge is not the only reason leading to a habit of eating raw fish but that there are also economic and social factors at play. Therefore, to control FZTi in Yen Bai province, particularly in the lakeside areas, an integrated control including, health education, fish/snail habitat interventions and safe food processing is essential.

Acknowledgements

Conflict of interest statement

The authors declare no conflict of interest.

Authors' contributions

NTTP, DDT, ML, BL, OV, DTB developed study design and research methodology. NTTP, TTBN, TIHL contributed in data collection. NTTP, MVG, MBB contributed in data analysis. NTTP, DTB contributed in manuscript's writing. NTTP, PD, MVG, MBB, DTB contributed in manuscript review and edited.

References

[1] Chai JY, Jung BK. Fishborne zoonotic heterophyid infections: An update. Food Waterborne Parasitol 2017;8-9:33-63. https://doi.org/10.1016/j.fawpar.2017.09.001

[2] Pal M, Ayele Y, Hadush A, Kundu P, Jadhav VJ. Public health significance of foodborne helminthiasis: A systematic review. J Exp Food Chem 2018;4:4-9. https://doi.org/10.4172/2472-0542.1000135

[3] Tolan RW. Fascioliasis due to Fasciola hepatica and Fasciola gigantica infection: An update on this "neglected" neglected tropical disease. Lab Med 2011;42:107-16. https://doi.org/10.1309/LMLFBB8PW4SA0YJI

[4] WHO. WHO estimates of the global burden of foodborne diseases: foodborne disease burden epidemiology reference group 2007-2015. 2015. Available at: https://www.who.int/foodsafety/publications/foodborne_disease/fergreport/en/

[5] Nguyen V De, Murrell DK, Le DC, Phung DC, Le VC, Nguyen DT, et al. The foodborne trematode zoonoses of Vietnam. Southeast Asian J Trop Med Public Health 2003;34:12-34.

[6] Doanh PN, Horii Y, Nawa Y. Paragonimus and paragonimiasis in Vietnam: An update. Korean J Parasitol. 2013;51:621-7. https://doi.org/10.1016/j.actatropica.2019.105074

[7] Thach D, Cam T, Yajima A, Nguyen K, Montresor A. Prevalence, intensity and risk factor of Clonorchiasis and possible use of questionnaire to detect individuals at risk in northern Vietnam. 2017;102:1263-8. https://doi.org/10.1016/j.trstmh.2008.06.002

[8] Hung NM, Dung DT, Lan Anh NT, Van PT, Thanh BN, Van Ha N, Hien HV, Canh LX. Current status of fish-borne zoonotic trematode infections in Gia Vien district, Ninh Binh province, Vietnam. Parasites Vectors 2015;8:1-10. https://doi.org/10.1186/s13071-015-0643-6

[9] Dao TTH, Bui T Van, Abatih EN, Gabriël S, Nguyen TTG, Huynh QH, Nguyen CV, Dorny P. Opisthorchis viverrini infections and associated risk factors in a lowland area of Binh Dinh Province, Central Vietnam. Acta Trop 2016;157:151-7. http://doi.org/10.1016/j.actatropica.2016.01.029

[10] Grundy-Warr C, Andrews RH, Sithithaworn P, Petney TN, Sripa B, Laithavewat L, Ziegler AD.. Raw attitudes, wetland cultures, life-cycles: Socio-cultural dynamics relating to Opisthorchis viverrini in the Mekong Basin. Parasitol Int 2012;61:65-70. http://doi.org/10.1016/j.parint.2011.06.015

[11] Doanh PN, Nawa Y. Clonorchis sinensis and Opisthorchis spp. in Vietnam: Current status and prospects. Trans R Soc Trop Med Hyg 2015;110:13-20. http://doi.org/10.1093/trstmh/trv103

[12] Bui TD, Doanh PN, Saegerman C, Losson B. Current status of fasciolosis in Vietnam: An update and perspectives. J Helminthol 2016;90:511-22. http://doi.org/10.1017/S0022149X15000929

[13] Trieu N, Nguyen V, Huynh H. Human fasciolosis in central-highland region of Vietnam and efficacy of interventional measures (2006-2009). Vietnamese J Mil Pharmaco-Medicine 2012;KC10:130-7.

[14] CDC. Parasites-Fascioliasis. 2018. Available at: https://www.cdc.gov/parasites/fasciola/

[15] Saijuntha W, Sithithaworn P, Petney TN, Andrews RH. Foodborne zoonotic parasites of the family Opisthorchiidae. Res Vet Sci 2020;135:404-11. http://doi.org/10.1016/j.rvsc.2020.10.024

[16] Bui NT. Current status of fishborne zoonotic trematode metacercariae in fish of the Northern Mountain Region Vietnam. Vietnam Graduate University of Science and Technology 2017.

[17] Nguyen V, Bui N, Nguyen V, Dao X, Pham T, Phan T. The eating raw fish habits and knowledge of people in mountain regions of northern Vietnam about the transmission of trematodiasis. Proceeding of the 43th Vietnam National Conference on Parasitology 2016, pp. 295-9.

[18] Kaliyaperumal K. IEC; Expert, Diabetic Retinopathy Project. Guideline for Conducting a Knowledge, Attitude and Prac-

tice (KAP) Study. AECS Illum Community Ophthalmology 2004;4:7-9.

[19] Goutille F, Crini V, Jullien P. Knowledge, Attitudes and Practices for Risk Education: how to impelement KAP surveys. Handicap I. Handicap International; 2009.

[20] Nguyen TTB, Dermauw V, Dahma H, Bui DT, Le TTH, Phi NTT, Lempereur L, Losson B, Vandenberg O, Do DT, Dorny P. Prevalence and risk factors associated with clonorchis sinensis infections in rural communities in northern Vietnam. PLoS Negl Trop Dis 2020;14:1-17. http://doi.org/10.1371/journal.pntd.0008483

[21] Benjamin S, Dhew E, Bloom BS. Learning for Mastery. Encycl Sci Learn 2012;(2):1854-1854. https://doi.org/10.1007/978-1-4419-1428-6_4645.

[22] Kaewpitoon N, Kaewpitoon SJ, Pengsaa P, Pilasri C. Knowledge, attitude and practice related to liver fluke infection in northeast Thailand. World J Gastroenterol 2007;13:1837-40. http://doi.org/10.3748/wjg.v13.i12.1837.

[23] Plecher H. Gross domestic product (GDP) per capital in the ASEAN countries 2020. 2020. Available at: https://www.statista.com/statistics/804307/gross-domestic-product-gdp-per-capita-in-the-asean-countries/

[24] Do TH. Situation of small liver fluke infection in people over 14 years old and some related factors in Nga An commune, Nga Son district, Thanh Hoa province in 2005. Hanoi University of Public Health, Vietnam, 2005.

[25] Le HT. Knowledge, attitude and practice towards prevention of Opisthorchis viverrini infection among above 15 years-old people at one commune of Phu Yen province. Vietnamese J Prev Med 2014;24.

[26] Nguyen NT, Le TC, Vo MDC, Cao HV, Nguyen LT, HO KT, Nguyen QN, Tran VQ, Matsumoto Y. High prevalence of cattle fascioliasis in coastal areas of Thua Thien Hue province, Vietnam. Vietnamese J Vet Med Sci 2017;79:1035-42. http://doi.org/10.1292/jvms.16-0331

[27] Nguyen V. Study on the current status of human fasciolosis and the effectiveness of some interventions in the community of Quang Nam province, 2012. National Institute of Malariology Parasitology and Entomology, Vietnam, 2012.

Assessment of oral health status and treatment needs of HIV positive transgenders in Odisha - a cross-sectional study

GUNJAN KUMAR, SHILPA RAI

Department of Public Health Dentistry, Kalinga Institute of Dental Sciences, KIIT deemed to be University Bhubaneswar, Odisha, India

Summary

Introduction. *Human Immunodeficiency virus (HIV) causes the human immunodeficiency infection which is a major global health problem. Oral health status of people infected by HIV is also compromised. There is limited literature on oral health status of HIV/AIDS transgenders in Odisha.*

Aim. *This study was conducted to assess the oral health status of HIV-positive transgenders.*

Methodology. *A cross-sectional study was conducted among the HIV positive transgenders in Odisha. Snowball sampling technique was employed to reach the population. Oral health was recorded using modified WHO 2013 proforma. Clinical examination using disposable mouth mirror and explorer. Chi square statistics was used for finding the association between the sociodemographic variables and DMFT, CPI, and LOA scores.*

Results. *The study included 153 participants out of which seventy participants belonged to the age group 18-30 years. Majority of the participants were unemployed and most of them had spent around 6-10 years in school. Majority of the participants*

used toothbrush for cleaning their teeth and the average duration of cleaning tooth was less than two minutes. Toothpick was the most common method used for cleaning interdental areas and none of the participants used dental floss or interdental brushes. The mean DMFT score which was recorded to be 1.424. Around 28.10% (43) inmates had pockets of depth 4 mm to 5 mm. Loss of attachment of 6 mm to 8 mm was found in majority (57, 37.25%) of the participants. Most of the participants did not require any prosthesis both in the upper and lower arches. Around 32 participants (20.91%) had very mild fluorosis, 29 participants (18.95%) exhibited signs of moderate fluorosis. Age was found to be significantly associated with loss of attachment score (p = 0.023). Occupation had an association with the DMFT score (p = 0.002) while years in school was found to be significantly associated with CPI score (p = 0.045).

Conclusion. *The oral health status of transgenders is poor and needs immediate attention.*

Introduction

Human Immunodeficiency virus (HIV) causes the human immunodeficiency infection which is a major global health problem. In India, the prevalence of HIV infection among adults was 0.22% in 2017 with 21.4 lakh people infected with HIV [1]. According to the recent HIV estimates report (2019) of the Government, India was estimated to have around 23.49 lakh people living with HIV/AIDS (PLHIV) in 2019 [2]. The aggregated overall HIV prevalence observed among transgenders was 7.5% in 2014-2015. As per the latest HIV estimates report (2019), HIV/AIDS prevalence in Odisha in 2018 and 2019 was 0.50 and 0.49 respectively [3].

HIV not only destroys the immune system but also results in an elevated tendency to acquire and manifest diseases that are usually resistible by the normal body [4]. Oral health status of people infected by HIV is also compromised. Studies show that HIV patients are more likely to have heavier oral burdens of lactobacilli and streptococci than others [1]. Poor oral health ultimately affects the quality of life by causing pain, discomfort, dry mouth, and eating restrictions and are a constant

source of opportunistic infection [5]. There is limited literature on oral health status of HIV/AIDS transgenders in Odisha. The treatment of oral health problems can considerably improve quality of life and well-being of this group. Hence, this study was conducted to assess the oral health status of HIV-positive transgenders.

Materials and methods

A cross-sectional study was conducted among the HIV positive transgenders in Khurda, Cuttack, Angul and Ganjam districts of Odisha. All the HIV positive transgenders who had medical documentation of HIV infection,who took and did not take antiretroviral drugs and gave their consent to participate were included in the study. The transgenders who did not give consent and tobacco associated oral lesions were excluded from the study. Snowball sampling technique was employed as transgenders are a difficult group to reach and HIV status not only adds social stigma but also discriminates making them more vulnerable. Oral health was recorded using modified WHO 2013 proforma. Data collection

Tab. I. Socio-demographic profile of the participants.

Socio-demographic Variables		n	%
Age (years)	≤ 18	4	11.76%
	> 18 & ≤ 30	70	45.75%
	> 30 & ≤ 40	53	34.64%
	> 40 & ≤ 50	16	10.46%
	> 50	10	6.54%
Occupation	Professional	0	0.00%
	Semi-professional	2	1.31%
	Clerical	15	9.80%
	Skilled	12	7.84%
	Semi-skilled	45	29.41%
	Unskilled	11	7.19%
	Unemployed	69	45.10%
Years in school	≥ 16 years & ≤ 20 years	4	2.61%
	≥ 11 years & ≤ 15 years	28	18.30%
	≥ 6 years & ≤ 10 years	88	57.52%
	≤ 5 years	33	21.57%

was carried out during four consecutive months from November 2019 to March 2020. It was initiated in ART centre; Khurda where the first HIV positive transgender and the outreach worker were encountered. With the help of this participant further clusters of HIV positive transgenders were reached in Bhubaneswar. Subsequently other transgender groups in Berhampur and Bhanjanagar (Ganjam), Angul and Cuttack districts were reached. Clinical examination using disposable mouth mirror and explorer, was performed on a total of 153 participants by the chief investigator in the presence of a recording assistant who was trained and calibrated in the department. A maximum of 25 inmates were examined in every visit.

Permission to conduct the study was obtained from the Odisha State AIDS Control Society. Ethical clearance was obtained from the Institutional Review Board.

Statistical Analysis

The collected data was analyzed using SPSS version 21.0 (IBM SPSS statistics for Windows, Version 21.0, Armonk, NY:IBM Corp). Chi square statistics was used for finding the association between the socio-demographic variables and DMFT, CPI, and LOA scores. The level of statistical significance was set at 0.05 with a confidence interval of 95%.

Results

The study included 153 participants out of which seventy participants belonged to the age group 18-30 years. Majority of the participants were unemployed and most of them had spent around 6-10 years in school (Tab. I).
Majority of the participants used toothbrush for cleaning their teeth and the average duration of cleaning tooth was less than two minutes for around 88 (57.52%) number of participants. Around 56.86% of the participants cleaned their teeth only once a day. Toothpick was the most

common method used for cleaning interdental areas and none of the participants used dental floss or interdental brushes. Warm saline was used by around twenty eight participants while majority did not use any additional cleaning aid (Fig. 1).

The mean number of filled, decayed, and missing teeth was found to be 0.078, 1.424, and 0.176 respectively. The mean DMFT score which was recorded to be 1.424 (Tab. II).

28.10% (43) inmates had pockets of depth 4 mm to 5 mm. Fifty eight participants only presented with bleeding while 36 (23.53%), had deep pockets. Loss of attachment of 6 mm to 8 mm was found in majority (57, 37.25%) of the participants. Around 49 participants (32.03%) had loss of attachment of 4-5 mm (Tab. III).

Around 27 participants (17.65%) had partial denture in the upper arch and around 13 participants (8.49%) had partial denture in the lower arch. Most of the participants did not require any prosthesis both in the upper and lower arches (Tab. IV).

The study participants exhibited signs of enamel fluorosis. Around 32 participants (20.91%) had very mild fluorosis, 29 participants (18.95%) exhibited signs of moderate fluorosis while two of the participants exhibited severe enamel fluorosis (Fig. 2).

Age was found to be significantly associated with loss of attachment score (p = 0.023). Occupation had an association with the DMFT score (p = 0.002) while years in school was found to be significantly associated with CPI score (p = 0.045) (Tab. V). The distribution of CD4+ T cell among the study participants has been depicted in Figure 3.

Discussion

The present study was carried out on the transgenders residing in Odisha. Around 153 transgenders participated in the study, out of which the majority belonged to the age group 18-30 years, were unemployed and had spent around 6-10 years in school. In a study done by Sivabakya and Srinivas [6], the mean age of the particpants was found to be 37.58 ± 10.44. Similar findings was reported by Kumar et al. [7].

In the present study, majority of the participants used toothbrush for cleaning their teeth and the average duration of cleaning tooth was less than two minutes. In a study done by Kumar et al., 65.9% were using toothbrush and paste for oral hygiene maintenance [7].

Aleixo et al. [8] had reported a high number of decayed teeth detected among patients undergoing ART which resulted in a mean DMFT of 16.9 teeth. In a study done by Chaudhary the mean decayed, missing, and filled teeth (DMFT) score was 4.03 ± 1.54 and only 12% of the patients had healthy periodontium [9]. The mean DMFT in the present study was 1.424 and 10.46% of the participants had healthy periodontium.

In the present study, 28.10% inmates had pockets of depth 4 mm to 5 mm. Loss of attachment of 6 mm to 8 mm was found in majority of the participants in the

Fig. 1. Oral health practices among the participants.

Oral hygiene practices
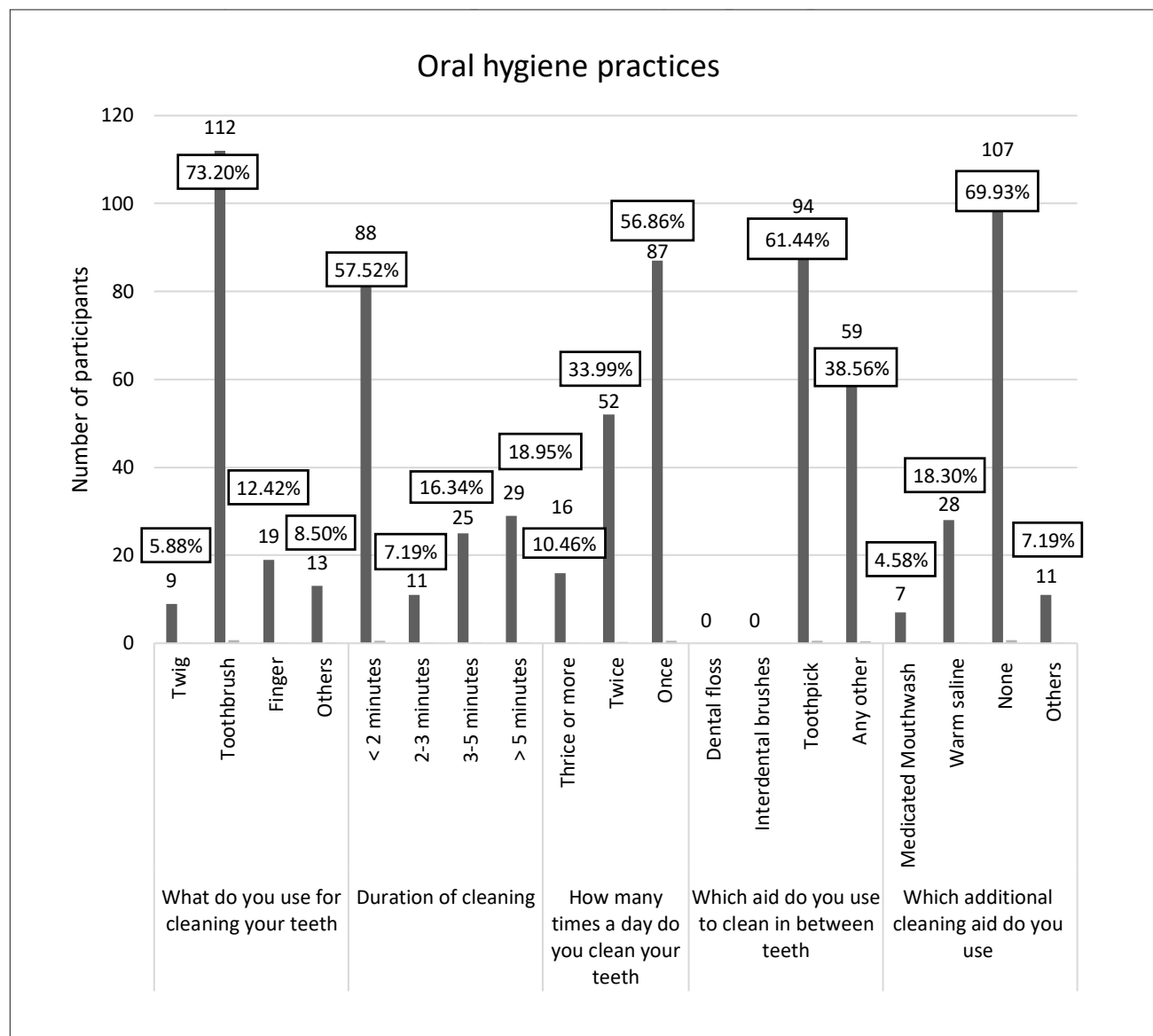
Tab. II. Dentition status of the participants.

Category (n = 153)	Minimum	Maximum	Mean	SD
Decayed teeth	0	8	1.424	1.707
Missing teeth	0	4	0.176	0.551
Filled teeth	0	4	0.078	0.493
DMFT score	0	9	1.679	1.958

DMFT: Decayed, missing, and filled teeth; SD: Standard deviation.

Tab. III. Periodontal status of the participants.

Dentition status of the participants

Category (n = 153)		Minimum	Maximum	Mean	SD
Decayed teeth		0	8	1.424	1.707
Missing teeth		0	4	0.176	0.551
Periodontal status	CPI highest score n (%)	Healthy periodontium			16 ; 10.46%
		Bleeding only			58 ; 37.91%
		Shallow pocket (4 mm-5 mm)			43 ; 28.10%
		Deep pocket (≥ 6 mm)			36 ; 23.53%
	LOA highest score n (%)	LOA 0-3 mm			16 ; 10.46%
		LOA 4-5 mm			49 ; 32.03%
		LOA 6-8 mm			57 ; 37.25%
		LOA 9-12 mm			26 ; 16.99%
		LOA ≥ 12 mm			5 ; 3.27%

Tab. IV. Prosthetic status of the participants and their prosthetic needs.

Presence of denture n (%)	Upper arch	No denture	126 ; 82.35%
		Partial denture	27 ; 17.65%
	Lower arch	No denture	140 ; 91.50%
		Partial denture	13 ; 8.49%
Prosthetic needs n (%)	Upper arch	No prosthesis needed	58; 37.91%
		Need for 1 unit prosthesis	37 ; 24.18%
		Need for multi-unit prosthesis	43 ; 28.10 %
		Need for a combination of 1 &/multi-unit prosthesis	15 ; 9.80 %
	Lower arch	No prosthesis needed	44 ; 28.76%
		Need for 1 unit prosthesis	56 ; 36.60%
		Need for multi-unit prosthesis	31 ; 20.26%
		Need for a combination of 1 &/multi-unit prosthesis	22 ; 14.38%

Tab. V. Association between age, education and years in school with various oral health status components.

Category	DMFT Score (p-value)	CPI Score (p-value)	LOA Score (p-value)
Age	0.492	0.186	0.023*
Occupation	0.002*	0.943	0.121
Years in school	0.671	0.045*	0.829

* $p < 0.05$ is considered as statistically significant. CPI: Community periodontal index; LOA: Loss of attachment; DMFT: Decayed, missing, and filled teeth.

present study. Muralidharan et al., reported that a higher percentage of people with 4 to 5 mm of pockets was seen with those who cleaned their teeth with a finger [10]. Kumar et al., reported that nearly 50% of people suffering from HIV had CPI score and LOA score > 27. These findings indicated poor periodontal health among patients suffering from HIV.

In this study, around 17.65% of the participants had partial denture in the upper arch and around 8.49% of them had partial denture in the lower arch. Most of the participants did not require any prosthesis both in the upper and lower arches. Soares GB reported that around 35.0% of HIV positive participants used dentures, 41.5% needed denture in the maxilla, and 62.0% in the mandible [11].

Around 32 participants in the present study had very mild fluorosis, 29 participants exhibited signs of moderate fluorosis while two of the participants exhibited severe enamel fluorosis. In a study done by Sivabakya TK, it was found that only 20.9% of the HIV patients had questionable fluorosis, followed by 7% with very mild and 7% with moderate dental fluorosis [6]. About 2.3% of the study participants had severe fluorosis [6].

Our study has few limitations. The sample size was small and as we used a crosssectional design the accurate temporal sequence of exposure and effect could not be established. There was no HIV uninfected population to compare the frequency of comorbidities.

Conclusion

The oral health status of transgenders is poor and needs immediate attention. Oral health education needs to

Fig. 2. Enamel fluorosis among the participants.
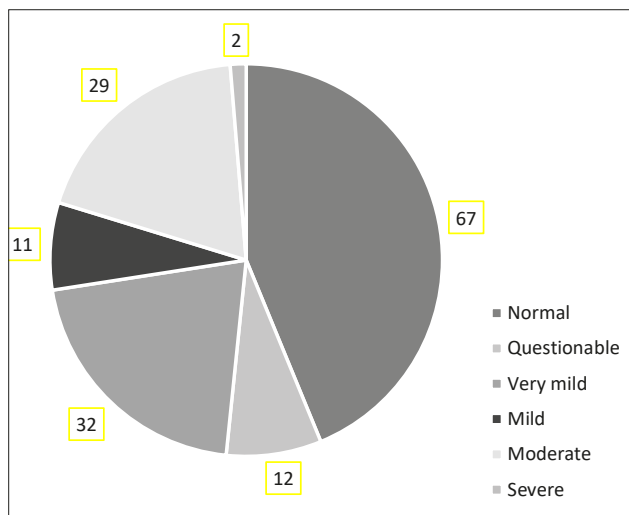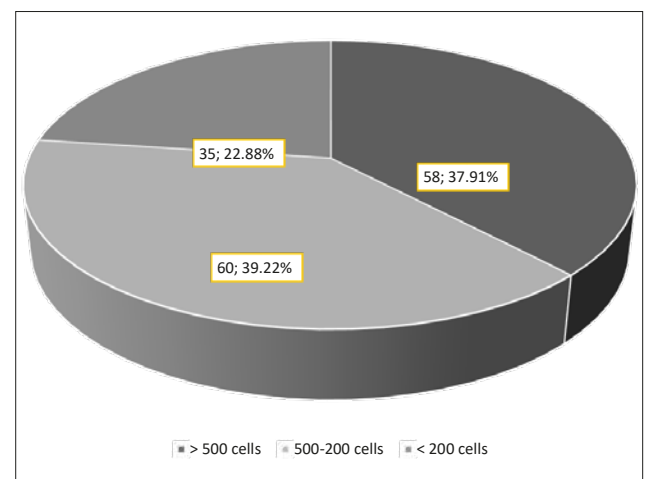

Fig. 3. Distribution of CD4+ T cell count.

imparted among this socially deprived group and their oral health needs must be met to ensure good and equitable oral health for all. Effective policies need to be drafted to take care of the oral health of this highrisk group.

Acknowledgements

Financial support and sponsorship

Conflict of interest statement

There are no conflicts of interest.

Authors' contributions

All authors reviewed the results and approved the final version of the manuscript.

References

[1] Annual Report 2010-2011. Department of AIDS Control Ministry of Health & Family Welfare. Accessed from: http://naco.gov.in/sites/default/files/NACO%20Annual%20Report%202010-11.pdf

[2] HIV/AIDS Patients in India. Ministry of health and family welfare. Accessed from: https://pib.gov.in/PressReleaseIframePage.aspx?PRID=1657057

[3] National AIDS Control Organization (2016). National Integrated Biological and Behavioural Surveillance (IBBS), Hijras/Transgender People, India 2014-15. New Delhi: NACO, Ministry of Health and Family Welfare, Government of India. Accessed from: http://naco.gov.in/sites/default/files/IBBS%20Report%202014-15.pdf

[4] Patton LL, Phelan JA, Ramos-Gomez FJ, Nittayananta W, Shiboski CH, Mbuguye TL. Prevalence and classification of HIV-associated oral lesions. Oral Dis 2002;8 (Suppl 2):98-109. https://doi.org/10.1034/j.1601-0825.2002.00020.x

[5] Ranganathan K, Hemalatha R. Oral lesions in HIV infection in developing countries: an overview. Adv Dental Res 2006;19:63-8. https://doi.org/10.1177/154407370601900113

[6] Sivabakya TK, Srinivas G. Oral health status among human immunodeficiency virus-positive patients visiting ART center in Chennai: A cross-sectional study. Indian J Oral Health Res 2020;6:38-41. https://doi.org/10.4103/ijohr.ijohr_19_20

[7] Kumar S, Mishra P, Warhekar S, Airen B, Jain D, Godha S. Oral health status and oromucosal lesions in patients living with HIV/AIDS in India: A Comparative Study. AIDS Res Treat 2014;2014:480247. https://doi.org/10.1155/2014/480247

[8] Aleixo RQ, Scherma AP, Guimaraes G, Cortelli JR, Cortelli SC. DMFT index and oral mucosal lesions associated with HIV infection: crosssectional study in Porto Velho, Amazonian region - Brazil. Braz J Infect Dis 2010;14:449-56. https://doi.org/10.1016/S1413-8670(10)70092-1

[9] Chaudhary P, Manral K, Gupta R, Bengani AKS, Chauhan BI, Arora D. Oral health status and treatment needs among HIV/AIDS patients attending antiretroviral therapy center in Western India: A cross-sectional study. J Family Med Prim Care 2020;9:3722-8. https://doi.org/10.4103/jfmpc.jfmpc_411_20

[10] Muralidharan S, Acharya AK, Margabandhu S, Kalekhan S, Ahsan S, Kulkarni D. Prevalence of Periodontitis and Soft Tissue Lesions among Human Immunodeficiency Virus-positive Patients on Antiretroviral Therapy in Raichur Taluk, Karnataka, India. J Contemp Dent Pract 2018;19:42-46. https://doi.org/10.5005/jp-journals-10024-2209

[11] Soares GB, Garbin CA, Moimaz SA, Garbin AJ. Oral health status of people living with HIV/AIDS attending a specialized service in Brazil. Spec Care Dentist 2014;34:176-84. https://doi.org/10.1111/scd.12056

Impact of the state of emergency on trends in the care of three major diseases at Showa University Hospital, Japan: a retrospective and descriptive study

AKIRA MINOURA[1], KOUZOU MURAKAMI[2], MASAAKI MATOBA[3], YOSHINORI ITO[2],
YUMI KAMIJO[3], AKATSUKI KOKAZE[1]

[1] Department of Hygiene, Public Health and Preventive Medicine, Showa University School of Medicine, Tokyo, Japan;
[2] Department of Radiology, Division of Radiology, Showa University School of Medicine, Tokyo, Japan;
[3] Department of Health Management, Showa University Graduate School of Health Sciences, Tokyo, Japan

Summary

Introduction. *This study aimed to examine the trends in patient consultations for three major diseases (cancer, heart disease, and stroke) at Showa University Hospital, Japan during the state of emergency for the Coronavirus 2019 (COVID-19) pandemic.*
Methods. *The present study was a retrospective and descriptive study of Showa University Hospital in Tokyo, Japan. Subjects were patients who had received medical treatment at Showa University Hospital and were diagnosed from 2017 to 2020. To examine the impact of the state of emergency, the number visits to hospital by the top three causes of death or other diseases were summarised from 21 weeks of data, from week 8 to week 28, for each year.*

Results. *Compared to the average of the previous 3 years, a comparison of the three periods before and after the state of emergency showed a V-shaped curve in 2020, with a large drop in the number of cancer patients during the state of emergency, both from within Tokyo and from outside the city.*
Conclusions. *This study showed a long-term decrease in cancer patient visits to Showa University Hospital since the beginning of the COVID-19 pandemic compared to the previous 3 years. It is also possible that medical care that would have been available may not have been provided due to the state of emergency, so it is necessary to follow up patients while keeping a close eye on measures other than infectious diseases.*

Introduction

Coronavirus 2019 (COVID-19) caused a global public health emergency in 2020 [1]. During the COVID-19 pandemic, there was a shortage of medical staff and resources, intensive care units, ventilators, and personal protective equipment (especially medical masks) due to an urgent increase in the number of infected and severe patients. To deter the spread of COVID-19, many countries have imposed a lockdown with restrictions on outings and service closures. The lockdown in most of these countries has compelling force with penalties for violations. The lockdown can be expected to deter the spread of the infection, which would otherwise become destructive, resulting in not only economic damage, but also delays in treatment of patients [2]. In particular, cancer treatment delay is a problem in health systems worldwide. Hanna et al. demonstrated that a 4-week delay of cancer treatment is associated with increased mortality across surgical, systemic treatment, and radiotherapy indications for seven cancers [3]. Japan was in "mild lockdown," which was not enforceable and non-punitive, during the state of emergency; nevertheless, the impact attracted attention [4]. On 7 April 2020, the Japanese government declared a state of emergency due to a COVID-19

outbreak in seven prefectures (Tokyo, Kanagawa, Osaka, Saitama, Chiba, Hyogo, and Fukuoka). Tokyo, host of the 2020 Olympics, had the highest number of infections among the 47 prefectures, and the Tokyo Metropolitan Government imposed its own transferal restrictions on citizens [5]. The state of emergency expanded nationwide on 16 April 2020, and was lifted in a phased manner beginning 14 May 2020. While many countries were in lockdown with penalties for violations, Japanese policy for COVID-19 was distinguished as the government "requesting" the public to refrain from going out except for emergencies and to temporarily close certain businesses without penalties for violations. This lockdown significantly transformed public activity as well as patients' medical examination behaviours in Japan. For example, the number of monthly train users in April 2020 prominently decreased by 45.5% compared with the same month in 2019 [6]. The mild lockdown in Japan had a diverse range of influence on people's lives, similar to other countries, including changes in domestic circumstances due to teleworking or school closure and economic damage due to decreased income or job loss. It has been suggested that patients with cancer are more likely to become severely ill due to COVID-19 infection, and it is possible that cancer

patients may have been discouraged from seeing a doctor [7]. The top three causes of death in Japan are cancer, heart disease, and stroke, but cancer has been number one since the 1980s [8]. Examining the impact of the COVID-19-related emergency on the behaviour of the top cause of death is a critical issue that directly affects the mortality rate in Japan.

This study hypothesised that the state of emergency suppressed patient visits to hospital for cancer, heart disease, and stroke in Japan. The aim of this study was to compare trends among cancer, heart disease, and stroke patient consultations at one university hospital in Tokyo before and after the issuance of the state of emergency. Moreover, we examined changes in patient consultations, including transfers between prefectures.

Methods

The present study was a retrospective and descriptive study of Showa University Hospital in Tokyo, Japan. Subjects were patients who had received medical treatment at Showa University Hospital and were diagnosed from 2017 to 2020. To examine the impact of the state of emergency, the number of visits to Showa University Hospital for the top three causes of death or other diseases were summarised from 21 weeks of data, from week 8 to week 28, for each year (Tab. I). Showa University Hospital is located near the border between Tokyo (the most populous prefecture in Japan) and Kanagawa (the second most populous prefecture). This is one of the areas most affected by the COVID-19 pandemic in Japan, because the number of COVID-19 infections has remained high since the early stages of the pandemic. In case of return to the hospital, subjects were defined only as patients with newly diagnosed diseases. The effectiveness of COVID-19 measures was assessed by calculating the 7-day moving average of the interval from symptom onset to isolation in hospital or quarantine. The trends of patient visits to hospital from Tokyo were divided into cancer, cardiovascular disease, stroke, and others (Fig. 1). The trends of patient visits to hospital from outside Tokyo were also divided into cancer, cardiovascular disease, stroke, and others (Fig. 2). For each disease, we examined the parallelism between 2020 and the average of the previous 3 years. As a secondary analysis, a difference-in-difference analysis was performed for diseases with parallelism. Table II shows parallel trends in both patients from within and outside Tokyo.

This study was approved by the Medical Ethics Committee of Showa University School of Medicine (Approval No. 2954).

All statistical analyses were conducted using JMP 15.0 (SAS Institute Inc. Cary, NC USA). All analyses were carried out at a 95% confidence interval. P-values less than 0.05 (two-tailed) were considered statistically significant.

Targeted disease	All periods (21 weeks)	Before the state of emergency(7 weeks)	During the state of emergency(7 weeks)	After the state of emergency (7 weeks)	p-value*
Patients from Tokyo (n = 47,136)					
All disease (2020)	21.240	6.877	5.565	8.798	< 0.001
All disease (2017-2019)	25.896	8.746	8.210	8.940	
Cancer (2020)	1.396	502	328	566	< 0.001
Cancer (2017-2019)	1.848	629	577	642	
Cardiovascular disease (2020)	241	79	82	80	0,718
Cardiovascular disease (2017-2019)	249	83	80	86	
Stroke (2020)	285	85	78	122	0,004
Stroke (2017-2019)	262	88	83	91	
Others (2020)	19.318	6.211	5.077	8.030	< 0.001
Others (2017-2019)	23.537	7.946	7.470	8.121	
Pateints from outside Tokyo (n = 6,782)					
All disease (2020)	2.831	941	696	1.194	< 0.001
All disease (2017-2019)	3.951	1.334	1.276	1.341	
Cancer (2020)	211	73	47	91	< 0.001
Cancer (2017-2019)	351	117	115	119	
Cardiovascular disease (2020)	22	9	5	8	0,370
Cardiovascular disease (2017-2019)	28	10	9	9	
Stroke (2020)	19	6	5	8	0,327
Stroke (2017-2019)	26	9	8	9	
Others (2020)	2.579	853	639	1.087	< 0.001
Others (2017-2019)	3.546	1.198	1.144	1.204	

Tab. I. Changes in the number of patient visits to Showa University Hospital before, during and after the COVID-19 state of emergency.

* Chi-square test.
The number of patients with the targeted diseases in 2020 was calculated data from weeks 8-28.
The number of patients with the targeted diseases from 2017 to 2019 was calculated as a 3-year average from data from weeks 8-28.

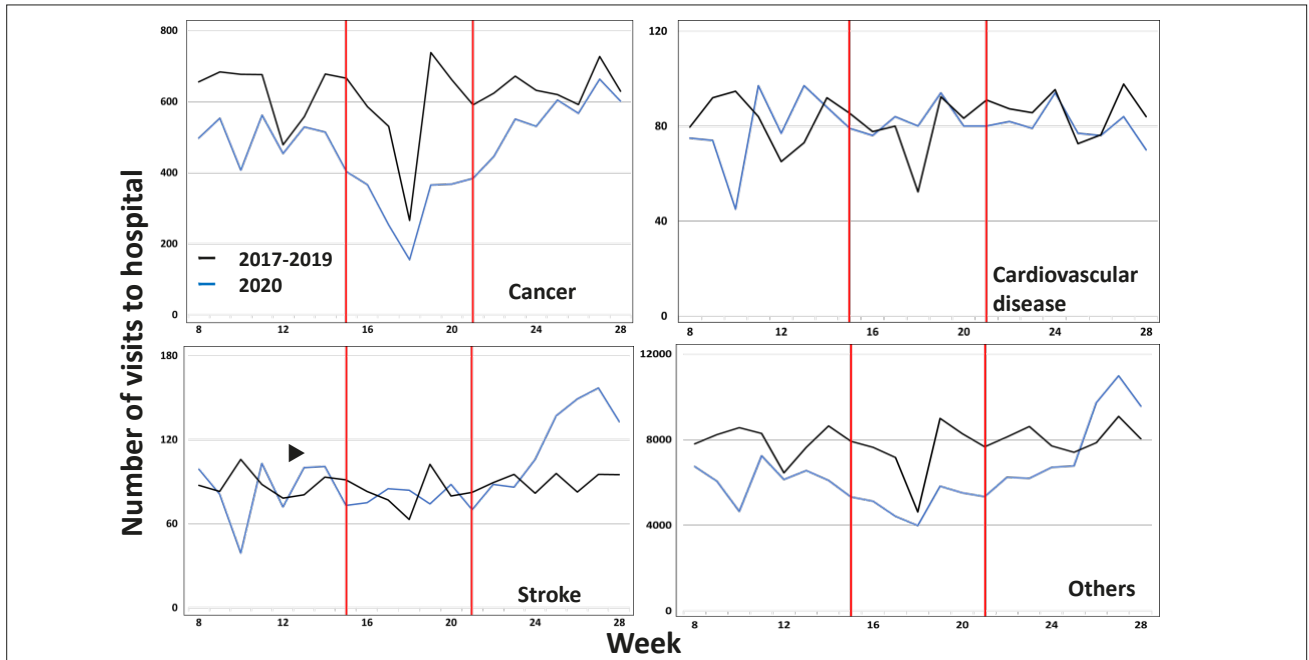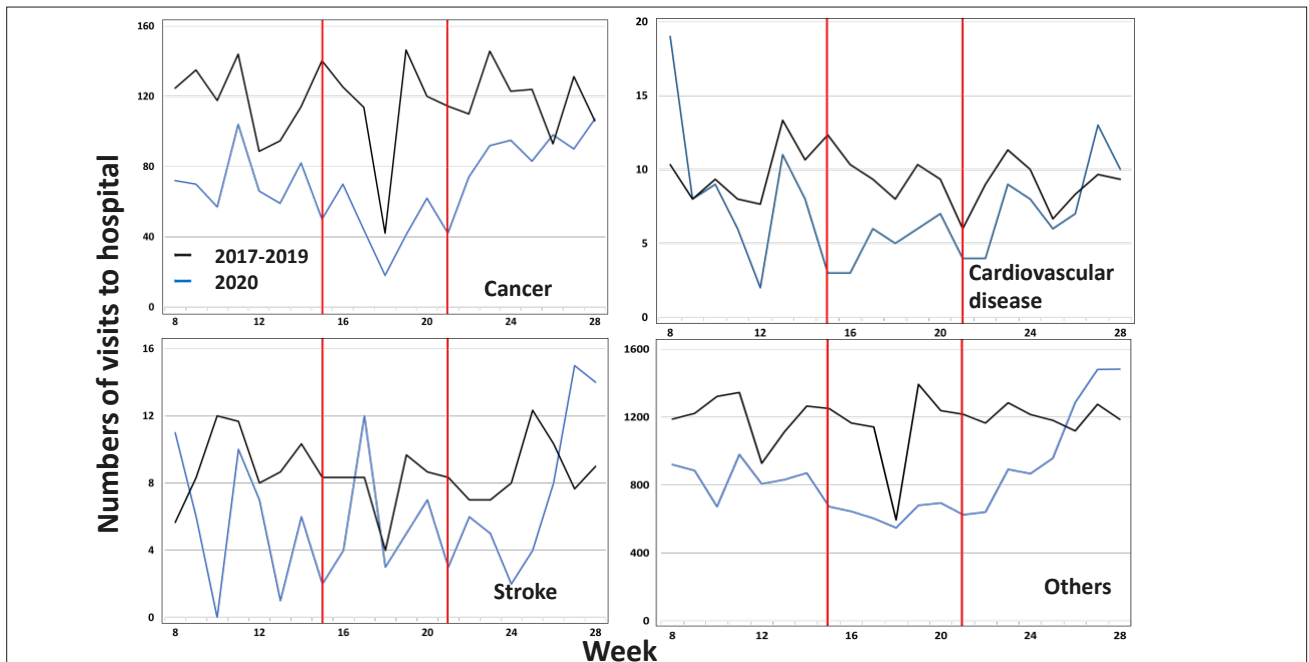Fig. 1. Number of visits to hospital by patients from Tokyo by disease.

Fig. 2. Number of visits to hospital by patients from outside Tokyo by disease.

Results

Table I summarises changes in the number of patient visits to Showa University Hospital before and after the state of emergency. Figures 1 and 2 summarise the weekly trends in visits to Showa University Hospital by patients from Tokyo and from outside Tokyo during the COVID-19 pandemic, respectively. In both figures, the start and end of the state of emergency are indicated by red lines. A comparison of the average number of visits for the three periods before and after the state of emergency during the previous 3 years and 2020 shows a V-shaped curve in 2020, with a large drop in the number of visits by cancer patients during the state of emergency, both from within Tokyo and from outside the city. Trends in visits by cardiovascular disease patients showed no significant difference when comparing the average of the previous 3 years to 2020. Visits by stroke patients from Tokyo tended to increase after the state of emergency was lifted when comparing the average of the

Tab. II. Difference-in-differences analysis for cancer patient visits to Showa University Hospital before, during and after the COVID-19 state of emergency.

	Before to during state of emergency	During to after state of emergency
	OR (95% CI)	OR (95% CI)
Patients from Tokyo	0.98 (0.95-1.00)	0.99 (0.97-1.00)
Patients from outside Tokyo	0.89 (0.78-1.00)	0.93 (0.88-1.00)

OR: Odds ratio; CI: Confidence interval.

previous 3 years with 2020. Without including the top three disease causes of death, a comparison of the three periods before and after the state of emergency between the previous 3 years and 2020 shows a V-shaped curve in 2020, with a large drop in the number of visitors during the state of emergency, both from within Tokyo and from outside the city.

Among the three major diseases, only cancer showed parallelism between 2020 and the average of the previous 3 years. The results of the difference-in-difference analysis for cancer patients showed that the number of patients during the state of emergency was significantly lower than before (Tab. II). Furthermore, the number of visits by patients from outside Tokyo [odds ratio (OR): 0.89; 95% confidence interval (CI) (0.78-1.00)] decreased more than the number of visits by patients from Tokyo [0.98; (0.95-1.00)]. The number of patient visits after the state of emergency was significantly lower than during the state of emergency. The number of visits by patients from outside Tokyo [0.93; (0.88-1.00)] decreased more than the number of visits by patients from Tokyo [0.99 (0.97-1.00)].

Discussion

The results of this study suggest that cancer patients at Showa University Hospital tended to refrain from seeing a doctor during the COVID-19 state of emergency, compared to before the state of emergency. Furthermore, compared to the situation during the state of emergency, there was a tendency to continue to refrain from seeing a doctor after the state of emergency was lifted. Among the top three disease causes of death, there was no significant difference in the trends of patients with cardiovascular disease and stroke between 2020 and the previous 3 years. The number of cancer patients decreased monotonically for 21 weeks, including the 7 weeks both before and after the state of emergency.

The effect of public holidays and weekends should be noted. A study of emergency medical visits to a district general hospital in southwest Scotland admissions showed statistically higher mortality associated with admission on public holidays both on weekdays and weekends, but not with weekend admissions generally [9]. In Japan, holidays usually fall between 29 April and 5 May, and the number of hospital visits tends to decrease significantly during this period. It is

possible that the effects of this vacation (about a week) overlapped with the effects of the state of emergency. However, since the number of cancer patient visits continued to decrease even after the state of emergency was lifted, it is possible that COVID-19 is having a long-term effect on consultation behaviour regardless of the impact of the state of emergency.

A global survey elucidates the role of pancreatic surgery during the COVID-19 pandemic, regarding patient selection for the surgical and oncological treatment of pancreatic diseases to support clinical decision-making [10]. It has also been suggested that the response should be divided by cancer site.

Xiao et al. demonstrated that the lockdown in China due to the COVID-19 pandemic has had a significant psychological impact on cancer patients and their families and showed the importance of psychological support during the pandemic [11].

Emergency infection control measures are essential in hospitals. Although Japan was spared from the 2003 severe acute respiratory syndrome (SARS) epidemic, hospitals were placed on high alert. In 2003, substantial differences in emergency infection control measures, as perceived by health care workers, exist among hospitals in Japan, with differences across institutions exceeding those across disciplines. To achieve a higher level of preparedness for infectious diseases, institutions should designate and implement effective emergency infection control measures [12]. It is necessary to compare multiple medical institutions and examine regional differences because each region has its own universal health insurance system, and the health care system varies greatly depending on population density and the number of medical institutions in each municipality.

Lapointe-Shaw et al. demonstrated that patients discharged from hospital during the December holiday period were less likely to have prompt outpatient follow-up and were at higher risk of death or readmission within 30 days [13]. Collection of longitudinal data could help examine the effect of public holidays, weekends and the state of emergency among Japanese patients.

This study suggests that the COVID-19 state of emergency may have inhibited the movement of patients with three major diseases across prefectures in Japan. However, it is also possible that the medical care that would have been available may not have been provided due to the state of emergency, so it is necessary to follow up patients while keeping a close eye on measures other than those for infectious diseases. Moreover, Inoue et al. suggested that the lack of social capital was associated with refraining from seeking medical care among Japanese [14]. When examining regional differences in Japan, it will be necessary to show individual or regional social factors as well.

Our study has limitations. This study is based on the trend of consultation at a single hospital, and its generalizability is a challenge. In light of the COVID-19 epidemic, this study provides valuable information showing that patients refrained from attending medical

examinations due to the state of emergency using data from a single hospital; however, further study using data from multiple hospitals is necessary. Although this study was conducted in one hospital in Tokyo, which has the highest number of confirmed COVID-19 cases in Japan, it has the advantage of being geographically suitable for confirming the effectiveness of the state of emergency. Because the COVID-19 epidemic has continued worldwide, and this study is based only on data up to September 2020, a longer-term study is needed.

It should also be noted that the number of patients for each disease varied. Compared to cancer, this study had a smaller number of patients with cardiac disease and stroke, and the trends for these conditions may not be readily detectable due to this smaller sample size.

Conclusions

In conclusion, our study showed a long-term decrease in cancer patient visits to Showa University Hospital since the beginning of the COVID-19 pandemic compared to the same period in the previous 3 years. Among cardiovascular disease and stroke patients, there was no significant decrease in long-term visits at the beginning of the COVID-19 pandemic compared to the previous years. It is also possible that the medical care that would have been available may not have been provided due to the state of emergency, so it is necessary to follow up patients while keeping a close eye on measures other than infectious diseases.

Acknowledgements

Funding

Conflict of interest statement

All authors declare that they have no conflicts of interest.

Author contributions

AM and KM planned this study. YI, YK and AK contributed to improving this study in a meaningful way. AM drafted the manuscript. KM performed data collection. MM supervised data collection. KM supported the draft of this manuscript and data collection. AM contributed to the statistical analysis. AK made substantial contributions to the conception of this study and the revision of the manuscript. All authors read and approved the final manuscript.

References

[1] World Health Organization. Coronavirus disease (COVID-19) Weekly Epidemiological Update and Weekly Operational Update. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports

[2] Wright A, Salazar A, Mirica M, Volk LA, Schiff GD. The Invisible Epidemic: Neglected Chronic Disease Management During COVID-19. J Gen Intern Med 2020;35:2816-7. https://doi.org/10.1007/s11606-020-06025-4

[3] Hanna TP, King WD, Thibodeau S, Jalink M, Paulin GA, Harvey-Jones E, O'Sullivan DE, Booth CM, Sullivan R, Aggarwal A. Mortality due to cancer treatment delay: systematic review and meta-analysis. BMJ 2020;371:m4087. https://doi.org/10.1136/bmj.m4087

[4] Yamamoto T, Uchiumi C, Suzuki N, Yoshimoto J, Murillo-Rodriguez E. The Psychological Impact of 'Mild Lockdown' in Japan during the COVID-19 Pandemic: A Nationwide Survey under a Declared State of Emergency. Int J Environ Res Public Health 2020;17:9382-400. https://doi.org/10.3390/ijerph17249382

[5] Murakami M, Miura F, Kitajima M, Fujii K, Yasutaka T, Iwasaki Y, Ono K, Shimazu Y, Sorano S, Okuda T, Ozaki A, Katayama K, Nishikawa Y, Kobashi Y, Sawano T, Abe T, Saito MM, Tsubokura M, Naito W, Imoto S. COVID-19 risk assessment at the opening ceremony of the Tokyo 2020 Olympic Games. Microb Risk Anal 2021. https://doi.org/10.1016/j.mran.2021.100162.100162

[6] Ministry of Land Infrastructure, Transport and Tourism. Monthly report of the Statistical Survey on Railway Transport in April 2020. Available at: https://www.e-stat.go.jp/stat-search/files?page=1&layout=datalist&toukei=00600350&kikan=00600&tstat=000001011026&cycle=1&year=20200&month=12040604&result_back=1&result_page=1&tclass1val=0. 2020 (Japanese).

[7] Takahari D, Shinozaki E, Wakatsuki T, Ooki A, Ozaka M, Suzuki T, Nakayama I, Osumi H, Kamiimabeppu D, Sato T, Ogura M, Suenaga M, Chin K, Yamaguchi K. Managing a gastrointestinal oncology practice in Japan during the COVID-19 pandemic: single institutional experience in The Cancer Institute Hospital of Japanese Foundation for Cancer Research. Int J Clin Oncol 2021;26:335-44. https://doi.org/10.1007/s10147-020-01806-7

[8] Ministry of Health, Labour and Welfare Japan. Vital Statistics of Japan, Statistics & Information Department, Minister's Secretariat 1975-2016; MHLW: Tokyo, Japan, 2016. https://www.mhlw.go.jp/english/database/db-hw/populate/dl/E03.pdf

[9] Smith S, Allan A, Greenlaw N, Finlay S, Isles C. Emergency medical admissions, deaths at weekends and the public holiday effect. Cohort study. Emerg Med J 2014;31:30-4. https://doi.org/10.1136/emermed-2012-201881

[10] Oba A, Stoop TF, Lohr M, Hackert T, Zyromski N, Nealon WH, Unno M, Schulick RD, Al-Musawi MH, Wu W, Zhao Y, Satoi S, Wolfgang CL, Abu Hilal M, Besselink MG, Del Chiaro M, Pancreas Club EPCCPSAECoMIPSSGoPTfPCSGoPDAw, International Study Group on Cystic Tumors of the P. Global Survey on Pancreatic Surgery During the COVID-19 Pandemic. Ann Surg 2020;272:e87-e93. https://doi.org/10.1097/SLA.0000000000004006

[11] Xiao H, Zhang Y, Kong D, Li S, Yang N. Social Capital and Sleep Quality in Individuals Who Self-Isolated for 14 Days During the Coronavirus Disease 2019 (COVID-19) Outbreak in January 2020 in China. Med Sci Monit 2020;26:e923921. https://doi.org/10.12659/MSM.923921

[12] Imai T, Takahashi K, Hoshuyama T, Hasegawa N, Chia SE, Koh D. Substantial differences in preparedness for emergency infection control measures among major hospitals in Japan: lessons from SARS. J Infect Chemother 2006;12:124-31. https://doi.org/10.1007/s10156-006-0436-0

[13] Lapointe-Shaw L, Austin PC, Ivers NM, Luo J, Redelmeier DA, Bell CM. Death and readmissions after hospital discharge during the December holiday period: cohort study. Bmj 2018;363:k4481. https://doi.org/10.1136/bmj.k4481

[14] Inoue A, Tsutsumi A, Eguchi H, Kachi Y, Shimazu A, Miyaki K, Takahashi M, Kurioka S, Enta K, Kosugi Y, Totsuzaki T, Kawakami N. Workplace social capital and refraining from seeking medical care in Japanese employees: a 1-year prospective cohort study. BMJ Open 2020;10:e036910. https://doi.org/10.1136/bmjopen-2020-036910

Correspondence: A. Minoura, Department of Hygiene, Public Health and Preventive Medicine, Showa University School of Medicine, Tokyo, Japan. E-mail: minoaki@med.showa-u.ac.jp

Advancing nursing in Italy through the development and evaluation of an innovative postgraduate programme in Family and Community Nursing - A pilot study

MARIA EMMA MUSIO[1], LUCIA VASSALINI[2], ROBERTA CENTANARO[2], MARTINA BARIOLA[3], MARCO GHIOZZI[3],
MARINELLA SANTACROCE[3], LUCIA BACIGALUPO[2], GIOVANNA RAZETO[2], GIULIA SOLDANO[4], LORENZO BRACCO[4],
GIUSEPPE ALEO[1], MILKO ZANINI[1], GIANLUCA CATANIA[1], FLAVIO MANGANELLO[5], FRANCESCA POZZI[5],
LOREDANA SASSO[1], ANNAMARIA BAGNASCO[1]
[1] Department of Health Sciences, University of Genoa, Italy; [2] IRCCS Ospedale Policlinico San Martino, University of Genoa, Genoa,
Italy; [3] Polo di Chiavari ASL4 Regione Liguria, Chiavari, Italy; [4] ASL1 Regione Liguria, Imperia, Italy;
[5] Istituto per le Tecnologie Didattiche, Consiglio Nazionale delle Ricerche, Genoa, Italy

Keywords

Summary

Introduction. *Due to the impact on the public health systems of the ageing and the increasing frailty of the population, the European Union and the World Health Organisation have emphasised how family and community nurses (FCNs) could play an important role in supporting the ageing process through prevention, promotion, and protection in the territory.*

Methods. *This study describes the first experience in Italy of a one-year postgraduate blended-learning master course divided into 5 modules for FCNs piloted as part of the EuropeaN curriculum for fAmily aNd Community nursE (ENhANCE) 2018-2020 project, funded by the European Commission. The 5 modules focused on: Epidemiology and Prevention (14 ECTS); Fundamentals of care (19 ECTS); Organisational Models and Priority Health Problems (12 ECTS); Communication Models and Continuity of Care (5 ECTS); and Nursing Research (10 ECTS).*

Participants included a total of 45 students and 23 lecturers and a team of clinical tutors.

Results. *The Italian pilot course for the FCNs proved to be a successful example of innovative teaching methods using blended didactic methods, which enabled participants to achieve high-standard learning outcomes and competencies in the field of family and community nursing.*

Conclusions. *The pilot course is well suited to preparing competent family and community nurses to meet the growing healthcare needs of the population. Therefore, we have planned to replicate this course to increase the workforce of family and community nurses, who through their healthcare services aimed at prevention, promotion and protection, will ensure high quality services to the public and consequently relieve the burden on acute hospitals.*

Introduction

Increase in life expectancy is one of the greatest achievements of modern medical and technological progress. According to the 2019 Eurostat Report, in 28 European countries, almost one fifth (19.7%) of the population was over the age of 65 and, by 2050, the older population is expected to rise to 149.2 million, equivalent to 28.5% of the entire population [1]. Economic progress has also played an important role in allowing a significant improvement in general living conditions.

In this context of our modern society, it is possible to contemplate a new and stronger sensitivity towards individuals with disabilities and frailties who, as suggested by the United Nations Convention on the Rights of Persons with Disabilities, have the right to live and be socially involved in the community, in complete safety, autonomy and comfort (United Nations, 2006). The European Union highlights the important role that

the family and community can play in preventing frailty, and promoting primary health care (PHC), education, and early diagnosis [1]. Several WHO (World Health Organization) documents identify the family and community nurse (FCN) in playing a key role in the new health model focused on primary care [3, 4].

Currently, there is no standardised professional profile for the Family and Community Nurse (FCN) at a European level which, in line with the European Standards of Skills/Competences, Qualifications and Occupations (ESCO) [5] and the European Credit System for Vocational Education and Training [6], can meet the demands of the frail population in the European Union, a long-term process which poses significant health challenges at all levels.

The ENHANCE project, therefore, aimed to fill this gap by developing a standardised professional curriculum for FCNs at a European level.

To identify the core competencies for family and community nurses, an e-Delphi study was conducted

involving a panel of experts from various European countries [7]. Through the development of this project the level of specialisation of FCN nurses will increase, focusing on specific primary health care competencies and enhancing the transition from the old model of primary health care to a more innovative and advanced model, based on evidence.

The European core FCN curriculum developed on the competencies identified through the e-Delphi study, was localized and piloted in Finland, Greece, and Italy. This led to the implementation of 3 national curricula, each preceded by a local teacher training course, which involved guidelines and methodological advice on how to effectively use the online tools and blended learning methodologies proposed by the ENHANCE Project, and support the sharing of good practices among nurses. The three pilot courses all aimed at bridging the gap between currently available nursing competences and the competences required by both public institutions and private service providers.

In Italy, the pilot course was the first experience of postgraduate education based on blended learning delived through a one-year pilot Master Course for Family and Community Nurses (FCNs), organised and implemented by the Department of Health Sciences of the University of Genoa (Italy) as part of the EuropeaN curriculum for fAmily aNd Community nursE (ENhANCE) 2018-2020 project, funded by the European Commission. Starting from the European Core Curriculum, this pilot Master course was adapted to target the healthcare needs and priorities of the Italian population.

The Italian pilot course was based on a blended learning approach, alternating e-learning and face-to-face activities.

The face-to-face activities were conducted at the University of Genoa, while the work-based learning activities were conducted in various community settings in the Liguria Region. However, it should be noted that the pilot course was held during the COVID-19 pandemic, raising many problems due to the lockdown imposed by the Italian government. Within each module, different levels of learning were identified, which could be achieved through complementary learning strategies, such as gamification [8-10]. Learning strategies were designed to ensure consistency between theory and practice. Classroom learning was supported by active teaching methods (i.e., Problem Based Learning and Case Studies) linked with laboratory activities. Internships, described as work-based learning, were conducted in person and involved introductory workshops.

STUDY DESIGN

A pilot course organised by the Department of Health Sciences of the University of Genoa in collaboration with the Istituto Tecnologico Didattico (ITD) of the National Research Council of Italy. This pilot course was based on a blended learning approach (i.e., alternating e-learning and face-to-face activities) and was divided into 5 modules.

The face-to-face activities of the Italian pilot were conducted at the University of Genoa, while the "Work-based learning' activities (or internships) were conducted in various community settings throughout the Liguria Region.

Participants

Students

Participants included a total of 45 students. Students had to have at least one of the following qualifications (equal to EQF 6):

a) Degree or University Diploma in General Nursing;
b) University Degree or Diploma in Paediatric Nursing;
c) University Degree or Diploma in Midwifery.

According to Italian legislation, university nursing degrees and diplomas are equivalent qualifications (Law n.42 of 26th February 1999).

The participants in the pilot course were predominantly female nurses (91%), with an average age of 40 years, and an average working experience as registered nurses of 12 years. All, except one, were working as nurses at the time of the course.

Students could apply to participate in the course by responding to a public announcement by Rectoral Decree of the University of Genoa (Italy).

A maximum of 50 students could be admitted to the pilot course. If the applicants exceeded the maximum number of places available, the selection would have included a written test on nursing related to the topics covered in the course, and an interview.

All the students completed the Italian pilot course for its entire duration, from January to December 2020.

Teachers

A total of 23 academic teachers we enrolled in the Italian pilot of the Family and Community Nursing Curriculum. Work-based learning was supported by a team of academic tutors experienced in community nursing.

THE PILOT COURSE STRUCTURE

Based on the 53 learning outcomes defined in the ENHANCE European Family and Community Nurse (FNC) reference curriculum, the Department of Health Sciences at the University of Genoa, delivered the FNC localised curriculum in the format of a 12-month postgraduate master course, consisting of 60 ECTS (European Credit Transfer and Accumulation System), for a total of 1500 hours of study. The ECTS system is an instrument of the European Higher Education Area (EHEA) that provides transparency to study courses by facilitating the recognition of qualifications and the valorisation of study periods abroad for students transferring from one country to another.

The modular structure of the FNC master course was designed according to the educational academic guidelines established by the Italian national legislation on professional practice and population health needs.

Five key areas of community and family nursing were used as a reference to structure the pilot course into 5 modules:

- module 1: Epidemiology and prevention (14 ECTS);
- module 2: Fundamentals of care (19 ECTS);

- module 3: Organisational Models and Priority Health Problems (12 ECTS);
- module 4: Communication Models and Continuity of Care (5 ECTS);
- module 5: Nursing Research (10 ECTS).

Module 0 (zero): The Florence Nightingale Role Model

Since this was the first time ever that in Italy a similar postgraduate course was being provided, before starting the 5-module FCN pilot course, module 0 was added to help the students familiarise with the innovative educational strategy of this course, with the new tools, such as the Open Online Tool (OOT), and with the other students attending the course.

THE OPEN ONLINE TOOL FUNCTIONALITIES

Due to the specific theoretical and practical nature of the professional profile of the family and community nurse, the teaching and learning methods involved blended learning activities, including face-to-face lectures and workshops, online learning activities supported by the use of the ENhANCE Open Online Tool (OOT) functionalities. Considering the instrumental importance of clinical training, Work-Based Learning was conducted entirely face-to-face.

The pilot course-integrated various innovative teaching and learning methods, supported by technological features, such as webinars, online forums, an online community, uploading and sharing individual tasks, gamification using "Level up" and digital badges.

The OOT also enabled gamification techniques within the pilot course to direct students towards the content by engaging them, motivating them to action, promoting learning and problem solving [8-10]. Gamification refers to the "use of game design elements (levels, badges, point systems, scores and time constraints) in non-game contexts" [8] as a powerful approach to motivate and engage learners. Challenge, curiosity, interactivity, feedback, freedom to fail are typical elements of gamification techniques [9]. The design of a pilot course promoting Self-Regulated Learning (SRL) had to meet some basic requirements, such as online learning and assessment, sharing of practices and collaboration, evaluation of online activities,

a social dimension and community building, self-regulated learning, recognition, and validation of non-formal/informal prior learning, personalisation, and openness. This was made possible using the Online Open Tool (OOT), which enabled students to practice and monitor the 4 actions of the so-called "4Cs model" (their behaviours in terms of Create, Connect, Consume, and Contribute), track and reflect on their learning progress, discuss and reflect on it with other students and teachers, plan and/or monitor and/or self-reflect on their learning journey.

The 4Cs framework for Self-Regulated Learning (SRL) can be effectively applied in knowledge-intensive domains [11, 12] of the different OOT functionalities are suited to support specific activities.

Module 1: Epidemiology and Prevention

This module included learning outcomes related to the health determinants of the population and provided an epidemiological background about the population and a general overview of the topic involved in this specific system of care. It also offered tools and methods to assess families' health status and health needs. The learning outcomes were related to how the students competently performed their skills and activities in this field. At the end of the first module, students were awarded 14 ECTS (Tab. I).

Module 2: Fundamentals of Care

The second module on fundamentals of nursing care, focused on the values and ethics of nursing to support the safe provision of nursing care in the community. It was based on the essential needs of patients, whether they were physical, psychological or relational, and it drew students' attention on the respective nursing sensitive outcomes. This was the key module of the entire Master course, comprising 19 ECTS (Tab. II).

Module 3: Organizational models and Priority health problems

The third module focused on organizational models, interprofessional work and nursing leadership. It aimed to develop students' ability to work and collaborate within a multidisciplinary team, but also knowledge and

Tab. I. Module 1: Epidemiology and prevention.	
EU Core Curriculum Learning Outcomes	
LO 1a	Identify and assess individuals' health status and health needs
LO 1b	Identify and assess families' health status and health needs
LO 1c	Contextualize and apply needs assessment taking into account cultures and communities
LO 3a	Plan nursing care to meet the needs of individuals, families, and the community within their scope of competence
LO 3c	Assess nursing care to meet the needs of individuals, families, and the community within their scope of competence
LO 19a	Assess community health needs in a multidimensional perspective
LO 19b	Identify the appropriate clinical interventions and care management strategies for communities
LO 17a	Know community health promotion goals
LO 17b	Carry out health promotion programs and activities that meet the community's goals
LO 18a	Evaluate policies for health promotion at family and community level
LO 18b	Effectively coordinate, develop, and implement policies for health promotion at family and community level

Tab. II. Module 2: Fundamentals of care.

EU Core Curriculum Learning Outcomes	
LO 21a	Assess the social, cultural, and economic context of patients and their families
LO 2a	Know the main professional ethical standards
LO 2b	Take decisions based on professional ethical standards
LO 23a	Know and apply communication, counselling and negotiation strategies and techniques with different actors
LO 25a	Know strategies and techniques for mentoring students and apply them in daily practice
LO 6a	Know the main communication strategies and techniques which can be adopted by a FCN and apply them to specific contexts and needs
LO 15a	Know professional standards and act in compliance with them
LO 20a	Know the main ethical principles to manage disparity and diversity and apply them in daily practice
LO 27b	Effectively address problems related to health and illness through the multidisciplinary team
LO 9a	Know the main guidelines, procedures and tools for the monitoring and the definition of the outcomes and apply them in daily practice
LO 12a	Know the main standards about nursing activities in people's homes and apply them in daily practice
LO 12b	Know the main standards about nursing activities in the community and apply them in daily practice
LO 12c	Evaluate the outcomes related to nursing activities in people's homes
LO 12d	Evaluate the outcomes related to nursing activities in the community
LO 7a	Know the main guidelines and procedures for palliative care and apply them in daily practice
LO 7b	Know the main communication and counselling techniques to manage relations with patients (and families) in palliative care

skills on how to apply leadership techniques, decision making, advanced strategies and teamworking skills. At the end of this module the students were able to:
- recognize the main characteristics of chronic and rare diseases that could be remotely monitored;
- apply main guidelines regarding the monitoring process and the expected outcomes;
- plan and prioritize the activities of the multidisciplinary team to address problems related to health and illness;
- after completing the third module, the students were awarded 12 ECTS (Tab. III).

Module 4: Communication Models and Continuity of Care

The fourth module on communication focused on the management of the healthcare processes to ensure care continuum between the hospital setting and the community, as well as educational strategies for individuals and families. It included learning outcomes related to the main educational strategies, which could be adopted to promote health and safety of individuals and families, as well as the main educational strategies for patient education and for building an effective therapeutic relationship with patients and families and applying them in daily practice. The module also explained how to engage individuals and families in the decision-making process, and how to apply strategies and techniques to motivate health workers and engage them in the promotion of community healthcare (Tab. IV).

Module 5: Nursing Research

The fifth module was developed to support evidence-based nursing practice, ensure the safety and appropriateness of nursing care, and provide the appropriate knowledge and skills to maintain the level achieved. It included

Tab. III. Module 3: Organizational models and priority health problems.

EU Core Curriculum Learning Outcomes	
LO 3b	Implement nursing care to meet the needs of individuals, families, and the community within their scope of competence
LO 22a	Know and apply leadership techniques that ensures clinical and healthcare effectiveness and appropriateness
LO 22b	Know and apply decision-making techniques that ensure clinical and healthcare effectiveness and appropriateness
LO 4b	Know unique needs of sub-populations and detect and contrast the main inequities which affect them
LO 15b	Know advanced strategies and techniques of team working and professional collaboration and apply them to specific contexts and needs
LO 8a	Know and evaluate the main problems and needs which could affect workers in a specific community context.
LO 14a	Know which changes are needed to improve FCN practice and act in order to target and reach them
LO 13a	Work and collaborate in a multidisciplinary team to address problems related to health and illness
LO 13b	Plan and prioritize the activities of the multidisciplinary team in order to address problems related to health and illness
LO 27a	Work and collaborate in a multidisciplinary team to prevent disease and to promote and maintain health
LO 24b	Know the main characteristics of chronic and rare diseases which could be monitored at distance and apply the main guidelines about the monitoring process and the expected outcomes

Tab. IV. Module 4: Communication models and continuity of care.	
EU Core Curriculum Learning Outcomes	
LO 11a	Involve individuals and families in decision-making process
LO 5a	Know and apply the main educational strategies which can be adopted to promote health and safety of individuals and families
LO 16a	Know the main educational strategies for patient education and apply them in daily practice
LO 16b	Know the main strategies and techniques for building an effective therapeutic relation with patients and families and apply them in daily practice
LO 8b	Know and apply strategies and techniques to motivate workers and to engage them in community healthcare promotion

learning outcomes related to the main elements/guidelines/procedures/theories to enhance and promote health and prevent disease and injuries in individuals, families, and communities, to foster inclusiveness, and effectively use scientific evidence. It also focused on learning outcomes related to the knowledge and use of standardized and validated tools in order to evaluate their own practice, and the main monitoring and reporting procedures to document their own practice. This module also focused on learning outcomes related to knowing the main computer technologies that enable to support health promotion, education, and treatment of patients remotely and how to use the most common digital tools. At the end of the fifth module, students were awarded 10 ECTS (Tab. V).

THE PILOT COURSE AND THE APPLIED LEARNING STRATEGIES

The learning strategies and outcomes were designed to foster continuity between theory and practice; classroom learning is supported by active teaching methods (e.g., practice-based learning and case studies), which allow to link with laboratory activities (e.g., role playing in the simulation lab). Work-based learning (e.g., through placements in community care centres) are always provided in presence and require introductory workshops. In addition, an Open Online Tool was available, which served as a platform for sharing information, learning, teaching and assessing students' progress.

"Online Collaborative Learning" involves learning processes based on computer-mediated interactions between members of a learning community. This educational approach emphasises the active and collective participation and interaction of both students and teaching staff, mainly through communication via the Internet [12].

The structure of the Italian pilot course for Family and Community Nurses (FCN) was built considering the "Learning Designer (LD)" tool. The Learning Designer is a web-based tool created by the London Institute of Education to integrate technology into the teaching and learning process. It can be used in any educational sector and for any learning context: traditional classroom, online or mixed.

When designing learning and defining which methodologies to use, the following elements need to be taken into account: the size and composition of the student cohort, the students' background and preferred learning styles, the teachers' skills and preferences, the students' self-regulation skills, the technological skills of teachers and students, the time available, the resources available (human, material and digital) and the nature of the content. The interplay between these elements guides teachers' decision-making to create a coherent learning plan that effectively addresses students' needs. The preparation of Technology-Enhanced Learning (TEL) interventions is the most challenging part of the process [14].

Different teaching methodologies are generated by the different orchestration of the 4 fundamental elements (4Ts) of collaborative online learning: the script/scenario (TASK), the cast (TEAM), the duration of each scene (TIME) and the set (TECHNOLOGY) [15].

Below are some of the methodologies used in the Italian pilot course.

Tab. V. Module 5: Nursing research.	
EU Core Curriculum Learning Outcomes	
LO 4a	Know the main elements/guidelines/procedures/theories to enhance and promote health and prevent disease and injuries in individuals, families and communities and to be able to apply them in daily practice
LO 20b	Know the main guidelines to foster inclusiveness and apply them in daily practice
LO 10a	Know and use standardized and validated tools in order to evaluate their own practice
LO 10b	Know and use the main monitoring and reporting procedures in order to document their own practice
LO 26a	Know the main scientific evidence databases and make an effective search
LO 26b	Use the best scientific evidence properly and apply them in daily practice
LO 24a	Know and use the main procedures and tools for monitoring people affected by chronic and rare illnesses
LO 28a	Know the main ICTs supporting health promotion and education and use the most common ones
LO 28b	Know the main ICTs supporting the treatment of patients at distance and use the most common ones
LO 28c	Know the main ICTs supporting distance health monitoring and use the most common ones

The Jigsaw methodology

Jigsaw, one of the techniques used in the implementation of cooperative learning, offers support to help students work together, replacing competition with cooperation. It is often considered as an alternative to traditional teaching methods [16]. The Jigsaw technique can be applied in different areas of science, including social and medical sciences [17, 18].

It consists of two phases and enables knowledge construction through collaboration, such as collaborative problem solving [19], provides equal learning opportunities and facilitates communication between students with different learning experiences [20].

Individuals need to cooperate with others to complete learning tasks that are not based on a predetermined set of answers and solutions. In this way, cooperative learning becomes meaningful (logical) for individuals [21].

Students exhibit different learning and social behaviours while seeking information and identifying possible solutions to questions or problems. In this process, students change their views about a topic, expand their understanding, and discuss how to combine the data they have collected with their plans to perform a task [22]. As a result of this active participation, each group member is able to learn the concepts they are focusing on [23].

The Peer Review methodology

The potential benefits of peer learning have long been recognised. In the academic world, various forms of peer, collaborative or cooperative learning, particularly small group activities, have increasingly been used to help students meet a variety of learning outcomes [24]. Therefore, the "Peer Review" methodology has been used for decades in across a wide range of disciplines, from Architecture to Music and Computer Science or Mathematics [25].

This methodology is associated with collaborative learning because it requires students to evaluate the work of their peers and provide them with feedback and effective feedback can increase students' motivation, change their behaviour, and improve their learning.

However, the application of peer assessment entails a change in the traditional assessment modelling the sense that students play a more active role, managing their own learning and participating in it. Peer review is one way of doing this. Since peer review reduces dependence on "experts", it could be useful also in the workplace [26].

The Learning Pyramid methodology

The "pyramid of learning", sometimes referred to as the "cone of learning", developed by the National Training Laboratory, suggests that most students remember only about 10% of what they read from textbooks, but retain almost 90% of what they learn through teaching others. The pyramid of learning model suggests, therefore, that some study methods are more effective than others and that varying study methods results in deeper learning and longer-term retention [27].

The pyramid technique usually has at least three phases and it is used when there is a need for convergence of a large group on a shared solution for a wicked problem (i.e., one that does not have only one right solution). In the first phase, each student devises a solution to the problem. In the second phase, dyads or groups of three work together by comparing the individual solutions and working out a better one by negotiating between the individual solutions. In the subsequent phases, groups merge and participants build new "shared" solutions based on those elaborated during the previous phase, until the whole cohort of students produces a single solution progressively built on top of the pre-existing ones.

Therefore, this usually involves the teacher or lecturer providing students with a learning task that they can observe, where active learning leads to a greater understanding. The key to mastering a concept is to teach it to others. In order to be able to teach or explain a topic to others requires an excellent grasp of the concepts, and superior retention.

The "Debate" and "Role Play" methods

Debate and Role Play are increasingly used in various undergraduate medical schools around the world, as they have proven to be particularly effective for learning critical thinking and communication skills [28]. Since these techniques are easily adaptable for use in the nursing profession and to be combined with other approaches, they enabled to integrate case studies, simulations, and PBL in the present Italian pilot course. The "Debate" technique has a low degree of structuredness and involves two main phases: in the first phase students are asked to study learning materials concerning a given problem (or case or theme) assigned by the teacher or tutor, while in the second phase they work in groups to negotiate their solution to the problem and produce an artefact reflecting the negotiation results. The debate technique lends itself to tackling complex problems such as, for example, case studies, where critical thinking, reflection and creativity need to be fostered and reflection is fostered by the asynchronous nature of the interactions.

The "Role Play" technique requires participants to "play a role", putting themselves in the shoes of someone else, whose perspective of a situation or an issue is different from their own, so that they better understand and appreciate their point of view. There are two phases to this technique: the first phase entails role uptake and study of materials (keeping an eye on the role taken), the second entails producing a common artefact by negotiating with peers its content from the perspective previously assumed. This technique has been used to recreate meaningful and realistic simulations.

Using a combination of the "Role Play" and "Debate" learning modes, students are encouraged to reflect on their progress towards their professional roles and responsibilities.

In debates, students argue two or more sides of an issue by bringing in important facts and points. Role-playing is a technique in which students are presented with roles in the form of a case or scenario, and then act out the roles,

in order to experience them for educational purposes and is, therefore, a spontaneous human interaction involving realistic behaviour in artificial or imagined conditions.

If used correctly, role-play and debate can create educational memories that could last a lifetime and offer students to opportunity to step out of their role of learners, which often tends to be passive. This brings diversity, fun, motivation, and a change of pace in teaching and learning. In the end, students gain a better understanding of the topic simply because they play an active role along the learning process [28].

Problem-based Learning methodology

Problem-based learning (PBL) is an educational approach that is increasingly used by many health professional training programs around the world [28]. The PBL approach promotes the use of social learning principles, which prompts group discussion and therefore contributes to the development of interpersonal, communication, and presentation skills, increased knowledge retention, improved problem-solving skills and better integration of basic science and clinical skills. Factors proposed to influence the effectiveness of PBL include the problems presented, facilitators, students, and the small group discussion process [29].

Instead of requiring students to study content knowledge and then context-free problems, PBL incorporates students' learning processes into real-life problems. The effectiveness of PBL in facilitating students' problem-solving and self-directed learning skills has been widely reported in medical education [30, 31]. PBL has also become increasingly popular across all disciplines in higher education [32, 33].

In PBL classes, students encounter the problem before learning, which contrasts with centuries of formal education practice, where students are expected to master the content before encountering a problem and attempt to apply the content. PBL is supported by theories of situated learning, which assume that learning is most effective when embedded in authentic tasks that are anchored in everyday contexts. In everyday life and professional life, people are constantly solving unstructured problems, those that have multiple or unknown objectives [34, 35].

Knowledge construction is stimulated by the problem and applied back to the problem. This teaching methodology is student-centred and self-directed, so that students individually and collaboratively take responsibility for generating questions and learning processes through self- and peer assessment and access to their own learning materials. In this context, teachers are not disseminators of knowledge, but facilitators who support and shape reasoning processes, group processes and interpersonal dynamics, probe students' knowledge in depth, and never intervene in the content or provide direct answers to questions.

The PBL learning process normally involves the following steps:

- students in groups of five to eight meet and discuss about the problem. They try to define and

articulate the problem and set learning objectives by identifying what they already know, what hypotheses or conjectures they have, and what learning activities are required and who will perform them;
- during self-directed study, individual learners complete their own learning tasks. They collect and study resources and prepare reports to the group;
- students share their learning with the group and revisit the problem, generating further hypotheses and rejecting others based on their learning;
- at the end of the learning period, which is usually one week, students summarise and integrate their learning [36, 37].

The Italian pilot course, by making use of Self-regulated Learning, also enabled students to control their own learning actively and consciously in terms of cognition, motivation and behaviour through experience and self-reflection [38, 39]. Teachers, as suggested by Pintrich (1995), stimulated and helped students to take responsibility for their own learning by offering instructional activities that provided opportunities for self-regulation.

Work-Based Learning

Work-Based Learning (WBL) activities are instrumental for the professional preparation of Family and Community Nurses, and in fact these were implemented throughout the pilot to achieve 11 specific learning outcomes (Tab. VI).

COURSE OUTCOMES

Twelve months after its inception, the first Italian blended learning Master Course for FCN was completed, highlighting a number of important outcomes that are described below.

Module 0

As already mentioned, the 0 module was introduced into the course structure to allow students to become familiar with the innovative teaching methods used and the functionalities of OOT.

Online activities were initiated by drawing from the story of Florence Nightingale's life, which was used as a virtual exemplar that the students could use while learning about family and community nursing during the pilot course.

After all the students had practised using the OOT, Florence (one of the Pilot's tutors) launched the first Forum to facilitate socialising. All the students introduced themselves to the others and talked about their professional experiences, skills, and expectations after the successful completion of the one-year pilot course. This also facilitated the recognition of prior learning.

This activity was completed in 2 weeks, and all the 45 students actively participated by posting their contributions on the Forum. At the end of this activity, Florence (the tutor) summarised the students' presentations and described their most relevant characteristics. The students' work experiences varied greatly, thus increasing the richness of their skill mix and potential as Family and Community Nurses. Many of the students demonstrated

Tab. VI. General outline targeted learning outcomes, Work-Based Learning topics, and learning assessment tools.

Targeted learning outcomes	WBL topics	Tools for assessment
LO1b Identify and assess families' health status and health needs	Nursing assessment and plan of care in community and family setting	OSCE
		WBL-REPORT
LO3a Plan nursing care to meet the needs of individuals, families, and the community within their scope of competence	Nursing assessment and plan of care in community and family setting	OSCE
		WBL-REPORT
LO19b Identify the appropriate clinical interventions and care management strategies for communities	Ageing and chronic disease processes	OSCE
		WBL-REPORT
LO21a Assess the social, cultural, and economical context of patients and their families	Fundamentals of care in community and family nursing care	OSCE
		WBL-REPORT
LO23a Know and apply communication, counselling and negotiation strategies and techniques with different actors	Communication patterns and family relationship in community and family setting	OSCE
		WBL-REPORT
LO27b Effectively address problems related to health and illness through the multidisciplinary team	Diagnostic therapeutic care pathways	OSCE
		WBL-REPORT
LO12c Evaluate the outcomes related to nursing activities in people's homes	Nursing-sensitive outcomes in community and family nursing care	OSCE
		WBL-REPORT
LO12d Evaluate the outcomes related to nursing activities in the community	Fundamentals of care in community and family nursing care	OSCE
		WBL-REPORT
LO13a Work and collaborate in a multidisciplinary team.	Team building in the community and family setting	OSCE
		WBL-REPORT
LO13b Plan and prioritise the activities of the multidisciplinary team in order to address problems related to health and illness	Organisational models in community and family setting	OSCE
		WBL-REPORT
LO10b Know and use the main monitoring and reporting procedures in order to document their own practice	Evidence-based nursing in community and family setting	OSCE
		WBL-REPORT

OSCE: Objective Structured Clinical Examination; WBL: Work-based learning.

significant levels of competence, which enabled to improve the quality of the group activities. By sharing their competencies with all their peers, these students became the key facilitators of all the group activities implemented in the 5 modules of the Italian pilot course.

The impact of the Open Online Tool on students

An *ad hoc* questionnaire was developed to evaluate the impact of the OOT on the students at the end of the course. Of the 45 students, 23 completed the questionnaire on a voluntary basis.

The questionnaire was composed of 43 items, the first 19 investigated personal experience with the OOT tool, a second section consisting of 12 items investigated the functionality of the tool in terms of ease of use, and the last 12 items, which constituted the third section of the questionnaire, investigated the functionality of the tool in terms of usefulness.

Each question asked respondents to express their level of agreement on a 5-point Likert scale (strongly agree, agree, neither agree nor disagree, disagree, strongly disagree). For the data analysis, the responses were categorised into three levels: positive (strongly agree and agree), neutral (neither agree nor disagree, no response), negative (disagree, strongly disagree).

In general, no items reported a negative evaluation, 2 items (4.7%) reported a neutral evaluation, 41 items reported a positive evaluation (95.3%) of the OOT tool.

First section students' "general experience with the instrument"

Overall values of the section: for 51.9% of the students their general experience with the instrument was positive, neutral for 39.1%, and negative for 8.9%.

The items with the best ratings were the following:

- "In general, I could complete any desired task with the OOT if I had specific training on it" (73.9%);
- "The OOT has good functionalities (e.g. those that support participation, sharing, evaluation of students' previous skills, etc.) (65.2%);
- "The use of the OOT in my vocational training has increased the effectiveness of my learning process" (56.5%);
- "As an overall evaluation at the end of the training, I can say that navigation within the OOT was intuitive"(56.5%);
- "As an overall evaluation at the end of the training, I can say that it was easy to remember how to perform tasks using the OOT"(56.5%);
- "In general, I could complete any desired task with the OOT if I could ask someone to help me when I get stuck"(56.5%);
- "In general, I could complete any desired task with the OOT because I saw someone else using it before I tried it myself" (56.5%).

All the items in the section related to experience with the Open Online Tool (OOT) received a positive evaluation, except for two items "The use of OOT in my professional training made me to save time" and "As an overall evaluation at the end of the training, I can say that interacting with the OOT was effortless" which received a neutral evaluation.

Second section, "Ease of using the Open Online Tool (OOT)"

Overall results of the section: for 61.2% of the students, the OOT was perceived as easy to use, moderately difficulty for 33.7%, and difficult for 5.1%.

"Group Webinar" was found to be the easiest section to use (82.6%), followed by "Webinar" (78.3%) and "Forum" (73.9%); no functionality was rated as not useful, while the "Nurse Sally" functionality was rated as easy to use for 50% and neutral for the remaining 50%.

Third section, "Usefulness of the Open Online Tool (OOT)"

In general, this section is the one that reported the highest positive values; overall, 63.4% of the students found the OOT useful, 34.10% expressed a neutral opinion, while 2.5% found it useless or not very useful.

More specifically, "Group Choice" and "Group Webinar" were the activities evaluated as most useful (78.3%), followed by "Forum" (73.9%) and "Quiz" (69.6%).

All activities were evaluated as useful except "Digital Badges", which was assessed as neutral.

STUDENTS' WORK-BASED LEARNING EXPERIENCE

To complete the work-based learning experience envisaged in the Italian pilot course project all students were assigned to a specific location, where they mainly conducted observation activities to collect information about the geography of their area and conduct a general description of their district, such as boundaries, land mass, traffic patterns, amenities, and services available

in the community using a validated community profile template.

They also collected data describing the socio-economic characteristics of their area, such as, type of family and networks, main religious beliefs, health literacy, language, types and rates of employment, type of housing, deprivation index, specific community development projects, and cases of self-neglect. Students were also asked to collect data on public, private and voluntary health services available in their assigned area. Then they collected data regarding health status indicators for the summarised care groups, including caseload data (all care groups) and target data (i.e., key performance indicators) at local, regional and national levels, as well as data regarding (a) the number of families connected to social workers, the number of people with disabilities, in mental health services, groups of adults living in the area under and over 65 years and the age decades (65, 75, 85, 95 years), the number of people with respite or home care packages, and the number of people with clinical needs.

Finally, their Work-Based Learning activities included describing existing and proposed workloads based on the information they had collected.

Once the students had collected all these data using a dedicated template on a mobile device (e.g., iPad, laptop, iPhone, etc.), they uploaded their templates with this information and shared them with other students and their teachers using the OOT Forum feature, through which they conducted a discussion to identify the top 3 priorities that were needed to meet the needs of the population living in their community. This process will enable them to identify, design and deliver the most appropriate interventions to address the priorities they identify.

Community Profiling is the collection of data about a particular community as descried above that can be used as a resource for change, where practice can be managed, measured, and evaluated [40] and is the tool through which FCNs can proactively meet the needs of the population by developing appropriate services.

Through the "Community Profile Template" tool, the needs of the following districts in Liguria were analysed: Pedemonte (Serra Riccò), Mezzanego, Savona, Murialdo (SV), Calice al Cornoviglio, Carcare (Val Bormida), Lumarzo (Tab. VII, Fig. 1). For each of these districts, the "Community Profile Template" enabled to identify the priorities useful for meeting the needs of the population in line with regional and national objectives.

LIMITATIONS

The Italian pilot course was held during the COVID-19 pandemic, raising many problems due to the lockdown imposed by the Italian government, especially regarding face-to-face teaching sessions and work-based learning modules. Furthermore, the use of an *ad hoc* unvalidated questionnaire to investigate students' satisfaction with the OOT may have undermined the quality of the data collected with this instrument.

Tab. VII. The healthcare needs of the population in the Liguria Region.

Areas	Priorities to meet the needs of the population in line with regional and national targets
Pedemonte di Serra Ricco'	Set up home care services and/or outpatient clinics to provide services (those provided by local health authorities were insufficient) Open a new nursing home for older people (the closest ones are in Sant'Olcese, Bolzaneto, Pontedecimo)
Mezzanego	Reduce the fragmentation of services (facilitating accessibility) Increase communication between the hospital and the community Introduce FCNs
Savona	Strengthen cooperation between local public authorities and the headquarters of the respective Ministries and Institutes Reinforcing the exchange of knowledge and information specific to each of the sectors involved Implementing the development of organisational arrangements
Murialdo	Organising activities aimed at identifying apparently healthy people with increased risk for metabolic syndrome and introducing them to specific programmes to decrease future adverse outcomes of hypertension and hyperglycaemia Intervene with activities to promote greater adherence to organised screening programmes, with a focus on the cervix uteri and colon-rectum Designing actions to increase participation in flu vaccination campaigns by people with at least one chronic disease in the 18-69 age bracket, given the importance of this indication, especially during the current COVID-19 pandemic, and contrasting misinformation on the subject Strengthening public transportation by providing alternative means of transport for a specific category of users who have difficulty walking and are therefore unable to use the few available public means of transport with stairs, and for all the disabled: setting up a time bank involving associations and social services Delivering hot meals at home for the inhabitants of the hamlets or for those who cannot move with details to be defined with the social services (family income, multimorbidity, unable to walk) using the kitchen of the Al Ponte di Murialdo restaurant, already offers this service privately on a daily basis for villagers who can leave their homes
Calice al Cornoviglio	Collaboration with the Municipality and local health authority to introduce the Family & Community Nurses and their mandate to the population, by sending out information leaflets Create a meeting place at the local ACLI association for possible recreational/sports activities Have a means of transport (e.g. minibus) to help to gather the population for meetings at a pre-established location and other needs (e.g. Adaptive physical activity, recreational activities ....)
Carcare (Val Bormida)	A nursing outpatients' clinic next to the office of the GP, to preventively intercept chronic diseases, such as diabetes, hypertension and obesity Improve transportation network for older people Healthcare education in the community regarding chronic diseases, like diabetes, hypertension, and obesity
Lumarzo	Increase involvement, awareness-raising of the population Increase the involvement of the population in public interventions concerning health status and its determinants: increase information and educational for individuals and groups Go from the "FCN interview" to the relationship of trust to build the reliability that the FCN role requires

Fig. 1. Map of the territories of the Liguria Region where the work-based learning sessions were carried out.

Discussion

The strengthening of an integrated care network among all social and health workers has been recognised as a common need throughout the Liguria Region. This is where the new professional figure of the family and community nurse (FCN) plays a key role. The geological characteristics of the Ligurian territory also brought to light the need to invest in a dedicated transportation network for disabled people, currently lacking in several areas of the Region, so that social and healthcare services are easily accessible also to the older population.

The pilot course described in this paper is well suited to the growing healthcare needs of the population and to appropriately address the important public health challenges also in the near future. Therefore, there is a great demand for highly competent family and community nurses also in the long term. Consequently, we plan to refine and replicate this course to prepare a highly skilled and competent workforce of family and community nurses, ready to provide their high-quality services to the public and at the same time relieve the healthcare burden on acute hospitals. This new generation of family and community nurses will also have the skills and knowledge to collect essential data to create a community profile, which will be essential for defining, designing, and delivering targeted interventions that effectively address the needs and health priorities of the community, and which could be used by nursing leaders to help public health policymakers make informed decisions.

FCNs will need to stay united and collaborate to share a path of progressive growth to unleash the potential of this "new' professional through measurable and verifiable results.

Conclusions

This study describes an innovative model for defining a postgraduate course based on a validated European core curriculum of the Family and Community Nurse, a new and emerging key professional to practising prevention, promotion, and protection of the public more extensively in the territory.

The Italian pilot course for the FCNs was a successful example of innovative teaching which, by using blended didactic methods achieved high levels of participant involvement and effective teaching and learning tools and activities. In fact, the OOT was perceived as a useful tool especially regarding group activities (choice of groups, group webinars) demonstrating that group work and debate generate professional growth.

The Family and Community Nurse is an emerging professional figure that needs to develop, consolidate, and establish itself. This process can be facilitated and enhanced through inter-professional teamwork. The OOT, which was set up during the pilot course and remained alive even after the end of the training course, constitutes the virtual commonplace where to build professional unity, debate, and exchange to establish this new type of nurse professional.

Furthermore, the structure of the pilot course proved to be effective in conveying the educational contents of the FCN curriculum, in fact new editions of this master course are being planned for the future. This will increase the number of highly competent FCNs and consequently improve the fulfilment of community needs.

Acknowledgements

Conflict of interest statement

The authors declare that there are no existing or potential conflicts of interest of financial, personal or any other nature that could affect or bias the results of this study.

Authors' contributions

The individual contributions of authors to the manuscript are as follows:

AB, LS, FP, GC, MZ, RC, and LV contributed to the conception and the design of this study.

AB, LS, LV, RC, MB, MG, MS, LB, GR, GS, LB, MZ, GC, and FM contributed to data collection, analysis, and interpretation.

MEM, GA, AB, and LS have been involved in drafting, editing and revising critically this manuscript.

All authors have read and approved the final manuscript

References

[1] EUROSTAT. Ageing Europe – Looking at the Lives of Older People in the EU 2019. https://doi.org/10.2785/811048

[2] United Nations, 2006. United Nations, 2006 Convention on the rights of persons with disabilities and optional protocol. New York: UN 2006. Available at: http://www.un.org/disabilities/documents/convention/convoptprot-e.pdf (Accessed in: February 2022).

[3] World Health Organization. Regional Office for Europe. (2005).Fourth workshop on WHO family health nurse multinational study: intercountry evaluation: report, Glasgow, Scotland 20-21 January 2005. Copenhagen: WHO Regional Office for Europe. Available at: https://apps.who.int/iris/handle/10665/107656 (Accessed in: December 2019).

[4] World Health Organization. Regional Office for South-East Asia. (2012). A framework for community health nursing education. WHO Regional Office for South-East Asia. Available at: https://apps.who.int/iris/handle/10665/204726 (Accessed in: November 2019).

[5] ESCO. European Skills/Competencies, Qualifications and Occupations. Available at: https://ec.europa.eu/esco/portal/occupation?resetLanguage=true&newLanguage=en (Accessed in: November 2019).

[6] ECVET - European Credit System for Vocational Education and Training. Available at: http://www.ecvet-projects.eu/About/Default.aspx (Accessed in: November 2019).

[7] Bagnasco A, Catania G, Zanini M, Pozzi F, Aleo G, Watson R, Hayter M, Sasso L. Core competencies for family and community nurses: a European e-Delphi study nursing. Nurse Educ Pract 2022;60:103296. https://doi.org/10.1016/j.nepr.2022.103296

[8] Deterding S, Sicart M, Nacke L, O'Hara K, Dixon D. Gamification: using game-design elements in non-gaming contexts. In: CHI'11 extended abstracts on human factors in computing systems, 2011. pp. 2425-2428.

[9] Kapp KM. The Gamification of learning and instruction. Game-based methods and strategies for training and education. San Francisco, CA: Pffeifer 2012.

[10] Kapp KM, Blair L, Mesch R. The Gamification of learning and instruction. Fieldbook: ideas into practice. San Francisco, CA: Pffeifer 2014.

[11] Milligan C, Littlejohn A, Margaryan A. Workplace learning in informal networks. JIME 2014. Available at: http://www-jime.open.ac.uk/jime/article/view/2014-06.

[12] Littlejohn A, Milligan C, Margaryan A. Charting collective knowledge: Supporting self-regulated learning in the workplace. J Workplace Learn 2012;24:226-238. https://doi.org/10.1108/13665621211209285

[13] Ng EMW. Online Collaborative Learning. In: Seel NM, eds. Encyclopedia of the Sciences of Learning. Boston, MA: Springer 2012. https://doi.org/10.1007/978-1-4419-1428-6_459

[14] Persico D, Pozzi F, Goodyear P. Teachers as designers of TEL interventions. Br J Educ Technol 2018;49:975-80. https://doi.org/10.1111/bjet.12706

[15] de Nooijer J, Schneider F, Verstegen DM. Optimising collaborative learning in online courses. Clin Teach 2021;18:19-23. https://doi.org/10.1111/tct.13243

[16] Tran VD, Lewis R. The effects of jigsaw learning on students' attitudes in a Vietnamese higher education classroom Int J High Educ 2012;1:1-13. https://doi.org/10.5430/ijhe.v 1n2p9

[17] Buhr GT, Heflin MT, White HK, Pinheiro SO. Using the jigsaw cooperative learning method to teach medical students about long-term and post-acute care. J Am Med Dir Assoc 2014;15:429-34. https://doi.org/10.1016/j.jamda.2014.01.015

[18] Zacharia ZC, Xenofontos NA, Manoli CC. The effect of two different cooperative approaches on students' learning and practices within the context of a WebQuest science investigation, Educ Technol Res Dev 2011;59:399-424. https://doi.org/10.1007/s11423-010-9181-2

[19] Masukawa H. Theory and Practice of the Constructive Jigsaw Method in Advancing Domain Knowledge and Skills in Parallel. Yakugaku Zasshi 2016;136:369-379. https://doi.org/10.1248/yakushi.15-00231-2

[20] Maden S. Effect of jigsaw I technique on achievement in written expression skill. Educ Sci: Theory Pract 2011;1:911-7.

[21] Karacop A. The Effects of Using Jigsaw Method Based on Cooperative Learning Model in the Undergraduate Science Laboratory Practices. Univers J Educ Res 2017;5:420-34. https://doi.org/10.13189/ujer.2017.050314

[22] Sharan Y. Learning to cooperate for cooperative learning. Anales De Psicología 2014;30:802-7. https://doi.org/10.6018/analesps.30.3.201211

[23] Berger R, Hänze M. Impact of expert teaching quality on novice academic performance in the jigsaw cooperative learning method. Int J Sci Educ 2015;7:294-320. https://doi.org/10.1080/09500693.2014.985757

[24] Boud D, Cohen R, Sampson J. Peer learning and assessment. Assess Eval High Educ 1999;24:413-26. https://doi.org/10.1080/0260293990240405

[25] Iacono UD, Pierri A, Taranto E. Peer review methodology in a blended course for mathematics teacher education. Int J Technol Math Educ 2019;26:49-54. https://doi.org/10.1564/tme_v26.2.01

[26] Conde MA, Sánchez-González L, Matellan-Olivera V, Rodriguez-Lera FJ. Application of peer review techniques in engineering education. Int J Eng Educ 2017;33:918-926.

[27] Lalley J, Miller R. The learning pyramid: Does it point teachers in the right direction. Education 2007;128:64-79.

[28] Latif R, Mumtaz S, Mumtaz R, Hussain A. A comparison of debate and role play in enhancing critical thinking and communication skills of medical students during problem based learning. Biochem Mol Biol Educ 2018;46:336-342. https://doi.org/10.1002/bmb.21124

[29] Zhou C, Kolmos A, Nielsen JFD. A problem and project-based learning (PBL) approach to motivate group creativity in engineering education. Int J Eng Educ 2012;28:3-16.

[30] Barrows H, Tamblyn RM. Problem-based learning: An approach to medical education. Springer Publishing Company 1980.

[31] Schmidt HG. Problem-based learning: rationale and description. Med Educ 1983;17:11-16. https://doi.org/10.1111/j.1365-2923.1983.tb01086.x

[32] Dochy F, Segers MSR, van den Bossche PG, Gijbels D. Effects of problem-based learning: A meta-analysis. Learn Instr 2003;3:533-568. https://doi.org/10.1016/S0959-4752(02)00025-7

[33] Hmelo-Silver CE. Problem-Based Learning: What and how do students learn? Educ Psychol Rev 2016;16:235-266. https://doi.org/10.1023/B:EDPR.0000034022.16470.f3

[34] Hung W, Jonassen DH, Liu R. Problem-based learning. Handbook of research on educational communications and technology 2008;3:485-506.

[35] Owen C. Problem-based learning. In learning and teaching in higher education. Edward Elgar Publishing 2019.

[36] Savery JR. Overview of Problem-based Learning: Definitions and Distinctions. Interdisciplinary Journal of Problem-Based Learning 2006;1(1). https://doi.org/10.7771/1541-5015.1002

[37] Schwartz, P. Problem-based learning. Routledge 2013.

[38] Zimmerman BJ. Models of self-regulated learning and academic achievement. In: Zimmerman BJ, Schunk DH, eds. Self-regulated learning and academic achievement. Theory, research and practice. New York: Springer 1998, pp. 1-25.

[39] Pintrich PR. Understanding self-regulated learning. New Dir Teach Learn 1995;63:3-12. https://doi.org/10.1002/tl.37219956304

[40] Hawtin M, Percy-Smith J. Community profiling: A practical guide: Auditing social needs. McGraw-Hill Education (UK) 2007.

Correspondence: Milko Zanini, Department of Health Sciences, University of Genoa, Via Pastore, 1, 16132 Genoa, Italy. Tel.: +39 010 3538590 - E-mail: milko.zanini@edu.unige.it

Adverse Effects of Sit and Stand Workstations on the Health Outcomes of Assembly Line Workers: A Cross-sectional Study

AMIR-MILAD MOSHREF JAVADI[1], ALIREZA CHOOBINEH[2], MOHSEN RAZEGHI[3],
HALEH GHAEM[4], HADI DANESHMANDI[5]
[1] Department of Ergonomics, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran;
[2] Research Center for Health Sciences, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran;
[3] Physiotherapy Department, School of Rehabilitation Sciences, Shiraz University of Medical Sciences, Shiraz, Iran;
[4] Department of Epidemiology, School of Health, Shiraz University of Medical Sciences, Shiraz, Iran;
[5] Research Center for Health Sciences, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran

Summary

Introduction. *Sitting and standing workstations can affect individual's health outcomes differently. This study aimed to assess the effects of sit and stand workstations on energy expenditure and blood parameters, including glucose and triglyceride, musculoskeletal symptoms/pain and discomfort, fatigue, and productivity among workers of assembly line of a belt factory.*
Methods. *This cross-sectional study was conducted on 47 male assembly line workers (24 workers in sitting workstation and 23 workers in standing workstation) with at least one year of working experience. Data were gathered via demographic/occupational characteristics, Fitbit system, medical records, the Persian version of the Nordic Musculoskeletal Questionnaire (P-NMQ), the Persian version of the Numeric Rating Scale (P-NRS), the Persian version of the Swedish Occupational Fatigue (P-SOFI), and Persian version of the Health and Work Questionnaire (P-HWQ).*
Results. *The results showed that there were no statistically significant between the demographic/occupational details of the participants in sitting and standing groups, except work experience.*

The findings of the present study revealed that the energy expenditure, and blood glucose/triglyceride there are not statistically differences between sitting and standing groups. In addition, the prevalence of musculoskeletal symptoms in the neck, lower back, knees, and ankles/feet in standing group was significantly higher than the sitting group. The means of severity of discomfort/pain in all body regions were significantly higher in standing group compared to other group. Generally, occupational fatigue was higher among the standing group compared to sitting group. About productivity, the 'concentration/focus' and 'impatience/irritability' subscales in sitting group were higher than the standing group. Contrariwise, other subscales of the productivity, including 'productivity', 'supervisor relations', 'non-work satisfaction', 'work satisfaction' in the standing group were higher than the sitting group.
Conclusions. *To reduce the adverse effects of sitting and standing workstations on individual's health outcomes, planning to use sit-stand workstations is recommended.*

Introduction

Prolonged and uninterrupted sitting is a significant risk factor for physical and mental well-being. In sitting position, trunk posture of the individual changes from its neutral position. On the other hand, long period standing is an important factor for developing the musculoskeletal discomfort in lower limbs, varicose veins and other known problems [1]. These situations can lead to individuals' inability, change in work efficiency, and bring significant costs for employees, employers and the community [2].

A person may only use one workstation during work, or may be moved between different workstations due to the type of activity. Generally, workstations can be divided into three categories in terms of performance: 1) sitting workstation, 2) standing workstation; and 3) sit-stand workstation (combined) [3].

Complications of sitting workstation are including blood pressure [4], type 2 diabetes, obesity, cardiovascular diseases [5], some types of cancers such as breast, colorectal, endometrial, ovarian, prostate, and lung cancers [6], Musculoskeletal Disorders (MSDs) [7, 9], and premature mortality [5]. In addition, some studies have stated a relationship between working in sitting workstation and the risk of fatigue [10, 11].

Standing posture (standing workstation) has advantages that include better access than sit workstation. Also in the standing position, the spine is positioned in its neutral posture and retains its natural curvature (S-mode). In this case, lower pressure is applied to the intervertebral discs. Also, standing can be maintained with less muscular activity and the strength of the trunk muscles in standing position is twice as much as sitting [12]. In addition, some studies have pointed out that heart rate, blood flow, and energy expenditure are significantly elevated in the standing working position vs the seated working position [13].

This study aimed to assess the effects of sit and stand workstations on energy expenditure and blood parameters, including glucose and triglyceride, musculoskeletal symptom/pain and discomfort, fatigue, and productivity among workers of an assembly line of a belt factory.

Methods

This cross-sectional study was conducted on 47 male assembly line workers (24 workers in sitting workstation and 23 workers in standing workstation) with at least one year of working experience. Employees with underlying diseases (cancer, heart diseases, chronic lung diseases, diabetes (type 1 and type 2), chronic liver diseases, physical disabilities, mental health disorders), accidents affecting the musculoskeletal system, cardiovascular diseases, and mental and hormonal disorders were excluded from the study.

All subjects voluntarily participated in the study after receiving information about the study objectives. They also signed informed consent forms before the commencement of the study. This study was approved by the ethics committee of Shiraz University of Medical Sciences. It also was performed in accordance with the Helsinki Declaration of 2013 [14].

DATA GATHERING TOOLS

Data were collected via demographic/occupational characteristics questionnaire, the Persian version of the Nordic Musculoskeletal Questionnaire (P-NMQ), the Persian version of the Numeric Rating Scale (P-NRS), the Persian version of the Health and Work Questionnaire (P-HWQ), the Persian version of the Swedish Occupational Fatigue (P-SOFI), Fitbit system, and medical records:

* demographic and occupational characteristics: This questionnaire included questions about age, height, weight, work experience, working hours per day, sex, marital status, number of children, and education level;
* Persian version of the Nordic Musculoskeletal Questionnaire (P-NMQ): P-NMQ examined the reported prevalence of musculoskeletal symptoms in different body regions among the study population [15]. In the present study, the reported musculoskeletal symptoms were limited to the past week. The psychometric properties of the P-NMQ have been examined by Choobineh et al. [16];
* Persian version of the Numeric Rating Scale (P-NRS): P-NRS is a unidimensional measure of discomfort and pain intensity [17]. In order to assess the intensity of musculoskeletal discomfort/pain, the subjects were required to rate P-NRS at the beginning, and end of the shift. Then, difference between the P-NRS scores at the beginning and end of the shift was calculated and was considered as musculoskeletal discomfort/pain in the work shift [18];
* Persian version of the Health and Work Questionnaire (P-HWQ): HWQ was developed by Shikiar et al. (2004) to assess various aspects of workplace productivity. HWQ consists of 30 questions responded through a 10-point Likert scale. The items are divided into six subscales, including productivity (own assessment and other's assessment), concentration/focus, supervisor relations, work and non-work satisfaction, and impatience/irritability in this questionnaire [19]. It is worth mentioning that concentration/focus and impatience/irritability subscales are in reverse mode. This means that higher scores represent lower concentration/focus and impatience/irritability. The psychometric properties of the P-HWQ have been examined by Daneshmandi et al. ($\alpha \geq 0.65$ for all subscales) [20];
* Persian version of the Swedish Occupational Fatigue (P-SOFI): The SOFI-20 consists of 20 items using an 11-point numerical rating scale (0 = not at all, and 10 = to a very high degree) for each item. The items have been categorized into five dimensions, including (1) lack of energy, (2) physical exertion, (3) physical discomfort (4) lack of motivation, and (5) sleepiness. Scores on each dimension range from a minimum of 0 to a maximum of 40. Based on the SOFI-20 users' guide, the score on each dimension was also rated on severity as follows: low (mean score < 8.5), medium (8.5 < mean score < 23.5), and high (mean score > 23.5) levels of fatigue, based on quartiles of the score distribution [21]. Psychometric properties of the Persian version of SOFI-20 (P-SOFI-20) were reported by Javadpour et al. [22];
* Fitbit system: The Fitbit apparatus (Charge model; made in China) was used to estimate energy expenditure during the work shift. Diaz et al. stated in their study that Fitbit was an accurate and reliable device for wireless physical activity tracking and estimation of energy expenditure [23]. In the present study, energy expenditure during the work shift was estimated;
* medical records: Data related to individuals' blood parameters, including glucose and triglyceride were extracted from their medical records. Normal range of glucose was considered ≤ 99 mg/dl and > 100 mg/dl shows a high level of the blood glucose [24]. In addition, normal range of triglyceride was ≤ 200 and > 200 mg/dl was considered high [24].

DATA ANALYSIS

The Statistical Package for Social Sciences 16 (SPSS Inc., Chicago, IL, USA) was used to analyze the data. At first, Kolmogorov-Smirnov and Shapiro-Wilk tests were used to test the normality of the data. To analyze the data, descriptive statistics (frequency/percentage, and mean/standard deviation), independent sample t-test, chi-square test, and Fisher's exact test were used. A p-value < 0.05 was considered to be statistically significant.

Results

The demographic/occupational characteristics of the subjects are presented in Table I. Based on the results,

Tab. I. Comparison of demographic/occupational characteristics between sitting and standing groups (n = 47).

Quantitative variable	Sitting group (n = 24)	Standing group (n = 23)	P-value[†]
Age (years)	36.45 ± 8.997	35.37 ± 3.639	0.091
Height (cm)	173.26 ± 7.927	175.93 ± 6.627	0.174
Weight (kg)	74.25 ± 12.659	74.44 ± 9.204	0.946
BMI (kg.m^{-2})*	30.37 ± 3.639	30.37 ± 3.639	0.379
Work experience (years)	11.44 ± 6.444	6.12 ± 3.344	< 0.001
Qualitative variable	Sitting group (n = 24)	Standing group (n = 23)	P-value
Marital status Single Married	 2 (12.5%) 22 (87.5%)	 3 (15.4%) 20 (84.6%)	0.522**
Education level Diploma and lower Associate degree and higher	 24 (90.3%) 0 (0%)	 21 (70.4%) 2 (29.6%)	0.061[‡]
Dominant hand Right Left	 23 (97.1%) 1 (2.9%)	 22 (85.2%) 1 (14.8%)	0.147[‡]
Smoking Yes No	 2 (9.5%) 22 (91.4%)	 1 (0%) 22 (100%)	0.477[‡]

* Body Mass Index; † Independent sample t-test; ** Chi-square test; ‡ Fisher's exact test.

Tab. II. Comparison of the energy expenditure between sitting and standing groups (n = 47).

Variable	Sitting group (n = 24)	Standing group (n = 23)	P-value*
Energy expenditure (kcal.min^{-1})	3.13 ± 0.77	3.50 ± 0.63	0.114

* Independent sample t-test.

Tab. III. Comparison of the glucose and triglyceride between sitting and standing groups (n = 47).

Variable	Sitting group (n = 24)	Standing group (n = 23)	P-value
Glucose (mg/dl) Normal High	 23 (95.83) 1 (4.17%)	 23 (100%) 0 (0%)	0.251*
Triglyceride (mg/dl) Normal High	 19 (79.16%) 5 (20.84%)	 18 (78.26%) 5 (21.74%)	0.936[†]

* Fisher's exact test; †Chi-square test.

Tab. IV. Prevalence rate of the reported musculoskeletal symptom in different body regions amongst the studied workers during the past 12 months (n = 47).

Body region	Sitting group (n = 24) No. (%)	Standing group (n = 23) No. (%)	P-value
Neck	9 (37.50)	16 (69.56)	0.016*
Shoulders	11 (45.83)	10 (43.47)	0.912*
Elbows	2 (8.33)	5 (21.74)	0.089[†]
Wrists/Hands	6 (25.00)	11 (47.82)	0.072*
Upper back	13 (54.16)	15 (65.21)	0.511*
Lower back	9 (37.50)	16 (69.56)	0.022*
Thighs	6 (25.00)	10 (43.47)	0.163*
Knees	9 (37.50)	17 (73.91)	0.040*
Ankles/Feet	9 (37.50)	20 (86.95)	0.001*

* Chi-squared test; † Fisher's exact test.

there is a significant relationship between the work experience of the sitting and standing groups:
- energy expenditure: the working energy expenditure of the participants is compared in Table II in sitting and standing groups. As shown in the table, the energy expenditure there is not statistically differences between sitting and standing groups;
- blood parameters: in Table III, the levels of the blood

parameters, including glucose and triglyceride have been compared in the sitting and standing groups. The findings revealed that the blood glucose and triglyceride there are not statistically differences between sitting and standing groups;
- musculoskeletal symptoms/pain and discomfort: Table IV shows the prevalence rate of the reported musculoskeletal symptom in different body regions

Tab. V. Comparison of severity of discomfort/pain in different body regions of the participants (n = 47).

Body region	Sitting group (n = 24)	Standing group (n = 23)	P-value*
Neck	1.60 ± 0.09	3.70 ± 0.03	0.001
Shoulders	2.00 ± 0.79	2.50 ± 0.40	0.004
Elbows	1.00 ± 0.06	2.60 ± 0.30	0.001
Wrists/Hands	1.70 ±0.40	1.80 ± 0.33	0.006
Upper back	1.00 ±0.48	2.80 ± 0.60	0.001
Lower back	0.90 ±0.35	2.90 ± 0.40	0.001
Knees	2.00 ±0.21	3.00 ± 0.60	0.001
Ankles/Foot	1.00 ±0.21	4.00 ± 0.70	0.001

* Independent sample t-test.

Tab. VI. Comparison of occupational fatigue subscales between sitting and standing groups (n = 47).

	Occupational fatigue subscale	Sitting group (n = 24)	Standing group (n = 23)	P-value*
Lack of energy	Low	11 (34.4%)	6 (22.2%)	> 0.001
	Moderate	21 (65.6%)	9 (33.3%)	
	High	0 (0%)	12 (44.4%)	
Physical exertion	Low	14 (43.8%)	8 (29.6%)	0.170
	Moderate	16 (50%)	13 (48.1%)	
	High	2 (6.3%)	6 (22.2%)	
Lack of motivation	Low	14 (45.2%)	6 (22.2%)	0.181
	Moderate	15 (48.4%)	18 (66.7%)	
	High	2 (6.5%)	3 (11.1%)	
Sleepiness (drowsiness)	Low	17 (53.1%)	8 (29.6%)	0.011
	Moderate	15 (46.9%)	13 (48.1%)	
	High	0 (0%)	6 (22.2%)	
Physical discomfort	Low	15 (48.4%)	6 (22.2%)	0.004
	Moderate	13 (41.9%)	8 (29.6%)	
	High	3 (9.7%)	13 (48.1%)	

* Chi-square test.

Tab. VII. Comparison of productivity dimensions between standing and sitting groups (n = 47).

Productivity subscale	Sitting group (n = 24)	Standing group (n = 23)	P-value*
Productivity	7.66 ± 2.34	7.95 ± 2.65	0.655
Concentration/Focus	2.52 ± 1.19	2.32 ± 0.95	0.333
Supervisor relations	1.48 ± 0.42	1.49 ± 0.45	0.906
Non-work satisfaction	1.66 ± 0.57	2.05 ± 0.69	0.020
Work satisfaction	2.28 ± 0.77	2.32 ± 0.75	0.867
Impatience/Irritability	2.26 ± 0.66	1.98 ± 0.75	0.139

* Independent sample t-test.

amongst the workers during the past 12 months. The prevalence of the musculoskeletal symptoms in the neck, lower back, knees, and ankles/feet in standing group was significantly higher than the sitting group. Mean ± standard deviation of severity of discomfort/pain in different body regions among the sitting and standing groups has been compared in Table V. As the table depicts, the means of severity of discomfort/pain in all body regions were significantly higher in standing group compared to other group;

• occupational fatigue: Table VI shows comparison of the occupational fatigue subscales between sitting and standing groups. As shown, the 'lack of energy', 'sleepiness', and 'physical discomfort' subscales were statistically significant between two studied groups; so that, occupational fatigue was higher among the standing group compared to sitting group;

• productivity: Table VII compares the subscales of productivity between sitting and standing groups. As shown in the Table, the 'concentration/focus' and 'impatience/irritability' subscales in sitting group were higher than the standing group. Contrariwise, other subscales of the productivity, including 'productivity', 'supervisor relations', 'non-work satisfaction', 'work satisfaction' in the standing group were higher than the sitting group.

Discussion

The results of the current study showed that there were no statistically significant between demographic/

occupational details of the participants in sitting and standing groups, except work experience. This means that the mean of work experience in the sitting group (11.44 years) was statistically higher than standing group (6.12 years) (p < 0.001). In fact, it seemed that workers with higher work experience were more likely to use sit workstations:

- energy expenditure: findings the present study revealed that the energy expenditure in the sitting group was slightly lower than the standing group, but no significant difference was obtained between the mentioned groups; In the current study, evaluated activities in the sitting and standing groups (3.13 *vs* 3.50 kcal.min[1], respectively) placed in the moderate jobs [25]. In a study by Forkan et al. [26] in order to assess the energy expenditure in the sitting and standing groups on office workers for six weeks, no significant results were found. On the other hand, Daneshmandi et al. [20] in their study stated that the sit-stand workstation can be effected on the energy expenditure of the individuals. Similar results have also been obtained in other studies conducted in this context [27, 28]. For example, Fryar et al. stated that 2 to 4 hours of standing per day could lead to an additional 25-57 kcal/day for an average-sized American man (88.9 kg) and an additional 21-48 kcal/day for an average-sized American woman (75.5 kg) [29].

- blood parameters: the findings of the study depict that there are not statistically differences between blood glucose/triglyceride in sitting and standing groups. In this context, a study showed a relative improvement in individuals' blood parameters at the sit-stand workstation [30]. In a study conducted by Mantzari et al. [31] concluded that sit-stand workstation had no a significant effect on energy expenditure, heart rate, and metabolic diseases. Conflicts with the findings of various studies can be attributed to the: 1) type of workstation (sit or stand or sit-stand workstation), 2) duration of use the workstation, and 3) demographic differences. In order to have a more accurate and consistent comparison of blood parameters between the two standing and sitting groups, it is recommended that a larger sample size be examined;

- musculoskeletal symptoms/pain and discomfort: the results of the study showed that the prevalence of musculoskeletal symptom in the neck, lower back, knees, and ankles/feet in standing group was significantly higher than the sitting group. Standing position is expected to exert more biomechanical pressure to the above-mentioned body regions. Therefore, the long-term standing in the subjects could provide a good reason for the high prevalence of musculoskeletal symptoms in these regions. In addition, findings revealed that severity of pain/discomfort in all individuals' body regions in standing group was statistically higher than the sitting group. Daneshmandi et al. in a study amongst assembly line workers reported a high prevalence of musculoskeletal symptom in the lower back, wrist/

hands, and neck [32]. Roelofs and Straker in their study pointed out that greatest musculoskeletal discomfort is related to the lower limb and back in standing bank tellers group [33]. In the same line, Daneshmandi et al. noted that longer standing in office workers could lead to musculoskeletal symptoms in some body regions, such as shoulders, wrists/hands, and ankles/feet [20];

- occupational fatigue: the findings of the present study showed that the 'lack of energy', 'sleepiness', and 'physical discomfort' subscales of the occupational fatigue were higher (statistically significant) among standing group compared to sitting group. In a study to compare sit, stand and sit-stand workstations, the results showed that long standing over than 90 minutes resulted in fatigue in the legs and back regions, and people tend to reduce pain and discomfort during standing by leaning backwards. According to the study, the standing condition causes fatigue in the legs and the sit-stand situation causing more discomfort in the buttocks region [34];

- productivity: the results of this section showed that the 'concentration/focus' and 'impatience/irritability' subscales in sitting group are higher than the other group (standing group), but, these differences are not statistically significant. On the other hand, our findings revealed that other subscales of the productivity, including 'productivity', 'supervisor relations', 'non-work satisfaction', 'work satisfaction' in the standing group were higher than the sitting group, but, only 'non-work satisfaction' subscale was statistically significant. In the same line, Pronk et al. [35], Hedge et al. [36], and Nevala et al. [37] stated that using the sit-stand workstation improved productivity. Thorp et al. also demonstrated that there is a significant improvement in total productivity among the individuals who used the sit-stand workstation compared to the sitting position, but this result was contrariwise about the 'concentration/focus' subscale [38].

Limitations

Given the cross-sectional nature of the study and a significant difference in work experience between sitting and standing groups, the findings should be interpreted cautiously. Additionally, due to the fact that the study was conducted in the field under real conditions, the outcomes might have been affected by confounding variables such as workplace policies, management issues, stress, lifestyle factors, financial and family commitments. Moreover, the sample sizes in each group were small. Therefore, using larger sample sizes could lead to achievement of more robust results.

Conclusions

In summary, the energy expenditure, blood glucose/

triglyceride there are not statistically differences between in sitting and standing groups. In addition, the prevalence of musculoskeletal symptom in the neck, lower back, knees, and ankles/feet in standing group was significantly higher than the sitting group. Generally, occupational fatigue was higher among the standing group compared to sitting group. About productivity, the 'concentration/focus' and 'impatience/irritability' subscales in sitting group were higher than the standing group. Contrariwise, other subscales of the productivity, including 'productivity', 'supervisor relations', 'non-work satisfaction', 'work satisfaction' in the standing group were higher than the sitting group. To reduce the adverse effects of sitting and standing workstations on individual's health outcomes, planning to use sit-stand workstations is recommended.

Acknowledgements

Conflict of interest statement

None declared.

Authors' contributions

AMMJ: idea, data gathering, data interpretation, article drafting, final approval of the article. AC, MR, HD: idea, data interpretation, article drafting, final approval of the article. HG data analysis and interpretation, article drafting, final approval of the article.

References

[1] Westgaard R, Vasseljen O, Holte KA. Trapezius muscle activity as a risk indicator for shoulder and neck pain in female service workers with low biomechanical exposure. Ergonomics 2001;44:339-53. https://doi.org/10.1080/001401301119649

[2] Noben CY, Evers SM, Nijhuis FJ, de Rijk AE. Quality appraisal of generic self-reported instruments measuring health-related productivity changes: a systematic review. BMC Public Health 2014;14:115. https://doi.org/10.1186/1471-2458-14-115

[3] Choobineh A, Solaymani E, Mohammad Beigi A. Musculoskeletal symptoms among workers of metal structure manufacturing industry in Shiraz, 2005. Iran J Epidemiology 2009;5:35-43.

[4] Patel AV, Bernstein L, Deka A, Feigelson HS, Campbell PT, Gapstur SM, Colditz GA, Thun MJ. Leisure time spent sitting in relation to total mortality in a prospective cohort of US adults. Am J Epidemiol 2010;172:419-29. https://doi.org/10.1093/aje/kwq155

[5] Thorp AA, Owen N, Neuhaus M, Dunstan DW. Sedentary behaviors and subsequent health outcomes in adults: a systematic review of longitudinal studies, 1996-2011. Am J Prev Med 2011;41:207-15. https://doi.org/10.1016/j.amepre.2011.05.004

[6] Lynch BM. Sedentary behavior and cancer: a systematic review of the literature and proposed biological mechanisms. Cancer Epidemiol Biomarkers Prev 2010;19:2691-709. https://doi.org/10.1158/1055-9965.EPI-10-08

[7] Daneshmandi H, Choobineh A, Ghaem H, Karimi M. Adverse effects of prolonged sitting behavior on the general health of office workers. J Lifestyle Med 2017;7:69-75. https://doi.org/10.15280/jlm.2017.7.2.69

[8] Choobineh A, Daneshmandi H, Saraj Zadeh Fard SK, Tabatabaee SH. Prevalence of work-related musculoskeletal symptoms among Iranian workforce and job groups. Int J Prev Med 2016;7:130. https://doi.org/10.4103/2008-7802.195851

[9] Choobineh A, Daneshmandi H, Aghabeigi M, Haghayegh A. Prevalence of musculoskeletal symptoms among employees of Iranian petrochemical industries: October 2009 to December 2012. Int J Occup Environ Med 2013;4:195-204.

[10] Stenlund T, Ahlgren C, Lindahl B, Burell G, Knutsson A, Stegmayr B, Slunga Birgander L. Patients with burnout in relation to gender and a general population. Scand J Public Health 2007;35:516-23. https://doi.org/10.1080/14034940701271874

[11] Daneshmandi H, Choobineh A, Ghaem H. Psychometric properties of the persian version of the "Multidimensional Assessment of Fatigue Scale". Int J Prev Med 2019;10:53. https://doi.org/10.4103/ijpvm.IJPVM_172_17

[12] Júdice PB, Hamilton MT, Sardinha LB, Zderic TW, Silva AM. What is the metabolic and energy cost of sitting, standing and sit/stand transitions? Eur J Appl Physiol 2016;116:263-73. https://doi.org/10.1007/s00421-015-3279-5

[13] Beers EA, Roemmich JN, Epstein LH, Horvath PJ. Increasing passive energy expenditure during clerical work. Eur J Appl Physiol 2008;103:353-60. https://doi.org/10.1007/s00421-008-0713-y

[14] World Medical Association. World Medical Association Declaration of Helsinki - 2013.

[15] Kuorinka I, Jonsson B, Kilbom A, Vinterberg H, Biering-Sørensen F, Andersson G, Jørgensen K. Standardised Nordic questionnaires for the analysis of musculoskeletal symptoms. Appl Ergon 1987;18:233-7. https://doi.org/10.1016/0003-6870(87)90010-X

[16] Choobineh A, Lahmi M, Shahnavaz H, Khani Jazani R, Hosseini M. Musculoskeletal symptoms as related to ergonomic factors in Iranian hand-woven carpet industry and general guidelines for workstation design. Int J Occup Saf Ergon 2004;10:157-68. https://doi.org/10.1080/10803548.2004.11076604

[17] Childs JD, Piva SR, Fritz JM. Responsiveness of the numeric pain rating scale in patients with low back pain. Spine 2005;30:1331-4. https://doi.org/10.1097/01.brs.0000164099.92112.29

[18] Daneshmandi H, Choobineh A, Ghaem H, Alhamd M, Fakherpour A. The effect of musculoskeletal problems on fatigue and productivity of office personal: a cross-sectional study. J Prev Med Hyg 2017;58:252-8.

[19] Shikiar R, Halpern MT, Rentz AM, Khan ZM. Development of the Health and Work Questionnaire (HWQ): an instrument for assessing workplace productivity in relation to worker health. Work 2004;22:219-29.

[20] Daneshmandi H, Choobineh AR, Ghaem H, Hejazi N. Proper sit-stand work schedule to reduce the negative outcomes of sedentary behavior: a randomized clinical trial. Int J Occup Saf Ergon 2021;27:1039-55. https://doi.org/10.1080/10803548.2019.1679972

[21] Choobineh A, Javadpour F, Azmoon H, Keshavarzi S, Daneshmandi H. The prevalence of fatigue, sleepiness, and sleep disorders among petrochemical employees in Iran. Fatigue: Biomed Health Behav 2018;6:153-62. https://doi.org/10.1080/21641846.2018.1461252

[22] Javadpour F, Keshavarzi S, Choobineh A, Aghabaigi M. Validity and reliability of the Swedish Occupational Fatigue Inventory (SOFI-20) among Iranian working population. Iran J Ergonomics 2015;3:50-8.

[23] Diaz KM, Krupka DJ, Chang MJ, Peacock J, Ma Y, Goldsmith J, Schwartz JE, Davidson KW. Fitbit®: An accurate and reliable device for wireless physical activity tracking. Int J Cardiol 2015;185:138-40. https://doi.org/10.1016/j.ijcard.2015.03.038

[24] Mahan LK, Raymond JL. Krause's food & the nutrition care process, mea edition e-book. Amsterdam: Elsevier; 2016.

[25] Bridger R. Introduction to ergonomics. Boca Raton: CRC Press; 2008.

[26] Forkan TA. Differentiating between low level activities in sedentary occupations utilizing fitbits. Montana: Montana Tech 2016.

[27] Burns J, Forde C, Dockrell S. Energy expenditure of standing compared to sitting while conducting office tasks. Hum Factors. 2017;59:1078-87. https://doi.org/10.1177/0018720817719167

[28] Thorp AA, Kingwell BA, English C, Hammond L, Sethi P, Owen N, Dunstan DW. Alternating sitting and standing increases the workplace energy expenditure of overweight adults. J Phys Activ Health 2016;13:24-9. https://doi.org/10.1123/jpah.2014-0420

[29] Fryar CD, Gu Q, Ogden CL. Anthropometric reference data for children and adults; United States, 2007-2010. Vital Health Stat 2012;252:1-48.

[30] Desmond PA, Neubauer MC, Matthews G, Hancock PA. The Handbook of operator fatigue. Farnham: Ashgate Publishing; 2012.

[31] Mantzari E, Galloway C, Wijndaele K, Brage S, Griffin SJ, Marteau TM. Impact of sit-stand desks at work on energy expenditure, sitting time and cardio-metabolic risk factors: multiphase feasibility study with randomised controlled component. Prev Med Rep 2019;13:64-72. https://doi.org/10.1016/j.pmedr.2018.11.012

[32] Daneshmandi H, Kee D, Kamalinia M, Oliaei M, Mohammadi H. An ergonomic intervention to relieve musculoskeletal symptoms of assembly line workers at an electronic parts manufacturer in Iran. Work 2018;61:515-21. https://doi.org/10.3233/WOR-182822

[33] Roelofs A, Straker L. The experience of musculoskeletal discomfort amongst bank tellers who just sit, just stand or sit and stand at work. Ergon SA 2002;14:11-29.

[34] Hosseinzadeh K, Choobineh A, Ghaem H. Validity and reliability of the Farsi version of the individual strength questionnaire checklist in the Iranian working population. Armaghane Danesh 2013;18:295-304.

[35] Pronk NP, Katz AS, Lowry M, Payfer JR. Peer reviewed: reducing occupational sitting time and improving worker health: the take-a-stand project, 2011. Prev Chronic Dis 2012;9:154. https://doi.org/10.5888/pcd9.110323

[36] Hedge A, Ray EJ, editors. Effects of an electronic height-adjustable worksurface on computer worker musculoskeletal discomfort and productivity. Proceedings of the human factors and ergonomics society annual meeting; 2004: SAGE Publications Sage CA: Los Angeles, CA.

[37] Nevala N, Choi DS. Ergonomic comparison of a sit-stand workstation with a traditional workstation in visual display unit work. Ergonomics 2013;6:22-7. https://doi.org/10.2174/1875934301306010022

[38] Thorp AA, Kingwell BA, Owen N, Dunstan DW. Breaking up workplace sitting time with intermittent standing bouts improves fatigue and musculoskeletal discomfort in overweight/obese office workers. Occup Environ Med 2014;71:765-71. https://doi.org/10.1136/oemed-2014-102348

HISTORY OF MEDICINE AND ETHICS

Health policy analysis in Eastern Mediterranean region using a health policy triangle framework: Historical and ethical insights from a systematic review

MASOUD BEHZADIFAR[1], MAHBOUBEH KHATON GHANBARI[2], HAMID RAVAGHI[3,4], AHAD BAKHTIARI[5],
SAEED SHAHABI[6], LEILA DOSHMANGIR[7], SAEIDE ALIDOOST[3], SAMAD AZARI[2], MARIANO MARTINI[9],
SEYED JAFAR EHSANZADEH[10], NICOLA LUIGI BRAGAZZI[11]

[1] Social Determinants of Health Research Center, Lorestan University of Medical Sciences, Khorramabad, Iran;
[2] Health Management and Economics Research Center, Iran University of Medical Sciences, Tehran, Iran;
[3] School of Health Management & Information Sciences, Iran University of Medical Sciences, Tehran, Iran;
[4] World Health Organization Regional Office for the Eastern Mediterranean, Cairo, Egypt; [5] Health Equity Research Center (HERC), Tehran University of Medical Sciences (TUMS), Tehran, Iran; [6] Health Policy Research Center, Institute of Health, Shiraz University of Medical Sciences, Shiraz, Iran; [7] Tabriz Health Services Management Research Center, Iranian Center of Excellence in Health Management, Tabriz University of Medical Sciences, Tabriz, Iran; [8] Hospital Management Research Center, Health Management Research Institute, Iran University of Medical Sciences, Tehran, Iran; [9] Department of Health Sciences, University of Genoa, Genoa, Italy; [10] English Language Department, School of Health Management and Information Sciences, Iran University of Medical Sciences, Tehran, Iran; [11] Laboratory for Industrial and Applied Mathematics (LIAM), Department of Mathematics and Statistics, York University, Toronto, ON, Canada

Summary

Background. *Health policy can be defined as an agreement and consensus on a health-related program and set of actions taken to achieve the goals expected by programs in the area of policy. Policy analysis involves a wide range of methods, techniques, and tools in a way to reach awareness of the impacts of the developed and implemented policies. Whereas policy analysis in developed countries has a long history, in developing countries, it is instead in its first developing stages. Our paper aimed to collect systematically the studies using health policy triangle framework in doing analysis in one of the health policy issues in the Eastern Mediterranean region organization.*

Methods. *To conduct our literature search, ISI/Web of Science, PubMed/MEDLINE, Embase, The Cochrane Library, Global Health Database, Scopus, as well as Google Scholar from 2003 up to June 2020 were systematically mined. To evaluate the meth-odological quality of the included studies, the Critical Appraisal Skills Program checklist was used.*

Results. *We selected 30 studies, conducted between 2011 and 2020. According to the findings of these studies, in the Eastern Mediterranean region, organization region, and the role of evidence-based research in policy-making has been repeatedly emphasized, but its use in health program decision-making has been limited, and health research systems in Eastern Mediterranean region organization are still under scrutiny. There is still a gap between evidence-based research in health systems and its use in policy-making.*

Discussion. *Based on the present systematic review, studies based on policy analysis should focus on all the elements of health policies and provide evidence to inform decisions that can strengthen health systems, improve health and improve existing inequalities.*

Background

Strengthening health systems with the aim of achieving sustainable development goals and universal health coverage requires evidence-based policy interventions [1]. Each component of the policy process plays its proper part within the health system and the country in which is implemented as a whole [2, 3]. The process of developing health policies is complex, and many actors in this field, such as government agencies, stakeholders, political parties, the mass media, researchers, and other governments, are pursuing goals in this area. They are self-sufficient and are influential in this process based on their position, goals, and impact on politics [4].

Due to the distinctive characteristics of the health system with respect to other sectors of the society, dealing with human lives, making policies to avoid unwanted effects has a special place [5]. Policy making concerning human and financial resources to deliver health care services in due time increases the importance of decisions made in this sector [1].

The World Health Organization (WHO) defines health policy as an agreement and consensus on a health-related program and set of actions taken to achieve the goals expected by programs in the area of policy [6]. Policy analysis involves a wide range of methods, techniques, and tools in a way to reach awareness of the impacts of the developed and implemented policies.

Health policy examines the laws that directly or indirectly affect health and its various aspects. Health policy can be performed through the public and private sectors [7]. The scope of health policy is broad and varied, and is likely to be gradual, fragmented, and incomplete. The health policy process evaluates and analyzes the best opportunity to identify appropriate strategies for the health sector [8].

How a policy is achieved, how it is designed, who is affected by the policy (including proponents and opponents), and what the consequences will be is the main questions that policy analysis tries to answer. The subject of policy analysis and how to carry it out is intensively discussed in many scientific and academic circles [9]. Policy analysis is a multidisciplinary process that seeks to examine the interaction between organs, ideas, and its benefits in a political process [10].

In policy analysis, researchers seek a proper understanding of the policy process and intend to examine its nature. This can provide a better understanding of the health policy process as well as very credible evidence for the problems and issues that arise in the field of health and for future decisions that need to be made [11].

To conduct a policy analysis, various theories and models are generally used [10]. Policy analysis in developed countries has a long history [12]. In developing countries, it is instead in its first developing stages [13]. The use of policy analysis models, theories, or frameworks is very important for policymakers, and they should use these analyzes to make more accurate and useful decisions [14]. In recent decades, the tendency to use theories and models of policy analysis in the health sector has increased, and many studies have been done in this regard [12].

Health policy triangle framework

In 1994, Walt and Gilson introduced a framework for health policy analysis. This framework has four main domains, including context, content, process, and actors. This framework can be used as a retrospective or prospective approach to policy analysis, and a comprehensive understanding of decision-making, planning, and policy implementation can be achieved [9]. This framework allows health researchers to examine the impact of political, social, cultural, economic, and international factors. It also discusses the process in which the policy in question is formulated, then designed, implemented, and evaluated by the policymaker, and analyzes the role of different actors in relation to the policy (Fig. 1).

In many countries with diverse health systems, this framework has been used to examine health-related policies and their impact on their community [9]. This framework can be used retrospectively or prospectively [15]. In addition to developed countries, the use of this framework has increased in recent years in developing countries [13]. Examining and summarizing the application of this framework in health-related policies can strengthen and implement more appropriate policies for countries [5]. The use of

Fig. 1. Health policy triangle framework.
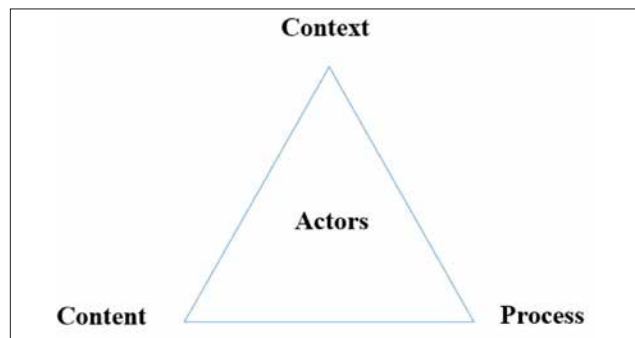
this framework can also provide a valuable platform for more comprehensive policy analysis [12]. Our paper aimed to collect systematically the studies using Health policy triangle framework in doing analysis in one of the health policy issues. In particular, the focus of our study is on health policy analysis studies in the Eastern Mediterranean region organization (EMRO). EMRO is one of the six regions of the WHO, having 21 members: namely, Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Palestine (West Bank and Gaza Strip), Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates (UAE), and Yemen [16].

Methods

Literature search

To conduct our literature search, ISI/Web of Science, PubMed/MEDLINE, Embase, The Cochrane Library, Global Health Database, Scopus, as well as Google Scholar from 2003 up to June 2020 were systematically mined. Also, to increase the chance of finding relevant studies, reference lists of the studies included were assessed. Specific keywords were employed using Boolean operators (AND, OR, NOT). First, a preliminary search was performed using MeSH on the PubMed/ MEDLINE database, and the keywords were identified after familiarization with the literature. The following search strategy was used:

("Policy "OR "Policy analysis" OR "Health policy" OR "Public policy" OR "Policy process" OR Health politics" OR "Document analysis" OR" Agenda setting" OR" "Stakeholder analysis OR "Framework" AND" Walt AND Gilson framework" OR "Health Policy Triangle Framework" OR "Policy triangle framework" OR "Walt AND Gilson's framework") AND ("Afghanistan "OR "Bahrain "OR "Djibouti "OR "Egypt "OR "Iran" OR "Iraq "OR "Jordan "OR "Kuwait "OR "Lebanon "OR "Libya "OR "Morocco "OR "Oman "OR "Pakistan "OR "Qatar "OR "Saudi Arabia "OR "Somalia "OR "Sudan "OR "Syrian" OR "Tunisia "OR "Emirates "OR "Yemen "OR "Eastern Mediterranean Region Organization "OR "EMRO ""OR "Middle East " OR "developing countries") NOT ("America" OR "USA" OR "Australia" OR "Canada" OR "UK" OR "Europe").

The search of the databases was carried out by two researchers independently. Any differences between them were resolved through discussion.

INCLUSION CRITERIA

1. Studies conducted in the EMRO region.
2. Studies that used the health policy triangle framework to analyze policy.
3. Studies published in English.
4. Studies published in journals with the peer-review system.
5. Studies published between 2003 up to June 2020.
6. Articles whose working method was acceptable.
7. Articles whose full text was available.

EXCLUSION CRITERIA

1. Studies published in Non-EMRO countries.
2. Studies published in Non-English language.
3. Studies the findings of which were not sufficient for analysis.
4. Theses and chapters of books.

QUALITY ASSESSMENT OF INCLUDED STUDIES

To evaluate the methodological quality of the included studies, the Critical Appraisal Skills Program (CASP) checklist was used. This checklist contains ten questions. There are three answers (Yes, No, and Unclear) to each question. For the answer Yes, score 1 and for the answer No, score 0 were considered. Based on the scores obtained, the studies were divided into three categories: good, moderate, and weak quality (1-3: poor, 4-7: moderate and 8-10: good).

DATA EXTRACTION

Two researchers independently extracted selected study data. In case of disagreement between them, one person acted as the arbitrator, and the dispute was resolved via discussion. Name of the first author, the year of publication, the country, the title of the topic of the policy, and the most important findings related to the items of the framework were extracted.

DATA ANALYSIS

Data were analyzed using deductive content analysis guided by policy triangle framework components (namely, content, context, processes, and actors). In qualitative research, deductive content analysis is similar to inductive content analysis. Deductive content analysis is applied usually has prior theoretical knowledge as the starting point and guided by a half-structured or structured analysis matrix.

Results

This study adhered to the "Preferred Reporting Items for Systematic Reviews and Meta-Analyses" (PRISMA) guidelines.
863 articles were found in the initial search. 172 articles

were duplicated and, as such, were removed. The titles of 691 articles were reviewed. 572 were removed, being unrelated studies. 30 studies were finally selected based on the study criteria. Figure 2 shows the process of searching and selecting studies [17-46].

Selected studies were conducted between 2011 and 2020. Studies were conducted in Iran (16), Pakistan (4 studies), Saudi Arabia (2 studies), Lebanon (2 studies), Sudan (2 studies), Tunisia (2 studies), Egypt (1 study), Afghanistan (1 study), Syria (1 study) and Palestine (1 study). One study was conducted in four countries (Tunisia, Syria, Palestine, and Turkey). Figure 3 shows the studies according to the EMRO countries in which they have been performed.

THE METHODOLOGICAL QUALITY OF THE SELECTED STUDIES

Table I and Figure 4 show the quality of studies broken down according to the previously mentioned classification (good, moderate, and poor quality). Based on the scores obtained, 20 had good quality, 9 had moderate quality, and 1 had poor quality.

The main characteristics and findings of the selected studies are shown in Table II.

Discussion

Policy analysis is a valuable process for understanding policy processes, identifying the determinants of the failures and successes of past policies, and planning for future ones [13], and is also complex due to the diverse nature of health issues [13, 47]. The present study assessed published studies related to health issues in the Eastern Mediterranean region using a Health policy triangle framework. The findings of the present study were selected from thirty extracted articles. With the exception of one study [34], all studies were retrospective. It seems that in order to evaluate the programs of the health system, it seems that in order to evaluate health system programs, it is better to pay attention to studies with prospective design and put it on the agenda, because evidence arising from these researches in improving the health systems and providing services by policymakers and researchers would be of higher quality and strength. Policy analysis can show the agility and dynamism of countries' health systems [48, 49]. Findings of studies based on four elements of study (context - why do you need this policy -, content - what is the policy mainly about-, process - how this policy is designed and implemented - and actors - who participate and influence policy formulation and implementation) were analyzed and reported.

CONTEXT

The policy analysis process should be such as to reflect a thorough understanding of the context, decision-making, planning and implementation of policies. Because health issues go beyond health care and are influenced by psychosocial, economic and environmental factors [13,

Fig. 2. Flow-chart showing the process of study retrieval, selection and inclusion adopted in the present systematic review.
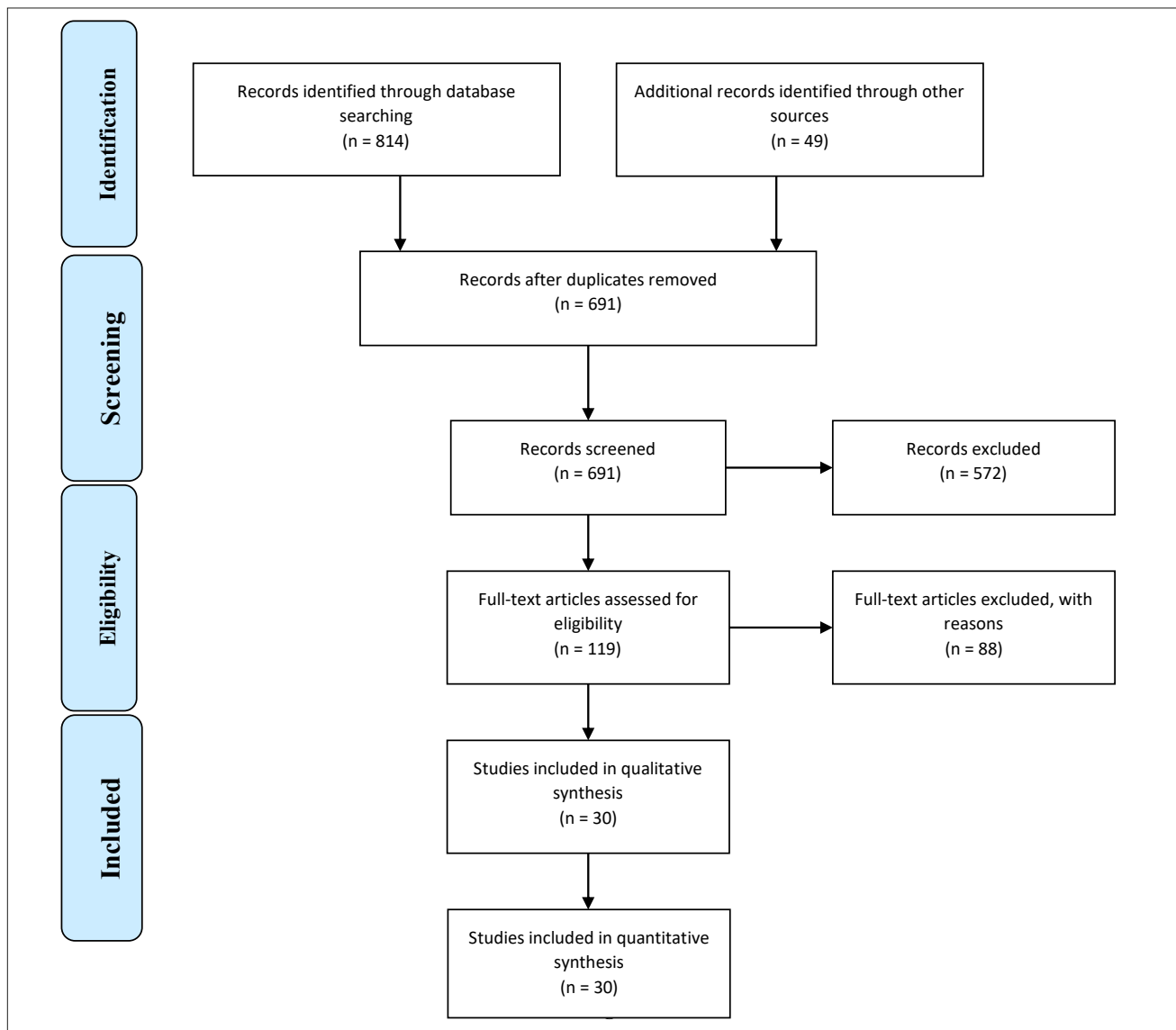

47], health policy-making is an inherently political process, which is influenced by the social and political context, and therefore understanding and analyzing political systems can help better assess the context and why a given policy is chosen [50].

Demographic, epidemiological, educational, technological, cultural, as well as social developmental, economic and financial issues, the specific type of political regime are some of the issues that should be seen in context [51]. In the included studies, political and administrative factors, as well as economic and financial one, and social and cultural variables, personal and political interests, promotion of international standards of sectarianism, urgency and values of policymakers and media policies are the most important underlying parameters determining the success of a given health policy. Impacts on specific policies were reported. In most of the selected studies, the contextual factors of the country of the study did not have a direct impact on the

choice of policy for analysis. It seems that the priority criteria for policy analysis in EMRO countries should be more transparent and the use of evidence should be increased. This could contribute to a more efficient and effective use of financial resources for policy analysis research [52]. Topics analyzed by researchers in selected studies included high prevalence or mortality rates, WHO reports, the Sustainable Development Goals (SDGs), Universal Health Coverage (UHC) achievement. Researcher evaluated also whether political decisions to solve a problem were taken based on evidence. Despite the fact that the type of political system, financing and Gross Domestic Product (GDP) per capita allocated to health programs are important elements in health policy making and can influence health policies related processes, none of the studies included in the present systematic review focused specifically on these factors and their impact on the policy in question.

The health policy triangle framework states that

Fig. 3. Studies included broken down according to the EMRO countries in which they have been performed.
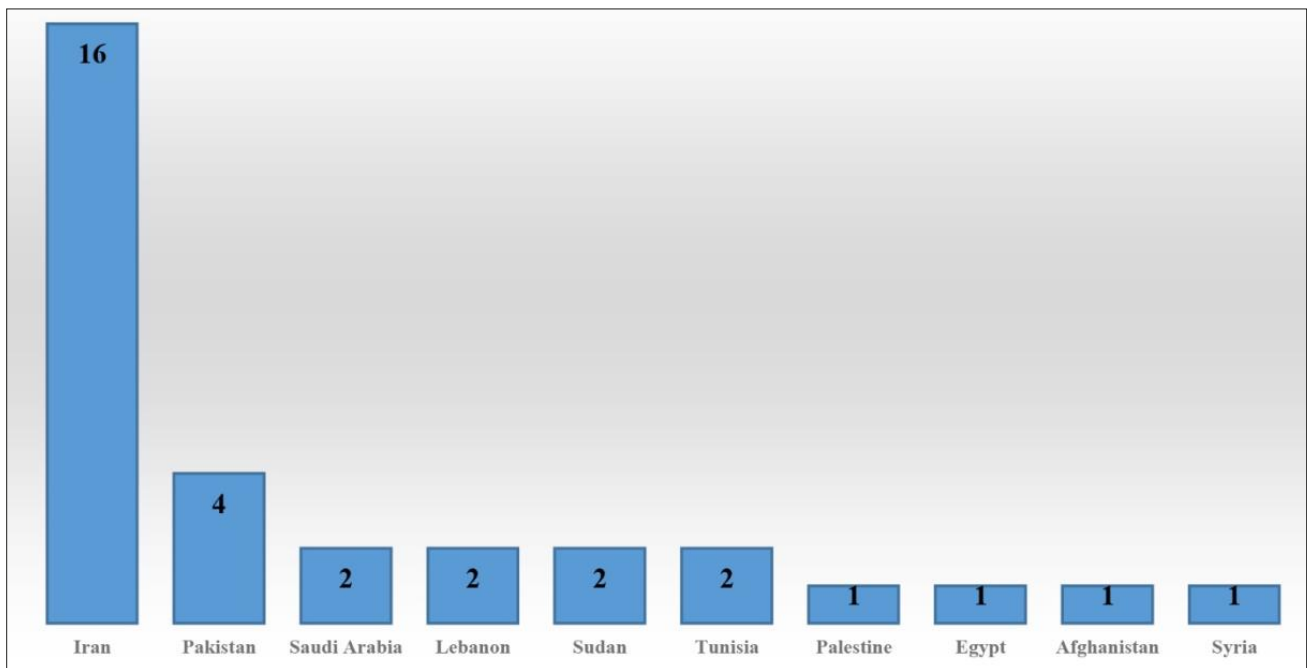
national, international, political, economic and social factors can influence health policies. However, based on the Leicher's classification of these factors, some of which depend on circumstances, structural, cultural, and international factors, most of the selected studies did not pay full attention to these issues and paid less attention to their impact. These issues can be effective in creating a tendency to analyze or not analyze a policy in the health sector. One of the important points was the attention of the researchers of the selected studies to the selection of topics related to diseases and issues such as health justice, health finance, governance, use of evidence whereas other issues were less analyzed. Perhaps one of the reasons for choosing diseases for policy analysis is easier access, greater participation of people in these studies, which encourages EMRO researchers to analyze them. Of course, the nature of some issues in the health sector may make researchers less interested in analyzing them. They may be conservative and not accept the problems they need to gather information about them.

On the other hand, due to political issues such as wars and sanctions in the EMRO region and its great impact on the health sector, the influence of these issues has received less attention. Ethnic and national prejudices have not been accounted for in the analysis of health sector policies in the countries of this region. Religious tendencies in this area have not been considered in selected studies. The existence of wars in Afghanistan, Syria and Yemen and the sanctions on Iran can affect the process of policy analysis of health-related issues. Lack of full vaccination coverage, failure to achieve the Millennium Development Goals (MDGs) goals, inadequate access to health services, reduced health budgets, issues related to children, women and the elderly, immigrants and refugees problems, as well as

economic-financial problems and declining incomes, can dramatically impact health funding and resources allocation, which in its turn further complicates these problems.

To analyze a policy in the health sector, one should not be utilitarian and conservative. You have to see the underlying issues. These affect the success or failure of that policy. Policy analysis is a dynamic and political process. The diversity of EMRO countries' political systems is crucial in implementing or not implementing health sector policies. The attention and priorities of policymakers in these countries can influence the choice of a given issue for policy analysis. Unfortunately, this issue has received less attention. Researchers seem to have sought to analyze issues that are more influenced by international factors.

CONTENT

Content is the body of policy, which includes the nature and details of a policy proposal or document and is expressed through all its components, including: programs, projects, specific activities, goals, general objectives and observable goals [53, 54]. The content of the selected studies is given in Table II.

Some articles referred to the formulation of policies, guidelines, and related laws, and some referred to its communication to related organizations and some other articles described the goals of the strategies. However, some studies did not fully explain the content of the programs under study and the relevant documentation and program outputs were not explained. Some studies did not mention or were vague.

The programs referred to for framework analysis were mainly developed by the Ministry of Health of these countries. The selected studies did not document any

Tab. I. Quality appraisal of the studies included in the present systematic review.

The first author (References)	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	The score of the quality	Categories
Beesley (14)	1	1	1	1	1	NA	1	1	1	1	9	Good
Zaidi (15)	1	1	1	1	1	1	1	1	1	1	10	Good
Phillimore (16)	1	1	1	1	1	1	1	1	1	1	10	Good
Seef (17)	NA	NA	NA	NA	1	NA	NA	1	1	1	4	Moderate
Zaidi (18)	1	1	1	1	1	1	1	1	1	1	10	Good
El-Jardali (19)	1	1	1	1	1	1	1	1	1	1	10	Good
El-Jardali (20)	1	1	1	1	1	1	1	1	1	1	10	Good
Markazi-Moghaddam (21)	NA	1	NA	1	1	NA	1	1	1	1	7	Moderate
Speakman (22)	1	1	1	1	1	1	1	1	1	1	10	Good
Awadalla (23)	1	NA	0	0	1	1	1	0	NA	1	5	Moderate
Ben Romdhane (24)	1	1	1	1	1	1	1	1	1	1	10	Good
Faraji (25)	1	1	NA	NA	1	NA	1	1	NA	1	6	Moderate
Alharbi (26)	NA	0	1	1	NA	1	1	1	1	NA	6	Moderate
Goshtaei (27)	NA	1	0	0	1	1	1	NA	1	1	6	Moderate
Moshiri (28)	NA	0	1	1	NA	1	1	1	1	1	7	Moderate
Sarfraz (29)	1	1	1	1	1	1	1	1	1	1	10	Good
Abolhassani (30)	1	1	1	NA	1	NA	1	1	1	1	8	Good
Aljumah (31)	1	NA	0	1	NA	1	1	NA	NA	1	5	Moderate
Azami-Aghdash (32)	1	1	1	1	1	1	1	1	1	1	10	Good
Haq (33)	1	1	1	1	1	1	1	1	1	1	10	Good
Yousefinezhad (34)	1	1	1	NA	1	1	1	1	1	1	9	Good
Ansari (35)	1	1	1	NA	1	NA	1	1	1	1	8	Good
Al-Ansari (36)	1	0	NA	1	0	1	0	1	1	1	6	Moderate
Edalati (37)	1	1	1	1	1	1	1	1	1	1	10	Good
Gharaee (38)	1	1	0	1	1	1	1	1	1	1	9	Good
Loloei (39)	1	1	1	1	1	1	1	1	1	1	10	Good
Mohseni (40)	1	1	1	1	1	1	1	1	1	1	10	Good
Behzadifar (41)	1	1	1	1	1	1	1	1	1	1	10	Good
Doshmangir (42)	1	1	NA	NA	1	1	1	1	1	1	8	Good
Raoofi (43)	1	NA	NA	NA	NA	1	NA	0	0	1	3	Week

health initiatives and related issues or programs that were felt needed and pursued by other health-related organizations. It seems that in EMRO countries, the main focus for the implementation and start of health programs is only the Ministry of Health, and due to over-reliance on this ministry, the process of programs is unipolar and still or other organizations are not sensitive in this regard or if there were no documents.

While health should be current and considered in all policies in countries. At the heart of "Health in All Policies" is the study of health determinants, which are largely controlled by policies of sectors other than those involved in health, because in the "Health in All Policies" process, addressing the social factors of health and disease can be a powerful tool for reducing health inequalities [55].

Health is highly influenced by lifestyle and environment and many health issues are simultaneously deeply affected by factors outside the traditional realm of health and healthcare. Factors such as literacy, poverty, employment and racism contribute to differences in life expectancy as well as health-related quality of life. Concerns about how to address these factors have led to a focus on "health in policies", in which policies in the

social sectors such as transport, housing, employment and agriculture can ideally focus on health and access to health contribute to equity in health [56]. Once the problems are identified, the content analysis will focus on the suggestions and goals themselves. Sources (material and political) should be mentioned in the discussion of the content of a policy. Material resources, such as equipment and money and technical and organizational resources, this type of resources means the knowledge and organizational and managerial abilities to implement the proposals. Moreover, political resources are essentially the power to implement a policy. None of the studies addressed this issue.

PROCESS

In the analysis of this section, what should be considered is to describe the process of health policies, ie policy formulation and implementation of policies and issues related to them. If Walt considers the three main aspects of the policy process to be the following: The issue of power in terms of who makes decisions and who influences them. The concept and types of policies in terms of what politics is and how it is policy-making, and the logic and rules of politics in terms of its formation as a logical process.

Tab. II. Characteristics of included studies.

First author	Year of publication	Country	Subject analyzed (title of policy)	Retrospectively or prospective	Data collection	Main finding		Process	Actors
						Context	Content		
Beesley (14)	2011	Sudan	The disrupted health sector	Retrospective	This study has been obtained by comparing and searching for documents in reputable databases and comparing them not enough information has been provided in this regard	One of the ways to help restore the functioning of the disrupted health sector is the effective and extensive participation of the international community in the form of providing technical assistance to the Ministry of Health to complete any shortcomings in specialization or experience. Creating a new health management by outsiders is also an opportunity to correct problems and introduce innovations. An example of international technical support in 2007 was the provision of technical assistance to the Sudanese Ministry of Health in the form of a manpower program	With the signing of the Comprehensive Peace Agreement in Sudan, the analysis of the situation and development plans of the health system and an improvement strategy were developed and designed and drafted by the new health officials. The World Health Organization (WHO) has launched a USAID-funded bilateral to provide full-fledged technical services to improve health care, especially in the area of human resources. The Youssid-funded capacity project to provide technical, managerial and financial support for the development and management of human resources and labor, as well as the African Medical and Research Foundation (AMREF), is the only clinical officer training school (with a track record in human resources in southern Sudan and other countries) Who were involved in developing human resource programs	Between 2005 and 2006, World Health Organization advisers supported the Sudanese Ministry of Health in conducting human resource assessments to provide the basis for a human resource development program for the Reconstruction Workforce Reconstruction Process for a Human Resource Development Program, a working group chaired by the Director of Human Resources of the Ministry of Health prepared the reference conditions for a comprehensive assessment. A multi-agency team, including three consultants, 10 data collectors and an IT specialist, coordinated with the Ministry of Health, as well as the main human resources organizations in the field of health and treatment, reviewed and collected the human resources inventory after completion. No further discussion took place after the data collection phase and after the delivery and internal rotation of the situation analysis and draft recommendations. The recommendations, the main focus of which is the proposed Human Resources Strategic Plan, were published in 2006 by the Ministry of Health	The Ministry of Health The World Health Organization (WHO) The African Medical and Research Foundation (AMREF) Not enough information has been provided in this regard
Zaidi (15)	2012	Pakistan	NGO–government contracting for health service delivery	Retrospective	Case study data (conducted by NGOs to prevent human immunodeficiency virus HIV) using in-depth interviews, semi-structured interviews, document review and direct observation and review of national policy plans, provincial contract management, and local contract implementation	Contracts outside of preventive health services and primary health care (PHC) by providing international assistance in a number of developing countries, such as Cambodia, Guatemala, Senegal, Costa Rica, Nicaragua, Afghanistan, Pakistan, Bangladesh and India, tend to be handed over to organizations. Non-governmental organizations have contracts (non-governmental organizations) that are more important in order to provide health care services in low-income and middle-income countries. The term non-governmental organization usually includes the non-profit sector, which aims to give these institutions better access to the deprived population and more responsiveness	The contract for the AIDS control program, which relied on NGOs, had four distinct features: first, contracting on a large scale, including large contracts and several bidding periods, and second, emphasizing performance-based contracts and health-related goals. The general was low cost. Third, the strength of the market to attract potential contenders for the AIDS program. Although inexperienced, the public sector played a key role in managing the contracting process. The program coordinated new and energetic leadership to prevent HIV	Even after its implementation, activities were limited and lacked strategic direction. But in the early 2000s, services began to follow the international pursuit of HIV / AIDS prevention and the frustration of international donors with Pakistan's efforts to control the search for new and daring ways to search for disease, and the government lobby was conducted with international donors at the Ministry of Finance level. This led to extensive contracting initiatives with donor budgets and an increase in the national budget allocation for HIV control from $ 2.5 million to nearly $ 10 million. It also envisages the development of a comprehensive service package (including public health measures as well as client empowerment and rehabilitative measures) in contracts that were necessary at the international level to attract HIV interventions	The Ministry of Health (MoH) The Ministry of Finance The World Bank UK Department for International Development (DFID) United States Agency for International Development (USAID) European Commission (EC) Canadian International Development Agency (CIDA)

Author	Year	Countries	Title	Type	Data collection		
Phillimore (16)	2013	Tunisia, Turkey, Palestine (oPt), and Syria	Health system challenges of cardiovascular disease and diabetes	Retrospective	Data collection of the qualitative study was done in three ways: Analysis of published and unpublished official documents on the details of the health care system of all 4 countries (Tunisia, Turkey, oPt, and Syria) focusing on cardiovascular disease and diabetes, semi-structured interviews with key informants at the national and regional level in the management of these diseases have major responsibilities in the health system of countries, case studies based on fieldwork including interviews with staff, patients and care professionals as well as clinical performance observations, as well as primary and secondary level facilities and equipment And some diabetes clinics	Increasing the prevalence of diseases such as CVD and diabetes and increasing the cost of managing these diseases requires the development of new techniques for managing diseases through which patients and their care costs can be monitored and monitored. If costs are not managed and monitored, the health care system will become " illegible." In Palestine: One of the problems of fragmentation of the health system, which is due to three reasons: the multiplicity of providers, the multiplicity of goals and priorities of donor organizations, and the problems caused by the political separation of the West Bank and Gaza,and the Palestinian health care system relies on funding from a variety of sources, with out-of-pocket payments accounting for the largest share of the budget. In Syria, because the government's budget for health care is unsustainable and limited, especially due to the high long-term costs of patients with NCD. In Tunisia, the health care system is budget-based and tax-based, and health care monitoring is poor. Social insurance covers a large portion of the population (more than 80%). In the private sector, the Ministry of Health's medical guidelines for patients with non-communicable diseases are rarely followed. Expenses are out of pocket. The introduction of the family physician system (in 2006) marked a change in the system. However, prevention and treatment services in the new system have not been integrated, and there is no proper referral system, especially for infectious diseases.	In Palestine, managing non-communicable diseases, which put the most pressure on the health system, is one of the four strategic goals of the Palestinian Ministry of National Health and other health care providers, and there are screening, diagnosis and treatment protocols for diabetes

In Palestine, the management of non-communicable diseases, which put the most pressure on the health system, is one of the four strategic goals of the Palestinian Ministry of National Health and other health care providers, and there are screening, diagnosis and treatment protocols for diabetes

In Palestine, the health system for policy making and implementation of programs in the field of these two diseases with problems such as lack of cohesion of the health system, reliance of the system on foreign donors, lack of stable information systems and lack of access to patient data and non-sharing of this information. There are differences between different parts of the health system and the lack of retention of employees, especially doctors.

In this country, despite spending 64% of expenditure on health on health care, only 7% of it is spent on the prevention of public services.

Although these two diseases are one of the main challenges in Syria, there is a lack of coordination and planning in different parts of the health care system. There was no systematic follow-up of weak patients to refer patients from primary to secondary care.

There is no system for recording patient records, especially in rural and rural areas, and there has also been a severe shortage of skilled staff in the health system, especially outside major cities.

In Tunisia, there are four frameworks and structures for NCD management, but there are no coordination, monitoring, and implementation mechanisms, and fragmentation of the system prevents coherent management of the disease. Strategic partnerships have not been strengthened, and policymakers are reluctant to see the disease as part of an economic and social development strategy, and the focus of participation is on health care, not prevention, and so inter-sectoral and conscious participation is weak.

There was coordination and integration in the Turkish health system, and the structure (The new Family Health Center framework) was formed, which was inconsistent. Moreover, the Health Transformation Programme (HTP) reforms play an important role in primary care (for prevention, diagnosis and treatment). However, the diagnosis and monitoring of non-communicable diseases has been neglected and poor, and there is no proper referral system.

In oPt:
The Palestinian MoH
The United Nations Relief and Works Agency (UNRWA)
A Non-Governmental Organisation (NGO) small private sector
In Syria: the government and private sectors the MoH
The Ministries of Defense, Interior and Education
The private sector, Private clinics, private hospitals Syria's pharmaceutical industry
In Tunisia:
the MoH private sector private polyclinics
In Turkey:
The Ministry of Health
expanding private health care sector, private hospitals
The Social Security Institution (SSI), the pharmaceutical sector, professional associations and, increasingly, the media

Author	Country	Year	Policy	Design	Methods	Problem	Policy narrative	Actors
Seef (17)	Egypt	2013	The H1N1 flu pandemic control	Retrospective	Data from the study, which looked at Egypt's health policies to control the epidemic, were reviewed from policy documents and literature review	The 2009 flu pandemic spread internationally. The new flu virus, known as the swine flu virus, killed hundreds of thousands of pigs while controlling the disease (despite recommendations from health officials). This was unnecessary because the disease does not occur through contact with pigs or eating meat	On March 4, 2009, the Egyptian parliament debated a law banning the breeding of pigs and their products, and lawmakers approved a request to kill all pigs in the country. The Minister of Health presented a plan to address the flu pandemic and proposed a plan for all relevant ministries, including the Ministries of Education, Transport, Environment and Agriculture. In 2009, Egypt began slaughtering about 300,000 pigs in the country. Policies were implemented through a top-down approach, with well-defined goals, the necessary political, administrative, technical, and financial resources available, the command chain established from the center to the fringes, and a system of communication and control. . But pig farmers, who were predominantly Christian, protested vehemently. International health officials say the swine flu virus, which has caused global fear, is not being transmitted by pigs and must be stopped. The World Health Organization also criticized the Egyptian government's decision	The Ministry of Health (MoH) The parliament No details were given about the actors
Zaidi (18)	Pakistan	2013	Nutrition Policy	Retrospective	Qualitative research data were obtained through in-depth interviews and focal group discussions with government stakeholders, donor agencies, civil society organizations (CSOs) and nutritionists, along with review of published and gray literature documents	Malnutrition in Pakistan is high and malnutrition is a chronic problem, and the most at-risk groups include pregnant and lactating women and children under the age of five. Moreover, there is no proper nutrition strategy	Interventions and policies included the establishment of Baby-Friendly Hospitals to promote newborn breastfeeding, the establishment of places in medical centers for nutrition counseling, the distribution of iron supplements and folic acid to pregnant women, and vitamin A to children. Food fortification was implemented with training and providing equipment and goods for food processing in the private sector. Pilots of targeted nutrition projects for girls' schools (ages 6-11 years) were implemented in deprived rural areas in all provinces. The projects were funded by UN agencies, the World Food Program and international NGOs. 770/5000 In 2008, the Food Safety Working Group and the Ministry of Food Safety were formed in Pakistan. Around the same time, a draft of Pakistan's federal-style integrated nutrition strategy was formed with UNICEF's support for the global Scaling Up Nutrition (SUN) movement. The release of the National Nutrition Survey NNS in early 2012, along with media advertising, raised the issue of support for researchers, the media and development partners, raising the issue of malnutrition. The provincial transfer in 2011 provided development partners with easier implementation and direct partnership with executives, and nutrition and related issues became a new public policy program led by development partners	The Ministry of Health (MoH) The UN agencies The World Food Program and international NGOs The Provincial Education Departments
El-Jardali (19)	Lebanon	2014	The voluntary health insurance system	Retrospective	Data collection was conducted by comprehensive and chronological media review, interviews with policymakers, stakeholders and key journalists, and review of legal documents, minutes, statistical studies, and official documents.	Out-of-pocket expenditures are very high in Lebanon (56.5%). Analysis of insurance policy Voluntarily examines how and why this policy is implemented. Public policy is a complex process. The typology of public policy consists of three aspects; distributive, regulatory and redistributive. Distribution policies provide specific benefits or services to specific segments of the population regardless of limited resources. Regulatory policies include a direct choice as to who will be exaggerated and who will be deprived. Meanwhile, redistribution policies include large groups of citizens who benefit from or receive losses. In fact, NSSF Voluntary insurance is a distributed policy typology.	11 The Social insurance Law on the Establishment of the voluntary insurance branch was issued by the Council of Ministers The decree was implemented by the President of the Republic on the basis of the recommendations of the NSSF board of Directors of the Minister of Labor, consultation with the Advisory Council and the approval of the Council of Ministers. the voluntary health insurance policy in Lebanon was adopted by the government and adopted as a political decision to address an immediate problem, and scientific, statistical and financial evidence was not used to develop policy and implement the policy.Moreover, policy makers and other stakeholders were not involved in policy making.	Although the Lebanese political system is democratic, the government insisted that the policy be adopted without the participation of the Ministry of Finance and the NSSF, which was not a participatory and transparent decision-making processbecause stakeholders and civil society did not participate in political discussions and decisions.

Reference	Year	Country	Topic	Design	Data collection	Description	Implementation	Actors
El-Jardali (20)	2014	Lebanon	Nursing practice Law	Retrospective	Qualitative research data were collected using informant interviews with key stakeholders as well as a roundtable to validate the findings, identify any gaps, and obtain insights and feedback on the panels.	Lebanese nursing practice law was drafted to modernize an existing 40-year law. This draft law was made with the aim of organizing and promoting the nursing profession by upgrading and standardizing the conditions for entering the nursing profession and changing the level of nursing.	The draft nursing practice law should be able to provide the changes required by educational programs to be promoted from a higher professional degree (TS) to a university degree (BS).	In order for this policy to be successful, there must be obstacles to implementation at the program development stage. The draft law on nursing practice was difficult to draft due to the lack of clarity in solving the problem and the lack of implementation barriers.	The main sponsors of the Nursing Act were the Ministry of Health and the Ministry of Education. All actors agree on the need to improve nursing in Lebanon. There are many differences in how to do this.
Markazi-Moghaddam (21)	2014	Iran	Establishment of Autonomous Hospitals and the Barriers	Retrospective	In the present qualitative study, the data were obtained in two stages. In the first stage, a questionnaire with open questions was sent to all medical universities and all 54 university hospitals that were granted independence in Iran. Then, a semi-structured interview of the key respondents of the first stage was conducted and analyzed.	In some developing countries, as well as in Iran, the Ministry of Health has started the liberalization and decentralization of the public sector. In fact, autonomous hospitals are likely to be run by the university rather than their own policies and programs within the hospitals themselves.	In 2003, when the government allowed eighty percent of government assets to be privatized or decentralized under Article 44 of the Iranian constitution, the Ministry of Health aimed to speed up service delivery, increase patient satisfaction with services across hospitals, increase productivity, and improve continuous quality. Gradually, in 2006, he moved to self-governing public university hospitals.	To implement this program, MOHME is open to all medical universities (they operate on behalf of the Ministry of Health in each province and are responsible for providing health care, university education in medical sciences, and overseeing public and private health care organizations). He ordered that at least one public hospital be declared. Therefore, 18 hospitals were finally selected and independent, but the Ministry of Health and insurance organizations did not pay for the reforms. The steps of formulating and implementing the policy were carried out separately in Iran, and therefore the major organizational reforms faced serious obstacles in the implementation and were not successful.	The Ministry of Health (MoH) The medical universities The insurance organization The Hospitals
Speakman (22)	2014	Afghanistan	Midwifery Education initiative and its influence on women's health and empowerment	Retrospective	Qualitative data collection was performed by reviewing documents published in reputable databases and interviews with knowledgeable key individuals. Documents related to policies, institutional reports, guidelines, and media articles were obtained by searching databases and websites.	Following the political transition in Afghanistan, which paved the way for the reconstruction and improvement of the destroyed health system, maternal health became a priority due to the high mortality rate. The Community Midwifery Education Program (CME) began teaching rural midwives in 2002 and expanded nationally in 2005.	The Community Midwifery Education (CME) programme, which was initially launched as a pilot project for non-governmental organizations but became an internationally recognized program. It is currently used as a model for other countries (eg Pakistan, Ethiopia, Laos). In the CME program, the two indicators used in Afghanistan were the maternal mortality ratio (MMR) index and the number of the skilled birth attendant (SBA) that were developed to achieve the Millennium Development Goals (MDGs), which was predicted (from 2002 to 2015) to reduce MMR by 50% and in line with the goal. Second, increase the SBA from 6 percent to 50 percent. CME improves maternal care and provides an example of women's empowerment. And it has had a wider social impact than expected.	The Community Midwifery Education (CME) began in 2002 with rural midwifery training and continued until 2005. It expanded nationally in 2005. In the same year, the Afghan Midwives Association (AMA) was established as a professional association for midwives. HealthNet-TPO (HNTPO) presented a program with the budget of the Dutch government to complete the short-comings of the Afghan government and inject financial resources. The CME pilot began with a Dutch government budget and Jhpiego technical support to develop a curriculum for target groups. Moreover, it improved the indicators and eventually became a well-known international program.	Afghan Ministry of Health officials NGOs, Ministry of Public Health, Ministry of Women's Affairs, inter-national donors (World Bank, European Commission, USAID, UN agencies Unicef, UNFPA, WHO), implementing NGOs (HealthNet-TPO, Jhpiego), and civil society organisations (AMA). Dutch INGO HealthNet-TPO (HNTPO) and other partners in the health sector.
Awadalla (23)	2015	Sudanese	Quality assurance program	Retrospective	The study was a review of documents about Sudan. Study data were conducted by searching valid sources and databases.	The use of quality improvement programs (QAP) in healthcare systems is essential Sudan launched its National Quality Assurance Program in 2001 in the health sector. However, the obstacles facing the program have led to poor performance and inefficiency.	The program began vertically from top to bottom, but there was no structural system for regular reporting and monitoring in Sudanese state hospitals.	There was no redistribution of financial and technical resources from the federal level to the states Adequate information on how the program was implemented was not provided to states and hospitals, and communication between different levels was not effective.	Physicians are influenced by both their professional power and their managerial role in implementing the program.

Ben Romdhane (24)	2014	Tunisia	Health system challenges of NCDs	Retrospective	The present qualitative study data were obtained through the analysis of official documents of hypertension, diabetes and obesity and tobacco programs, and case studies of fieldwork conducted in four clinics and semi-structured interviews with key individuals.	The challenges of the health system in non-communicable diseases in Tanzania and its analysis are highly dependent on routine social and demographic indicators, and research in this area has been in its early stages. And this gap must be filled through policy analysis and solutions	There was no capacity in the Tunisian Ministry of Health for an integration strategy, nor was there a platform for private sector intervention in the management of communicable diseases.	The WHO The Ministry of Health(MoH) The emerging private sector The private polyclinics National legislators, regional councils, researchers, the pharmaceutical industry, Capitalists and the mass media
Faraji (25)	2015	Iran	Control of Diabetes	Retrospective	Searching for information sources on policies and programs for the prevention and control of diabetes in Iran since 1989 (the first program of the World Health Organization in the field of prevention and control of diabetes) were done in reputable databases	Due to the increasing prevalence of diabetes in Iran (trend analysis from 2005 to 2011) and also the possibility of increasing its prevalence in the future, it is necessary to analyze policies and programs related to the prevention and control of diabetes.	In line with the Global Diabetes Program in 1989, the National Diabetes Prevention and Control Program was piloted at 17 Iranian University of Medical Sciences for people over 30 and pregnant women between 1999 and 2001.	internal stakeholders included the national diabetes committee members, the representatives of the medical universities; Department of Endocrinology and Metabolic of Center for Non-communicable Disease Control, Center for Network Development and Health Promotion, Bureau of Population & Family Health, and Office of Community Nutrition Improvement of Ministry of Health and Medical, Office of hospital administration and Clinical Service Excellence, Endocrinology & Metabolism Research Institute of Tehran University of Medical Sciences, the chancellors and vice-chancellors of the medical universities, Iranian Society of Nephrology, the financial director of treatment deputy, the general manager of Center for Non-communicable Disease Control and the program experts at the medical universities internal stakeholders participated in the development of the diabetes program, and the main stakeholders outside the field of healthcare did not participate in the development of the program.
Alharbi (26)	2016	Saudi Arabia	Diabetes	Retrospective	Articles on diabetes and healthcare policy were searched by PubMed and Medline Database to find research sources. The sources were manually screened by the authors before entering the study.	Rapid economic development and urbanization" in Saudi Arabia, along with behavioral changes, has led to a change in lifestyle, followed by a decrease in physical activity, increased consumption of refined carbohydrates and increased obesity, as well as non-communicable diseases such as diabetes.	Saudi Arabia's Ministry of Health has approved a ten-year national executive plan and sought to implement targeted health care methods in all areas of health care. It is also designed to prevent, treat and rehabilitate patients and has created a network of integrated facilities with the aim of providing appropriate health standards for 20 specialized centers for the treatment of diabetics.	In Saudi Arabia, the Ministry of Health is responsible for health care, monitoring and planning policies and responsibility for health promotion, early diagnosis and treatment of the disease. several governmental bodies, including the Ministry of Defense and Aviation (the second-largest health services provider), the Ministry of the Interior and the National Guards, also provide health care

Goshtaei (27)	2016	Iran	Nutrition policy process challenges	Retrospective	The qualitative data of the present study were obtained through semi-structured interviews with 59 policymakers, knowledgeable key stake-holders and nutrition experts at the Iranian University of Medical Sciences.	The nutrition transition is rapidly taking place in the world due to lifestyle changes, especially in developing countries. On the other hand, food shortages are due to economic factors and lack of awareness. Nutritional policies play an essential role in improving the health of society. Analyzing these policies can help design and implement interventions and programs to improve the nutritional status of the community, especially the low-income population. In Iran, this has happened rapidly and has led to overweight and obesity. Although many nutritional policies have been developed, no systematic research has been conducted to analyze and evaluate these policies in the context of policy analysis.	Despite the statement of the National Nutrition Policy in Iran, the absence of some senior policy makers in the preparation of the National Nutrition Policy Statement has not been signed by the President. Thus, this led to the failure of organizations to implement the National Nutrition Policy Statement. There are insufficient coordination mechanisms to address the challenges in the field of nutrition. Nutritional policies are often not evidence-based interventions, and there is not enough support for nutrition policy makers. The weakness of agreement in society and the main policy in prioritizing and arranging interventions and the role and responsibilities of institutions is an issue. Nutritional studies are performed only once every 10 years, so it is difficult to analyze the status of micronutrients and identify the trend. There is often disagreement between policies at the national level and existing programs. National capacity in public health nutrition is limited, especially human resources to implement nutritional programs. Some policies clearly do not specify operational plans and work plans. The nutrition policy process is a top-down approach in Iran, and national surveys do not show enough nutritional indicators and program success. There is not enough food monitoring system in Iran. The impact of most programs and policies is not systematically assessed. Evaluating nutrition policy is expensive and time consuming.	National nutrition policy statement policy, which was not approved by the High Council for Health and Food Safety due to a change in council officials and was not sent to organizations for implementation. However, the Minister of Health, Treatment and Medical Education signed the statement and sent it to the country's medical universities, and the university's presidents were required to implement it through the provincial health council.	The Ministry of Health MoHME The High Council of Health and Food Security The Universities of Medical Sciences (UMS)
Moshiri (28)	2016	Iran	The Formation of Primary Health Care in Rural Iran	Retrospective	Qualitative study data that examined the process of PHC implementation as well as the status of referral system in Iran from 1982 to 1989 through semi-structured and in-depth individual interviews (with 35 participants with different roles and situations during development and They also ran PHC (as well as extensive data from you) and collected resources in libraries.	In the late 1970s and even early 1980s, many people in need of treatment went to traditional healers, and the number and distribution of primary care centers with a public budget, and the number of licensed physicians, most of them working in urban areas. Life expectancy was low and infant and maternal mortality was high, and there was no coherent vaccination program, so PHC network formation was required.	Primary health care in Iran has created an effective model for the effectiveness of health and population indicators. Since its inception, Iran has had two main goals in mind: improving justice and access. Demographic and health indicators (eg, life expectancy, Birth rate per 1000 population, Birth rate per 1000 population, Population doubling time year and etc.) after the start of the program. Improved primary health care program concluded that the provision of health care could no longer depend on the presence of a physician. He was determined to provide social services for all citizens.	In 1980, during the meetings of the Organizational Council of the Ministry of Health (which included the Minister of Health, all Deputy Ministers and some experts), discussions and decisions were made on general issues, but the details were mainly discussed by Dr Kamel Shadpour, Cyrus Pileroudi and Ayyub Espandar wrote with great care and was ready to perform. The purposeful interaction of PHC designers with local actors before the performance stage led to the formation of an extensive and cohesive network and the participation of groups was strengthened. The implementation of the program began with determining the location of health houses and main villages and satellite villages. After preparing the program for the expansion of the required budget network, the Ministry of Health estimated the year, and then the members of the parliament added a reference line for the expansion of the PHC network by creating a budget line when approving the budget. After the implementation of health centers throughout the country; it was done in a serious and accurate way.	The Ministry of Health (MoH) The parliament Dr. Shadpour and Dr. Pileroudi Former UNICEF president, Mr. James P. Grant

Sarfraz (29)	2016	Pakistan	Pakistan's Maternal, Newborn and Child Health (MNCH) Program	Retrospective	The data presented in this qualitative paper were collected over a 3-month period in 2011. To find a wide range of challenges, qualitative data were collected from program managers, midwives, and members of the local community, such as mothers, wives, and mothers-in-law. There was also a comprehensive review of policy and planning documents on the subject	The Mother, Infant and Child Health Program were launched in 2006 with the aim of improving maternal health indicators (reducing maternal mortality), especially in order to improve MDG indicators. Moreover, trained midwives and licensed maternal health care services in rural communities.	Under the MNCH program, the Department of Health has developed important goals for PC-1, executive strategies, operational procedures, and estimated costs. The MNCH program consists of two parts, one of which is to strengthen the region's health sector technically, including improving management capacity, simplifying services to provide basic and comprehensive emergency care services for women and children and EMONC infants, and integrating MNCH services at the regional level. The other part was training experienced community-based staff to provide services	To implement the program, the Ministry of Health and the Ministry of Foreign Affairs have each pledged to pay 50 percent of the cost of the program, other international organizations through the Ministry of Health. The continuation of this program was shaky due to the lack of financial resources of the government. There is no transparency about the future management methods of program management. Given that the transfer of the Ministry of Health was imminent at the time of data collection, there were no plans for financial management and long-term sustainability. The process of monitoring and evaluating program progress has been defined but not implemented. Resource delivery was recorded to strengthen the health care system to provide care for mothers and children, but this information was not in line with the goals of the service. Local cultural values were not included in the guidelines, and the culture of patriarchy and religious values that usually existed in Pakistani society, especially in rural areas, posed challenges to the implementation of the program and prevented the program's goals from being achieved.	The Ministry of Health (MoH) and the Department for International Development) The USAID The UNICEF The UNFPA
Abolhassani (30)	2017	Iran	The establishment of the Drug Naming	Retrospective	The present qualitative study data were collected first (semi-structured interview with main experts, observation) and secondary (documents).	Common medical errors due to significant human and financial costs and the safety of the patient have been high on the health policy agenda. Due to the high rate of drug errors in Iran and the warnings of the World Health Organization about the name of the drug, policymakers of the Food and Drug Organization (FDO) have addressed this issue. Structural, situational, international and cultural factors play a major role in this	In order to reduce drug errors and increase patient safety, the Food and Drug Organization of Iran (FDO)adopted a multifaceted and integrated approach to the initial naming of drugs, and activated the National Drug Naming Committee, which was appointed the names of the drugs should not be misleading and should not be similar to other names of drugs registered in Iran and other countries. Branded brands should not be taken from International Non proprietary Name (INNs) of worldwide acceptability INNs, and the similarity in or writing the name of the drug with other names registered in the Iranian pharmaceutical system is mandatory (the name of the drug must be at least two consecutive letters different from the names of other registered drugs).	The National Committee for the Appointment of Medicines within the Food and Drug Organization is in charge of implementing the naming program. The pre-committee evaluation must comply with the criteria prepared by the FDO The National Committee for the Appointment of Medicines within the Food and Drug Administration is in charge of implementing the naming program. Pre-committee evaluation must comply with the criteria developed by the FDO, which will lead to better decision-making by committee members. The committee has processes so that all drug manufacturers are required to approve the committee before registering their products. First, submit the initial submission (maximum three special names) based on FDO criteria. After evaluating the pre-committee, send it to the main committee, and if approved, according to the rules of the trademark, manufacturers can register in the General Office of Trademarks Registry (GOTR	The Ministry of Health Patient safety officials in the Ministry of Health and affiliated medical sciences universities, hospitals and deputies of health the Food and Drug Organization of Iran (FDO) The General Office of Trademarks Registry (GOTR) the Department of Medicines (DoM) SCOs (the Iran Medical Council) health care providers (hospitals, pharmacies, physicians, nurses) and academics in this field the syndicate of pharmaceutical manufacturers and pharmaceutical manufacturers

First author (ref)	Year	Country	Topic	Type	Method	Background	Policy level	Findings	Actors
Aljumah (31)	2017	Saudi Arabia	Colorectal cancer	Prospective	This forward-looking study has been obtained by comparing and searching for documents in reputable databases and comparing them	Following the increase in the incidence of colorectal cancer and due to high demand, A forward-looking and systematic analysis of Colorectal cancer (CRC) screening policy was conducted in Saudi Arabia Despite the increasing prevalence of colorectal cancer in Saudi Arabia, there is no policy to prevent and screen for colorectal cancer.	This policy must be carried out at the national level (country-wide) of Saudi Arabia and can be used by the general public	Due to the forward-looking nature of the present study, steps will be taken to develop CRC policy in Saudi Arabia Although this policy does not currently exist in Saudi Arabia, it is expected that the effect of its development and its subsequent implementation will be provided in the near future.	Actors who make policies will include the following Influential individuals, local scientific associations, international organizations, governmental and non-governmental organizations and institutions International organizations: WHO, American Gastroenterology Association, the American Cancer Society, the European Society for Medical Oncology, the Association of European Cancer Leagues, the United European Gastroenterology State or government institutions: Regional Health Directory, The Saudi Commission for Health Specialties (SCHS) is a scientific body founded by virtue of the Royal Decree in 1992 that provides licensing and privilege for all health care providers Non-state actors: Civil society organizations and charities, Saudi Cancer Society
Azami-Aghdash (32)	2017	Iran	Road Traffic Injury Prevention	Retrospective	A qualitative study was conducted as a case study. Study data were collected by three methods of semi-structural interview, published reports and review of literature and documents of the last ten years and analysis of data and policies.	In Iran, RTIs are the first cause of injury and the second cause of death Injury prevention policies in road traffic are essential due to a large number of road traffic injuries in Iran. Due to the increase in Road Traffic Injuries (RTIs), the identification of seat belts has emerged as an effective tool for reducing injuries in accidents and the need to increase safety equipment in vehicles and its training.	Policies that were implemented with the two topics of seat belt and explaining prevention policies in students which was done in the form of four topics: program planning, policy formulation, policy implementation, policy evaluation	The Incident Prevention Training Policy was implemented in 2007 for elementary and middle school students and aims to improve the culture of safety and social discipline among students and their parents, strengthen responsibility and self-confidence among students, and teach. Safety and traffic tips for students were familiarity with traffic violations.Also, the proposal of the law of compulsory wearing of seat belts,The traffic police issued a circular on the implementation of the executive directive by the Ministry of Justice, the Ministry of Interior, the Ministry of Industry and Mines, the Ministry of Roads and Transportation, and the approval of the executive directive by the parliament (Majlis)	Actors in Student Policy: Ministry of Education, Ministry of Culture and Islamic Guidance, Management and Planning Organization, Teachers 'Parents' Council, Traffic Police and Parents' Council in Seat Belt Policy: Ministry of Interior, Ministry of Industry and Mines, Ministry of Education, Ministry of Culture and Islamic Guidance, Ministry of Justice and Management and Planning Organization, and Traffic Police
Haq (33)	2017	Pakistan	Evidence-informed health policy making	Retrospective	The data of the present study were performed in three ways: Review the literature and then a counseling session with key experts and informants to explore broad areas of policy development and in-depth interviews with participants from different levels of the health system, and finally a roundtable discussion with experts to share and consolidate and analyze information and data.	Health is not a priority for administrative or political levels, but reliance on basic evidence to maintain public acceptance and efficiency in public policy as well as effective measures in fundamental interventions. In Pakistan, various actors - local and global - are working to facilitate the development of evidence-based health policies. However, effective intervention requires knowledge of the country's context and knowledge of the complexities of how to formulate policies in Pakistan.	The PC-I is the initial form according to which all projects and projects required are prepared by the planning commission And the approval of the package of necessary health services was approved as part of the health policies of the provinces But the 2001-2002 Health Policy Document was in fact a hollow document and not a policy Rather, it was a practical plan that was approved quickly over a period of days because it was merely a symbol of the government's efforts to have a new policy that could serve as another sign of that government, but no evidence. The discourse or measurement process of the options available was not anticipated.	In the two key periods before and after the transfer of health to the provinces, the policy-making process was formed primarily at the federal and provincial levels, but the implementation process has faced many challenges. Political decisions have taken place in an unorganized and almost aimless manner. Furthermore, there is no process for knowing the evidence. Decisions are usually delayed and few are made arbitrarily, usually by the Office of the Minister of Health. Where political leadership is strong (for example, the senior minister of Punjab province) plays an active role, but this situation is less desirable in other provinces and regions. Programs are either not approved or are implemented incompletely. The current system for data collection and management, including the health management information system and the district health information system, is only running in five of the 50 areas.	The Ministry of Health The WHO The Provincial Experts

Author	Year	Country	Policy	Study type	Method	Description	Policy content	Stakeholders
Yousefinezhadi (34)	2017	Iran	Hospital Accreditation Policy	Retrospective	Qualitative study data were obtained by reviewing documents related to the policy-making and accreditation process (official letters, laws, legal regulations, instructions, reports and meetings of the Ministry of Health) and face-to-face semi-structured face interviews.	Hospital accreditation is an external evaluation system aimed at assessing patient quality and safety and encouraging continuous quality improvement. It is developed by an independent accreditation body and local professional institution to evaluate the hospital in terms of structures, processes and results (outputs/ outcome) using pre-defined and optimal standards.	2157 accreditation criteria for the accreditation of 36 departments of the hospital Two accreditation criteria were developed for accreditation of 36 hospital wards and it was taught at the university and hospital level. It was mandatory and monitored by hospital evaluators, and then Non-standard hospitals were required to address problems and improve performance over a specified period of time	In 2012, the hospital's appraisal system was renamed and upgraded to a hospital accreditation system, which used the department's method to develop accreditation standards for Iranian hospitals. After reviewing the accreditation standards of some of the leading countries, such as the United States, France, and the Middle East, the accreditation standards of Iranian hospitals were implemented. The Office for the Accreditation of Healthcare Institutions (OAHI) finalized the first draft of the standards and piloted it in eight hospitals and as a result, the standards were modified using the comments received after discussions and expert meetings. 2157 accreditation criteria for the accreditation of 36 departments of the hospital were placed in the accreditation program with a focus on structures and processes. The whole process of compiling this program in six stages And it lasted three years	The Ministry of Health Patient safety officials in the Ministry of The Office for the Accreditation of Healthcare Institutions (OAHI) The hospitals The Universities of Medical Sciences and Health Services (UMSS) The authorities at the hospital evaluation department
Ansari (35)	2018	Iran	Palliative Care Policy	Retrospective	Data were collected through semi-structured in-depth interviews	Because cancer is the third leading cause of death in Iran and cancer patients need supportive care and pain management, providing palliative care services, the main need of health systems is to provide services to cancer patients.	The integration of palliative care and support services within health care systems should be one of the most important goals and human resources, financial resources and physical equipment (resource management) should be considered. Political feasibility, social feasibility, and structural feasibility must also be considered	To implement this policy, standardization of care, the participation of stakeholders and strategies and educational management are required.	The Ministry of Health Health care providers Volunteers Governmental and non Governmental Medical-education and research centers
Al-Ansari (36)	2019	Iran	Alcohol policy in Iran	Retrospective	Search and extract resources on the websites of official organizations such as the Ministry of Health and the Ministry of Justice Also, literature and political documents that are available to the public	Despite restrictions on alcohol consumption in most Muslim countries, alcohol consumption has recently increased And because of the civil ban on alcohol and the lack of enough information about alcohol policies, it is not in line with global policies	Among the ten policy areas of the WHO that each country can choose according to the local conditions, In this regard, Iran has developed and implemented all its policies in the framework of a comprehensive program for prevention, treatment and reduction of alcohol poisoning in 2011-2015.	In 2006, the Supreme Leader's General Policy on Combating Drug and Alcohol Abuse was announced and the fight against planting, production, import, export, storage and distribution of various types of drugs and alcohol consumption became illegal. Health was set up, and in the same year, the office estimated the size of the alcoholic population. Under the Eleventh Government (2013-2017), health was a top priority, leading to a larger national health budget for treatment. The policy adopted in 2011 forced the Ministry of Health to make progress in the treatment of alcoholism and in accordance with the recommendations of the World Health Organization in response to alcohol. The overall policy was set out in broad perspective and in the plan of the "Fifth National Development Plan"in 2014, some of these general policies aimed at improving mental health, especially among students. , and prevention of harm caused by drugs, psychedelics and alcohol.	The Ministry of Health The Ministry of Health's Mental Health office The governmental funding institute The State Welfare Organisation of Iran decision-makers and Policy developers The Law Enforcement Force of the Islamic Republic of Iran (NAJA) The Border Guard Command Community and religious actors International agencies Researchers Industry(very little role)

	Year	Country	Title		Methods				Stakeholders
Edalati (37)	2019	Iran	Nutrition labelling	Retrospective	Review relevant documents and articles and semi-structured interviews with stakeholders	Implementing a nutrition labelling strategy to promote healthy eating and fight non communicable diseases is essential.	Provide and implement accepted executive guidelines on nutrition guidelines Forcing to label food guidance And provide on nutritional facts And nutrition guidelines on food packaging and products	In 2014, after the introduction of the traffic light and nutrition program, the National Committee for the Development of Food Labels was formed, and after reviewing its executive instructions, it was implemented voluntarily for 2 years and then compulsorily.	Food and Drug Administration Iran Broadcasting organization
Gharaee (38)	2019	Iran	Public-Private Partnership in Providing Primary Health Care Policy	Retrospective	Data were collected through stakeholder interviews and document analysis and analyzed through content analysis.	the public-private partnership (PPP) is one of the basic strategies for achieving (the third goal of the Sustainable Development Goals) UHC, and in Iran's upstream documents and in many legal articles, PPP has been considered by national policymakers	The major policies that need to be designed are: Reduce public sector ownership using private sector power Attract people's participation Improving the efficiency of the PHC system Repair of the payment system Increase justice	In implementing the policy, the issues of coordination, creating a suitable environment, necessary tenders, employing and training the required human resources, creating a referral system, and formulating the Board of Trustees of the people should be considered.	Deputy of health of ministry of health Minister of Health University of Medical Sciences Health insurance companies University's office for Legal Affairs Municipality Department of education Public sector employee Politicians people (households) planning and budget organization Supportive organizations Foundation, State Welfare Organization) physicians Private sector
Loloei (39)	2019	Iran	Salt reduction in bread	Retrospective	In the present qualitative study, data were collected from three methods: interview (with 37 informed and key frames), observation (directly from the work of traditional and industrial bakeries, as well as traditional flour factories) and focused group discussion (five group discussions with people were waiting in the queue of bakeries)	In Iran, the average decrease in salt consumption (which is approximately 15-10 grams per day, especially from sodium hidden in bread, cheese and fast foods) has been seriously pursued since 2009. However, although the Supreme Council of Health and Food Security is the coordinator of organizations working in the field of public health, all government agencies involved in wheat, flour and bread are pursuing their goals and related issues. With the health of bread and the reduction of salt in this main food, there is less mutual cooperation	Following the establishment of a specialized working group at the Ministry of Health, Treatment and Medical Education of Iran in 2013, effective and practical solutions to eliminate the use of baking soda and reduce salt content in the bread production process were presented. Moreover, industrialization of traditional bread production (changing the pattern of bread consumption), reviewing the list of permitted and used materials in the cooking industry, revising national standards and guidelines, creating a proper culture in the field of healthy consumption of bread (through the broadcasting of the Republic Broadcasting) Islamic Iran, Newspapers, Books, Educational Brochures, and Urban Advertising P. quality wheat for domestic purchases and imports of wheat, food industry to hire graduates of technical supervision and strict implementation of health on traditional bread and bakery also close to traditional industrial complexes.	Due to changes in the government and the priorities of the Ministry of Health, the results of the meetings of the specialized working group for improving the quality of bread were ineffective, and the mentioned policies and efforts made in bread production were not carried out.	The Ministry of Health The Council of Health and Food Security The bread producers (industrial and traditional) The Bakers

First author (ref)	Year	Country	Topic	Study type	Data/Methods	Findings	Stakeholders/Organizations
Mohseni (40)	2019	Iran	Malnutrition among children under 5 years old	Retrospective	The study data were obtained by reviewing policy and state and organizational policy documents, including the Constitution of the Islamic Republic of Iran, Iran's 20-Year Vision Plan, Iran's Fourth and Fifth Five-Year Development Plans, Comprehensive Scientific Map of Iran, a comprehensive scientific roadmap of the health system, health indicators in the Islamic Republic of Iran, document of poverty reduction and targeting of subsidies, reports published by the Health and Food Security High Council, and other relevant organizations (in scientific databases and data database searches) and semi-structured face-to-face interviews.	Malnutrition is one of the leading causes of death in children under 5 years of age and is a life-threatening factor in children's health. Despite economic development in developing countries, it is still a major health problem in these countries. The UNICEF Global Health Program for Children is GOBI-FFF, which includes seven programs. The content of policies adopted in Iran includes two main categories in accordance with UNICEF policy: quality-based of life policies (the most important of which include nutrition promotion policies), which are the three main policies of breastfeeding, nutrition of children under 5 years and control of micro-nutritional deficiencies include iron, iodine, vitamin A and vitamin D. In the above documents, the issues of mother and child are important and it is necessary to take care of them. Politicians are more focused on mother and child issues than on other groups. After examining the current situation and prioritizing the problems of the provinces of the country based on malnutrition and indicators were created to measure the deficiency of micronutrients, efforts were made to involve other organizations and test policies. Appropriate policies were adopted and implemented as executive guidelines. Has been notified Feedback has been received from other organizations involved in child affairs, and self-assessment of the activities of the organizations and monitoring of the implementation of the activities has been done.	The Ministry of Health The Ministry of Co-operation, Labor and Social Welfare The Ministry of Agriculture The Ministry of Industry, Mine and Trade The Ministry of Education The Ministry of Culture and Islamic Guidance The Ministry of Research Science andTechnology The Ministry of Interior The Islamic Consultative Assembly The Targeting Subsidies Organization The Welfare Organization The Planning and Budget Organization The National Standards Organization Literacy Movement The Islamic Republic of Iran Broadcasting The Imam Khomeini Relief Committee NGOs (Saman) The Iranian Children's Nutrition Science Association The Iranian Nutrition Forum The Scientific Society of Food and Nutrition Supporter of Health The Experts The Researchers The University professors The World Health Organization UNICEF The Food and Agriculture Organization The World Food Program Office
Behzadifar (41)	2019	Iran	The hepatitis C	Retrospective	After searching and collecting the relevant documents between September 2017 and July 2018, the relevant form was prepared, then the title, content and year of publication of the policies and documents were collected. Qualitative study data were extracted using semi-structured and face-to-face interviews with participants over two different time periods.	In Iran, the general public has a negative attitude towards HCV Therefore, in order to increase public awareness, educational activities are carried out at different levels of the health sector, especially in PHC. However, generally, they are weak and unorganized. Most HCV research activities are carried out by research centers of the Ministry of Health, which pay less attention to socio-cultural and economic dimensions. The Ministry of Health of Iran has developed its plans and policies for the control and management of the disease in accordance with the WHO and other relevant international organizations. Health policies and decision-makers are working to prioritize HCV. Iran's Hepatitis Network provides many educational and therapeutic activities in this field for patients. The formation of the National Hepatitis Committee is an essential step in the HCV decision-making process in Iran The key members of this committee include researchers, health policy- and decision-makers, and their responsibilities are policy and planning, management, and monitoring.	In Iran, the Ministry of Health is the most important actor in designing and supporting HCV policies that implement disease control policies, including planning, budgeting, medical, educational, and screening activities.

Author	Year	Country	Topic	Type	Methods	Content	Actors/Stakeholders
Doshmangir (42)	2020	Iran	Policy analysis of the Iranian Health Transformation Plan in primary healthcare	Retrospective	It was a qualitative study data were collected through document analysis, round-table discussion, and semi-structured interviews with stakeholders	Health systems reform is inevitable due to the never-ending changing nature of societal health needs Iran needed to change its health care system. After the 8-year war with Iraq, Governments focused more on health care While little attention was paid to public health and prevention. Following several amendments, Dr. Hassan Rouhani, The President of Iran put the issue of health at the center. Soon after coming to power and fulfilling its campaign promise, HTP was apparently the most important Ubud's government social project. Focus areas include Medical care, public health and PHC, medicine Training and improvement of the medical pricing system.	The Government of Iran launched the "Health Transformation Plan" (HTP) in May 2014, to facilitate the attainments of UHC The goals of the reforms are: 1) to increase global health Insurance coverage 2) Ensure financial support from Patients 3) Ensure fair and equitable distribution Doctors and subspecialties across the country 4) Improving hoteling and renovation in the public health sector 5) Expand outpatient services in the public health sector. 6) Promote delivery (NVD) and Prevent the increase in the number of unnecessary cesarean sections 7) Improve care and financial support From patients with special needs and end-stage diseases and 8) Establishment of air ambulance services.	Health systems reform)HTP(focused on health problems and issues, and hospitals affiliated with the Department of Health. The scheme was later extended to cover PHC HTP focused on health problems and issues,hospitals affiliated with the Department of Health. The scheme was later extended to cover PHC Initiated PHC modification includes programs including: Developments in the proper structure of the health team, development of family functioning, service delivery and PHC services in rural areas and cities with a population of less than 20,000 and in suburban areas and cities with a population of about 20,000 to 50,000, a new integration of services including smoking cessation, nutrition improvement, prevention of traffic accidents, promotion of physical activity Prevent cancer, prevent cardiovascular disease, prevent diabetes, improve oral health Prevent mental illness and improve the health status of people with mental illness, create and Strengthen cross-sectoral collaboration, and create and modify FP and referral systems.	the Ministry of Health and Medical Education (MoHME) The explanation was not complete
Azam Raoofi (43)	2020	Iran	COVID-19	Retrospective	Qualitative study data were obtained from the analysis of the targeted content of documents, programs, reports of actions and documents and official news of the Ministry of Health and Iranian websites related to COVID-19, as well as China and the World Health Organization.	Following the global outbreak of the COVID-19 virus, the Iranian Ministry of Health announced on February 19 that the disease was spreading in Iran (Qom city), and as of March 5, 2020, all 31 provinces were infected. The total number of confirmed cases on April 3 was 53,183, of which 3,294 died and 17,935 were recovered Due to unilateral US political sanctions against Iran, it has raised major concerns about the country's health care. Iran has made great efforts to defeat this prevalence, so it is very important for Iran policies to formulate appropriate policies and implement them accordingly.	The content of Iran's policy regarding the prevalence of corona can be divided into two categories: pre-outbreak and post-outbreak. Examination of incoming passengers from China and transfer of suspicious cases to certain hospitals, return of Iranian students residing in China and quarantining them for two weeks and allocation of special funds to provide the necessary resources, such as personnel, medicines, equipment, etc. And actions After the outbreak, it was based on the WHO six building blocks, which included Including Inter-sectoral cooperation, legislation Obtaining a license to import equipment and medical universities with permission to recruit new personnel Service delivery for providing, equipping and operating medical centers and ambulances, and providing and equipping paraclinical centers Disinfection of public places, insurance, resource allocation, employment and human resources, informing and increasing public awareness, research, technology and information system, medicines and medical equipment.	The Ministry of Health MoHME The governmental and non-governmental organizations The Universities of Medical Sciences (UMS) The MoHME various deputies (particularly Deputies for Curative Affairs, Public Health, Nursing, and Administration and Finance) The Food and Drug Organization, The Emergency Services Organization, The Iran Health Insurance Organization are the main intra-organizational actors within the MoHME, almost 200 The Medical Associations, The General Medical Council, The General Nursing Council, The Social Security Organization (and other insurance organizations), the Islamic Consultative Assembly (Parliament), The Cabinet of Ministers and Officials Planning and Budget The COVID-19 National Committee was set up at the Iranian Ministry of Health, which needs to be strengthened Corona's countermeasures are a major concern for public health, which requires inter-sectoral collaboration and government agreement through various coalitions. There are several factors to consider when planning and implementing programs, Including : paying attention to the capacity of medical universities and their ability to implement programs, the need for inter-sectoral collaboration and attention to formal multi-disciplinary working groups given the complexity of the issue, The need for regular negotiations between policymakers and the so-called street-level bureaucrats (SLBs) to optimize service delivery and achieve the best possible results. Paying attention to the attitudes, strategies and knowledge of frontline employees that unofficially influences policy implementation The government's attention to the evaluation and monitoring of frontline staff and the provision of financial and non-financial incentives for stakeholders, Considering the importance of the role of political agents and other stakeholders, including the clergy, governors, mayors and Friday prayer leaders of Qom and Mashhad, member of parliamentarians MPs, as well as some experts and academics in making some decisions such as closure of holy shrines and cancellation of Friday prayers for the implementation of social distancing and pay attention to their role as mediators or political intermediaries To compromise and limit differences between coalitions to reach a collective agreement.

Fig. 4. Quality assessment of the studies included in the present systematic review.

In some of the articles included in the present systematic review, some explained the program and its purpose, while others described the activities of care centers and decision-making committees such as the National Committee for Hepatitis and Acquired Immunodeficiency Syndrome (AIDS), etc. Some considered the reason for the programs to be due to the urgency of the issue and other than political decisions. Some studies have pointed to the implementation and structural challenges of programs and policies, the latter of which has been highlighted in these studies as one of the factors in the failure of health programs. Other reasons for the programs' failure include internal wars and crises, weak financial and technical capacity, disputes between states, sanctions, and declining funding for national standards produced without infrastructure. It seems that one of the reasons for the failure of the programs was the lack of proper prioritization to solve the problems under study, as mentioned in the articles. Because in order to succeed in promoting health programs, it is very important to pay attention to prioritization and criteria (which must be clearly defined and understood by decision makers and stakeholders in each country) and should not be the sole responsibility of specific institutions or ministries. Therefore, in all policies, stakeholders and supporters should be considered as key factors. As shown in these studies, programs that sought advocacy were more successful because advocacy as a key strategy to achieve the goals of health promotion and Advocacy organizations play a key role in promoting justice in health, given global challenges, research and policy [57].

Also, health should be separated from political issues and levels of health governance, policies and measures should be complementary to each other because participation in health governance, policy-making and development of interventions and its implementation by sectors other than health is important and health is mainly outside. Areas and levels of health are created and attention to the creation and implementation of health in all policies strengthens the potential that other sectors have for health [58]. It should be noted that developing countries underestimate the role of education in their policies, and the budgets allocated for health education in these countries are very small and health policy makers pay very little attention to this issue. Therefore, indigenous educational projects should be designed in accordance with the context of communities, and on the other hand, executive decision-making groups should be multidisciplinary, and their roles should be clearly defined before determining program priorities, and involving groups other than Medical teams are very effective in advancing goals [44, 45, 52].

ACTORS

The WHO in its 2000 report defined health systems as "all organizations, institutions, and resources dedicated to the production of health measures," which includes a full range of actors and health care providers, including sectors. Private, non-profit, non-governmental organizations (NGOs) as well as international donor foundations [59]. Therefore, health systems are operating at the central, regional, local, social and home levels, and all of these institutions must be considered at all levels of strengthening health systems. Actors include any institution, character, or social movement that has the ability to influence health events, and a common feature of all social actors is that they have a certain amount of power.

The most important actor mentioned in the present study was the Ministry of Health. Several articles referred to the role of domestic and foreign NGOs. NGOs play an important role in providing health services and health policies, and the importance of these organizations in providing health services in low- and middle-income countries has become increasingly important [60]. In poor countries, they are more effective and efficient than public organizations and act as agents of change in international economic, social and environmental policies. It seems that EMRO countries have not yet been able to use the effective potential of NGOs in advancing health policies, ignoring the need to strengthen government health programs and cooperate with organizations to achieve the goals set in the SDGs and improve the quality and efficiency of health care. Non-governmental support is therefore essential [61].

The involvement of NGOs with the public sector should play a key role in addressing justice issues and improving the quality of services provided, along with addressing system access and accountability issues. In these studies, the role of the private sector as actors was very small and in some studies it was not explicitly mentioned, while policymakers, who want to move health systems towards UHC must play appropriate roles to provide, identify and rely on private providers and health markets. The importance of strengthening public and private health systems has been repeatedly emphasized in various documents by various international, regional and national institutions related to health care such as WHO, USAID, Global Fund, etc. The non-governmental sector and the private sector, due to their potential and capabilities, can fill the gaps and shortcomings that exist in the public sector, so a serious partnership between them can ultimately increase accountability, equity and efficiency in the health care system. It should be noted that health care outsourced to the private sector in low- and middle-income countries (LMICs) is very widespread, even though weak, and highly heterogeneous. It seems that in EMRO member countries, the role of these two sectors, namely non-governmental organizations and the private sector as a very important player in health system policy, is very small and has led to the lack of progress in existing policies in the health sector.

LIMITATIONS

In this context, it seems that the place of the result and the cause of the failure of the programs is empty, and also there are no solutions to the problems in the research. Gilson and Rafaeli pointed out some of the

gaps and weaknesses in the analysis of health policies in low- and middle-income countries mentioned in special cases [13].

Conclusion

In the EMRO region, the role of evidence-based research in policy-making has been repeatedly emphasized, but its use in health program decision-making has been limited and health research systems in the EMR are still under scrutiny. We think that they have not been able to produce needed evidence and inject it into health systems. There is still a gap between evidence-based research in health systems and its use in policy-making, as well as in the analysis of health policies in LMICs. The findings of these studies also confirm this, and therefore studies based on policy analysis should be aimed at achieving this goal because evidence-based decisions can strengthen health systems, improve health and improve existing inequalities. Also, considering that this analysis triangle has 4 specific components, studies should be selected that can be analyzed based on the four elements of this study, but some studies did not have these conditions. On the other hand, this framework should be re-examined and its components should be up-to-date and more standardized in order to enable deeper analyses.

Acknowledgements

Not applicable.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Funding

Not applicable.

Authors' contributions

MB and HR designed the study. MB, SA, MM, SJE, MKG, AB, SA, SS, LD and NLB collected the data and performed the data analysis. HR, NLB, MB, SS, SJE and LD edited and revised the paper for grammar. All authors read and approved the final paper for publication.

References

[1] Correa-de-Araujo R. Evidence-based practice in the united states: Challenges, progress, and future directions. Health Care Women Int 2016;37:2-22. https://doi.org/10.1080/07399332.2015.1102269

[2] van de Goor I, Hämäläinen RM, Syed A, Juel Lau C, Sandu P, Spitters H, Eklund Karlsson L, Dulf D, Valente A, Castellani T, Aro AR; REPOPA consortium. Determinants of evidence use in public health policy making: Results from a study across six EU countries. Health Policy Plan 2017;121:273-81. https://doi.org/10.1016/j.healthpol.2017.01.003

[3] Contandriopoulos D, Benoît F, Bryant-Lukosius D, Carrier A, Carter N, Deber R, Duhoux A, Greenhalgh T, Larouche C, Leclerc BS, Levy A, Martin-Misener R, Maximova K, McGrail K, Nykiforuk C, Roos N, Schwartz R, Valente TW, Wong S, Lindquist E, Pullen C, Lardeux A, Perroux M. Structural analysis of health-relevant policy-making information exchange networks in Canada. Implement Sci 2017;12:116. https://doi.org/10.1186/s13012-017-0642-4

[4] Cheung KK, Mirzaei M, Leeder S. Health policy analysis: a tool to evaluate in policy documents the alignment between policy statements and intended outcomes. Aust Health Rev 2010;34:405-13. https://doi.org/10.1071/AH09767

[5] Robert E, Rajan D, Koch K, Muggleworth Weaver A, Porignon D, Ridde V. Policy dialogue as a collaborative tool for multi-stakeholder health governance: a scoping study. BMJ Glob Health 2020;4(Suppl 7):e002161. https://doi.org/10.1136/bmjgh-2019-002161

[6] World Health Organization. Health policy 2020 [updated 28 August 2020. Available from: https://www.who.int/topics/health_policy/en/.

[7] Mulcahy G, Boelsen-Robinson T, Hart AC, Pesantes MA, Sameeha MJ, Phulkerd S, Alsukait RF, Thow AM. A comparative policy analysis of the adoption and implementation of sugar-sweetened beverage taxes (2016-19) in 16 countries. Health Policy Plan 2022;37:543-64. https://doi.org/10.1093/heapol/czac004

[8] Kind J, Maeschli B, Bruggmann P. How to set the agenda for hepatitis C: a theory-driven policy analysis. Health Res Policy Syst 2022;20:20. https://doi.org/10.1186/s12961-022-00824-3

[9] Gilson L, Raphaely N. The terrain of health policy analysis in low and middle income countries: a review of published literature 1994-2007. Health Policy Plan 2008;23:294-307.https://doi.org/10.1093/heapol/czn019

[10] Browne J, Coffey B, Cook K, Meiklejohn S, Palermo C. A guide to policy analysis as a research method. Health Promot Int 2019;34:1032-44. https://doi.org/10.1093/heapro/day052

[11] Walt G, Gilson L. Can frameworks inform knowledge about health policy processes? Reviewing health policy papers on agenda setting and testing them against a specific priority-setting framework. Health Policy Plan 2014;29 (Suppl 3):6-22. https://doi.org/10.1093/heapol/czu081

[12] Montenegro Martínez G, Carmona Montoya A, Franco-Giraldo Á. Models for public health policy analysis reported in scientific publications. Gac Sanit 2020;S0213-9111:30275-4. https://doi.org/10.1016/j.gaceta.2019.11.007

[13] Walt G, Shiffman J, Schneider H, Murray SF, Brugha R, Gilson L. 'Doing' health policy analysis: methodological and concep-

tual reflections and challenges. Health Policy Plan 2008;23:308-17. https://doi.org/10.1093/heapol/czn024

[14] Shiffman J, Sultana S. Generating political priority for neonatal mortality reduction in Bangladesh. Am J Public Health 2013;103:623-31. https://doi.org/10.2105/AJPH.2012.300919

[15] O'Brien GL, Sinnott SJ, Walshe V, Mulcahy M, Byrne S. Health policy triangle framework: Narrative review of the recent literature. Health Policy OPEN 2020;1:100016. https://doi.org/10.1016/j.hpopen.2020.100016

[16] World Health Organization. WHO's Eastern Mediterranean Region comprises 2020 [updated 28 August 2020. Available from: http://www.emro.who.int/countries.html.

[17] Beesley M, Cometto G, Pavignani E. From drought to deluge: how information overload saturated absorption capacity in a disrupted health sector. Health Policy Plan 2011;26:445-52. https://doi.org/10.1093/heapol/czq083

[18] Zaidi S, Mayhew SH, Cleland J, Green AT. Context matters in NGO-government contracting for health service delivery: a case study from Pakistan. Health Policy Plan 2012;27:570-81. https://doi.org/10.1093/heapol/czr081

[19] Phillimore P, Zaman S, Ahmad B, Shoaibi A, Khatib R, Khatib R, Husseini A, Fouad F, Elias M, Maziak W, Tlili F, Tinsa F, Ben Romdhane H, Kılıç B, Kalaça S, Ünal B, Critchley J. Health system challenges of cardiovascular disease and diabetes in four Eastern Mediterranean countries. Glob Public Health 2013;8:875-89. https://doi.org/10.1080/17441692.2013.830756

[20] Seef S, Jeppsson A. Is it a policy crisis or it is a health crisis? The Egyptian context--analysis of the Egyptian health policy for the H1N1 flu pandemic control. Pan Afr Med J 2013;14:59. https://doi.org/10.11604/pamj.2013.14.59.1631

[21] Zaidi S, Mohmand SK, Hayat N, Acosta AM, Bhutta ZA. Nutrition policy in the post-devolution context in Pakistan: An analysis of provincial opportunities and barriers. IDS Bull 2013;44:86-93.

[22] El-Jardali F, Bou-Karroum L, Ataya N, El-Ghali HA, Hammoud R. A retrospective health policy analysis of the development and implementation of the voluntary health insurance system in Lebanon: learning from failure. Soc Sci Med 2014;123:45-54. https://doi.org/10.1016/j.socscimed.2014.10.044

[23] El-Jardali F, Hammoud R, Younan L, Nuwayhid HS, Abdallah N, Alameddine M, Bou-Karroum L, Salman L. The making of nursing practice law in Lebanon: a policy analysis case study. Health Res Policy Syst 2014;12:52. https://doi.org/10.1186/1478-4505-12-52

[24] Markazi-Moghaddam N, Aryankhesal A, Arab M. The first stages of liberalization of public hospitals in Iran: establishment of autonomous hospitals and the barriers. Iran J Public Health 2014;43:1640-50.

[25] Speakman EM, Shafi A, Sondorp E, Atta N, Howard N. Development of the community midwifery education initiative and its influence on women's health and empowerment in Afghanistan: a case study. BMC Womens Health 2014;14:111. https://doi.org/10.1186/1472-6874-14-111

[26] Awadalla H. Implementation of quality assurance program in Sudanese public hospitals: lessons learned. J Med Med Res 2015;3:7-14.

[27] Ben Romdhane H, Tlili F, Skhiri A, Zaman S, Phillimore P. Health system challenges of NCDs in Tunisia. Int J Public Health 2015;60 (Suppl 1):S39-46. https://doi.org/10.1007/s00038-014-0616-0

[28] Faraji O, Etemad K, Akbari Sari A, Ravaghi H. Policies and programs for prevention and control of diabetes in Iran: A document analysis. Glob J Health Sci 2015;7:187-97. https://doi.org/10.5539/gjhs.v7n6p187

[29] Alharbi NS, Alotaibi M, de Lusignan S. An analysis of health policies designed to control and prevent diabetes in Saudi Arabia. Glob J Health Sci 2016;8:233-41. https://doi.org/10.5539/gjhs.v8n11p233

[30] Goshtaei M, Ravaghi H, Sari AA, Abdollahi Z. Nutrition policy process challenges in Iran. Electron Physician 2016;8:1865-73. https://doi.org/10.19082/1865

[31] Moshiri E, Rashidian A, Arab M, Khosravi A. Using an analytical framework to explain the formation of primary health care in rural Iran in the 1980s. Arch Iran Med 2016;19:16-22.

[32] Sarfraz M, Hamid S. Exploring managers' perspectives on MNCH program in Pakistan: a qualitative study. PLoS One 2016;11:e0146665. https://doi.org/10.1371/journal.pone.0146665

[33] Abolhassani N, Akbari Sari A, Rashidian A, Rastegarpanah M. The establishment of the drug naming committee to restrict look-alike medication names in Iran: a qualitative study. Int J Risk Saf Med 2017;29:69-79. https://doi.org/10.3233/JRS-170740

[34] Aljumah AA, Aljebreen AM. Policy of screening for colorectal cancer in Saudi Arabia: a prospective analysis. Saudi J Gastroenterol 2017;23:161-8. https://doi.org/10.4103/sjg.SJG_468_16

[35] Azami-Aghdash S, Gorji HA, Shabaninejad H, Sadeghi-Bazargani H. Policy analysis of road traffic injury prevention in Iran. Electron Physician 2017;9:3630-8. https://doi.org/10.19082/3630

[36] Haq Z, Hafeez A, Zafar S, Ghaffar A. Dynamics of evidence-informed health policy making in Pakistan. Health Policy Plan 2017;32:1449-56. https://doi.org/10.1093/heapol/czx128

[37] Yousefinezhadi T, Mosadeghrad AM, Arab M, Ramezani M, Sari AA. An Analysis of hospital accreditation policy in Iran. Iran J Public Health 2017;46:1347-58.

[38] Ansari M, Rassouli M, Akbari ME, Abbaszadeh A, Akbarisari A. Palliative care policy analysis in Iran: a conceptual model. Indian J Palliat Care 2018;24:51-7. https://doi.org/10.4103/IJPC.IJPC_142_17.

[39] Al-Ansari B, Thow AM, Mirzaie M, Day CA, Conigrave KM. Alcohol policy in Iran: policy content analysis. Int J Drug Policy 2019;S0955-3959:30210-5. https://doi.org/10.1016/j.drugpo.2019.07.032

[40] Edalati S, Omidvar N, Haghighian Roudsari A, Ghodsi D, Zargaraan A. Development and implementation of nutrition labelling in Iran: A retrospective policy analysis. Int J Health Plann Manage 2019;45:e28-e44. https://doi.org/10.1002/hpm.2924

[41] Gharaee H, Tabrizi JS, Azami-Aghdash S, Farahbakhsh M, Karamouz M, Nosratnejad S. Analysis of public-private partnership in providing primary health care policy: an experience from Iran. J Prim Care Community Health 2019;10:2150132719881507. https://doi.org/10.1177/2150132719881507

[42] Loloei S, Pouraram H, Majdzadeh R, Takian A, Goshtaei M, Djazayery A. Policy analysis of salt reduction in bread in Iran. AIMS Public Health 2019;6:534-45. https://doi.org/10.3934/publichealth.2019.4.534

[43] Mohseni M, Aryankhesal A, Kalantari N. Prevention of malnutrition among children under 5 years old in Iran: a policy analysis. PLoS One 2019;14:e0213136. https://doi.org/10.1371/journal.pone.0213136

[44] Behzadifar M, Azari S, Gorji HA, Martini M, Bragazzi NL. The hepatitis C virus in Iran: health policy, historical, ethical issues and future challenges. J Prev Med Hyg 2020;61:E109-E18. https://doi.org/ 10.15167/2421-4248/jpmh2020.61.1.1438

[45] Doshmangir, Rashidian A, Kouhi F, Sergeevich Gordeev V. Setting health care services tariffs in Iran: half a century quest for a window of opportunity. Int J Equity Health 2020;19:112. https://doi.org/10.1186/s12939-020-01224-1

[46] Raoofi A, Takian A, Akbari Sari A, Olyaeemanesh A, Haghighi H, Aarabi M. COVID-19 pandemic and comparative health policy learning in Iran. Arch Iran Med 2020;23:220-34. https://doi.org/10.34172/aim.2020.02

[47] Embrett MG, Randall GE. Social determinants of health and health equity policy research: exploring the use, misuse, and

nonuse of policy analysis theory. Soc Sci Med 2014;108:147-55. https://doi.org/10.1016/j.socscimed.2014.03.004

[48] El-Jardali F, Lavis JN, Ataya N, Jamal D. Use of health systems and policy research evidence in the health policymaking in eastern Mediterranean countries: views and practices of researchers. Implement Sci 2012;7:2. https://doi.org/10.1186/1748-5908-7-2

[49] Barnish M, Tørnes M, Nelson-Horne B. How much evidence is there that political factors are related to population health outcomes? An internationally comparative systematic review. BMJ Open 2018;8:e020886. https://doi.org/10.1136/bmjopen-2017-020886

[50] Casey M, Rohde D, Brady AM, Fealy G, Hegarty J, Kennedy C, McNamara M, Nicholson E, O'Connell R, O'Connor L, O'Leary D, O'Reilly P, Stokes D. Developing a new health-related policy analysis tool: An action research cooperative inquiry approach. J Nurs Manag 2019;27:1233-41. https://doi.org/10.1111/jonm.12804

[51] Frenk J. Comprehensive policy analysis for health system reform. Health Policy 1995;32:257-77. https://doi.org/10.1016/0168-8510(95)00739-f

[52] Gibson JL, Martin DK, Singer PA. Setting priorities in health care organizations: criteria, processes, and parameters of success. BMC Health Serv Res 2004;4:25. https://doi.org/10.1186/1472-6963-4-25

[53] Walt G, Gilson L. Reforming the health sector in developing countries: the central role of policy analysis. Health Policy Plan 1994;9:353-70. https://doi.org/10.1093/heapol/9.4.353

[54] Araújo Jr JLCd, Maciel Filho R. Developing an operational framework for health policy analysis. Rev Bras de Saúde Matern Infant 2001;1:203-21. https://doi.org/10.1590/S1519-38292001000300002

[55] Zaidi S, Bhutta Z, Hussain SS, Rasanathan K. Multisector governance for nutrition and early childhood development: overlapping agendas and differing progress in Pakistan. BMJ Glob Health 2018;3(Suppl 4):e000678. https://doi.org/10.1136/bmjgh-2017-000678

[56] Collins J, Koplan JP. Health impact assessment: a step toward health in all policies. JAMA 2009;302:315-7. https://doi.org/10.1001/jama.2009.1050

[57] Carlisle S. Health promotion, advocacy and health inequalities: a conceptual framework. Health Promot Int 2000;15:369-76. https://doi.org/10.1093/heapro/15.4.369

[58] De Leeuw E. Engagement of sectors other than health in integrated health governance, policy, and action. Annu Rev Public Health 2017;38:329-49. https://doi.org/10.1146/annurev-publhealth-031816-044309

[59] World Health Organization. The world health report 2000 - Health systems: improving performance 2000 [updated 9 November 2020. Available from: https://www.who.int/whr/2000/en/

[60] Ejaz I, Shaikh BT, Rizvi N. NGOs and government partnership for health systems strengthening: a qualitative study presenting viewpoints of government, NGOs and donors in Pakistan. BMC Health Serv Res 2011;11:1-7. https://doi.org/10.1186/1472-6963-11-122

[61] Shaikh B, Kadir M, Hatcher J. Health care and Public health in South Asia. Public Health 2006;2:142-4. https://doi.org/10.1016/j.puhe.2005.08.018

ERRATA CORRIGE

ERRATA

J Prev Med Hyg 2022;63:E69-E75. https://doi.org/10.15167/2421-4248/jpmh2022.63.1.2299

CORRIGE

J Prev Med Hyg 2022;63:E374. https://doi.org/10.15167/2421-4248/jpmh2022.63.2.2299

ERRATA

Factors related to the voluntary interruption of pregnancy in Spain

SOFÍA GARCÍA SENSO[1], MARTA CARA RODRÍGUEZ[1], MARÍA ÁNGELES RODRÍGUEZ-ARENAS[2]

CORRIGE

Factors related to repeated voluntary interruption of pregnancy in Spain

SOFÍA GARCÍA SENSO[1], MARTA CARA RODRÍGUEZ[1], MARÍA ÁNGELES RODRÍGUEZ-ARENAS[2]

ERRATA

How to cite this article: García Senso S, Rodríguez MC, Rodríguez-Arenas Ma. Factors related to the voluntary interruption of pregnancy in Spain. J Prev Med Hyg 2022;63:E69-E75 https://doi.org/10.15167/2421-4248/jpmh2022.63.1.2299

CORRIGE

How to cite this article: García Senso S, Cara Rodríguez M, Rodríguez-Arenas MA. Factors related to repeated voluntary interruption of pregnancy in Spain. J Prev Med Hyg 2022;63:E374. https://doi.org/10.15167/2421-4248/jpmh2022.63.2.2299

MSD INVENTING FOR LIFE

Pfizer Vaccines

Seqirus
A CSL Company

SANOFI PASTEUR

VISMEDERI
ANALYSES FOR LIFE IMPROVEMENT

AstraZeneca