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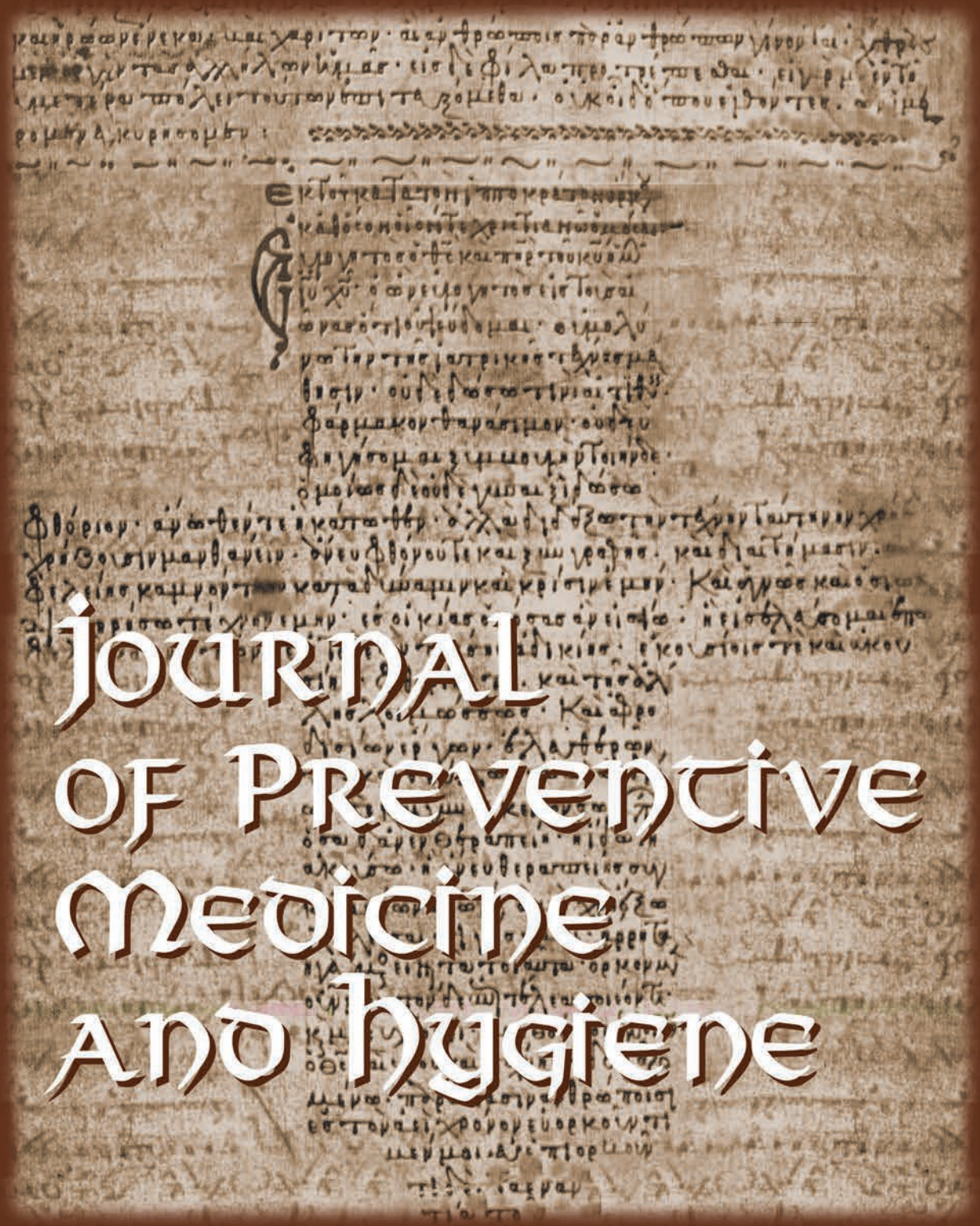

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The original document of Hippocrates' oath

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Keywords

Diabetic patients • Vaccinations

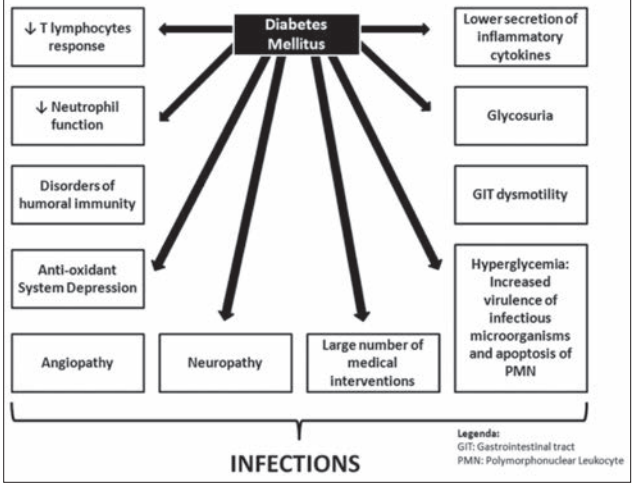
Introduction

It is widely recognized diabetes represents a relevant public health issue worldwide, due to the remarkable social, economic and healthcare burden this disorder is responsible for, mainly through the development of chronic complications leading to increased morbidity and mortality in the affected individuals [1].
Diabetes-associated burden has been progressively becoming even more relevant, due to the overwhelming increase in the number of patients diagnosed with this disorder which has already attained the status of an epidemic condition, as demonstrated by the doubling of people living with diabetes observed over the last two years, reaching, overall, 415 million of individuals worldwide, in 2015 [2].
Notably, as reported by the International Diabetes Federation (IDF), such a trend is expected to continue over the next years, even to a greater extent, with estimates indicating a further increase in the number of subjects suffering from diabetes reaching 642 million by 2040 worldwide [2].

Increased likelihood of infections in diabetic patients

There's increasing body of evidence supporting diabetes leads to an increased risk of developing and dying from infectious diseases [3-5].
It has been shown that certain infectious diseases, such as influenza, not only are more likely to occur in diabetes patients, but may generally have a more severe course (e.g., higher incidence of complications) in this patient group [4].
In fact, as compared to subjects with normal glucose metabolism, diabetics have been shown a higher relative risk (RR) for infection-related adverse outcomes such as hospitalization [RR: 2.17 ($p < 0,0001$)] or death [RR: 1.92 ($p < 0,0001$)] [6].
Multiple mechanisms may account for the increased risk of infections in patients with diabetes (Fig. 1), most of them related to chronic hyperglycemia which may affect several physiological pathways involved in the immune response against pathogens which virulence also appear to be higher in diabetics [3-5].
It has been described that also comorbidities, such as obesity (which often affects diabetic subjects), may contribute to pose individuals with diabetes at increased risk of developing infectious diseases [3, 4, 6].

Fig. 1. Pathophysiology of infections associated with diabetes mellitus [3].



The major points of interest are:

- Diabetes is associated with an increased likelihood of infections [3-5].
- Multiple factors appear to be involved in diabetic patients' increased risk to infections [3-5].
- Infectious diseases' course is likely to be more severe in diabetics, with higher risk for hospitalization and death compared to euglycemic subjects [6].

Influenza infection in patients with diabetes

Susceptibility to & burden of influenza, and vaccination-related benefits

Influenza infection has been shown to affect patients with diabetes to a greater extent than it does with individuals with normal glucose homeostasis, as highlighted by available literature [3, 4].

Subjects with diabetes not only have an increased risk to develop influenza during winter season, but they're more likely to experience a more severe course of this infection, as compared to general population, with higher incidence of flu-related major adverse outcomes such as all-cause hospitalizations, intensive care unit admissions, and all-cause mortality, as well [7-9].

Notably, these findings have been reported not only in diabetic elderly patients, but also in younger diabetics, as well as in both subjects with type 1 and those with type 2 diabetes [7-9].

The higher risk for severe/complicated flu in diabetic patients has been reported not only by published studies, but arises also from real-life surveillance data from, for example, 2017-2018 flu season in Italy, where the majority of individuals either hospitalized at intensive care unit or died due to laboratory-confirmed influenza suffered from at least a chronic disorder such as diabetes, COPD, cardiovascular disease [10].

Importantly, these subjects were younger than 65 years, having a mean age of 60 years, therefore, for whom recommendations by health authorities and scientific societies to get vaccinated against flu derives from the presence of a chronic disease (e.g., diabetes), rather than their age [10-13].

The increased severity of seasonal flu seen in patients with diabetes may, at least partially, result from influenza-associated deleterious impact on cardiovascular system. In fact, as reported by a recently published study by Kwong et al., a relevant association between laboratory-confirmed influenza and the likelihood of acute myocardial infarction (AMI) occurrence after laboratory confirmation was found. Indeed, study subjects (half of whom suffered from diabetes) showed a six-fold increased risk to develop AMI within 7 days after confirmed influenza which, interestingly, was mainly driven by influenza B which accounted for a ten-fold increased risk of AMI, overall, whereas influenza A was associated with a five-fold increased risk, accordingly [14].

Several mechanisms have been hypothesized to account for such an increased risk to develop AMI following influenza infection, especially in at-high cardiovascular risk individuals such as diabetics [15]. These mechanisms – leading to a worsening of atherosclerotic process – include cytokine release during acute inflammation, atherosclerotic plaque damage, hypoxia, tachycardia, vasoconstriction (following sympathetic system activation), as well as a direct harmful effect by influenza virus on myocardial tissue (Fig. 2) [15].

Influenza vaccination has been shown to be beneficial to diabetic patients, as reported by available studies conducted in this at-risk group for flu-related complications [1]. Initial evidences supporting flu vaccination-induced benefits in subjects with diabetes came from a UK study performed by Colquhoun et al. that clearly demonstrated a relevant relative risk reduction (i.e., by 79%) in hospitalization due to influenza, pneumonia, bronchitis, as well as diabetic ketoacidosis and diabetes without complications, over two flu seasons [16]. Findings from Colquhoun's et al. study were consistent with results from more recently published studies which reported improved outcomes in diabetic subjects, across different age, after receiving flu vaccination [17, 18].

Accordingly, Vamos & Coll. found how influenza vaccination, administered to over 120,000 type 2 diabetes patients, resulted in a significant relative risk (RR) reduction in major outcomes such as hospitalization due to stroke (-30%) (RR: 0.70; 95% confidence interval [CI]: 0.53-0.91), heart failure (-22%) (RR: 0.78; 95% CI: 0.65-0.92), pneumonia or influenza (-15%) (RR: 0.85; 95%CI: 0.74-0.99), and all-cause mortality (-24%) (RR: 0.76; 95%CI: 0.65-0.83) [17].

It has been shown as also diabetic elderly patient, a widely represented sub-group in daily clinical practice, may really benefit from getting vaccinated against seasonal flu, as reported by Kuan Wang et al. who found significantly lower incidence of pneumonia, influenza, respiratory failure, as well as reduced risk for hospitalization, intensive care unit admission and death in vaccinated vs. not-vaccinated elderly subjects with diabetes [18].

Protection provided by flu vaccination against influenza virus-induced harmful impact (either direct or indirect) on myocardial tissue may account for the reported im-

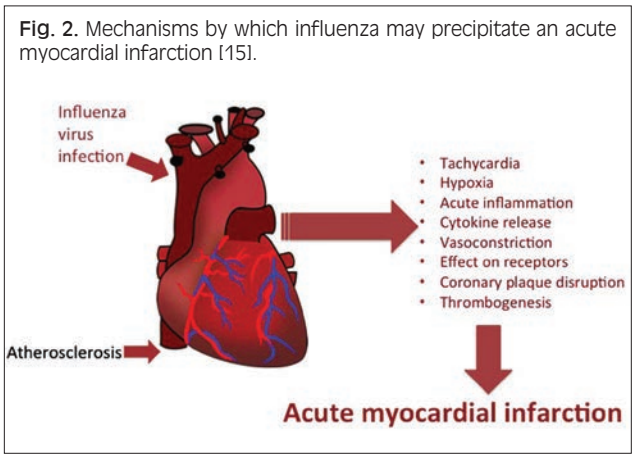


Fig. 2. Mechanisms by which influenza may precipitate an acute myocardial infarction [15].

Tab. I. Efficacy of accepted coronary interventions and influenza vaccine in the prevention of myocardial infarction [15].

Coronary intervention	Prevention	Intervention efficacy/ effectiveness against acute myocardial infarction (%)
Smoking cessation [4, 23-25]	Secondary	32-43
Statins [38]	Secondary	19-30
Antihypertensive drugs [26-29, 32]	Secondary	17-25
Influenza vaccine [5, 9, 18]	Secondary	15-45

provement of cardiovascular (CV) outcomes in patients with diabetes. This hypothesis may be supported by the flu vaccination's marked effectiveness in the secondary prevention of AMI occurrence in high CV-risk patients, which was similar to that reported by well-established CV preventive interventions such as smoking cessation, antihypertensive drugs, statins (Tab. I) [15].
It is important to point out as, although the above-mentioned impairment in the immune response seen in diabetic patients (accounting for their increased risk to experience severe flu), the latter have been shown to really benefit from receiving flu vaccination, being able to achieve an effective and sustained humoral immune response to flu vaccine, similar to that observed in subjects without diabetes [1, 19].

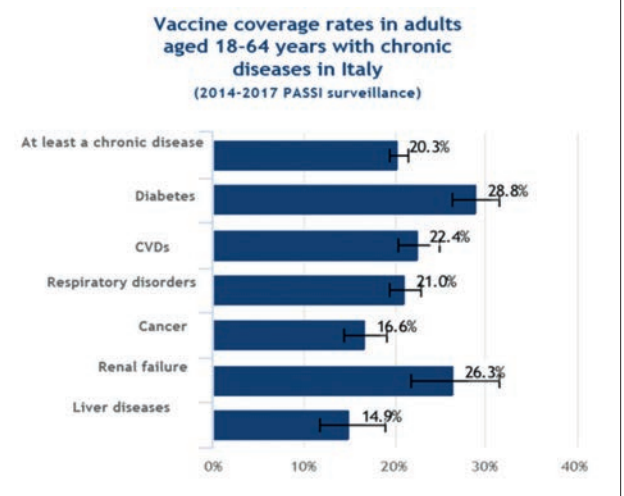
Recommendations by health authorities/ scientific societies and current coverage rates

Because of the flu-related relevant burden as well as well-established vaccination-associated benefits in diabetic subjects, both international and national bodies - such as the Italian Ministry of Health (MoH), and Diabetes Scientific Societies (i.e., AMD & SID) recommended that all individuals with diabetes (either type 1 or type 2) above 6 months of age would receive seasonal influenza vaccination to protect themselves against flu-associated adverse outcomes [11-13].
As reported in both the 2017-2019 National Immunization Plan (NIP) and Italian MoH's recommendations for 2018-2019 flu season, subjects with diabetes (as well as other chronic patients) will receive seasonal influenza vaccination via an active and free offer, being individuals at higher risk to develop flu-related morbidity and mortality [11, 12]. Both Italian MoH's 2018-2019 recommendations and 2017-2019 NIP recommend for patients with diabetes (and, in general, for those with chronic disorders) to achieve flu vaccination coverage rates of at least 75% (i.e., minimum recommended target), or, ideally, the value of 95% representing the optimal coverage goal for all at-risk individuals, regardless of their underlying disease [11, 12].
Nevertheless, despite influenza-associated burden and proven vaccination efficacy in improving major outcomes in diabetic patients aged 18-64 years, the current coverage rates in this patient group are still low (~29%), far away from the aforementioned MoH's recommended targets (Fig. 3) [12, 20].
Whereas, current influenza vaccination coverage rates in individuals with diabetes aged ≥ 65 years are unknown, so far (as other chronic conditions), since, to date, in Italy, for elderly people there's information only about the overall flu vaccination coverage rates (which were around 52% in 2016-2017 season), with no data available for each chronic disorder in this age group [12].

Patients' attitudes and/or barriers to flu vaccination

Patients' attitudes towards medical interventions - either therapeutic (i.e., pharmacological treatments) or preventive (i.e., vaccinations) - have been shown to play a key role to guarantee good patients' compliance, and therefore increase the likelihood that these interventions are successful.
Available literature has shown that multiple patient-related factors – including not being considered as at-risk individuals for flu-associated complications, fear of vaccine-associated side effects, low awareness/knowledge of vaccination-induced benefits – may account for influenza vaccination lower uptake among patients with diabetes [21].
On the other hand, advanced age, regular contacts with diabetes-treating physicians, more frequent visits at GP's office, higher number of previous influenza vaccinations, existing comorbidities (e.g., chronic respiratory disorders), longstanding diabetes, represented major factors associated with a higher likelihood to diabetic subjects to adhere to seasonal influenza vaccination [21, 22].
The above-mentioned findings highlight the critical role GPs and diabetes-treating physicians play to effectively promote influenza vaccination uptake among their diabetic patients [21, 22].
The key role played, in Italy, by both diabetes-treating physicians and GPs to promote diabetics' adherence to

Fig 3. Influenza vaccination coverage rates in patients with chronic disorders in Italy between 2014 and 2017 [20].



this vaccination has also resulted from an Italian-based research (published in 2017) carried out by Censis Institute, aiming at addressing knowledge/awareness, attitudes and behaviors of Italian people aged above 50 years with regard to influenza and the related vaccination [23]. The Censis research reported both influenza infection and flu vaccination were widely known by population involved, whereas less than 50% of the sample (i.e., 43%, overall) was aware of influenza-associated complications [23]. Moreover, this research clearly highlighted, according to 2016-2017 flu season data, that GPs play a key role, not only to administer flu vaccine, but also to actively promote patients/citizens' adherence to seasonal influenza vaccination (as reported by 63% of the interviewers) [23].

In summary the major points of interest are:

- Diabetic patients are more likely to experience severe influenza [3, 4].
- Diabetes confers an increased risk of acute myocardial infarction, admission to intensive care unit, as well as all-cause hospitalization and mortality following influenza infection [8, 9, 14].
- Vaccination against influenza results in improved outcomes in diabetics (including the elderly), leading to a reduced risk of hospitalization due to stroke, heart failure and flu/pneumonia, respiratory failure onset all-cause mortality [16, 18].
- Flu vaccination has been shown to be as effective as well-known CV preventive interventions to reduce the risk of acute myocardial infarction in high-CV risk patients [15].
- Although marked flu burden and established vaccination benefits, current coverage rates in diabetics < 65 years are less than 30% [8, 17, 20].
- 2017 Censis report and available literature have shown that advice from both diabetes-treating physicians and GPs are major factor to promote diabetic subjects' adherence to flu vaccination [21-23].

Pneumococcal infections in subjects with diabetes

Susceptibility to & impact of pneumococcal infections, and vaccination-associated benefits

Patients with diabetes have been shown to have a higher likelihood to experience pneumococcal-related infections such as pneumococcal pneumonia (1.4 fold increase) and pneumococcal invasive disease (1.4 to 1.6 fold increase), both responsible for increased rates of morbidity and mortality, as well as relevant costs for healthcare system [24, 25].

Hyperglycemia-induced deleterious effects on immune and/or pulmonary function has been hypothesized to account for diabetes patients' greater susceptibility to develop both pneumococcal pneumonia and pneumococcal invasive disease [24].

Notably, longstanding diabetes and poor glycemic control have been shown by available literature to account for an increased risk of hospitalization due to pneumococcal pneumonia in diabetic individuals [24].

A recently published retrospective Spanish study – including over 900,000 hospitalizations due to community acquired pneumonia (CAP), evaluated over 10 years – reported an increased incidence of hospitalizations, over this period, among diabetic patients compared with individuals with normal glucose metabolism [26].

Pneumococcal-associated diseases have been shown to be responsible for a high economic burden, with total direct costs of 3,7 billion of dollars yearly in U.S. adults aged > 50 years [11].

In this regard, the European Respiratory Society reported pneumonia-related costs to be higher than 10 billion of Euros within 51 European countries of WHO, with hospitalization-associated costs accounting for 6 billion of Euros yearly [11]. Because of the high clinical and economic burden of pneumococcal-related infections in diabetic patients, it is widely recognized the key role by pneumococcal vaccination to prevent pneumococcal infections-associated burden in these at-risk individuals.

Benefits associated with pneumococcal vaccination in diabetic patients have been reported by a randomized, placebo-controlled Dutch study, called *CAPiTA* (*Community-Acquired Pneumonia Immunization Trial in Adults*), which involved around 85,000 elderly subjects with chronic disorders (half of whom with diabetes) [25]. In fact, Suaya et al. showed 13-valent pneumococcal conjugate vaccine (PCV13) was associated with higher and sustained (over a 4-year period) efficacy than placebo in preventing both the first and all pneumococcal pneumonia episodes in subjects aged ≥ 65 years with chronic conditions, including diabetes [25].

Pneumococcal vaccination efficacy in diabetes patients has also been shown by a retrospective cohort study conducted in approximately 67,000 elderly subjects that, via assessing, across a 9-year period, the *Taiwanese National Health Insurance Research Database*, reported a reduced risk by 14% of pneumococcal invasive disease onset in the group who received 23-valent pneumococcal vaccine (PPV23) compared with the group not exposed to PPV23 [27].

Such a trial reported further benefits associated with Pneumococcal vaccination, since study subjects who received PPV23 experienced an improvement in – clinical and economic – outcomes such as hospitalization, respiratory failure, hospital stay and healthcare costs [27].

Importantly, it has been shown diabetes patients (including those aged ≥ 65 years) are able to mount a humoral immune response following pneumococcal vaccination which is similar (no significant differences detected) to that observed in subjects without diabetes, accounting for the ability to diabetic individuals to adequately respond to such a vaccination, thereby protecting themselves from Pneumococcal-associated diseases [28-30].

Notably, diabetic subjects who got vaccinated with pneumococcal vaccine showed similar safety profile to euglycemic individuals who received this vaccine [28].

Recommendations by health authorities/ scientific societies and current coverage rates

In Italy, both 2017-2019 NIP and 2018 AMD-SID Diabetes Mellitus Guidelines recommend patients with diabetes (either type 1 or type 2) to get vaccinated against pneumococcal-related infections [11-13]. In this regard, available recommendations state patients with diabetes should receive pneumococcal vaccination at least one time in their life, with a single revaccination for individuals aged > 64 years who got vaccinated > 5 years earlier [11-13].

Current NIP states pneumococcal vaccination should be administered all at once lifetime, in a single dose, either together with flu vaccination or not, and, in contrast to the latter, in any season of the year [11].

At this time, a relevant issue, in Italy, comes from the evidence of low pneumococcal vaccination coverage rates in patients with chronic disorders including diabetes which are far away from MoH's recommended target of 75%, although diabetics' increased likelihood to suffer from pneumococcal-related infections, as well as the well-established benefits associated with such a vaccination in these at-risk individuals [11, 31].

In fact, although In Italy pneumococcal vaccination coverage rates are not routinely collected, it has been reported these are quite low in the elderly, ranging from 0.7 to 50% across different regions [31].

Importantly, current NIP's objectives over 2017-2019 period include a progressive increase in pneumococcal vaccination coverage rates, with the goal to achieve MoH's recommended target of 75% in 2019 [11].

Patients' attitudes and/or barriers to pneumococcal vaccination

GPs' advice to diabetic subjects to get vaccinated against pneumococcal-related infections has been shown to represent a major predictive factor for this patient group to adhere to pneumococcal vaccination [32, 33]. In contrast, diabetic patients' reduced awareness/knowledge about vaccination recommendations, as well as concerns (from both patients' and physicians' side) about pneumococcal vaccination-associated potential side effects have been shown to represent relevant factors accounting for the reduced uptake of this vaccination in such individuals [32, 33].

In summary the major points of interest are:

- Diabetic patients are more likely to develop pneumococcal pneumonia and invasive disease, as well as their complications [24, 25].
- Hyperglycemia-associated harmful effects on immune and/or pulmonary function has been hypothesized to account for diabetics' greater likelihood to develop pneumococcal-related infections [24].
- Both MoH and scientific societies recommend pneumococcal vaccination in diabetics [11, 13].
- Influenza vaccination has been shown effective in diabetic patients, resulting in reduced risk of pneumonia, hospitalizations, respiratory failure, as well as shortening hospital stay [25, 27].
- In Italy, although vaccination-associated benefits and available recommendations, pneumococcal vaccination coverage rates in diabetic subjects are below MoH's established target of 75% [11, 31].
- Recommendations by GPs to diabetics to receive pneumococcal vaccination and vaccine-associated safety concerns by patients/HCPs represent major promoting and limiting factors, respectively, to diabetic patients' adherence to this vaccination [32, 33].

Herpes Zoster (HZ) in patients with diabetes

Susceptibility to HZ infection

Recently published studies reported diabetes represents a major risk factor for the development of HZ infection and its severe complication, namely the post-herpetic neuralgia (PHN) [5].

The current NIP recommends diabetes patients to get vaccinated also against herpes zoster (HZ) infection [11].

In Italy, vaccination against HZ is recommended and provided freely not only to people ≥ 65 years, but also to individuals suffering from chronic disorders such as diabetes mellitus [11].

Accordingly, a meta-analysis, conducted in the U.S., and based on 62 trials, reported patients with diabetes (especially those with type 2 diabetes [T2DM]) had an increased risk (by 30%) to develop HZ infection [34].

Another study (which was observational in the design) conducted in the U.S. showed diabetic patients were more likely to suffer from both HZ and PHN, which incidences were increased, as compared to individuals without diabetes, by 78% and 50%, respectively [35].

Consistent with findings from aforementioned trials, Weitzman's et al. retrospective cohort study, found HZ infection and PHN were associated with some risk factors including diabetes [36]. Moreover, it has been estimated each year in the U.S. that 13% of all cases of HZ occurred in subjects with diabetes the latter has also been shown to be associated with an increased severity of HZ infection course [5, 35].

Notably, it has been shown type 1 diabetes (T1MD), and not only T2DM, would represent a risk factor for HZ occurrence, as well as this infection would be more common in women and elderly diabetic individuals and also in patients with diabetic vascular complications [5].

HZ infection-related impact and vaccination-induced benefits

Diabetes subjects, in addition to being at higher risk of developing PHN, have also been shown, as compared to subjects without diabetes, to experience increased severity and persistence of PHN, the latter known to negatively affect diabetic patients' quality of life [5].

Importantly, HZ infection has also been shown to negatively affect diabetics' glycemic control, as well as increase healthcare resource utilization in this patient group, due to the higher number of outpatient visits, hos-

pitalizations, antiviral medications usage, loss of working days [5].
Based on above-mentioned data, prevention of HZ infection and PHN episodes in subjects with diabetes represent a key goal in these at-risk individuals and lies on the chance of providing such subjects with vaccination against HZ infection [5, 11].
To date, in Italy, anti-HZ vaccination is based on a marketed live attenuated vaccine, while in the future, a new, recombinant adjuvated vaccine, recently approved in Europe, and already employed in the U.S. for eligible individuals (including those with diabetes), would be made available also in Italy and in other EU countries [5].

Recommendations by health authorities/ scientific societies and current coverage rates

Although the relevant – clinical, social and economic – burden of HZ infection in patients with diabetes, as well as the proven benefits resulting from the related vaccination, the current coverage rates are still low in these high-risk subjects [5].
In Italy, vaccination against HZ infection is currently recommended in individuals with diabetes by, both 2017-2019 NIP and 2018 AMD-SID Diabetes Mellitus Guidelines [11, 13].
According to the current NIP, vaccination against HZ infection is recommended, and – actively and freely –offered (in addition to elderly individuals) to subjects aged ≥ 50 years suffering from chronic disorders such diabetes [11].
The current NIP has issued, over 2017-2019 period, the objective of a progressive increase in HZ-related vaccination coverage rates, in order to reach, in 2019, the MoH's recommended target of 50% [11].
In summary the major points of interest are:

- Diabetes represents a major risk factor for the onset of both HZ infection and PHN [5].
- Diabetes is responsible for a more severe clinical course of HZ infection [5].
- Diabetic patients show higher persistence and severity of PHN compared to subjects without diabetes [5].
- HZ infection has been shown to worsen diabetics' glycemic control and quality of life, as well as to increase related healthcare costs [5].
- Vaccination against HZ infection is recommended by both MoH and diabetes scientific societies, and is offered freely also to diabetic subjects aged > 50 years, with the goal of a progressive increase in vaccination coverage rates across 2017-2019 [11, 13].

Other vaccinations recommended in diabetic individuals

Anti-meningococcal disease

Current NIP's recommended vaccinations in diabetics also include meningococcal vaccination, to T1DM patients [11].
In this regard, NIP states subjects with certain diseases are more likely to develop meningococcal invasive infection; therefore, immunization through meningococcal conjugated vaccine is recommended in patients suffering from disorders such as T1DM [11].
Notably, the recommendation to diabetics to receive meningococcal vaccination has been included, for the first time, in 2018 AMD-SID Diabetes Mellitus Guidelines recommending meningococcal vaccinations to all subjects with T1DM [13].

Anti-Diphteria-tetanus-pertussis (dTp)

Vaccination against diphtheria, tetanus and pertussis (dTp) is also included in 2017-2019 NIP and provided (via an active offer) as a ten-year booster, and through an adult-based dosage [11].
Although current NIP doesn't specifically refer to diabetic patients while addressing anti-dTp vaccination, in contrast to the CDC (*Centers for Disease Control and Prevention*) which specifically refers to diabetics among individuals for whom such a vaccination is recommended, it is clear that current NIP-reported recipients (those aged 19-64 years) to anti-dTp vaccination also include patients with diabetes for whom this vaccination is recommended due to their increased likelihood to develop severe infections [3-5, 11, 37].

Scientific societies' recommendations about adult diabetic subject-related vaccinations

To actively promote vaccinations included in the national vaccine calendar approved by the Italian Ministry of Health, represents a deontology obligation for each Physician (Italian Ministry of Health circular. March 9, 2017. Operational aspects for the complete and consistent implementation of the 2017-2019 National Immunization Plan and the related Vaccine Calendar).
These recommendations include:

- Flu vaccination to be systematically offered by GPs to their diabetic subjects, together with also during the influenza campaign, pneumococcal vaccination (if possible and available) to diabetic individuals.
- Systematic counseling carried out by GPs to diabetic patients regarding influenza and pneumococcal vaccinations, together with, at any time, the evaluation of anti-tetanus vaccination coverage, as well as advice provided towards anti-HZ vaccination. Moreover, assessment of meningococcal vaccination coverage to be implemented in adults with type 1 diabetes.
- Diabetes-treating physicians and GPs, during the collection of patients' history, should systematically assess and report within medical records, diabetic patients' vaccinal status regarding the following vaccinations:
  - anti-flu;
  - anti-pneumococcal;
  - anti-diphtheria- tetanus-pertussis (dTp);
  - anti-herpes zoster (HZ);
  - anti-meningococcal (T1DM patients).
- Systematic vaccination counseling performed by diabetes-treating physicians, together with reporting, within either outpatient visit-associated documentation or hospital discharge-related letter (to be provid-

ed to diabetic patients) recommendations to receive the following vaccinations:
- anti-flu;
- anti-pneumococcal;
- anti-dTp;
- anti-HZ;
- anti-meningococcal (T1DM patients).

- Diabetes-treating physicians should attend educational events, organized by the related Scientific Societies, addressing the topic of vaccinations in adult patients with diabetes, in order to increase their knowledge & awareness about this matter.

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Conflict of interest statement

The topic addressed in this article by the authors (on behalf of their scientific societies) has already been addressed by the same authors (on behalf of their scientific societies) in another article comprising similar contents which has already been submitted to another journal.

Authors' contributions

All Authors have made a substantial contribution to the drafting of the article. All Authors approve the final version submitted to the Journal of Preventive Medicine and Hygiene.

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Overview

A new meningococcal B vaccine for adolescents and adults: characteristics and methods of use

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Keywords

Meningococcal B vaccine • Directions of use • Adolescent

Summary

The invasive disease from Neisseria meningitidis is one of the leading causes of death for meningitis and sepsis at all ages. The highest incidence of cases occurs at paediatric and adolescent age, but no age of life is considered protected from this infection and disease.
Prevention against the five main serogroups is possible using the combined conjugated polysaccharide vaccine against the ACWY (anti-MenACWY) serogroups and the meningococcal B (anti-MenB) protein vaccines.
Trumenba® vaccine, approved by the EMA (European Medicine Agency) for use in individuals aged ≥ 10 years, protects against serogroup B invasive disease.
This bivalent, recombinant vaccine is able, when given with a 0-6 month schedule, to induce a protective response in adolescents and young adults, comparable with a 3-doses schedule.
For this reason, the Trumenba® vaccine should be used routinely with the 2-dose schedule (0-6 months). The 3-doses use could be considered in particular situations, like an occurring epidemic or particular individual risk factors such as asplenia or complement deficit, but is not needed for underlying conditions like diabetes or heart diseases.

Introduction

The invasive disease from *Neisseria meningitidis* is one of the leading causes of death for meningitis and sepsis at all ages [1]. The highest incidence of cases occurs at paediatric and adolescent age, but no age of life is considered protected from infection and disease. There are five *Neisseria meningitidis* serogroups most frequently involved in invasive infections: A, B, C, W, Y [2, 3]. There is now the possibility of prevention against the five serogroups using the combined conjugated polysaccharide vaccine against the ACWY (anti MenACWY) serogroups and the meningococcal B (anti-MenB) protein vaccines.
The use of anti-meningococcal C and tetravalent anti ACWY vaccines is well established; data regarding safety, protective efficacy and administration protocols to be used are well known.
Prophylaxis against meningococcus B can be performed with two vaccines, the Bexsero® vaccine, marketed in Italy by GlaxoSmithKline and indicated for use both in childhood and adolescence and in adulthood, and the Trumenba® vaccine, marketed in Italy by Pfizer and registered for use in adolescents and adults. Both are protein vaccines. The proteins inserted in the vaccines are produced with recombinant DNA technologies. The Bexsero® vaccine is used with a 2-dose protocol in children > 2 years and adolescents; the Trumenba® vaccine, recently introduced in use in Italy, has a 2- or 3-dose posology [4, 5]. This has raised some issues in healthcare workers regarding the calendar to be used with this vaccine.
Moreover, since the University of Florence is conducting a Health Technology Assessment (HTA) study to support health policy makers in the use of Trumenba® within vaccine policies funded by the *Servizio Sanitario Nazionale* (National Health Service), it is crucial, to establish the conditions where the use of the two-dose schedule is indicated and, on the other hand, when three doses are advised. The aim of this work is therefore to provide the most recent scientific evidence that can support the use of one schedule or the other, and facilitate the HTA evaluation of the product.

Trumenba® vaccine in adolescents: immunogenicity studies and bactericidal activity.

The bivalent, recombinant Trumenba® vaccine contains two variants of factor H-binding protein (fHBP) and has been approved by the EMA (European Medicine Agency) for use in individuals aged ≥ 10 years [5]. Like in the past for meningococcal polysaccharide vaccines, also for meningococcal B protein vaccines, it was not possible to carry out clinical efficacy studies due to the low incidence of invasive meningococcal disease. Instead, several immunogenicity studies have been performed: antibody production and bactericidal activity have been considered as a correlate of protection.

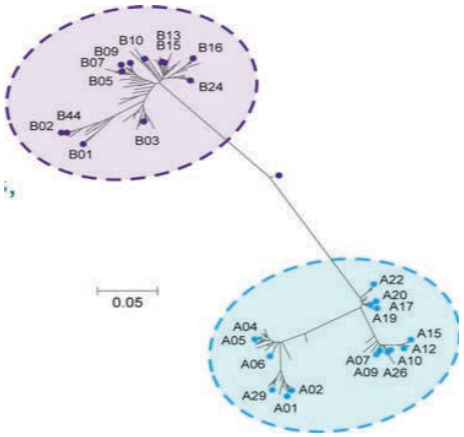
The fHbp protein is present on virtually all meningococci; however, for antibodies induced by the vaccine to guarantee bactericidal activity, the amount of fHbp present on the surface of the meningococcus needs to be sufficiently high as to be recognised by the antibodies. In this regard, the studies that analysed the amount of fHbp present on the meningococcal surface have been able to demonstrate, on more than 2,150 meningococcus strains, that over 90% of the isolates present a sufficient amount of fHbp to trigger the antigen-antibody reaction, and therefore the bactericidal activity of vaccine-induced antibodies [5, 6].

The peculiarity of the studies of bactericidal activity of the Trumenba® vaccine is that they were performed by testing the vaccine-induced antibody production against heterologous strains (i. e. strains that exhibit antigens other than those contained in the vaccine) of meningococci, expressing different sub-variants of fHbp, and a different amount of protein on the surface of the meningococcus. Another peculiarity is that the vaccine antigens of Trumenba® (A05 and B01) are derived from both existing subfamilies of fHbp (A and B) with the aim of including the set of circulating forms of meningococcus B (subfamily A comprises about 30% of circulating forms, whilst subfamily B comprises about 70%).

In detail, fHbp proteins are different from meningococcus to meningococcus: there are numerous forms that can be grouped in the two indicated subfamilies (in detail, subfamily A and B according to the Pfizer classification, or variants 1, 2, 3 according to the Novartis classification (Oxford classification), with Pfizer's subfamily A corresponding to the Oxford variants two and three, and Pfizer's subfamily B corresponding to the Oxford variant 1 [7]. Within these subfamilies, there are many (over 200) fHbp sub-variants. For this reason, it is very important to be sure that the antibodies produced by the vaccine are effective against most of these sub-variants (i. e. directed against both subfamilies) and therefore against different meningococcus strains. Today we know that not all the sub-variants are equally frequent and that in 80% of meningococcus strains, the same 10 sub-variants are present [8].

Regarding the bactericidal activity against different sub-variants, studies have been conducted towards the main sub-variants A22, A56, B24 and B44, detected by current epidemiological investigation (actual invasive MenB disease strains from reference laboratories in Europe and the United States) and belonging to both meningococcus subfamilies A and B. These aspects characterise the development of the vaccine. The studies were then further extended to other 10 sub-variants also circulating in Europe and the USA, for a total of 14 sub-variants expressed by current epidemiology [9]. Despite the antibody titre needed to induce protection (correlate of protection) being a hSBA 1:4 titre, in the Trumenba® development studies a higher dilution titre was used as a protection correlate (1:8 for A56, B24 and B44 and 1:16 for A22) to strengthen the certainty of achieving a sufficient antibody titre, using a higher threshold value. A 4-fold increase in the seroconversion index was also evaluated. These studies were conducted with different protocols, including two or three doses [5].

Fig. 1. Phylogenetic tree of meningococcal fHbp proteins (Donald et al., mod. [8]).



Trumenba® vaccine in adolescents: 2 or 3 doses?

The Vesikari study, conducted in Finland on adolescents and young adults, assessed the percentage of subjects who achieved or exceeded the antibody titre of bactericidal activity (hSBA) of 1:8 (i. e. with double dilution compared to the protection correlate 1:4). With the 2-dose protocol (0-6 months), the subjects who achieved this titre were respectively > 90% against the A22 variant, > 98% against the A56 variant, > 69% against the B24 variant and > 70% against the B44 variant [10].

The data therefore confirmed the ability of antibodies induced by the vaccine to induce a sufficiently protective response against meningococci expressing different variants of fHbp (i. e. heterologous to the vaccine). The data of the study allowed to conclude that the Trumenba® vaccine is able, when given with a 0-6 month calendar, to induce a protective response in adolescents and young adults comparable with a 3-dose schedule. The authors also conclude that increasing the time between the two doses improves the induced antibody response so much that protocol 0-6 month is preferable to protocol 0-4 or 0-2 or 0-1 month.

The results of the study were therefore that both the 2- and 3-dose calendars induce a robust immune response [10].

Precisely for this reason, the Trumenba® vaccine should be used routinely with the 2-dose schedule (0-6 months). The 3-dose use could be considered in particular situations, when it is necessary, for example in travellers heading to endemic areas, to be protected in a short time because of an outbreak occurrence; in that case, a schedule 0-1 month (before departure) can be used, followed by a third dose at month 6.

For example, this was indicated in the recommendations of the Advisory Committee on Immunization Practices

(ACIP) updated as of May 2017, which show that, in routine conditions, two doses are recommended in subjects not exposed to risk. It is important to remember that "patient at increased risk" does not mean a patient with an underlying disease (e. g. diabetes, heart disease, etc.). The first 2015 ACIP recommendations indicate precisely the conditions of increased risk and specifically: "*Persons with persistent complement component deficiencies, persons with anatomic or functional asplenia, microbiologists routinely exposed to isolates of Neisseria meningitides, persons identified as at increased risk because of a serogroup B meningococcal disease outbreak.* " The recommendations mentioned above also indicate that if the interval between the two doses is equal to or greater than 6 months, the third dose in those at risk is no longer necessary, demonstrating a 3-dose rationale linked solely to the need to accelerate the schedule [11, 12].

Adding further doses to vaccination calendars often causes a reduction in adherence to the prescribed number of administrations in patients and families, and this is especially true in adolescents, who are in any case difficult to reach. US data obtained on a typical adolescent vaccination, the anti HPV, have shown that vaccination coverage decreases with doses following the first: 60% for the first dose, 50. 3% for second and 39. 7% for the third dose [13]. A similar decreasing trend is also present in Italy.

The data obtained in the Vesikari [10] study were evaluated and analysed in further publications with the conclusion that a two-dose schedule (0-6 months) is perfectly usable in vaccination practice [14, 15].

Given the very rapid evolution of the clinical conditions characteristic of the disease (which may evolve towards a very serious or even fatal situation in less than 24 hours), it appears appropriate to provide a periodic booster dose for all subjects at risk for age or other conditions (work, travel) in order to take advantage of the immunological memory induced by vaccination. This procedure is appropriate also for vaccination against meningococcus B, just as for vaccinations against meningococcal vaccines C or ACWY [5, 15]. The timing recommended for carrying out this booster vaccine should be established in the future by monitoring the antibody kinetics in populations of vaccinated subjects followed in the years after the basic immunisation course.

Conclusions

Trumenba® vaccine is able, when given with a 0-6 month schedule, to induce a protective response in adolescents and young adults, comparable with a 3-doses schedule. For this reason, the Trumenba® vaccine should be used routinely with the 2-dose schedule (0-6 months). The 3-doses use could be considered in particular situations. These are clearly addressed in the recommendations of the Advisory Committee on Immunization Practices (ACIP) updated as of May 2017: three doses are recommended in subjects at increased risk, not meaning patients with an underlying disease (e. g. diabetes, heart disease, etc.) but, as the first 2015 ACIP recommendations precisely indicate: "Persons with persistent complement component deficiencies, persons with anatomic or functional asplenia, microbiologists routinely exposed to isolates of Neisseria meningitides, persons identified as at increased risk because of a serogroup B meningococcal disease outbreak. "

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Conflict of interest statement

The Authors previously participated in advisory boards, expert meetings, or were speakers or organizers of congresses/conferences on different vaccines sponsored by Pfizer, GlaxoSmithKline, Sanofi Pasteur MSD, MSD, Sanofi Pasteur, Seqirus, and occasionally received grants for scientific studies from the same manufacturers.

Authors' contributions

CA and PB have made equal contribution to the conception, design, analysis and interpretation of data, drafted the article; they approved the final version submitted to the Journal of Preventive Medicine and Hygiene.

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ORIGINAL ARTICLE

Levels of understanding of the rules of correct medical usage among vietnamese pharmacy students: a cross-sectional study

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Keywords

Health literacy • Medical terms • Drug usage • Pharmacy students

Summary

Background. *Comprehensive misunderstanding about medicine usage is often associated with high treatment risks which have led to unexpected and adverse effects or even death. Many researches assessing health literacy have been undertaken, but only in adults. This study was undertaken to evaluate the level of understanding in students of medical terms and its correlation with gender, grade and parental occupation.*
Methods. *A cross-sectional study was conducted from September to October 2017 with 594 students (28.6% of men and 71.4% of women) of Hanoi University of Pharmacy from freshman to fifth-year students chosen randomly. The knowledge of pharmacy students was assessed by a questionnaire including 25 medical terms. Descriptive statistics and Chi-square test were used with $p < 0.05$ as level of statistical significance.*
Results. *The level of understanding of students was high with most of medical terms reaching over 70% correct answers. A positive significant association between health literacy and education was found with higher knowledge demonstrated in upper years, while there was no difference among students with and without parents belonging to the medical field. Regarding the relation with gender, there was no significant correlation for most medical terms.*
Conclusions. *Levels of understanding of medical terms in pharmacy students was high, presenting a significant association with education. This study should be extended in order to assess the level of health literacy in various populations, thereby indirect evaluating implementation of medical preventive programs.*

Introduction

Nowadays, along with the continuous economic and social development, people have to face many health and mental problems which increase the demand for drugs. Increased drug use is often associated with high risks of error, abuse or non-compliance in use leading to significant adverse effects or even death [1]. Even if the rules of correct administration of medication are followed, many potential treatment risks still exist and greatly increase if they are not followed. Especially, the fact that people in the developing countries usually select the drug-stores as the first-choice when they have any health problems without the doctor's prescription or follow the social media from pharmaceutical companies which has a great potential for the public to be exposed to misleading or dangerous information about medicine [1-7]. As a result, enhancing the awareness and understanding of people in the rational use of medicines plays a crucial role which helps improve the quality of treatment, reduces costs for patients and society alike and avoids wasting scarce resources and widespread health hazards [8, 9]. One of the first steps to raise people's awareness about proper medicine usage is the better understanding of medical terminology which is commonly used in manuals or instruction sheets. A proper understanding of medical terminology helps avoid the risk of misunderstanding information on drug use and increases patients' ability to make a personal health-related decision based on available information, as found in the WHO definition about health literacy as "the cognitive and social skills which determine the motivation and ability of individuals to gain access to, understand and use information in ways which promote and maintain good health" [10-13].
Numerous researches assessing health literacy have been carried out in many countries but exclusively in adults [14-18], and there is still a lack of information about literacy in students and especially students of pharmacy, who will play an important role in health care in the future. As a result, this study was undertaken in order to (a) evaluate the awareness and knowledge of pharmacy students based on their understanding of 25 medical terms, (b) explore possible correlations with gender, education or parental occupation.

Methods

This is a cross-sectional study assessing levels of understanding of medical terms among university pharmacy students based on the questionnaire distributed to all years from freshman to fifth-year students during 2

months from September to October 2017 when students started the new school year. Participants were students of Hanoi University of Pharmacy (HUP). In HUP, each year was divided into 5 or 6 classes, depending on the number of students in each year. Two or three classes from each year were chosen randomly. After obtaining the permission from the heads of various departments, questionnaires were administered by the research group and collected when the students finished class. The questionnaire was administered only once, all students present on the day of survey were included and absent students were not considered. The completion of questionnaires was absolutely anonymous and voluntary.

The questionnaire was originally created and certified by the University of Camerino, Italy in an Italian and English version and was then translated into Vietnamese by the HUP research group. The questionnaire was divided into 2 parts. The first part concentrated on social and demographic facts and parental occupation, and the second part focused on the knowledge of medical terms which are frequently used in patient information leaflets. The medical terms were obtained from the list of the most used words on 50 OTC package information leaflets in Italy, which was published by the Italian Ministry of Health [19]. From the list, the 24 highest frequency terms were selected corresponding to the Anatomical Therapeutic Chemical Classification System including the following groups: A01, A02, A03, A06, A07, A11, C05, D01, G01, M01, M02, N02, R01, R05. This classification system was also applied in Vietnam. Moreover, the term "teratogenic" was also added to this evaluation in order to consider possible damage from using some medicines during pregnancy. As the result, a total of twenty five terms was used in this part, each term corresponded to 5 definitions including 4 possible answers explaining the term and 1 answer which stated "do not know" in order to add value to the results and avoid blank answers, but there was only one correct answer for each question.

The results were coded and processed using Statistical Package for the Social Sciences (SPSS) software, version 20.0. Descriptive statistics were used to examine the participants' socio-demographic profile and parental occupation. Chi-square test was used to find the relationship between the level of understanding of medical terms and gender, grade or parental occupation and $p < 0.05$ was considered as a level of statistical significance.

Results

Among the 730 questionnaires distributed, 594 students who agreed to participate and complete questionnaires were evaluated (81.4%). The sample included 170 male (28.6%) and 424 female (71.4%) students, with a mean (SD) of age of 20.34 years (± 1.719). The majority of students were Vietnamese (98%), the other foreign students (1%) came mainly from Cambodia, Laos and Mongolia and 1% did not answer the question on nationality. The percentage of students participating in the survey was not similar among the grades with most being fourth-year students (160 students, 26.9%). Next were the third-year and first-year students with 125 (21%) and 123 students (20.7%) respectively. The number of second-year and fifth-year students interviewed was much smaller, with 92 (15.5%) and 94 (15.8%) students respectively. The occupations of students' parents were very different, but agriculture accounted for the highest percentage with over 46% having either father or mother employed in this field and 42.6% having both of them working in this field. The proportion of parents employed in the medical field was very low, at approximately 2.5%.

Results evaluating the knowledge of 25 medical terms were displayed in Table I. Results were organized into the number and percentage of correct answers of each term in all students and the percentage of correct answers of each term in each grade.

According to Table I, the percentage of students choosing correct answers was high with 3/4 of questions getting over 70% correct answers. Around 50-70% students selected the right answers for the terms of "anuria", "parenteral" and "asthenia". However, the terms of "erythema", "exanthema", "interaction" and "antiaggregant" were not well known with a lower proportion of accurate selections (under 50%), especially "erythema" (14%).

An assessment of associations between levels of understanding of 25 medical terms with gender, grade and parents' occupation was also carried out with the results shown in Table II.

Table II showed a significant difference ($p < 0.05$) between male and female respondents on the following terms: "parenteral", "ophthalmic", "hyperkalemia", "dyspnea", "edema", "dyspepsia", "antipyretic", "antalgic", "analgesic" and "posology" with more correct answers given by female participants than males. The remaining terms showed no significant difference between male and female participants.

In the correlation with grade, there was a significant association ($p < 0.05$) for most terms. Students from upper years had higher rates of correct selections than those of lower years (with the exception of 5th year students, who gave a lower percentage of correct answers than 4th year students). However, the variable relating to year of study was not significant when associated with the following terms: "erythema", "parenteral", "dyspnea", "antipyretic", "spasm", "antalgic" and "posology".

On the contrary, in relation to parents' occupation, students whose father or mother were employed in the medical field did not show significant differences in their knowledge of most medical terms compared with the remaining students. However, a correlation was still found for the following terms: "anuria", "dyspnea", "asthenia", "antiaggregant", "hyperkalemia" and "edema". The occupation was classified according to 2 categories: (a) occupation in higher education such as doctor, pharmacist, teacher, scientific, business, … and (b) occupation in lower education such as farmer, unemployed, housewife, general worker. Results from Table II showed that there was a significant difference in health literacy for the following terms: "parenteral", "ophthal-

Tab. I. Correct answers of students.

Medical terms	Number of correct answers in all students	% of correct answers					
		All students (n = 594)	First-year students (n = 123)	Second-year students (n = 92)	Third-year students (n = 125)	Fourth-year students (n = 160)	Fifth-year students (n = 94)
Erythema	83	14.0	16.3	15.2	8.0	13.1	19.1
Anuria	353	59.4	23.6	37.0	67.2	85.0	74.5
Hematuria	479	80.6	62.6	78.3	81.6	91.3	87.2
Topical	426	71.7	46.3	54.3	72.0	91.3	88.3
Parenteral	346	58.2	50.4	57.6	57.6	66.3	56.4
Ophthalmic	474	79.8	65.0	76.1	80.8	90.0	84.0
Hyperkalemia	481	81.0	67.5	79.3	78.4	91.9	85.1
Anaphylaxis	431	72.6	43.1	57.6	77.6	91.9	86.2
Dyspnea	510	85.9	79.7	83.7	86.4	91.3	86.2
Edema	480	80.8	65.9	70.7	84.0	90.0	90.4
Asthenia	405	68.2	54.5	55.4	70.4	80.6	74.5
Dyspepsia	522	87.9	80.5	85.9	87.2	93.8	90.4
Constipation	502	84.5	76.4	78.3	83.2	91.9	90.4
Antipyretic	526	88.6	84.6	83.7	88.8	93.8	89.4
Exanthema	200	33.7	30.9	42.4	20.0	36.3	42.6
Spasm	417	70.2	66.7	69.6	69.6	75.0	68.1
Antiaggregant	274	46.1	41.5	33.7	42.4	56.9	51.1
Bradycardia	482	81.1	71.5	72.8	80.8	90.6	86.2
Excipient	452	76.1	40.7	71.7	84.0	94.4	85.1
Teratogenic	523	88.0	77.2	89.1	87.2	95.0	90.4
Interaction	221	37.2	21.1	34.8	33.6	47.5	47.9
Antalgic	527	88.7	84.6	85.9	87.2	94.4	89.4
Analgesic	524	88.2	80.5	85.9	87.2	95.6	89.4
Posology	436	73.4	74.8	77.2	76.0	74,4	62.8
Precautions	445	74.9	71.5	63.0	65.6	86.9	83.0

mic", "dyspnea", "edema", "asthenia", "antipyretic", "excipient", "antalgic" and "analgesic". The remaining terms showed no significant difference between type of occupation and the knowledge of medical terms.

Discussion

Based on the random sample of 694 students in HUP with 5 years (from first-year to fifth-year students) participating in the questionnaire, levels of health literacy and its association with gender, grade and parents' occupation were explored. Summing up, students in HUP left less blank questions and had a much higher percentage of correct answers, with most medical terms reaching over 70% correct answers compared with similar results in the Italian survey [20]. The reason for this might be that the respondents in Vietnam were pharmacy students at university level who were mainly educated in the medical field while Italian respondents were high school students as well as university students of various majors. This result was similar to the research of Montaqna in evaluating the knowledge of undergraduate health care students showing a high percentage of correct answers [21].

Gender

In this study, we found mixed results regarding the association between level of understanding of medical terms and gender which led to a controversial result about the relation between these 2 variables. The results of our study were similar to many studies which showed no significant correlation for most medical terms [16, 20] and were also similar to other researches which showed a significant difference in health literacy between male and female students, with higher levels of understanding found in women [16, 22-26]. The difference were

Tab. II. p-value between 25 medical terms and relevant variables.

No	Medical terms	p-value				
		Gender	Grade	Father's occupation	Mother's occupation	Occupation's classification
1	Erythema	0.744	0.161	0.456	0.408	0.590
2	Anuria	0.715	0.000	0.043	0.964	0.967
3	Hematuria	0.242	0.000	0.627	0.165	0.187
4	Topical	0.163	0.000	0.239	0.660	0.051
5	Parenteral	0.017	0.112	0.312	0.889	0.007
6	Ophthalmic	0.050	0.000	0.908	0.053	0.009
7	Hyperkalemia	0.014	0.000	0.357	0.006	0.084
8	Anaphylaxis	0.943	0.000	0.264	0.270	0.861
9	Dyspnea	0.009	0.088	0.019	0.159	0.041
10	Edema	0.009	0.000	0.367	0.006	0.008
11	Asthenia	0.178	0.000	0.04	0.018	0.025
12	Dyspepsia	0.020	0.014	0.280	0.080	0.699
13	Constipation	0.054	0.001	0.900	0.625	0.677
14	Antipyretic	0.000	0.078	0.736	0.292	0.050
15	Exanthema	0.415	0.001	0.191	0.599	0.067
16	Spasm	0.642	0.603	0.919	0.382	0.275
17	Antiaggregant	0.421	0.003	0.014	0.106	0.248
18	Bradycardia	0.494	0.000	0.803	0.909	0.075
19	Excipient	0.176	0.000	0.294	0.386	0.019
20	Teratogenic	0.062	0.000	0.785	0.331	0.146
21	Interaction	0.324	0.000	0.118	0.443	0.772
22	Antalgic	0.005	0.080	0.719	0.799	0.022
23	Analgesic	0.032	0.005	0.575	0.867	0.017
24	Posology	0.001	0.150	0.866	0.558	0.551
25	Precautions	0.362	0.000	0.749	0.455	0.221

in the following 10 terms: "parenteral", "ophthalmic", "hyperkalemia", "dyspnea", "edema", "dyspepsia", "antipyretic", "antalgic", "analgesic" and "posology". The reasons for these differences are not clear, women may be more familiar with the terms due to traditional gender roles regarding health and nutrition within the family. Moreover, men tend to have a lower overall awareness of common health conditions [27] and they also tend to seek help only after becoming ill [28]. Future research should consider men and women separately to ensure reliable results.

Year of study

In general, the more advanced the students were in study, the higher number of correct choices they made. This finding is consistent with many other studies [15-17, 20, 26, 28] which showed that there was a tight relation between levels of education and better understanding of health literacy. This indicates that education levels played an important role in raising people's awareness about health literacy which decreased high risks in incorrect medicine usage due to comprehensive misunderstanding. In our study, it was observed that the 5th year students had the lower percentage of right choices than the 4th year students which could be explained that the fifth year students began to focus on their majors, paid more attention to their final thesis and rarely applied the knowledge they had learned (except clinical pharmacy students), so they forgot most of their knowledge. This was also a warning that it was essential for students to apply and review their knowledge frequently. For widely used terminologies as "erythema", "parenteral", "dyspnea", "antipyretic", "spasm", "antalgic" and "posology", no significant difference was found.

Occupation

In contrast to gender and education, the research showed that students whose parents were employed in the medical field showed no significant difference in levels of health literacy compared with those whose parents were employed in other fields. This could be explained by the fact that the survey candidates were pharmacy

students, so the level of health knowledge was similar among students. However, when carrying out the part of the survey relating to occupation', the type of parental occupation was positively and statistically associated with nearly half the number of medical terms. Students with parents working in higher-level occupations gave higher percentages of correct answers than those with lower-level jobs. This finding was consistent with previous studies [16-18, 25]. Education level and subsequent occupation had a strong correlation, the effect of occupation on health literacy reflected the effect of education on health literacy in a similar way, so individuals with higher levels of family education were more likely to possess higher health literacy.

Strengths and limitations

A large representative sample of students in medical field with the various years of study is one of the strengths of this study, which provides an overview about the quality of knowledge in pharmacy students who play an important role in the national medical care system. Moreover, this study evaluated the association between many influencing factors and levels of understanding of students, which helps in detection of learning difficulties and set of policies to support and improve curriculum, learning methods or activities. Besides, the questionnaire was designed with the variety and representation of the most common medical terms corresponding to the Anatomical Therapeutic Chemical Classification System, which allows the accurate classification and assessment of health literacy among students.

Our study has some limitations. First, the questionnaire were created by an Italian University and the terms used in this survey were chosen at random from leaflets of the most commonly used OTC drugs in Italy with the intention of finding the level of understanding of some commonly used and some less commonly used but often encountered medical terms – so it was not standardized. As a result, it has not reflected reality in Vietnam. Second, although the initial sample sizes were estimated to be similar among grades, there was still a large disparity due to the absence of students and the difficult access of 2nd and 5th year students because these students were in the practice stage and rarely in classes. Third, the generalizing our findings to apply to all students was limited to pharmacy students, as it was difficult to obtain permission from the heads of other universities and schools, meaning there was a lack of comparison between universities and schools as well as between age groups.

Conclusions

This study explored levels of understanding of medical terms in students of Hanoi University of Pharmacy and its association with various variables including gender, grade and parental occupation. The results showed that pharmacy students in Vietnam have higher health literacy compared with multidisciplinary students in Italy. Among the factors, education had a positive effect on the knowledge and awareness of students. This study should be extended in order to assess the level of health literacy in various populations, thereby indirectly evaluating the implementation of medical preventive programs.

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Conflict of interest statement

None declared.

Authors' contributions

NTTC conducted the statistical data analyses and wrote the manuscript. SS, NTB contributed to the study design and interpretation of results. PF participated in designing the study protocol and completing the analyses. GI designed the study, built the questionnaire, and made the critical review of the manuscript. All authors gave substantial contribution to manuscript revising and editing.

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ORIGINAL ARTICLE

Promoting physical activity in upper elementary children using multi-theory model (MTM) of health behavior change

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Keywords

Schools • Exercise • Child • Behavior

Summary

Background. *Physical activity and exercise offer numerous benefits to children and Centers for Disease Control and Prevention guidelines require that school children engage in at least 60 minutes of moderate to vigorous physical activity every day. Unfortunately, up to 30% elementary students do not meet these requirements and 79% elementary schools do not provide students with physical education classes every day. The transition from elementary to secondary school is particularly deleterious for levels of physical activity. Therefore, there is a need to develop educational interventions for upper elementary school children to promote physical activity. A new theory multi-theory model (MTM) of health behavior change can be utilized to develop such interventions.*
Objectives. *The purpose of this article was to develop and introduce an instrument based on MTM for physical activity change in upper elementary school children and propose an approach for changing this behavior among sedentary students.*
Methods. *A review of literature in MEDLINE, CINAHL, Google Scholar, and ERIC databases was conducted for physical activity in upper elementary children and multi-theory model of health behavior change to prepare this article.*
Results. *An instrument with Flesch-Kincaid Grade level of 5.4 and the Flesch Reading Ease of 68 making it suitable for administration with upper elementary school children was developed. An approach utilizing the constructs of participatory dialogue, behavioral confidence and changes in physical environment to initiate physical activity and reifying the constructs of emotional transformation, practice for change and changes in social environment to sustain physical activity in upper elementary school children is presented.*
Conclusions. *MTM offers potential to augment current educational efforts to promote physical activity in upper elementary school children.*

Background

Regular physical activity and exercise performed by children helps in improving their academic performance [1], managing weight, and fostering cardiovascular and musculoskeletal health thereby reducing the chances of developing chronic diseases as adults [2]. Schools provide opportunities for children to be physically active that can contribute to their meeting the 60 minutes/day moderate-to-vigorous physical activity guideline [3]. Unfortunately, many schools are not providing adequate opportunities to children for becoming physically active. A nationally representative survey of 1,831 elementary schools in United States from 2009-2012 found that only about 21% provided students with physical education classes every day [4]. A meta-analysis found that elementary children do not meet CDC guidelines for physical activity lesson time in schools [5]. Furthermore, 2009-2010 National Health and Nutrition Examination Survey in the United States based on proxy reports found that 30% children in the ages 6 to 11 years did not meet CDC recommended levels of physical activity [6].

Transition from elementary to secondary school is particularly deleterious for levels of physical activity [7]. A study with upper elementary school children revealed that total physical activity and particularly moderate to vigorous physical activity significantly declined from fifth to sixth grades [8]. There is an ardent need to develop educational interventions for upper elementary school students to enhance their physical activity levels. In recent years various educational interventions have been tried in elementary school children to promote physical activity such as utilization of classroom instruction [9], curricular changes [10], health promotion programs consisting of educational and policy changes [11], peer-led programs [12], use of computer games [13], training of physical education teachers [14] and others. These interventions have had mixed results and many of these do not use any behavioral theory thus not aiding in evidence-based practice. The interventions in health education have progressed in four generations from knowledge-based to skill-based to theory-based to now multiple theory-based, precision interventions [15]. One such approach of utilizing multiple theories is the multi-theory model [MTM) of health behavior change [15, 16].

MTM divides the process of health behavior change into initiation and sustenance. The model advocates the constructs of participatory dialogue in which advantages of behavior change outweigh the disadvantages of making the proposed change; behavioral confidence that can come from any internal or external sources and is futuristic; and changes in physical environment that provide resources and opportunities for behavior change are instrumental in initiating the behavior change. In order to sustain the behavior change the constructs of emotional transformation in which one directs one's feelings toward behavior change; practice for change in which one actively reflects on changing one's behavior and devises ways of overcoming barriers; and changes in social environment in which one recruits support from family, friends, health professionals and others are reified.

The purpose of this article was twofold. First objective was to develop an instrument based on multi-theory model (MTM) of health behavior change that can gauge changes in physical activity among upper elementary school children. Second objective was to propose an approach for promoting physical activity in upper elementary school children based on MTM.

Methods

In order to prepare this article a review of literature in MEDLINE, CINAHL, Google Scholar, and ERIC databases was conducted for physical activity in upper elementary children and multi-theory model of health behavior change. Based on this review of literature, informal discussion with a group of upper elementary children in Mississippi, and a previous validated instrument with college students [15, 17] the instrument for this article was prepared by the authors (see Appendix 1).

Results

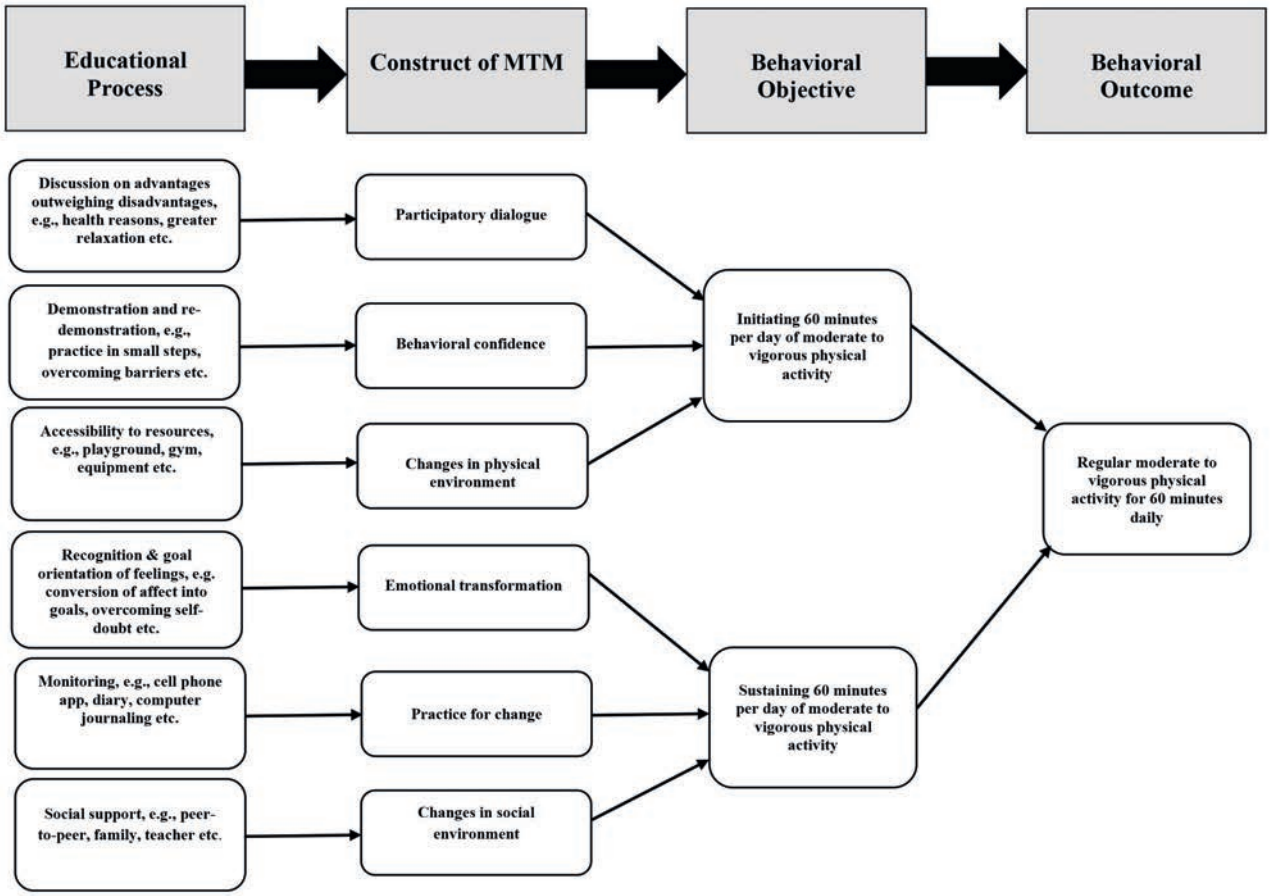
The instrument developed by the authors is presented in Appendix 1. The Flesch-Kincaid Grade level of this instrument was found to be 5.4 thus making it suitable for administration with upper elementary school children and the Flesch Reading Ease of this instrument was found to be 68 once again making it readily comprehensible in this age group. The construct of participatory dialogue is derived from a subtractive score of advantages minus disadvantages of being physically active for 60 minutes daily. Both advantages and disadvantages are measured on a scale of never (0), almost never (1), sometimes (2), fairly often (3), and very often (4). Some of the advantages that the instrument taps into include being healthy, being relaxed, getting sick less often, having more energy, and enjoying life more. Some of the disadvantages included in the instrument are getting tired, not having enough time for school or other activities, not having enough time for friends and getting injuries. The construct of behavioral confidence is based on a response to five items on a scale of not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), and completely sure (4). The behavioral confidence entails being physically active despite having school work, despite finding time for rest, without getting tired and without sustaining any injuries. The construct of changes in physical environment is also measured on a scale of not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), completely sure (4) and taps into having a place for being physically active, being able to afford it and be able to use tools to exercise. The construct of emotional transformation also uses the same scale of not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), completely sure (4) and gauges surety about directing feelings toward the goal of physical activity, inspiring oneself toward the goal and defying self-doubt. The construct of practice for change also utilizes the same scale of surety and measures ability to monitor, being active despite barriers and changing plans when faced with difficulties. The construct of changes in social environment also uses the same scale of surety and asks about getting help from a family member, friend or health worker. Finally, the intention to initiate and sustain physical activity are measured on scales of not at all likely (0), somewhat likely (1), moderately likely (2), very likely (3), and completely likely (4).

Discussion

The purpose of this article was to develop and introduce an instrument based on multi-theory model (MTM) for physical activity change in upper elementary school children and propose an approach for changing this behavior among sedentary students. The instrument that has been presented can be validated for face and content validity by a panel of experts that include a mix of experts on this theory, upper elementary school children and instrumentation. The instrument can further be subjected to construct validation by administering it to a sample of upper elementary school children and doing confirmatory factor analysis on the subscales using structure equation modeling or an extension of exploratory factor analysis (Sharma & Petosa, 2014). Internal consistency reliability of subscales can be established by computing Cronbach's alpha and test retest reliability assessment can also be done [18].

The proposed approach for promoting physical activity in upper elementary school children based on MTM is depicted in a logic diagram in Figure 1. While MTM has not been tested with school-aged children it has been tested with college students and found to be useful [17]. In order to facilitate participatory dialogue it is important to have personalized discussion with the kids about advantages and disadvantages of at least 60 minutes per day of physical activity and exercise. For building behavioral confidence demonstration and re-demonstration of skills by students will be helpful. This can also be complemented with a discussion on sources of behavioral confidence for being physically

Fig. 1. Using Multi-theory model (MTM) of health behavior change to promote physical activity in upper elementary children.



active and how to build it. Regarding changes in physical environment the educators must ensure that children have access to playgrounds in the premises of the school and that they utilize these. For bringing about emotional transformation interactive affective exercises (such as role play, psychodrama or simulation) can be deployed to explore feelings in children and how to direct them toward goals for being physically active. In order to foster practice for change cell phone apps or computer journaling should be encouraged for the students to monitor their daily physical activity. A growing number of upper elementary children are having access to these gadgets and spending greater time on these [19]. There is a potential to employ these measures in educational interventions to promote physical activity. Finally for building changes in social environment peer-to-peer social support is indispensable and must be utilized. Previous interventions have also found this approach to be beneficial [12] (Fig. 1).

In summary, it can be appreciated that MTM offers potential to augment current educational efforts to promote physical activity in upper elementary school children. MTM based interventions have an advantage of being brief and precise in fostering behavior change thus making them replicable. Careful and concerted operationalization of this model to this target group has the potential to help sedentary school children become more physically active.

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Conflict of interest statement

None declared.

Authors' contributions

Manuscript conceptualization: MS and VKN; Manuscript writing (First Draft): MS; Manuscript writing (Final Draft); Instrument development: MS.

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APPENDIX 1
MEASURING CHANGE IN PHYSICAL ACTIVITY IN UPPER ELEMENTARY CHILDREN

Directions: This survey is voluntary, which means you may choose not to complete it or not to answer some questions. There is no direct benefit of this survey to you. All data from this survey will be kept secret and not used for grading. Your responses will help in making good physical education programs. Please put an X mark by the response or fill the response that correctly describes your position. Thank you for your help!

1. During the past seven days, how many minutes did you participate in any physical activities or exercises such as running, playing ball, sports, or walking for exercise?

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
_____min.	_____min.	_____min.	_____min.	_____min.	_____min.	_____min.

Please add the total minutes up: _____ minutes/week
If your total is over 420 minutes, then you can stop taking this questionnaire. Thank you for your time.

2. Do you suffer from any medical condition including any physical disability that prevents you from being physically active?
   - □ No
   - □ Yes

If you answered Yes you may stop this questionnaire and thank you for your time.

3. What is your gender?
   - □ Boy
   - □ Girl
   - □ Other, _____

4. How old are you today? _____ years

5. What is your class?
   - □ 5th grade
   - □ 6th grade

6. Have you been taught about being physically active in school?
   - □ No
   - □ Yes, one class lesson
   - □ Yes, two class lessons
   - □ Yes, three or more class lessons

7. Do you participate in a physical education class at school?
   - □ No
   - □ Yes

8. How many times does your physical education class meet per week? _____ (write a numbe

9. How many minutes is your physical education class? _____ (minutes)

	Never	Almost Never	Sometimes	Fairly Often	Very Often
If you do more than 60 minutes of physical activity every day you will…					
10. … be healthy.	☐	☐	☐	☐	☐
11. … be relaxed.	☐	☐	☐	☐	☐
12. … get sick less often.	☐	☐	☐	☐	☐
13. … have more energy.	☐	☐	☐	☐	☐
14. … enjoy life more.	☐	☐	☐	☐	☐

| | Never | Almost Never | Sometimes | Fairly Often | Very Often |

If you do more than 60 minutes of physical activity every day you will…					
15. … be tired.	☐	☐	☐	☐	☐
16. … not have enough time for school.	☐	☐	☐	☐	☐
17. … not have enough time for other things.	☐	☐	☐	☐	☐
18. … not have time for friends.	☐	☐	☐	☐	☐
19. … get injuries.	☐	☐	☐	☐	☐

	Not At All Sure	Slightly Sure	Moderately Sure	Very Sure	Completely Sure
How sure are you that you will be physically active for 60 minutes …					
20. … from tomorrow?	☐	☐	☐	☐	☐
21. … this week while finishing all school work?	☐	☐	☐	☐	☐
22. … this week while finding time for rest?	☐	☐	☐	☐	☐
23. … this week without getting tired?	☐	☐	☐	☐	☐
24. … this week without getting injured?	☐	☐	☐	☐	☐

	Not At All Sure	Slightly Sure	Moderately Sure	Very Sure	Completely Sure
How sure are you that you will…					
25. … have a place to be physically active for 60 minutes per day?	☐	☐	☐	☐	☐
26. … be able to afford a place to be physically active for 60 minutes per day?	☐	☐	☐	☐	☐
27. … be able to use tools to be physically active for 60 minutes per day?	☐	☐	☐	☐	☐
How sure are you that you can…					
28. … direct your feelings to the goal of being physically active for 60 minutes every day?	☐	☐	☐	☐	☐
29. … inspire yourself to be physically active for 60 minutes every day?	☐	☐	☐	☐	☐

	Not At All Sure	Slightly Sure	Moderately Sure	Very Sure	Completely Sure
How sure are you that you can…					
30. … defy self-doubt in meeting the goal of being physically active for 60 minutes every day?	☐	☐	☐	☐	☐
How sure are you that you can…					
31. … keep a self-diary to monitor total time of your physical activity every day?	☐	☐	☐	☐	☐
32. … be physically active for 60 minutes every day even if you come across barriers?	☐	☐	☐	☐	☐
33. … change your plan for being physically active for 60 minutes every day if you face difficulties?	☐	☐	☐	☐	☐

	Not At All Sure	Slightly Sure	Moderately Sure	Very Sure	Completely Sure
How sure are you that you can get the help of a…					
34. …family member to be physically active for 60 minutes every day?	☐	☐	☐	☐	☐
35. …friend to be physically active for 60 minutes every day?	☐	☐	☐	☐	☐
36. …health worker to be physically active for 60 minutes every day?	☐	☐	☐	☐	☐

	Not At All Likely	Somewhat Likely	Moderately Likely	Very Likely	Completely Likely
How likely is it that you will…					
37. …increase your physical activity to 60 minutes from tomorrow.	☐	☐	☐	☐	☐
How likely is it that you will…					
38. … Increase your aerobic physical activity to 60 minutes every day from now on.	☐	☐	☐	☐	☐

SCORING

Construct of advantages: Scale: Never (0), Almost never (1), Sometimes (2), Fairly often (3), Very often (4). Summative score of Items 10-14. Possible range: 0- 20. High score associated with likelihood of initiation of behavior change.

Construct of disadvantages: Scale: Never (0), Almost never (1), Sometimes (2), Fairly often (3), Very often (4). Summative score of Items 15-19. Possible range: 0- 20. Low score associated with likelihood of initiation of behavior change.

Construct of participatory dialogue: Subtract disadvantages score from advantages score to calculate participatory dialogue construct score. Positive score will be indicative of behavior change.

Construct of behavioral confidence: Scale: Not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), completely sure (4). Summative score of Items 20-24. Possible range 0-20. High score associated with likelihood of initiation of behavior change.

Construct of changes in physical environment: Scale: Not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), completely sure (4). Summative score of Items 25-27. Possible range 0-12. High score associated with likelihood of initiation of behavior change.

Construct of emotional transformation: Scale: Not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), completely sure (4). Summative score of Items 28-30. Possible range 0-12. High score associated with likelihood of sustenance of behavior change.

Construct of practice for change: Scale: Not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), completely sure (4). Summative score of Items 31-33. Possible range 0-12. High score associated with likelihood of sustenance of behavior change.

Construct of changes in social environment: Scale: Not at all sure (0), slightly sure (1), moderately sure (2), very sure (3), completely sure (4). Summative score of Items 34-36. Possible range 0-12. High score associated with likelihood of sustenance of behavior change.

For modeling initiation dependent variable can be Item 37: not at all likely (0), somewhat likely (1), moderately likely (2), very likely (3), and completely likely (4) and multiple regression can be used. For modeling sustenance dependent variable can be Item 38: not at all likely (0), somewhat likely (1), moderately likely (2), very likely (3), and completely likely (4) and multiple regression can be used.

Flesch-Kincaid Grade level: 5.4
Flesch Reading Ease: 68

ORIGINAL ARTICLE

An educational intervention on based information, motivation and behavior skills model and predicting breast self-examination

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Keywords

Breast self-examination • Educational intervention and information • Motivation and behavior skills model

Summary

Introduction. *Breast self-examination recommend as a breast screening method in developing countries where there are limited access to other screening methods. Therefore promoting breast self-examination required to identify effective interventions and relevant factors.*
Methods. *This study was a quasi-experimental design carried out among 314 women 20-69 years in community cultural centers in Isfahan city, Iran. Sampling was conducted from April to 10 August, 2016. A structured questionnaire was used for data collection in before and after the educational intervention. Then participants were followed by phone call after one month for breast self-examination performance. We used descriptive statistical analysis (mean, standard division, frequency distribution), and also other statistical methods (Paired t-test, Pearson's correlation and logistic regression).The data were analyzed using SPSS version 18 with considering a significant level less than 0.05.*
Results. *There was significant difference between mean scores of information, motivation and behavior skill before and after intervention (P < .0001). After one month following 205 of women (72.2%) reported to perform breast self-examination. Pearson's correlation showed that breast self-examination significantly correlated with information (r = .305, p = .000), motivation (r = .128, p = .031) and behavior skills (r = .161, p = .006). Also the logistic regression results demonstrated that information (p < .001, OR = 1.071), motivation (p = .045, OR = .978) and behavior skills (p = .001, OR = 1.033) predicted breast self- examination.*
Conclusions. *Considering the results of this study, it appears that the use of educational interventions based on three constructs of information, motivation and behavior skills can be used to promote breast self-examination. Moreover these results can apply to improve breast self-examination among women by health care providers.*

Introduction

Cancer is the most common diseases leading mortality in world [1]. In recent years, breast cancer was one of the main diagnosed cancers among women (1.67 million) after lung cancer (1.82 million) globally. The data from Globocan in 2012 showed of the 1,600,000 new cases of breast cancer, 794,000 and 883,000 were in the more and less developed world respectively. But the deaths in the less developed world were higher, the 324,000 compared with 198,000 in more developed world [2]. Although the incidence of breast cancer was reported lower in less developed countries, the mortality rate of breast cancer in these countries was higher [3]. On the other hand in numerous developing countries, the incidence of breast cancer is rising severely [4]. The findings of the 10-year national cancer registry of Iran showed that breast cancer as the most common of cancer in Iranian females has the crude incidence 22.6 per 100,000 females annually [5].

Early detection of breast cancer is important, especially in low- and middle-income countries where breast cancer is diagnosed in late stages [6]. Mammography is an expensive method for breast cancer screening and requires logistic and trained manpower, while breast self-examination can be the only realistic method to the initial detection of breast cancer in developing countries [7]. For that reason there are no population-based mammography screening programs in Iran country and breast self-examination is recommended as a practical method for breast cancer screening [8]. However, Breast self-examination alone is not enough for early detection of breast cancer; it can increase breast health awareness of women and be responsible for their own health [9]. On the other hand breast self-examination can be performed by women and without help of health providers. Despite these advantages, Montazeri et al. revealed that only 17% of women performed breast self-examination regularly. They also indicated that 20% and 63% of women occasionally and never carried out breast self-examination, respectively [7].

Another study in 2012 noted that the rate of breast self-examination in Iranian women's was low and only 12.9% of women performed it regularly [10].
Numerous factors about participation of women in breast self - examination have been proposed. Avci et al. mentioned a relationship between health motivation and performing of breast screening methods [9]. Kawar showed embarrassment, fatalism, fear and stigmatization of cancer decreased breast cancer screening participation [11]. An American study revealed lack of knowledge as a barrier [12]. Others also demonstrated that women who never used from methods of breast screening, had lack of knowledge [7, 13]. Although a lot of women failure breast self-examination due to not know how to perform it correctly [14], there is evidence to show high self-efficacy was significantly associated with breast self-examination [15].
Consequently, a number of researches focused on interventions to increase breast cancer screening behavior [16]. The recently, information, motivation and behavioral skills model was introduced by Fisher and Fisher [17]. They firstly used this model to explain the behavior associated with HIV [18].This model mention to three constructs; information, motivation and behavioral skills. Each of these construct associate with performance a behavior. Moreover there are a numerous relationship among these constructs [17]. This model has useful aspects. First of all the IMB model is able to simply explain complex health behaviors [18].
Secondly, it can be considered as social psychological conceptualization and utility to increase health-related behavior [19]. Thirdly a successful self-management such as breast self- examination needs detect information, motivation and behavioral skills which are considered in this model [18].

Materials and methods

A quasi experimental design (before and after intervention) was used in this research. We invited women living in a region of Isfahan city to attend in educational classes using a numerous of advertising such as banners, flyers and free Messages.
Sampling was conducted from April to 10 August, 2016 in four community cultural centers of city. Community cultural centers have been created by municipality in numerous places of the district. In these centers, various classes are being held in different fields for women and children, such as arts, aerobics and healthcare. Likewise, these places have been appropriate settings for educational intervention in women who had lived in the region.
In this study inclusion criteria were included 20 to 69 years old women that have no history of breast cancer or specific diseases, being able to read and write and not having history of breast self- examination.
Women who have inclusion criteria participated in a two-hour class. They were educated by role playing, lecture and Power Point presentation. The education materials were provided based on Iranian Ministry of Health and Medical Education protocols. For performing role playing, first of all a scenario was written. Later some participants voluntarily were selected to play the scenario. The roles were included a client, a mother of client and a midwife. The researcher played as midwife. Then role playing was performed by players and rest of women observed it. Next women discussed and commented on the matter. Consequently all members of every group had an opportunity to share their experience and problems together.
Participation in this study was also on based written informed consent. A structured questionnaire was used for data collection. The data was collected using the questionnaire before and after the educational intervention on 314 women. The questionnaire included 40 questions in four domains: socio-demographic characteristics (n = 4), information (n = 22), and motivation (n = 7) and behavior skills (n = 7). A 5-point Likert scale from strongly disagree to strongly agree was used for answers to the questions of motivation and behavior skills. Yes/ no/ don't know questions were designed to check information.
The questionnaires were verified by a number of faculty members who were specialized in the field; such as health and midwifery. Also we determined reliability questionnaire by Cronbach's alpha. That was 0.80, 0.75 and 0.84 for information, motivation and behavior skills questions respectively. Consequently the questionnaire had adequate internal consistency. In addition, test retest method was used with 2-week interval in 15 women for reliability and in final sampling the 15 questionnaires were omitted.
In this study, the motivation was considered as personal and social motivation according to Fisher's proposition [18]. Social motivation encompassed perceived social support to perform breast self-examination and personal motivation comprised of beliefs about the outcome of interventions and attitude towards breast self-examination. Moreover, two concepts of objective individual skills and self-efficacy were considered as behavior skills in the model of information, motivation and behavior skills in this study [20].
Participants in the study were followed up with a phone call after a month of educational interventions for performing breast self- examination. Of the total samples (314 persons), 284 individuals responded to the call.

Data analysis

The data were analyzed using SPSS version 18 with considering a significant level less than 0.05. Descriptive statistical analysis (mean, standard division and frequency distribution), and also other statistical methods (Paired t-test, Pearson's correlation and logistic regression) were considered to analyze.
Pearson's Correlation was used for investigating the relationship between dependent variable (breast self-examination performance) and independent variables

(Age, Number of child, Education, Marital Status, Information, Motivation and Behavior skills). Moreover we used Logistic regression model to predict breast self-examination among the women.

In this study the sample size was concluded using $n = z^2 p(1-p)/d^2$. We assumed p = 25%, $Z^2 = 1.96$ and d = 0.05. In addition nonresponse was considered10%. The final sample size was determined to be about 300 in educational intervention.

Ethical consideration

This study was approved by Ethics Committee of the Medical Research of Isfahan University of Medical Sciences with the number of IR.MUI.REC.1394.3.256.

Results

A total of 314 participants with the average age and number of children (mean ± standard deviation) 45.53 ± 10.99 and 2.79 ± 1.74 respectively were entered into this study. Approximately majority of participants were married (90%). Moreover, 43.9% of them had obtained high school diploma.

Results of Paired t- test demonstrated that there was significant difference between mean scores of information, motivation and behavior skill before and after the educational intervention (P < .001) (Tab. I).

After one month following 205 of women (72.2%) reported to perform breast self-examination. Percentage of breast self- examination in women aged 50 to 59 (23.2%); married (66.2%), with high school education (42.3%) and two children (22.5%) were higher of other women in same groups (Tab. II).

Although the findings of Pearson's correlation revealed that there was positive significant correlation between education and breast self-examination (r = .129, p = .029), the study results indicated no significant correlation between other socio-demographic characteristics and breast self-examination. Additionally, Pearson's correlation showed that breast self-examination significantly correlated with information (r = .305, p = .000), motivation (r = .128, p = .031) and behavior skills (r = .161, p = .006) (Tab. III).

We used logistic regression analysis to predict breast self-examination behavior. Therefore, independent variables were considered in logistic regression analysis. The analysis results showed participants who had more information (p < .001, OR = 1.071), motivation (p = .045, OR = .978) and behavior skills (p = .001, OR = 1.033) were more probable to perform breast self-examination behavior. But logistic regression analysis didn't demonstrate a significant correlation between education (p = .299) and breast self-examination performance (Tab. IV).

Tab. I. Mean and standard division (SD) of information, motivation and behavior skills scores before and after intervention.

	Before		After		T test	P-value
	Mean	SD	Mean	SD		
Information	64.43	19.62	91.00	9.42	22.85	< .001
Motivation	79.46	13.71	89.41	10.02	11.78	< .001
Behavior skills	77.36	15.48	90.63	10.41	15.15	< .001

Tab. II. Frequency distribution of breast self- examination performance based on socio-demographic characteristics.

Socio-demographic characteristics	Breast self-examination performance - N (%)		
	No	Yes	Total
Age			
20-29	4 (1.4)	11 (3.9)	15 (5.3)
30-39	23 (8.1)	50 (17.6)	73 (25.7)
40-49	24 (8.5)	61 (21.5)	85 (30.0)
50-59	18 (6.3)	66 (23.2)	84 (29.5)
60-69	10 (3.5)	17 (6.0)	27 (9.5)
Education			
Primary	30 (10.6)	56 (19.7)	86 (30.3)
High school	39 (13.7)	120 (42.3)	159 (56.0)
University	10 (3.5)	29 (10.2)	39 (13.7)
Marriage status			
Marriage	68 (23.8)	188 (66.2)	256 (90)
Divorced	1 (.40)	3 (1.1)	4 (1.5)
Widow	5 (1.8)	11 (3.9)	16 (5.7)
Unmarried	5 (1.8)	3(1.0)	8(2.8)
Number of child			
0	4 (1.4)	13 (4.6)	17 (6.0)
1	8 (2.8)	27 (9.5)	35 (12.3)
2	29 (10.2)	64 (22.5)	93 (32.7)
3	15 (5.3)	39 (13.7)	54 (19.0)
4	11 (3.9)	26 (9.2)	37 (13.1)
≥ 5	12 (4.2)	36 (12.7)	48 (16.9)

Tab. III. Pearson's correlation of independent variables and breast self-examination performance.

Independent variables	Breast self-examination performance	
	Pearson correlation	Sig. (2-tailed)
Age	.012	.841
Number of child	.017	.779
Education	.129	.029
Marital Status	.11	.065
Information	.305	.000
Motivation	.128	.031
Behavior skills	.161	.006

Discussion

This study focused on investigation of educational interventions based on information, motivation and behavior skills model and predicting breast self-examination. The results of this study indicated that the use of lecture, Power Point presentation and role-playing as an educa-

Tab. IV. Results of logistic regression analysis.

Variable	B	S.E.	P value	Odds ratio	Confidence interval of Odds Ratio
Information	.066	.017	.000	1.071	1.033-1.105
Motivation	.033	.018	.045	0.978	0.947-0.981
Behavior skills	.051	.015	.001	1.033	1.010-1.075
Education	.088	.086	.299	0.981	0.957-1.198

tional intervention were accompanied by an increase in information, motivation and behavior skills in women.
These results agreed with findings of previous educational interventions which used a range of interventions. The study of Rahimparvar et al. (2017) demonstrated that audio visual teaching can increase the self-efficacy [21]. The findings of a research by Zeinomar showed Power Point presentations improved knowledge of breast cancer [22]. Avci and Gozum used video and the model group as educational interventions. They showed the video group improved knowledge of breast self- examination and the model group increased knowledge, perceived self-efficacy and skill of perform breast self- examination [23].
Other studies have found that role playing method improved knowledge, skills [24], intentions to health behavior [25] and self-efficacy [26].
Additionally, significant changes in awareness and perception of women about cancer and screening were reported through using lecture and movies [27].
The results of our study disclosed that three constructs of information, motivation and behavior skills had a significant correlation with breast self-examination after a month of interventions. In line with the findings of this study, results of Misovich's study revealed a correlation among breast self-examination, information, motivation and behavioral skills [28]. They mentioned the connection between IMB model`s constructs and a health behavior using a cross-sectional study and proposed designing interventions based on this model in order to improve health behavior.
In addition, the findings of present study showed that information, motivation and behavior skills in IMB model played a role in predicting the breast self-examination behavior. Therefore, based on the findings of present study, the model`s constructs could predict breast self-examination as a health behavior. The results of our study are consistent with findings of Huy's study which indicated IMB model`s constructs predicted using condoms [29].
In present study, there was a significant correlation between education and breast self-examination, however, education has not been reported as an effective predicator in breast self-examination. This result was supported by findings of other studies [30].
The findings of this study did not indicate any correlation between age and breast self-examination. There existed the same situation regarding variables of number of children and marital status. These findings were in accordance with results of Akhtari-Zavare`s study which demonstrated that there were not a significant correlation between breast self-examination and some demographic factors such as age and marital status [14].
The present study has strength points. Firstly, IMB model has been used as a framework in order to perform educational interventions in this study. Secondly, predicting breast self-examination behavior was investigated using IMB model`s constructs in a prospective study. There also have been limitations in our study. This study used samples that approached cultural centers. Therefore, generalizing the finding to whole community is being considered as limitation of this study. Moreover, the lack of control group, the short follow up and not considering information regarding women's predisposition to perform breast self-examination were other limitations of this study.

Conclusions

The results of this study shows that the use of educational interventions based on three constructs of information, motivation and behavior skills can be used to promote breast self-examination.
It is a fact that breast self-examination is a cheap and readily available screening test for breast cancer and a significant percentage of breast tumors are detected by self-examination. As using this method are proposed in some countries by world health organization, the findings of present study can apply to improve breast self-examination among women by health care providers.

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Conflict of interest statement

None declared.

Authors' contributions

Study design: MSE and FT and MT. Data collection: MSE. Data analysis: MSE and FT and MN. Study supervision: FT and MT and MN.Manuscript writing and revisions: MSE, FT and MN.

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ORIGINAL ARTICLE

Tackling breast cancer in developing countries: insights from the knowledge, attitudes and practices on breast cancer and its prevention among Nigerian teenagers in secondary schools

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Keywords

Breast self-examination • BSE • Breast cancer • Women • Secondary schools • Knowledge • Attitude • Practice

Summary

Background. *Breast cancer occurrences in developing countries are gradually matching caucasian levels. Since early detection is linked to reductions in morbidities and mortality, affordable screening techniques like breast self-examination (BSE) becomes imperative in these resource-limited economies. Ascertaining the Knowledge, Attitudes, and Practices (KAP) of breast cancers and BSE among young adult females will help provide baseline information for early and targeted interventions.*

Method. *A cross sectional survey involving 432 female senior secondary school students in Otuocha Educational Zone of Anambra State, Nigeria.*

Results. *A total of 321 (74.3%) valid questionnaires were returned. Mean age was 16.79 ± 1.48 years. Even though 84.6% and 55.2% had respectively heard about breast cancer and BSE, and the 'General Knowledge' of breast cancer was high (75.2%), specifics on 'Risk Factors' (41.5%) and 'Symptoms' (46.1%) were poor.*

Knowledge on correct BSE 'Techniques' was 52.9%, but few know when to commence (43.1%), the right frequency (31.5%), or the right timing (24.6%). A large majority (73.6%) had positive attitudes, but only 6.1% practice it monthly, while 55.3% had never done it at all. No significant predictors of Knowledge and Practice of BSE was identified.

Conclusion. *Health campaigns on BSE and breast cancers should provide specific details on techniques, risk factors and symptoms, while emphasizing on the right methods, timing and frequency. The positive attitudes identified raise optimism that health interventions would be effective and can have long term benefits. If possible, BSE and breast cancer teachings should be included in the secondary school academic curricula of resource-limited countries.*

Introduction

Besides lung and non-melanoma skin cancers, breast cancer is the commonest malignancy worldwide, constituting 11.9% of all cancers [1], with a male to female ratio of 1:67 [2]. It is the 5th commonest cause of deaths from cancers worldwide, accounting for 571,000 deaths in 2015 [3]. Its incidence among women has reportedly been on a steady increase, from 1:20 in 1960, to the current 1:8 [4].

Breast cancer reduces the life expectancy of affected population aged 31 and 50 years [5, 6], 3.5% of which are expected to die [6]. Early detection is associated with lower morbidities and mortalities [7], so it is not a surprise that 85% [8] to 95% [7, 9], of affected patients survive with early detection, while only 56% [8] survive if diagnosed late.

Two key facilitators of early detection are health education and screening [10]. Screening methods include breast self-examination (BSE), clinical breast examination (CBE), and mammography [11]. Even though CBE and mammography in developing countries are becoming increasingly available in recent years [7], their wide scale utilization in these resource-limited economies are poor due to significant financial and manpower limitations. Conversely, BSE offers a simple, cheap, and non-invasive screening option [10, 12, 13].

Breast cancers, unlike most others, occur in an organ (breast) that is easily visible [9, 14], and BSE is the visual and manual examination of breasts for lumps, bumps, and skin changes over nipples and breasts [4]. Monthly BSE is recommended from age 20 [4], Even though its efficacy in preventing breast cancer deaths is unproven [15, 16], it remains a free, painless and easy-to-practice technique, which helps improve body awareness, allowing changes potentially indicative of breast cancer to be picked up early [17, 18]. Alongside other screening methods, BSEs can improve outcomes and reduce mortality by as much as 25% [19].

Even though traditionally, Caucasian women have higher ocurrences, breast cancer incidence is reportedly rising in populations with previously low cases (mainly developing countries like Nigeria). This is presumably because more women increasingly adopt western lifestyles [6, 20] like the use of tobacco and alcohol, as well as the attainment of tetiary education by most females,

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which results in late marriages and delayed first pregnancies (> 30 years) [10].

Delayed presentations >3 months are considered prolonged [2], but notably, only 20%-30% of Caucasians delay this long, as against 70% of African women [2, 21, 22]. Overall, affected Africans present at least a decade earlier than their Caucasian counterparts [20], during which time their lesions are bigger, [23, 24] more aggressive [25-28], advanced [29], and with poor prospects of long-term survivals [23, 30]. Five-year survival rates of breast cancers in Nigeria is < 10% compared to the 70% from developed countries [13, 22]. These racially-observed variations may not be solely due to socioeconomic differences [28], but largely attributable to the lack of early detection programmes and poor diagnostic and treatment facilities [5, 10, 14].

Even though the mean age of presentation in Nigeria is 42 to 44 years [2, 26, 31], prognosis in younger patients aged < 40 years is poor [32], and early screening and detection is vital [17]. While reports vary, one study found that 12% of the cancers in Nigeria are among those aged < 30, the youngest being a 16 year old [33]. Another paper reported occurrences in patients aged 14-96 years, with 70% among 26-50 year olds and cumulative frequencies of 0.8% at ≤ 20 years and 3.3% at < 25 years [21]. These statistics suggest that breast cancer should not be neglected among the under 30s. Therefore, ascertaining their KAP regarding breast cancers and BSE provides baseline information valuable to concerned stakeholders in the design and implementation of targeted interventions aimed at early disease prevention [34], improving survival rates [4, 35, 36] and quality among survivors [37].

Unfortunately, only a handful of studies have ever looked at BSE among Nigerian secondary school students [10, 32, 38] and young undergraduates [37], and none has ever looked at South-East Nigeria, an area culturally and socially different from the rest of the country. This study reduces this knowledge gap, and contributes to the growing literature regarding early preventive approaches to breast cancer in resource-limited environments exemplified by a developing country like Nigeria.

Methods

Setting and participants

The participants included all female final year high school (called senior secondary school or SSS-3) students in the 26 government-owned schools within the Otuocha Post Primary Schools Service Commission (PPSSC) Educational Zone of Anambra State, Nigeria. The Otuocha PPSSC is one of the six Educational Zones in the State, [39] and covers three of the state's 21 Local Government Areas (LGAs), which include Anambra East, Anambra West, and Ayamelum. Anambra State is one of Nigeria's 36 states, and is predominantly inhabited by Christians of the "Igbo" tribe located in the South Eastern part of the country, in West Africa. It has a projected 2016 population of 5,527,800 (based on the 2006 census) [40].

Inclusion and exclusion criteria

Participants must be female final year (SSS-3) students enrolled in one of the eligible secondary schools as at the time of the study. Boys and students in privately-owned schools were excluded. Overall, 10 schools with 190 students were eligible from Anambra East LGA, 7 schools (with 92 students) from Anambra West LGA, and 9 schools (with 150 students) from Ayamelum LGA. Two schools (one each from Anambra East and Ayamelum LGAs) were all-boy schools, and these were excluded, leaving a total of 24 schools and 432 participants.

Study design

This study is a Cross Sectional, self-completed, questionnaire-based survey targeting all eligible participants, and is part of a larger study that explored the KAP of the participants regarding Breast Cancer, BSE and Cervical Cancers. Cervical cancer was not covered in this paper.

Questionnaire

This was developed from validated questions adapted from previous publications [4, 14, 32, 41]. However, given that some of the wordings were modified to suit our participants, the document was piloted using 20 SSS-3 students in different PPSSCs in Anambra State. Feedbacks from them, along with inputs from professional colleagues, were used to develop the final Questionnaire (Annex 1).

The questionnaire was divided into four parts. Part 1 contained the Introduction and Consent, while Part 2 (8 questions) covered the basic respondent demographics. Part 3 (12 questions) collects information on the participants' KAP on Breast Cancers and BSE. Under this Part 3, Knowledge questions for Breast Cancers were explored with Question Numbers 1 (Early Symptoms), 8 (Risk Factors) and 10 (General). BSE was covered by other questions in Part 3 as follows: General Knowledge (Number 2); Knowledge of BSE Methods (Questions 3, 4 and 12); Attitudes and Practices (Questions 9 and 11 respectively). Questions 5, 6 and 7 explored those that have heard about breast cancers and BSE, as well as their sources. To eliminate responses based on speculations by the participants, some of the questions were worded negatively, while others were presented positively.

Part 4 of the Questionnaire had 10 major questions, and explored the Knowledge and Attitudes on Cervical Cancers, which are not covered in this paper.

The final, validated tool was dispatched and returned within one week from September 18th 2017 through the Zonal Director to the various school principals, with each school getting exactly the number for their eligible students.

Data entry and analysis

All analysis were with IBM® SPSS version 25.0. Most responses to the questions and sub-questions in Part 3

had options of 'Yes or Agree', 'Not Sure or Unsure' and 'No or Disagree'. For positive questions, these attracted scores of 3, 2 or 1 respectively, and were reversed accordingly for all negative items. Percentages were worked out and interpreted in line with the methods of a previous publication,[4] with '≥70%' indicating Excellent, while '50-69%' and '< 50%' signify Moderate and Poor respectively.

The Binary Logistics Regression (BLR) was used to explore statistical associations,. Three Independent (Predictor) Variables and Three Dependent (Outcome) Variables were tested, with variables dichotomized as necessary. The three Predictor Variables include each of the "educational status of father and mother ('Primary/Not at all' Versus 'Secondary/Tertiary')" and "Knowledge of family member or anyone with breast cancer (Yes or No)". The three Outcome Variables include: "Whether BSE has ever been practised", "If BSE is Practised Monthly", and "If BSE is practised 7-10 days after periods". The responses to each Outcome Variable was dichotomized to "Yes or No". All associations with p-values of < 0.05 are significant.

Results

A total of 390 out of the 432 dispatched questionnaires were returned, but only 321 had enough components completed to warrant inclusion in the analysis. This gives a 74.3% response rate.

The basic respondent characteristics (Tab. I)

The ages range from 13-25 years (Mean of 16.79 ± 1.48). Only 4.1% have a family member that had been affected with breast cancer, while 82.1% know no one that is affected, be it a family member or anyone else. About 84.6% has heard about breast cancer, while 55.2% has heard about BSE.

The best sources of information include Television/Radio (50.5%), school teachers (49.2%), health workers (46.1%), and the print media (43.0%).

General knowledge, symptoms and risk factors of breast cancer (Tab. II)

Most respondents (75.2%) had an excellent 'General Knowledge' of breast cancer (Tab. IIA), but specific Knowledge on the 'Risk Factors' (41.5%; Tab. IIB) and 'Early Symptoms' (46.1%; Tab. IIC) were poor.

Knowledge, attitudes and practice of BSE (Tab. III)

Only one single question each correctly represented the 'Knowledge on who should do BSE', its 'Frequency', and its 'Timing', and all three responses were poor. Only 43.1% know that any woman above the age of 20 years should practice BSE (Tab. IIIA), while less than one-third (31.5%) know that it should be done monthly (Tab. IIIB). Only one-quarter (24.6%) know that BSEs are best carried out about one week after the monthly periods cease.

Multiple positive and negative questions explored the 'Knowledge on Techniques of BSEs' (Tab. IIID), and the average revealed a level that is just Moderate (52.9%).

'Attitude' to BSE is Excellent (73.6%; Tab. IV), but, as shown in Table V, about 55.3% of the respondents had never practised BSE, while only 6.1% do so at the correct monthly frequency.

Predictors of BSE (Tab. VIA-B-C)

No significant predictors of the Practice of BSE, or their Knowledge on its Frequency and Timing were identified.

Discussion

At 74.3%, the response rate from this study is decent, even though it is less than the 95.7% and the 91.7% recorded in similar studies of female secondary school students elsewhere in Nigeria [10] and Saudi Arabia [17] respectively. Also, the mean age (in years) of 16.79 ± 1.48 for the participants from our study bears a striking similarity to the rates from studies that looked at other Nigerian schools in Abuja [10] and Lagos [32], as well those from overseas studies of similar high school female students [42]. Our finding that only 4.1% of the respondents reported a positive family history of breast cancer is also consistent with the 4% reported in a previous Nigerian study [2]. These similarities to findings of previous publications, along with the decent response rate of this study, suggest that our findings might be representative, and hopefully, generalizable.

It is encouraging that over 4-in-5 (84.6%) and a little more than half (55.2%) of the respondents had respectively heard of breast cancer and BSE prior to our study. This would imply that a good knowledge base does exist for any health enlightenment campaign, since issues on these subjects would not be completely new. Interestingly, these proportions are consistent with levels reported in similar Nigerian studies from Abuja (100% on breast cancer and 58.5% on BSE) [10] and Lagos (97% on cancer and 56.4% on BSE) [32], but higher that the 37.9% of students that has heard about BSE in a Turkish study [42]. Cultural or religious differences may be responsible for the difference between the two nations.

Unfortunately, the fact that our participants have a moderate level of BSE awareness has not translated to reasonably high levels of Knowledge and Practice of BSEs. For instance, only 43.1% know that any woman above the age of 20 years should practice BSE, while one-third (31.5%) and one-quarter (24.6%) respectively know the correct Frequency and Timing. Even more disappointing is the fact that a much lower number (6.1%) actually do practice BSE on a monthly basis, while 55.3% had never practised it at all. These findings call for action, given the already-stated benefits of BSE in resource-limited economies like Nigeria, where it may be the only affordable screening measure available to millions of women. Compared to similar Nigerian studies, the 31.5% with proper knowledge of monthly BSEs is somewhat sim-

Tab. I. Demographics and characteristics of female senior secondary school students in State Government-owned schools of Otuocha Educational Zone, Anambra State, Nigeria.

S/N	Respondent variable	Various components	Number	Percent
1.	Age Details (n = 317)	Mean	16.79	
		Mode	17	
		Median	17.00	
		Standard deviation	1.475	
		Range	12 (13-25)	
2.	Local Government Area (n = 307)	Anambra East	158	51.5
		Anambra West	57	18.6
		Ayamelum	92	30.0
3.	Knowledge of someone with breast cancer (n = 290)	Yes: family member affected	12	4.1
		Yes: none family member	40	13.8
		No: I know no affected person	238	82.1
4.	Mother's highest educational attainment (n = 312)	Not educated at all	31	9.9
		Completed primary school	119	38.1
		Completed secondary school health	123	39.4
		Completed post-secondary education (university, polytechnic, etc.)	39	12.5
5.	Father's highest educational attainment (n = 307)	Not educated at all	29	9.4
		Completed primary school	117	38.1
		Completed secondary school	118	38.4
		Completed post-secondary education (university, polytechnic, etc.)	43	14.0
6.	Source of information regarding BSE* and breast cancers (This questions allowed respondents to tick multiple answers)	Television/radio	162	50.5
		School teachers	158	49.2
		Health workers (doctors, nurses, etc.)	148	46.1
		Newspaper/magazines/textbooks	138	43.0
		Friends/peers	113	35.2
		Internet (Facebook, Google, Twitter, etc.)	102	31.8
		Home/family	101	31.5
		Church	51	15.9
		Not sure	16	5.0
7.	Ever heard of BSE? (n = 315)	Yes	174	55.2
		No	114	36.2
		Not sure	27	8.6
8.	Ever heard of breast cancer? (n = 318)	Yes	269	84.6
		No	43	13.5
		Not sure	6	1.9

*BSE: Breast self-examination

ilar to the 36.4% found in Oyo State [38], but higher than the 18.8% reported from Abuja [10]. At 24.6%, the knowledge of the Timing of BSEs is much lower than the 51.8% from the Oyo State study [38], but higher than the 12.5% recorded in Abuja [10]. Similarly, the 6.1% that correctly practise BSE in our study is only slightly less than the 10.1% [10] and 14.5% [38] reported from the aforementioned studies, as well as the 19.0% found among slightly older undergraduates in a Nigerian University [37], while the 55.3% that had never practised BSE at all is similar to the 58.2% reported among a similar group of students in Oyo State, Nigeria [38].

Comparable overseas studies involving high school students of similar age and academic level also exist. Both of our findings on the knowledge of correct Frequency and Timing of BSEs were respectively higher than the 21.8% and 13.2% reported in a Turkish study [42], while the rate on actual practice of BSEs is nearly identical to the 6.7% [42] reported by the same Turkish study, but slightly higher than the 3.4% [17] from a Saudi Arabian study. International comparisons should be interpreted with caution though, given the likely difference in culture and religion among the two countries.

One more interesting finding on the knowledge of BSEs is that, when the responses of all the positive and negative questions are factored in (Tabl. IIIA), the general knowledge on BSE Practise moves from Poor (for the individual positive items), to Moderate level (65.9%). This shows that, even though the participants may have a poor knowledge of what is right, they seem to have a good idea of what is wrong regarding BSE. This observation has a huge implication for health education campaigns, since the emphasis has to be on promoting the right practices, and less so on potentially wrong ones. Compari-

Tab. II. Knowledge of breast cancer, its early symptoms, and its risk factors among female senior secondary school students in State Government-owned schools of Otuocha Educational Zone, Anambra State, Nigeria.

S/N	Description	Agree (%)	Unsure (%)	Disagree (%)	Total scores** (average: 1 to 3)	Correct scores* (% of average)
A. General knowledge on breast cancers (Q10, Part 3 of Questionnaire)						
1	Breast cancer is a common cause of cancers deaths among Nigerian women (n = 318)	242 (76.1)*	53 (16.4)	24 (7.5)	854 (2.69)	726 (85.0)
2	Any woman aged ≥20 can develop breast cancer (n = 317)	179 (56.5)*	88 (27.8)	50 (15.8)	763 (2.41)	537 (70.4)
3	Breast cancer is transmissible (n = 314)	56 (17.8)	100 (31.8)	158 (50.3)*	730 (2.32)	474 (64.9)
4	BSE can help detect and prevent breast cancers (n = 316)	209 (66.1)*	64 (20.3)	43 (13.6)	798 (2.53)	627 (78.6)
Totals					3,145 (2.49)	2,364 (75.2)
B. Knowledge of Risk Factors For Breast Cancers (Q8, Part 3 of Questionnaire)						
5	Early onset of menstruation; < 11 years (n = 316)	49 (15.5)*	140 (44.3)	127 (40.2)	554 (1.75)	147 (26.5)
6	Late onset of menstruation; > 16 years (n = 314)	37 (11.8)	164 (52.2)	113 (36.0)*	704 (2.24)	339 (48.2)
7	Having no babies at all (n = 317)	25 (7.9)*	130 (41.0)	162 (51.1)	497 (1.57)	75 (15.1)
8	Having many babies; > 4 (n = 309)	21 (6.8)	115 (37.2)	173 (56.0)*	770 (2.49)	519 (67.4)
9	Eating a high fatty diet (n = 314)	55 (17.5)	161 (51.3)	98 (31.2)*	671 (2.14)	294 (43.8)
10	Using the birth control pill (n = 305)	57 (18.7)	179 (58.7)	69 (22.6)*	622 (2.04)	207 (33.3)
11	Having a family history of breast cancer (n = 313)	85 (27.2)*	109 (34.8)	119 (38.0)	592 (1.89)	255 (43.1)
12	Early onset of sexual intercourse (n = 312)	69 (22.1)	144 (46.2)	99 (31.7)*	654 (2.10)	297 (45.4)
13	Having a urinary tract infection (n = 313)	79 (25.2)	158 (50.5)	76 (24.3)*	623 (1.99)	228 (36.6)
Totals					5,687 (2.02)	2,361 (41.5)
C. Knowledge of early symptoms of breast cancer (Q1, Part 3 of Questionnaire)						
14	Pain in the breasts (n = 319)	164 (51.4)	91 (28.5)	64 (20.1)*	538 (1.69)	192 (35.7)
15	Chest pain (n = 313)	59 (18.8)	152 (48.6)	102 (32.6)*	669 (2.14)	306 (45.7)
16	Headache (n = 309)	66 (21.4)	103 (33.3)	140 (45.3)*	692 (2.24)	420 (60.7)
17	Breast lump (n = 314)	141 (44.9)*	118 (37.6)	55 (17.5)	714 (2.27)	423 (59.2)
18	Lump in armpit (n = 309)	67 (21.7)*	145 (46.9)	97 (31.4)	588 (1.90)	201 (34.2)
19	Unilateral nipple discharge (n = 314)	103 (32.8)*	139 (44.3)	72 (22.9)	659 (2.10)	309 (46.9)
20	Nipple discharge in a pregnant person (n = 309)	62 (20.1)	148 (47.9)	99 (32.0)*	655 (2.12)	297 (45.3)
21	Nipple discharge when squeezed (n = 313)	73 (23.3)	165 (52.7)	75 (24.0)*	628 (2.01)	225 (35.8)
Totals					5,143 (2.05)	2,373 (46.1)
Grand totals for breast cancer knowledge		13,975 (2.19) 7,098 (50.8)				

-**Total Scores are derived by the sum of the following: Correct Responses (marked with *; multiply by 3) + Unsure (multiply by 2) + Incorrect (multiply by 1)
-Result Interpretation: ≥ 70% = Excellent knowledge; ≥ 50 to < 70% = Moderate knowledge; < 50% = Poor knowledge
-BSE = Breast Self-examination

sons reveal that these findings were broadly consistent with similar Nigerian [10, 38] and overseas [42] studies, which all either reported poor or moderate levels of knowledge (not practice) of BSEs.

A striking and very important finding of our work concerns the Attitude of the respondents towards BSE, where the 73.6% positive attitude is within the 'Excellent' range. A similar study in Abuja, Nigeria [10], also reported an 82.6% positive attitude. Combined, these high positive attitudes imply that, despite the low levels of knowledge and practise of BSEs in Nigeria, young females are keen to learn and follow recommendations, and, any well-designed and culturally-appropriate health intervention on BSEs, would be well received.

Regarding breast cancer, the poor levels of specific knowledge of the *Risk Factors* (41.5%) and *Early Symptoms* (46.1%) seem to agree with findings of similar groups in Nigeria [10],Turkey [42], and Saudi Arabia [17]. However, the seemingly high level of *General Knowledge* (75.2%) on breast cancer issues is likely to be due to the fact that we factored in both negative and positive knowledge. Again, these observations highlight the need for health educators to emphasize more on specific positive behaviours, rather than on more general and negative ones.

Tab. III. Knowledge of Breast Self-Examination (BSE) among female senior secondary school students in State Government-owned schools of Otuocha Educational Zone, Anambra State, Nigeria.

S/N	Description	Agree (%)	Unsure (%)	Disagree (%)	Total scores** (average: 1 to 3)	Correct scores* (% of average)
A. Knowledge of who should practice BSE (Q2, Part 3 of Questionnaire)						
1	All women ≥20 years (n = 320)	138 (43.1)*	103 (32.2)	79 (24.7)	699 (2.18)	414 (59.2)
2	Only married women (n = 313)	36 (11.5)	84 (26.8)	193 (61.7)*	783 (2.50)	597 (73.9)
3	Only sexually active women (n = 317)	55 (17.4)	93 (29.3)	169 (53.3)*	748 (2.36)	507 (67.8)
4	Only women that have been pregnant (n = 317)	32 (10.1)	117 (36.9)	168 (53.0)*	770 (2.43)	504 (65.5)
5	Only post-menopausal women (n = 318)	39 (12.3)	109 (34.3)	170 (53.5)*	767 (2.41)	510 (66.5)
6	Only women with positive family history of breast cancer (n = 319)	77 (24.1)	105 (32.9)	137 (42.9)*	698 (2.19)	411 (58.9)
Totals					**4,465 (2.35)**	**2,943 (65.9)**
B. Knowledge of BSE Frequency (Q3, Part 3 of Questionnaire)						
7	Once a day (n = 314)	72 (22.9)	118 (37.6)	124 (39.5)*	680 (2.17)	372 (54.7)
8	Once a week (n = 312)	74 (23.7)	131 (42.0)	107 (34.3)*	657 (2.11)	321 (48.9)
9	Once a month (n = 314)	99 (31.5)*	127 (40.4)	88 (28.0)	639 (2.04)	297 (46.5)
10	Once every 6 months (n = 311)	51 (16.4)	136 (43.7)	124 (39.9)*	695 (2.23)	372 (53.5)
11	Once every year (n = 312)	46 (14.7)	112 (35.8)	155 (49.5)*	735 (2.35)	228 (31.0)
Totals					**3,406 (2.18)**	**1,590 (46.7)**
C. Knowledge of BSE Timing (Q4, Part 3 of Questionnaire)						
12	Anytime during cycle (n = 317)	133 42.0	108 (34.1)	76 (24.0)*	577 (1.82)	228 (39.5)
13	During menstrual flow (n = 314)	88 (28.0)	130 (41.4)	96 (30.6)*	636 (2.03)	288 (45.3)
14	7 to 10 days after periods (n = 313)	77 (24.6)*	153 (48.9)	83 (26.5)	620 (1.98)	231 (37.3)
15	Midway through your cycle (n = 312)	49 (15.7)	175 (56.1)	88 (28.2)*	663 (2.13)	264 (39.8)
16	7 to 10 days before period (n = 313)	62 (19.8)	157 (50.2)	94 (30.0)*	658 (2.10)	282 (42.9)
Totals					**3,154 (2.01)**	**1,293 (41.0)**
D. Knowledge of BSE Techniques (Q12, Part 3 of Questionnaire)						
17	Standing in front of a mirror (n = 315)	174 (55.2)*	86 (27.3)	55 (17.5)	749 (2.38)	522 (69.7)
18	Lying down (n = 311)	77 (24.8)*	139 (44.7)	95 (30.5)	604 (1.94)	231 (38.2)
19	Use one hand to examine the opposite one, and vice versa (n = 312)	149 (47.8)*	118 (37.8)	45 (14.4)	728 (2.33)	447 (61.4)
20	Use finger pads/pulps (n = 312)	101 (32.4)*	146 (46.8)	65 (20.8)	660 (2.12)	303 (45.9)
21	Use fingernails to examine (n = 310)	45 (14.5)	135 (43.5)	130 (41.9)*	705 (2.27)	390 (55.3)
22	Use palms to examine (n = 310)	75 (24.2)	137 (44.2)	98 (31.6)*	643 (2.07)	294 (45.7)
23	Use one finger only (n = 311)	51 (16.4)	134 (43.1)	126 (40.5)*	697 (2.24)	378 (54,2)
24	Use the 3 middle fingers only (n = 308)	62 (20.1)*	154 (50.0)	92 (29.9)	586 (1.90)	186 (31.7)
25	Use circular motions till all parts are covered (n = 312)	125 (40.1)*	129 (41.3)	58 (18.6)	691 (2.21)	375 (54.3)
26	Use vertical motions till all parts covered (n = 313)	117 (37.4)*	143 (45.7)	53 (16.9)	690 (2.20)	351 (50.9)
27	Examine breasts in wedges till all parts examined (n = 311)	103 (33.1)*	162 (52.1)	46 (14.8)	679 (2.18)	309 (45.5)
28	Press the nipple to check for any discharge (n = 312)	126 (40.4)*	133 (42.6)	53 (17.0)	697 (2.23)	378 (54.2)
29	Examine the armpit for lumps (n = 305)	108 (35.4)*	134 (43.9)	63 (20.7)	655 (2.15)	324 (49.5)
30	Look for any changes in breast size or shape (n = 310)	167 (53.9)*	105 (33.9)	38 (12.3)	649 (2.42)	501 (77.2)
31	Look at shape of nipples (n = 312)	123 (39.4)*	147 (47.1)	42 (13.5)	705 (2.26)	369 (52.3)
32	Raise one hand above the head while examining breast on that side (n = 313)	147 (47.0)*	111 (35.5)	55 (17.6)	718 (2.29)	441 (61.4)
33	Undress to the waist (n = 311)	86 (27.7)*	135 (43.4)	90 (28.9)	618 (1.99)	258 (41.7)
Totals					**11,464 (2.19)**	**6,057 (52.9)**
Grand totals for BSE knowledge		**22,489 (2.18)** **11,883 (52.84)**				

-**Total scores are derived by the sum of the following: Correct responses (marked with *; multiply by 3) + Unsure (multiply by 2) + Incorrect (multiply by 1)

- Result interpretation: ≥ 70% = Excellent knowledge; ≥ 50 to < 70% = Moderate knowledge; < 50% = Poor knowledge

Tab. IV. Attitudes to Breast Self-Examination (BSE) among female senior secondary school students in State Government-owned schools of Otuocha Educational Zone, Anambra State, Nigeria.

S/N	Description (Question 9; Part 3 of the Questionnaire)	Agree (%)	Unsure (%)	Disagree (%)	Total scores** (average: 1 to 3)	Correct scores* (% of average)
1	I am healthy and do not need to examine my breasts (n = 319)	119 (37.3)	68 (21.3)	132 (41.4)*	651 (2.04)	396 (60.8)
2	Examining my breasts by myself is important and necessary (n = 317)	216 (68.1)*	55 (17.4)	46 (14.5)	804 (2.54)	648 (80.6)
3	I am not well informed on how to examine my breasts (n = 318)	148 (46.5)	65 (20.4)	105 (33.0)	NB: This item was not scored and not part of the calculations	
4	I feel shy and embarrassed about examining my breasts by myself (n = 318)	61 (19.2)	54 (17.0)	203 (63.8)*	778 (2.45)	609 (78.3)
5	Examining my breasts by myself will be painful (n = 314)	57 (18.2)	95 (30.3)	162 (51.6)*	733 (2.33)	486 (66.3)
6	I am afraid that examining my breasts might reveal breast cancer (n = 314)	61 (19.4)	88 (28.0)	165 (52.5)*	732 (2.33)	495 (67.6)
7	Examining my breasts by myself will waste a lot of my time (n = 311)	54 (17.0)	79 (24.9)	184 (58.0)*	764 (2.41)	552 (72.3)
8	Examining my breasts by myself is a dirty practice and against my values or beliefs (n = 318)	56 (17.6)	69 (21.7)	193 (60.7)*	773 (2.43)	579 (74.9)
9	I will not like to touch my breasts in the way required for me to examine it (n = 318)	76 (23.9)	74 (23.3)	168 (52.8)*	728 (2.29)	504 (69.2)
10	If I find a suspicious lump while examining my breasts, I will see a medical doctor rather than a traditional healer (n = 316)	230 (72.8)*	44 (13.9)	42 (13.3)	820 (2.59)	690 (83.8)
Grand totals for bse attitude					**6,738 (2.19)**	**4,959 (73.6)**

-**Total scores are derived by the sum of the following: Correct responses (marked with *; multiply by 3) + Unsure (multiply by 2) + Incorrect (multiply by 1)
-Result Interpretation: ≥ 70% = Excellent knowledge; ≥ 50 to < 70% = Moderate knowledge; < 50% = Poor knowledge

Tab. V. Practice of Breast Self-Examination (BSE) among female senior secondary school students in State Government-owned schools of Otuocha Educational Zone, Anambra State, Nigeria (n = 313).

S/N	Have you ever practised BSE	Number	Percent
1	Never	173	55.3
2	Once ever	47	15.0
3	Once daily	53	16.9
4	Once weekly	16	5.1
5	Once monthly	19	6.1*
6	Once six monthly	2	0.6
7	Once yearly	3	1.0

*Correct practice

This study also found that nearly all sources of information for the participants on BSE and breast cancers were poor, with the best source (Television/Radio) benefitting just 50.5%. The rest of the sources, including information from school teachers, health workers, print media, church, internet, family, and peers, were all below 50%. This observation opens up a huge window of opportunity, as measures to involve school teachers and religious institutions (churches and mosques) in these campaigns will improve the reach and efficacy of the programs. This is recommended because school and religious events are popular in Nigeria, with 75.6% of Nigerians aged 15 to 24 years being literate [43], while 90% of the entire population identify as Christians or Muslims [44]. Unfortunately, other supposedly effective and popular means of information dissemination in the developed world (internet and electronic media), are not easily accessible to most Nigerians, due to poor power supply and high costs. Their role, for now, can only be complementary to schools and churches/mosques.

Finally, it is surprising that no significant associations were found between the participants' knowledge of someone affected with breast cancer (family or otherwise) or their parents' educational attainments, on the

Tabl. VI. Influence of "parental educational attainment" and "the knowledge of someone with breast cancer" on the Practice, Frequency, and Timing of BSEs* among Senior Secondary School students in State Government-owned schools of Otuocha Educational Zone, Anambra State, Nigeria.

S/N	Characteristic	Odds Ratio (OR)	Confidence Interval		p-value
			Lower	Higher	
A. Respondent knows someone with breast cancer (family or other)					
1.	Have practised BSE* at least once before (n = 285)	0.79	0.43	1.46	0.46
2.	Knows that BSE* is recommended to be done monthly (n = 284)	1.12	0.58	2.17	0.74
3.	Knows that BSE* is recommended to be done 7-10 days after menses (n = 284)	1.10	0.54	2.24	0.79
B. Father's education less than secondary/tertiary level					
1.	Have practised BSE* at least once before (n = 301)	0.78	0.50	1.24	0.30
2.	Knows that BSE* is recommended to be done monthly (n = 301)	1.00	0.61	1.61	0.98
3.	Knows that BSE* is recommended to be done 7-10 days after menses (n = 301)	1.06	0.63	1.80	0.82
C. Mother's education less than secondary/tertiary level					
1.	Have practised BSE* at least once before (n = 306)	0.90	0.58	1.42	0.66
2.	Knows that BSE* is recommended to be done monthly (n = 305)	1.08	0.67	1.75	0.75
3.	Knows that BSE* is recommended to be done 7-10 days after menses (n = 306)	1.07	0.64	1.80	0.80

*BSE: Breast self-examination.

Knowledge of the Frequency and Timing of BSEs. Even though aspects of these none associations broadly agree with a study that showed no association between BSE and family history of breast cancer [42], as well as those of a few others [10, 17] that also found no association with age and other sociodemographic characteristics not covered in this work, these findings are generally not in line with majority of existing publications in this area. For instance, some previous studies have shown associations with family history of breast cancers [17, 37], knowledge of BSE [10, 42], and parental educational attainment [10].

Strengths

The fact that all eligible participants were contacted, and a reasonably high response rate received, indicate that our findings are likely to be representative, and thus generalisable. Also, the incorporation of both positive and negative questions, which were accounted for in the analysis, minimized the potential impact of speculative responses thereby making the findings more reliable. Finally, the wordings of the questionnaire were in simple, plain language, with efforts made to 'regularize' medical terms, ensuring that the respondents would have understood the questions asked.

Weakness

A higher response rate (≥ 90%) would have been welcomed, but, given that the responses are arguably representative and consistent with previously published data, the potential impact of this is likely to be minimal.

Conclusions

We conclude that, while most students have heard about breast cancer, the specific knowledge on its risk factors and early warning symptoms are poor, while the actual practise of BSE is very poor. While participants have an excellent attitude towards BSE, their Knowledge on its Timing and Frequency were poor, while that on Technique is only moderate. No significant predictors of BSE were identified, and popular sources of information are not in place for the respondents.

Recommendations

Firstly, health campaigns on breast cancer and BSE should be very specific on techniques, risk factors and symptoms, and emphasize more on the right methods, timing and frequency of the practices. Such programs are expected to be very effective and achieve long lasting impacts, given the hugely positive attitude of the respondents,

Secondly, more should be done to involve schools and religious institutions in the dissemination of information regarding breast cancers and BSE, given that these are popular and cheap avenues in Nigeria. In fact, including BSE and relevant breast cancers topics in the school curriculum of Nigerian (and overseas) senior secondary students is highly recommended, while religious institutions (churches and mosques), as well as healthcare workers, should be empowered to engage the masses on these issues.

Ethical considerations

Ethical clearance was obtained from the Griffith University Human Research Ethics Committee (GU Ref No: 2017/458). Participation was voluntary, and the Zonal Director in charge of the Otuocha PPSSC facilitated permissions for the study from the relevant State Agencies, school principals, the students and their parents.

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Conflict of interest statement

Both authors are involved in charity organizations which were involved in the delivery of a health symposium on breast cancer and BSE to female secondary students in Otuocha PPSSC, organized after the questionnaires for this study were returned.

Authors' contributions

Both authors contributed significantly in all aspects of the study.

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ANNEX 1

PART 2: Breast and Cervical Cancers
Basic Socio-Demographic Data

1. **What is your gender? (*please write*):**

2. **What is your age (*in years*)?**

3. **What is the LGA where your school is located? *(please tick only one):***
- ☐ Anambra East LGA
- ☐ Anambra West LGA
- ☐ Ayamelum LGA
- ☐ Other

4. **Which of the following applies to you (*please tick all that apply*)**
- ☐ A family member of mine or a close relative has had breast cancer
- ☐ I know someone (not a family member or relative) who has had breast cancer
- ☐ I do not know anyone (family, relative or otherwise) who has had breast cancer

5. **What is your father's ocupation (if alive):**

6. **What is your mother's ocupation (if alive):**

7. **What is/was your father's highest educational attainment:**
- ○ Not educated at all
- ○ Completed Primary School
- ○ Completed Secondary School
- ○ Completed Post Secondary Education (university, polytechnic, etc.)

8. **What is/was your mother's highest educational attainment:**
- ○ Not educated at all
- ○ Completed Primary School
- ○ Completed Secondary School
- ○ Completed Post Secondary Education (university, polytechnic, etc.)

PART 3: Breast Cancers and Breast Self-Examinations

Knowledge (Questions 1 to 8), Attitudes (Questions 9 to 10) and Practices (Questions 11 to 12) towards Breast Cancers and Breast Self-Examinations

1. **Which of the following may indicate early breast cancer (please tick one box for each question):**

	Agree	Unsure	Disagree
Pain in the breasts	☐	☐	☐
Chest pain	☐	☐	☐
Headache	☐	☐	☐
Breast lump or swelling	☐	☐	☐
Lump or swelling in the armpit	☐	☐	☐
Nipple discharge from one breast only	☐	☐	☐
Nipple discharge in a pregnant person	☐	☐	☐
Nipple discharge when it is being queezed	☐	☐	☐

2. **Who is advised to do breast self-examination? (*please tick only one box for each question*):**

	Agree	Unsure	Disagree
All women aged 20 years or older	☐	☐	☐
Only married women	☐	☐	☐
Only women who have started having sexual intercourse	☐	☐	☐
Only women that have ever been pregnant	☐	☐	☐
Only women whose periods (menstruation) have stopped (usually above 50 years of age)	☐	☐	☐
Only women that have had breast cancers or with breast cancers in their families	☐	☐	☐

3. **How often should breasts be examined? (*please tick only one box for each question*):**

	Agree	Unsure	Disagree
Once a Day	☐	☐	☐
Once a Week	☐	☐	☐
Once a Month	☐	☐	☐
Once every 6 months	☐	☐	☐
Once every year	☐	☐	☐

4. **At what stage of your monthly cylce should you examine your breasts (*please tick only one box for each question*)?**

	Agree	Unsure	Disagree
Anytime	☐	☐	☐
During your period (menstrual flow)	☐	☐	☐
7 to 10 days after your period (menstrual flow) stops	☐	☐	☐
Midway through your cycle	☐	☐	☐
7 to 10 days before your period (menstrual flow) starts	☐	☐	☐

5. **Have you ever heard of breast cancers?** ***(Please tick only one answer):***

- Yes
- No
- Not sure

6. **Have you ever heard of Breast Self-Examination?** ***(Please tick only one answer):***

- Yes
- No
- Not Sure

7. **If you have ever heard of breast cancer or breast self-examination, how did you hear about it? (*kindly tick all the sources of your information, which may be more than one):***

- Home/Family
- Friends/Peers
- TV, Radio
- Newspaper/Magazines/Textbooks
- School Teachers
- Health Workers (doctors, nurses, etc.)
- In the church
- Internet: Facebook, Google, Twitter, etc.
- I have never heard about any of them

8. **Which of the following may increase the risks of developing breast cancer (*please tick one box for each question*):**

	Agree	Unsure	Disagree
Starting your periods (menstruation) at an early age (before 11 years)	☐	☐	☐
Starting your periods (menstruation) at a late age (over 16 years)	☐	☐	☐
Having no babies at all	☐	☐	☐
Having many babies (more than 4)	☐	☐	☐
Eating a high fatty diet	☐	☐	☐
Using the birth control pill	☐	☐	☐
Having someone in the family with breast cancer	☐	☐	☐
Starting sexual intercourse at an early age	☐	☐	☐
Having a urinary tract infection (infection of urine)	☐	☐	☐

9. **Please answer the following about yourself (*tick only one box for each question*):**

	Yes	Unsure	No
I am healthy and do not need to examine my breasts	☐	☐	☐
Examining my breasts by myself is important and necessary	☐	☐	☐
I am not well informed on how to examine my breasts	☐	☐	☐
I feel shy and embarrassed about examining my breasts by myself	☐	☐	☐
Examining my breasts by myself will be painful	☐	☐	☐
I am afraid that examining my breasts might reveal breast cancer	☐	☐	☐
Examining my breasts by myself will waste a lot of my time	☐	☐	☐
Examining my breasts by myself is a dirty practice and against my values or beliefs	☐	☐	☐
I will not like to touch my breasts in the way required for me to examine it	☐	☐	☐
If I find a suspicious lump while examining my breasts, I will see a medical doctor rather than a traditional healer	☐	☐	☐

10. **How do you respond to the following questions (*please tick only one box for each question*):**

	Agree	Unsure	Disagree
Cancer of the breast is a common cause of deaths arising from cancers among females in Nigeria	☐	☐	☐
Any young woman aged 20 years or more can develop breast cancer	☐	☐	☐
Cancer of the breast can be passed on from one person to another	☐	☐	☐
Self breast examination can help detect and prevent breast cancers	☐	☐	☐

11. **Have you ever examined your breasts by yourself? (*please tick only one answer*):**

- ○ No
- ○ Yes, just once
- ○ Yes, at least once every day
- ○ Yes, at least once every week
- ○ Yes, at least once every month
- ○ Yes, at least once every 6 months
- ○ Yes, at least once every year

12. **What is the best position to adopt while examining your breasts (*please tick only one box for each row*)?**

	Agree	Unsure	Disagree
Standing in front of a mirror	☐	☐	☐
Lying down	☐	☐	☐
Use right hand to examine the left breast (and left hand to examine right breast)	☐	☐	☐
Use the finger pads (finger pulps) of the fingers to examine	☐	☐	☐
Use my fingernails to examine	☐	☐	☐
Use my palms to examine	☐	☐	☐
Use one finger only	☐	☐	☐
Use the 3 middle fingers only	☐	☐	☐
Examine the breast by moving fingers in circles around the breast till all parts are covered	☐	☐	☐
Examine the breasts by moving fingers from top of breast to bottom (vertically) till all parts covered	☐	☐	☐
Examine breasts by checking small sections of it (in wedges) till all parts examined	☐	☐	☐
Press the nipple to check for any discharge	☐	☐	☐
Examine the armpit for lumps	☐	☐	☐
Look for any changes in breast size or shape	☐	☐	☐
Look at the nipple to see if it is drawn inwards	☐	☐	☐
Raise one hand above the head while examining breast on that side	☐	☐	☐
Undress to the waist	☐	☐	☐

PART 4: Cervical Cancers
Knowledge (Questions 1 to 7) and Attitude (Question 8) towards Cervical Cancers, Screening and Vaccination

1. **Have you ever heard about "cancer of the cervix", which is also called "cervical cancer"? *(please tick only one answer)***
Note: Cervical Cancer is the cancer of the lower part (or entrance) to the womb. It is the part of the womb that connects it to the vagina.

- ○ Yes
- ○ No
- ○ Not sure

2. **Have you ever heard of "screening for cervical cancer"? *(please tick only one answer)***

- ○ Yes
- ○ No
- ○ Not sure

3. **Have you ever heard about "Pap Test", which is also called "Pap Smear"? *(please tick only one answer):***
Note: Pap Test is a test done to look for Cervical Cancer.

- ○ Yes
- ○ No
- ○ Not sure

4. **Have you ever heard about "Human Papilloma Virus (HPV)" and Vaccinations against it to prevent Cervical Cancer? *(please tick only one answer)***

- ○ Yes
- ○ No
- ○ Not sure

5. **If you have ever heard about cervical cancer, screening for cervical cancer, pap test or HPV vaccination, how did you hear about it? *(kindly tick all the sources of your information, which may be more than one):***

- ○ Home/Family
- ○ Friends/Peers
- ○ TV, Radio
- ○ Newspaper/Magazines
- ○ School Teachers
- ○ Health Workers (doctors, nurses, etc.)
- ○ In the church
- ○ Internet: Facebook, Google, Twitter, etc.
- ○ I have never heard about any of those terms

6. **Regarding cervical cancers, what do you think concerning the following? (*please tick only one box for each question*):**

	Agree	Unsure	Disagree
Pap smear (test) can help detect early cervical cancer	☐	☐	☐
Pap smear is only for married women	☐	☐	☐
Pap smear is advisable for women 18 years or over who have started having sexual intercourse	☐	☐	☐
Pap smear is advised for all women after 2 years of starting sexual activity	☐	☐	☐
Only women whose periods (menstruation) have stopped (usually above 50 years of age) should have pap smears	☐	☐	☐
Only women that have had cervical cancers or those whose family members have had it should have pap smears	☐	☐	☐
Pap smears should be done at least every 2 years for those who are eligible	☐	☐	☐
Pap smears should be done only once in a lifetime	☐	☐	☐
Human Papilloma Virus (HPV) Vaccine can help protect against cervical cancers	☐	☐	☐
To be effective, HPV Vaccine is recommended for adolescent girls before the first exposure to sexual activity	☐	☐	☐

7. **Which of the following may increase the risks of developing cervical cancer? (*please tick one box for each question*):**

	Agree	Unsure	Disagree
Early onset of unprotected sexual activities	☐	☐	☐
Having multiple sexual partners	☐	☐	☐
Smoking cigarretes	☐	☐	☐
Drinking lots of alcohol	☐	☐	☐
Having many babies (more than 4)	☐	☐	☐
Eating a high fatty diet	☐	☐	☐
Using the birth control pill	☐	☐	☐
Spiritual attack	☐	☐	☐
Having someone in the family with cervical cancer	☐	☐	☐
Having vaginal warts (caused by the Human Papilloma Virus, a type of viral infection)	☐	☐	☐
Having a urinary tract infection (infection of urine)	☐	☐	☐
Having sexually transmitted diseases (infections)	☐	☐	☐
Poison from enemies	☐	☐	☐
Cervical cancer can be inherited from one's parents	☐	☐	☐

8. **Which of the following may indicate early cervical cancer (please tick one box for each question):**

	Agree	Unsure	Disagree
Vaginal discharge with an offensive (foul) smell	☐	☐	☐
Bleeding after sexual intercourse	☐	☐	☐
Having pain during menstruation	☐	☐	☐
Having heavy bleeds during menstruation	☐	☐	☐
There may be no symptoms	☐	☐	☐
Rash in vaginal area (private part)	☐	☐	☐
Swelling in vaginal area (private part)	☐	☐	☐

9. **How do you respond to the following questions regarding cervical cancer screening through pap smears (*please tick only one box for each question*):**

	Agree	Unsure	Disagree
Cervical cancers kill women in Nigeria	☐	☐	☐
If I am eligible, I will like to do regular pap smears to detect early cervical cancer	☐	☐	☐
I am afraid that pap smear will be painful or dangerous	☐	☐	☐
I will like to know more about pap smears	☐	☐	☐
I can only undertake pap smear if it is free	☐	☐	☐
No matter the financial costs, I will like to undertake regular pap smears	☐	☐	☐
I will be too embarrased to discuss pap smears with my doctor	☐	☐	☐
I am worried about what the doctor will find from the pap smear test	☐	☐	☐
I will be too busy to find time for the pap smear	☐	☐	☐
I do not think that pap smear for early detection is necessary	☐	☐	☐
I do not know where to go for pap smears	☐	☐	☐
It is against my religious and cultural beliefs to undertake pap smear	☐	☐	☐

10. **How do you respond to the following questions regarding cervical cancer prevention through HPV Vaccinations (*please tick only one box for each question*):**

	Agree	Unsure	Disagree
If available, I will like to have the HPV Vaccine that prevents cervical cancer	☐	☐	☐
I am afraid that HPV vaccination will be painful or dangerous	☐	☐	☐
I will like to know more about HPV Vaccines	☐	☐	☐
I can undertake HPV vaccination only if it is free	☐	☐	☐
No matter the financial costs, I will like to have HPV vaccines if I am eligible	☐	☐	☐
I will be too embarrased to ask for HPV vaccination from my doctor	☐	☐	☐
I will be too busy to find time for HPV vaccination	☐	☐	☐
I do not think that HPV vaccination for preventing cervical cancer is necessary	☐	☐	☐
I do not know where to go for either the HPV vaccination	☐	☐	☐
It is against my religious and/or cultural beliefs to go for HPV vaccination	☐	☐	☐

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Overview

Re-organisation of the management of patients affected with chronic pathologies in Lombardy Region: critical points associated with the management of HIV positive patients

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Keywords

HIV • Chronic patients • Public health

Summary

The Regional Council of Lombardy Region published in 2017 two resolutions related to a re-organisation of the management pathway of patients affected with chronic pathologies, to meet the changing needs of the users. The objective of this document is to provide recommendations to the Regional Health Service of Lombardy Region to manage the implementation of the resolutions considering peculiar aspects related to the management of HIV positive patients.

These resolutions are a concrete answer to the changing needs of health care users within the regional context. The design of the new approach is coherent with the objectives stated, allowing a tighter integration between hospital services, primary care services and social services, however it should be adapted to each of the 62 chronic pathologies considered. In the case of HIV, not considering antiretroviral treatments within the tariff might limit the cost management capability of the case manager. The full implementation of the resolutions with the inclusion of social services will allow a complete management of chronic patients with positive consequences on their quality of life.

Introduction

The Regional Council of Lombardy Region published in 2017 two resolutions related to a re-organisation of the management pathway of patients affected with chronic pathologies [1, 2]. In details, the objectives of the Regional Health Service are to modify the organization of the health care services to meet the changing needs of the users within the Regional context.

In the last years, the number of chronic patients, in fact, is increasing due to better available health technologies, leading, as in the case of HIV infection, to an epidemiologic transition; and their clinical conditions are increasingly more complex, due to concomitant chronic pathologies.

Healthcare services related to chronic patients represents 70% of direct medical costs for the Regional Health Service, as reported in a Regional Bulletin of 2016, while chronic patients represents 30% of the total number of residents within Lombardy Region. Therefore, most of the regional healthcare resources are devoted to the management of a minority of the whole regional population [3].

The authors of this editorial, agree with the principles that lead the regional authorities to modify the approach to the management of chronic patients. The aforementioned resolutions, refer to the management of 62 chronic pathologies, with different health consequences in terms of clinical and humanistic burden for patients and different backgrounds in terms of available guidelines and clinical pathways implemented by pathology related scientific societies.

The objective of this document is to provide recommendations to the Regional Health Service of Lombardy Region to manage the implementation of the resolutions considering peculiar aspects related to the management of HIV positive patients.

The content of the two resolutions

With the resolutions of the Regional Council number x/6164 of the 30th of January 2017 and number x/6551 of the 4th of May 2017 [1, 2], Lombardy Region continued on the pathway of reforms of the Regional Health Service, started in 2015 with the Regional Law number 23 [4].

The focus of the two resolutions is the management of patients affected with chronic pathologies. In details, the principles of the documents are the shift of the actual curative pathway of patient to a pro-active approach in terms of programming on an annual basis the therapeutic and monitoring pathway of each patient, based on his/her needs; the identification of a single "managing provider" responsible for the management of the patient pathway (including co-morbidities); and the integration between health care and social services, and between different levels of care (i.e. hospitals and territorial services) at a regional level.
The objective is to increase the personalization of the curative pathway, overcoming the actual fragmentation of the health services, integrating the needs of the patient into a single pathway, defined and coordinated by the managing provider, that can be both identified at a hospital level or at a primary care level.
From a financial point of view, the resolutions indicate the overcoming of the actual remuneration system, based on the health services provided to patients (pay per service), to consider a single tariff per main chronic pathology and per level of complexity of the patient, that will cover all the health care needs of the patient associated with his/her chronic conditions. The tariffs will be based on the value of the health services provided in previous years to patients with homogeneous levels of complexity and main chronic pathology.
The three levels of complexity considered for each of the 62 chronic pathologies taken into consideration are based on the number of chronic co-morbidities: the third level consider patients affected by one chronic pathology, the second level consider patients affected by two or three chronic pathologies and the first level consider patients affected by four or more chronic pathologies.
The process of implementation of the new approach is based on four phases: the categorization of chronic patients; patients' enrollment; the organization of the curative pathway; and the monitoring of the activities and reimbursement of the managing provider.

HIV management peculiarity

Considering the level of complexity of the management of HIV positive patients and the specialization and experience needed to plan a medium-long term clinical pathway, we expect that the managing provider accredited for the management of HIV positive patients will be a hospital provider. HIV positive patients are nowadays already managed by hospital wards both for therapies dispensation and clinical pathway organization. From this point of view no differences are expected, beside the positive aspects related to the management of booking of examinations that will be performed by a service center, as indicated in the regional resolutions, to facilitate the access to health services for patients.
Furthermore, no differences in terms of patients' compliance to antiretroviral therapies and appropriateness of prescriptions are expected, due to their estimated actual high level.
The implementation of pathways for each chronic condition of the patients, might lead to synergies among them, in case of concomitant pathologies, however, no significant differences in the cost of management of HIV positive patients are forecasted, due to the severity of the pathology.

Critical points and proposals

Sources for the determination of the individual care pathways

Every year the clinical manager of each patient is responsible for the definition of an individual care pathway, indicating all the health care services expected for the monitoring and curative process of the patient.
The two referral documents should be the Italian national guidelines for the treatment of HIV positive patients and the Lombardy Region clinical pathway [5, 6]. These documents reports precise details related to the therapies to be provided to HIV positive patients, with limited indications related to diagnostic and monitoring activities.
The high variability of clinical decisions related to diagnostic activities grants the freedom of clinicians to identify the most appropriate diagnostic pathway but conflict with the objective to limit the variability of prescriptive choices.
According to the authors the Lombardy Region pathway for HIV patients should be revised, providing detailed information on the monitoring and diagnostic activities recommended for patients.

Services considered in the definition of the patients' managing tariffs

The applicability of the model depends on the congruity of the tariffs related to the level of complexity of patients. The resolution of the 4th of May 2017 reports tariffs equal to 1,727.05 € for level 1, to 1,146.28 € for level 2 and to 999.55 € for level 3. The tariffs should cover outpatient activities and, for level 1, hospitalizations [2].
A recent study conducted within the former Local Health Authority of Brescia [7], reports a per capita annual cost for HIV positive patients for outpatient activities equal to 1,544 € between 2012 and 2014. This value is higher, than the tariffs of the levels of complexity 2 and 3, however it is not clear how the patients of the cohort considered were distributed among the three levels of complexity. Adding the cost for hospitalizations, the annual per capita cost would be of 2,727 €, higher than the tariff considered for the level of complexity 1.
An estimation of the per capita outpatient activities to be carried out on a yearly basis per type of monitoring (excluding specialist visits) can be derived from the Italian Guidelines on HIV/AIDS as follow: viral, between 221.70 € and 1,330.20 €; immunologic, between 17.95 € and 215.40 €; cardiovascular disease risk, 291.83 €; hy-

pertension / dyslipidemia / diabetes mellitus, between 7.40 € and 9.10 €; liver disease, between 77.35 € and 155.95 €; pulmonary disease risk, 144.08 €; kidney disease risk, 15.40 € and bone disease risk, between 78.08 € and 129.18 €.
The minimum and maximum per capita cost for the Regional Health Service related to the monitoring activities recommended (excluding specialist visits) are 853.79 € and 2,291.14 €.
The analysis of the annex 1 of the resolution of the 4th of May, does not allow a calculation of the costs related to the health care services provided to HIV positive patients in Lombardy Region in the year 2016, due to the fact that some of the services are reported in aggregated form, i.e. "immune-hematology – transfusion", "clinical chemistry" and "laboratory in general". This information was partially clarified by the data presented in the resolution of the Directorate General for Health of Lombardy Region of the 3rd of August 2017 [8], which was, however, based on a lower number of patients compared with the previous resolution [2] and with the aggregated categories as "visit-clinical chemistry laboratory analysis, microbiology, etc…".
According to the authors, a higher degree of transparency should be provided by the Regional Health Service on the way the tariffs will be defined, i.e. considering historical data of reimbursements related to the services provided, or measuring the real cost of delivering the health care services within selected providers.
Furthermore, the level of each tariff should be revised on a yearly basis not only considering retrospective data, but also the most recent recommendations of Italian and international guidelines, the regional clinical pathway for HIV/AIDS and the availability of new health technologies.

The antiretroviral therapy

The capacity of clinical managers to control the health expenditures related to HIV patients are significantly limited due to the exclusion of antiretroviral therapies from the tariff. Antiretroviral therapies, in fact, represent around 80% of the direct health costs for the management of HIV positive patients.
To allow a higher control of expenditures, the authors recommend to include the cost of antiretroviral therapies in the reimbursement tariff for the management of patients.

Definition of tariffs for complexity levels 1 and 2

The tariffs considered for the management of pluri-pathologic patients depend on the main pathology they are affected with. Within the regional resolutions it is not explained how the main pathology is determined. The determination of the main pathology, in fact, influences the tariff considered for the management of patients and varies from almost 33,000 € for kidney failure to between 100 € and 200 €. The congruity of the tariff, therefore, depends on the pathology that is considered as the main one to assign a patient to a specific category.

The aforementioned study conducted in the former Local Health Authority of Brescia reports additional direct health costs for comorbidities equal to + 1,701.4 € for diabetes, + 2,087.7 € for cardiovascular disease, + 3,756.8 € for gastroenterology pathologies, + 4,103.3 € for respiratory chronic pathologies, + 4,388.8 € for liver diseases, + 7,557.6 € for tumors, + 13,665.3 € for kidney failure.
These values would not be sustainable considering the tariffs for level 1 and level 2 for HIV positive patients. The authors recommend more transparency related to the algorithm used to define the prevalent chronic pathology that assign pluri-pathologic patients to a specific category.

Integration between hospital and territorial services

To grant a real management of the health care needs of chronic patients, a further integration of the different care setting is necessary. The Regional law number 23 of 2015 [4], promoted the implementation of territorial services for the management of patients requiring low intensity of care, however, considering HIV positive patients, residential homes, as nursing homes, are often not able to offer services to these patients. A central role, in terms of integration between hospital and territorial services should be played by general practitioners.

Customer satisfaction

As reported in the resolution of May 2017 [2], the assessment of the customer satisfaction could identify critical aspects of the implementation of the new approach towards chronic patients.
It would be important to implement a regional document to be used within each managing provider, to provide homogeneous information within the regional context. Previous similar experiences at a primary care level (i.e. CReG) revealed high level of satisfaction among patients enrolled.

Conclusions

The resolutions on chronic patients management in Lombardy Region are a concrete answer to the changing needs of health care users within the regional context. The design of the new approach is coherent with the objectives stated in the regional documents, allowing a tighter integration between hospital services, primary care services and social services, however it should be adapted to each of the 62 chronic pathologies considered. In the case of HIV, for instance, not considering antiretroviral treatments within the tariff might limit the cost management capability of the case manager.
The full implementation of the resolutions with the inclusion of social services will allow a complete management of chronic patients with positive consequences on their quality of life. The overcoming of the critical aspects reported in this commentary might help the Regional Health Service to customize the approach pro-

posed to fit the needs related to a relevant pathology as that of HIV infection.

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Conflict of interest statement

None declared.

Authors' contributions

All authors contributed equally to this work.

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ORIGINAL ARTICLE

Quality and management care improvement of patients with chronic kidney disease: from data analysis to the definition of a targeted clinical pathway in an Italian Region

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Keywords

Clinical pathway • Kidney cronic disease • Patient centered care

Summary

Background. *Clinical Diagnostic Care Pathways (CDCP) are management tools widespread throughout the world to improve the quality of patient care through a well-organized care continuum and to enhance the patient's "risk-adjusted" outcomes; indeed they could optimize the management of resources. They are particularly effective in the management of patients with chronic degenerative diseases, such as chronic kidney disease, with increasingly incidence and prevalence, with an estimated 11-13% of the population being affected. The aim of this study is to apply the Health Services Research methods to estimate the relationship between need, demand and supply in patients with stage 5 Chronic Kidney Disease (CKD) for, then to describe the definition of a CDCP dedicated to patients in Lazio Region , so to allow an appropriate patient management, to reduce the likely complications and the patients' migration to facilities outside the region.*

Methods. *The study was conducted in 2017 in collaboration between the National Institute of Health, the University of Messina and the S. Giovanni Addolorata Hospital.*

Results. *We analyzed the data for the CKD in Roma and in the San Giovanni Addolorata Hospital Trust and we found a drop out in the patients' attendance towards other regions and/or hospitals. So we defined a CDCP to be adopted at the San Giovanni Addolorata hospital.*

Conclusions. *To define management and care tools to provide adequate, efficient and patient centered care is a nowadays "must", to ensure the sustainability of the Italian NHS, which today is comparable to a "ship that is heading towards a perfect storm".*

Introduction

Today, the right to health is universally recognized: each Country has in fact ratified at least one of the international human rights treaties sanctioning it [1]. Healthcare, however, is provided differently on different continents, ranging from private systems with the need for insurance coverage by citizens, as in the US, to public systems with costs borne by the National Health Service as in Italy, where public funds support healthcare provision [2]. All developed countries are putting more resources into health, but this increased investment is totally inadequate to meet the steady increase in community needs; which is primarily due to a change in the population that is "growing older" and as life expectancy increases so does the number of subjects with chronic degenerative diseases who require access to treatment [3]. This is linked to the greater availability of new and more expensive diagnostic technologies; since health is an asset to be safeguarded and all citizens, regardless of age, must be assured equal treatment opportunities. Thus, the demand for health care (and consequently the costs) is ever-increasing creating a vicious circle [4]. The continuous effort to improve health therefore requires the performance of healthcare systems and policies be measured, with subsequent adaptation of the system based on the assessment. Given the limited availability of funds in Italy, their correct and timely management is vital. This necessitates a well-structured therapeutic diagnostic process and this is where Clinical Diagnostic Care Pathways (CDCP) come into play. CDCPs are widespread throughout the world and their objectives are to improve the quality of patient care through a well-organized care continuum , and to enhance the patient's "risk-adjusted" outcomes; the third objective is to optimize the management of resources, not only economic but also structural and human [5, 6]. One of the most widespread chronic degenerative diseases is chronic kidney disease (CKD), and its incidence and prevalence is increasing worldwide: with an estimated 11-13% of the population being affected by CKD, particularly stage 3 [7]. Once the terminal stage of the disease has been reached, the patient must undergo renal replacement therapy by specialized dialysis. The main replacement methods of renal func-

tion are hemodialysis and peritoneal dialysis. In 2010, 284 individuals per million population were estimated to be receiving maintenance dialysis in the world. Although the use of peritoneal dialysis is increasing in some countries, including China, United States and Thailand, it has proportionally decreased in parts of Europe and in Japan [8, 9]. Well-functioning vascular access is a prerequisite for good dialysis treatment; vascular access failure (VAF) is the most common reason for hospitalization among hemodialysis (HD) patients. The economic burden of VAF is estimated to exceed 1 billion dollars per year and continues to rise. The possible acute complications related to vascular access (bleeding, stenosis and/or thrombosis, AVF malfunction, malfunction, dislocation, central venous catheter (CVC) infection) must be managed in a specialized environment and by highly specialized personnel [10-12]. Arterio-venous fistula (AVF) with native vessels is the preferred method of vascular access as it allows greater survival, reduced risk of infection and fewer complications. The Kidney Disease Outcomes Quality Initiative (KDOQI) guidelines recommend packing vascular access when creatinine exceeds 4 mg/dL or when the Glomerular filtrate is less than 25 ml/min (Guideline 8 of KDOQI) and at least one month before (better 3-4 months) cannulation [13]. In the Italian region of Lazio at 31/12/2015 there were 90 outpatient facilities providing dialysis services ("dialysis centers"), 37 public and 53 private, with a non-homogeneous coverage across the region. This wide supply availability induces high patient mobility in Rome area, with patients migrating towards dialysis centers located in healthcare districts other than that of residence. This phenomenon is also found in the other municipalities of Lazio, albeit to a lesser extent. Over the period 2008-2013, the rate of first hospital admissions in Lazio region due to cardio-circulatory problems was 21.0%, and a mortality rate of 20.9%, both within two years from the start of dialysis. Even taking into account the uneven distribution of clinical and demographic features among patients treated according to the P.Re.Val.E procedure (risk adjustment), there remains inconsistency between dialysis centers and areas of residence [14]. The aim of the present study is to: 1) analyse according to a Health Services Research perspective the relationship between need, demand and supply for patients with stage 5 CKD in a given area in Rome [15]; b) to define a clinical diagnostic care pathway for patients in the Lazio region that allows, first, a more appropriate and timely patient management by all medical figures involved, to to reduce the likely disease complications and, secondly, a reduction in patients' migration to facilities outside the region; c) to build up a monitoring system to evaluate the forthcoming impact of the implementation of the CDCP.

Materials and methods

The Health Services Research analysis was conducted in collaboration between the Istituto Superiore di Sanità (National Institute of Health), the University of Messina and the Complex Operative Unit of Vascular Surgery at the S. Giovanni Addolorata Hospital, a Hospital Trust in Rome metropolitan area. The database used was the national database of Hospital Discharge Cards (SDO) available at the ISS Statistical Technical Service, provided by the Ministry of Health. Reasons for hospitalization are classified by means of the international system called the ICD-9 CM (International Classification of Diseases - Clinical Modification), which is also used in Italy (the latest version is 2007) [16].

The analysis was carried out in November-December 2017 and covered residents in the Lazio Region admitted to facilities in the Lazio Region and to the San Giovanni Addolorata Hospital, in particular. The years analyzed were 2015 and 2016 with prevalent cases counted separately for these two years. The analysis covered both inpatients and outpatients; in order to obtain the most accurate estimate of the prevalence of pathological conditions. The SDO database was considered in its entirety including daytime admissions, while naturally excluding long-term hospitalizations and rehabilitations. Each SDO reports a "Diagnosis/main procedure" and up to five "secondary diagnoses/procedures"(Law Decree 380/2000). The database was queried for all the diagnosis/procedure fields thereby enabling the number of cases to be estimated more accurately.

Results

The application of the Health Services Research approach

The resident population in Lazio was 5,898,124 inhabitants at 31/1/17 (ISTAT data) and the total number of patients with stage 5 CKD (eg, Lazio cod. 5856) was 2,116 for the year 2016 (SDO data). Thus, the estimated prevalence of the disease stage in Lazio was 0.036% for the year 2016. The number of patients admitted under IRC cod 5856 were 2,695 and 2,926 for the years 2015 and 2016 respectively, with the number of admissions with severe complications of 1,757 and 1,826.

The population served by S. Giovanni Addolorata Hospital is 413,749 inhabitants, thus the predicted number of patients at the San Giovanni-Addolorata hospital with CKD Cod. 5856 (to be estimated according to the SDO database) is approximately 148.4. However, the number of patients treated was 90 and 102 for the years 2015 and 2016 respectively (estimated according to the SDO database). This means a likely migration of stage 5 CKD patients to other centers of as many as 46 patients for the year 2016. A more focused analysis of the data available showed migration to facilities outside the Lazio region of 6.3% of cases for the year 2015 and 6.4% of cases for the year 2016. The results obtained are summarized in Tables I and II.

The definition of the CDCP

The clinical pathway must be the tool to sensitize the problem of the "life line" of the uremic patient starting

Tab. I. Admissions and procedures in the Lazio Region and San Giovanni Addolorata hospital.

Lazio	Year 2015	Year 2016
Number of admissions for CKD (cod. 5856)	2,695	2,926
Number of admission for complications (V56.1, V56.2, 996.1, 996.62, 996.73)	1,757	1,826
Number of surgical procedures (39.27, 39.49, 39.50, 39.52, 39.29, 39.42, 39.43, 38.95, 86.07)	10,923	11,393
Numbers of surgical procedures outside region Cod. 39.27, 39.49, 39.50, 39.52, 39.29, 39.42, 39.43, 38.95, 86.07	703	780
Numbers of patients with CKD at end stage cod.5856	1,961	2,116
San Giovanni Addolorata		
Number of admissions cod. 5856	90	102
Number of admissions	82	84
Number of surgical procedures (39.27, 39.49, 39.50, 39.52, 39.29, 39.42, 39.43, 38.95, 86.07)	372	495
Number of admissions for complications (V56.1, V56.2, 996.1, 996.62, 996.73)	8	7

Tab. II. Codex of procedures and complications.

Procedures and complications	Cod.
Numberof admissions for CKD	5856
Number of admission for complications	
Placement and arrangement of extracorporeal dialysis catheter	V56.1
Positioning and arrangement of peritoneal dialysis catheter	V56.2
Mechanical complications of other devices, implants and vascular grafts.	996.1
Infection of vascular grafts	996.62
Other complications from prostheses, implants and renal dialysis grafts	996.73
Number of surgical procedures	
Arteriovenostomy for renal dialysis	39.27
Other revision of vascular interventions	39.49
Angioplasty or atherectomy of a non-coronary vessel	39.50
Other repair of aneurysms	39.52
Other vascular anastomoses or by-pass (peripheral)	39.29
Revision of arterio-venous anastomoses for renal dialysis	39.42
Removal of A-V anastomosis for renal dialysis	39.43
Venous catheterization for renal dialysis	38.95
Insertion of a totally implantable vascular access device	86.07

with the family physician who will single out which patients to send to the nephrologist to plan for the creation of a usable vascular access when the need arises for dialysis. It will be the nephrologist who will identify when the vascular surgeon will have to perform the surgery. The emergency doctor of the first aid who will manage the acute uremic patient through nephrological counseling, and will activate the path for urgent vascular or endovascular surgical treatment in order to avoid the insertion of a central venous catheter unless absolutely indispensable. It will be necessary to sensitize the hemodialysis centers of the territory on which the hospital company insists, in order to inform them of the possibility of using a 24-hour service for the management of complications of vascular access or for the creation of complex arteriovenous fistulas. It is therefore necessary to create an interdisciplinary team consisting of: emergency doctor, nephrologist, vascular surgeon and interventional radiologist. The aims of the clinical pathway are as follows:

- optimization of patency surveillance, the correct planning of vascular access packaging and avoiding the insertion of CVC for acute hemodialysis;
- reducing the number of uremic patients requiring urgent hemodialysis treatment, without vascular access (avoiding the insertion of central venous catheters that are linked to high morbidity in terms of infection and thrombosis of central veins thereby compromising the feasibility of future vascular accesses for hemodialysis);
- reducing the number of patients who acutely need revision of vascular access due to occlusion/thrombosis or malfunction (avoiding urgent repacking and insertion of CVC);
- intercepting patients with acute occlusion of the vascular access for surgical or endovascular correction in order to restore the functionality or eventual packaging of arteriovenous prosthetic fistula "early cannulation" in order to avoid insertion of CVC;
- avoiding extra-regional migration of hemodialysis patients who have difficulty accessing vascular surgeries in Lazio;
- clinical surveillance of vascular accesses for the early diagnosis of dysfunction in the dialysis room, with the aid of instrumental diagnostics (Color Doppler ultrasound, angiography);

- using the resources of 24-hour centers to deal with vascular access complications and to restore the patency and usability of the arteriovenous fistula as soon as possible. The "Quick access" CDCP complies with the National Kidney Foundation KDOQI guidelines and those of the Italian Society of Vascular and Endovascular Surgery [17, 18].

The aforementioned CDCP has therefore been adopted as a model in the San Giovanni Addolorata hospital and the reduction of outpatient migration and emergency hospital access have been included in the CDCP monitoring plan and are currently being monitored.

Discussion and conclusions

By applying the Health Services Research approach, we found that patients admitted with a IRC coding were 2,695 and 2,926 for the years 2015 and 2016, respectively, with the number of admissions with severe complications of 1,757 and 1,826. Thus, a unsatisfactory management of the uremic patient by both general physicians and specialists would be underlined.

In addition, 6.3% of cases of patients with stage 5 KCD in 2015 and 6.4% of cases in 2016 accessed to facilities outside the Lazio region.

In addition, our analysis highlights shortcomings in patient management, despite the professional and structural resources available so to induce a high extra-regional migration for surgical procedures, that is reasonably not due to boundary migration. This is particularly heavy for patients with CKD and for their carers and is unacceptable for a region where specialized facilities and highly qualified personnel are available.

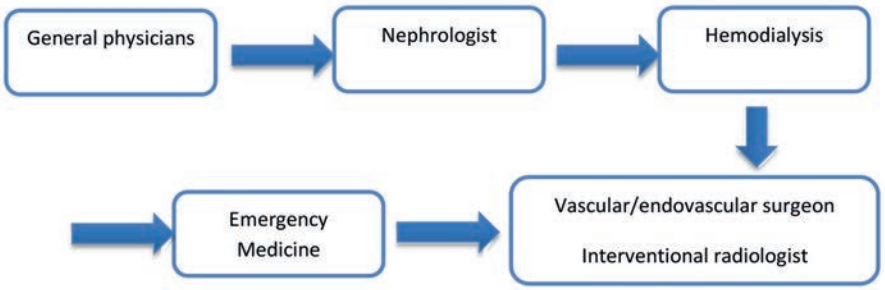
It is evident from clinical practice that the problems related to the packaging and maintenance of a vascular access usable for satisfactory hemodialysis are often neglected, despite their importance in terms of social and health impact. Since this surgical technique is specific to terminal uremic patients, while referrals for surgeryare made only by the nephrologist, it is difficult for the vascular surgeon, to respond promptly to a demand for treatment. Complex vascular surgery units often have no specific competence and demand from the nephrologist the packaging of native arteriovenous fistulas, but at the same time, they are called upon to solve urgent complications for which complex surgical or endovascular procedures are required. The result is an erratic and imprecise management in a "no man's land" that endangers the "life line" of the uremic patient, that is the Arteriovenous Fistula. It is therefore necessary, in our opinion, to delineate a care path that identifies a multidisciplinary team that will deal with all these patients, to plan the packaging of the vascular access and maintain its patency through clinical surveillance. This will lead to the reduction of complications related to any malfunction and reduce the need to insert CVC that compromise the quality of efferent blood vessels.

It is also necessary for diagnostic and therapeutic procedures to be implemented in environments where the patient's response can be constant within 24 hours. A systematic review and meta-analysis demonstrated a trend toward the benefit of the rate of thrombosis and access to patients with usual clinical monitoring [19]. Compliance with international guidelines, approved by the Italian scientific societies of nephrology and vascular and endovascular surgery, guarantees the correctness of procedures and result in improved outcomes [17, 18, 20]. Despite the presence of numerous hemodialysis centers and the same number of Vascular surgery units in the Lazio region, the data provided by the SDO cards, show an alarmingly high a number of urgent hospitalizations for chronic renal insufficiency that suggest incorrect planning and classification of uremic patients from that area. There is also a frequent need for urgent dialytic treatment and therefore the insertion of CVCs and vascular access packaging in post-acute conditions and this involves the reduction of the superficial venous heritage of the upper limbs for repeated venipuncture. All this translates into increased morbidity related to vascular access and a reduction of long-term patency, as also demonstrated by the existing literature [21]. These shortcomings in patient management, despite the professional and structural resources present, mean that there is also a discouraging and disconcerting fact:. a need for a prompt, timely and appropriate treatment, is not encountered by the supply system and its causes a high extra-regional migration for surgical procedures, that is reasonably not due to boundary migration. This is particularly heavy for patients with CKD and for their carers and is unacceptable for a region where specialized facilities and highly qualified personnel are developed and recognized by the scientific community!

Therefore, an appropriate management of the uremic patient is necessary both by general practitioners and by nephrologists with the creation of an adequate care path. The early management of the patient with CKD and the sharing with the nephrologist of these patients constitute the pivot on which the different levels of care are articulated; with at least three possible different levels of care: region, outpatient and hospital management. Each of the three levels is not an end in itself, but may overlap with others depending on the patient's clinical status, any complications and accelerations [13]. In order for care to be efficient, the creation of a clinical diagnostic care path based on the coordinated synergy of different professional figures is necessary to guarantee and enhance its effectiveness with the formulation of clear recommendations for shared management, to be reviewed periodically with any updates to be implemented, as new evidence arises [22, 23]. To enhance integration and continuity of care, the creation of shared data platform between the GP and the nephrologist is welcome as crucial to allow a useful exchange of information between the professionals involved and the monitoring of the process through shared indicators, in line with current Ministry of Health guidelines [24].

The optimization of patient management and the organization of adequate health care is therefore essential to ensure the sustainability of the Italian NHS, which today

Fig. 1. Clinical diagnostic care pathway.



is comparable to a "ship that is heading towards a perfect storm" [25, 26].

Some limitations of our study must be acknowledged. One limitation of the present study is the partial retrospective collection of cases.

Another one is due to the use of administrative data (eg, the SDO database) for epidemiological purposes, to describe the relationship between needs, demand and supply of care for patients with KCD. The national database of the SDO doesn't receive informations on the incidence, residences adress and it isn't possible to reason on the mobility of patients inside the area of Rome.

In addition, by calculating "incidence", we didn't analyse the likely increase over the years or other factors with an expected impact on access to care.

Such limitations in data source and integration also limited us in the analysis of an adequate relationship between demand and supply, that is of primary importance in a National Health Service like the Italian, were the free of choice of patients towards of providers of care in the health sectors care is an underpinning principle. We are confident that such a risk would be avoided by applying a ZIP code analysis or by studying patterns of patients fluxes due to other determinants by applying marketing strategies [27], internal "leaks" within the city of Rome, surveys on the customer preferences towards the delivery facilities. On the other hand, we consider of crucial importance to propose a quantitative approach to evaluate the capability to satisfy healthcare needs and to perform an advocacy role towards a better management of patients with CKD, who are at higher risk of inequalities and lower access to care in a period of economic costraints and of management weakness, as a consequence of the "perfect storm" [26].

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Conflict of interest statement

None declared.

Authors' contributions

CG and PT concepted and designed the study; VM acquised the data; CG, PT and RS analysed and interpretated the data; CG, PT and RM drafting the article; RS and AGdB revising it critically for important intellectual content; all authors give final approval of the version to be submitted and any revised version.

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Original article

Risk factors for voluntary interruption of pregnancy and possible preventive public health actions

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Keywords

Voluntary interruption of pregnancy • Risk factors • Prevention

Summary

Introduction. *Voluntary interruption of pregnancy (VIP) is one of the most frequent healthcare procedures in the world and a Public Health concern in many countries, especially after liberalization of the abortion laws. The study has been carried out to identify the factors that still influence a fraction of female population towards abortion in the absence of fetal malformations.*
Methods. *We conducted a cross-sectional study in the period 2012-2016. The survey was carried out on all VIPs performed at the Gynecology and Obstetrics Unit of the University Hospital "G. Martino" in Messina, Italy.*
Results. *The analyzed sample consisted of 1131 women, aged between 16 and 50 years. Only 4% of VIPs was due to a diagnosis of fetal malformation. In relation to the presence or absence of fetal malformations as the possible reason for VIP, the sample was split up into two groups and the socio-demographic characteristics were considered. VIPs in the absence of malformations were significantly more frequent in younger women with a lower educational level, in unmarried and unemployed women and in women who already had children. These results were confirmed to Pearson test that indicated that all these variables were related to VIP in the absence of malformations.*
Conclusions. *Based on our results, it is crucial to further prevent requests for VIPs through information and sex education programs for adolescents in schools and consultants, and responsible procreation promotion programs.*

Introduction

Voluntary interruption of pregnancy (VIP) is one of the most frequent healthcare procedures in the world [1-3]. In 2003, approximately 41, 600, 000 VIPs were carried out and this number has remained constant over the past ten years [4]. Abortion seems to be a Public Health concern in many countries, especially after liberalisation of the abortion laws. In Italy over the last twenty years, there has been a constant reduction of VIPs due to more frequent and better use of contraceptive methods and more effective family counselling. Before legalisation, clandestine abortions ranged between 220,000 and 600,000 per year. In Italy, in the years immediately following the introduction of the law 194/78, which established rules for the protection of maternity, there was an increase in the incidence of abortions; however, in subsequent years there was a continual decrease [5]. The provisional data for 2014 showed a total of 97,535 notified by Regions with a decrease of 5.1% respect the definitive data of 2013 (102,760) and a halving compared to 234,801 of 1982, the year in which the highest value was found in Italy [6].
The availability of detailed information concerning VIPs has been made possible by the constant monitoring provided by the above mentioned law, 194/78, which provides national annual presentations to parliament on reports about VIPs, curated by the Ministers of Health and Justice [7]. Data are collected from the VIPs-Epidemiological Surveillance System, which involves, at a central level, the Istituto Superiore di Sanità (National Institute of Health, also named ISS), the Ministry of Health and the National Institute of Statistics (ISTAT) and, at peripheral level, the Regions and the Autonomous Provinces. The Surveillance System is based on the use of a special form, the D12 form of the National Institute of Statistics, which contains various information such as the socio-demographic characteristics of women and other data not obtainable from those derived from the hospital discharge forms. The Regions collect this information monthly from the structures involved in the execution of the VIPs and transmit it to the central level. Since its inception in 1980, the Surveillance System has been able to follow the evolution of VIPs, the prevention of which is one of the primary goals of Public Health. This system has also allowed us to hypothesise the possible reasons women request VIPs and the effectiveness of the prevention programmes [6].
This survey, carried out on all VIPs performed at the Gynecology and Obstetrics Unit of the University Hospital "G. Martino" in Messina, Italy, during the five-year period 2012-2016, has been designed to identify the factors that still influence a fraction of female population towards abortion in the absence of fetal malformations.

This is essential to further reduce this practice, allowing development of more effective and targeted preventive interventions. To this aim, grouping cases according to the presence or absence of diagnosed fetal malformations, the socio-demographic characteristics were assessed to identify potential differences between the two groups.

Methods

Sample collection

We performed a cross-sectional study by analysing the D12 forms of the ISTAT, compiled by the healthcare workers in Gynecology and Obstetrics Unit of the University Hospital "G. Martino" in Messina, for each abortion in the five-year period 2012-2016. The Istat D.12 is individual and anonymous form in which are collected information about the woman and the pregnancy. To avoid bias caused by case selection and to have a more complete overview of the factors influencing VIP choice, no eligibility criteria were established and all D12 forms were examined. These include information on the socio-demographic features of the women (their residence, citizenship, age, marital status, education, occupation and reproductive history), the services involved in certification and the intervention, and the methods of intervention (gestational age, type of intervention, analgesic therapy, duration of hospital stay and complications). The D12 paper forms were subsequently forwarded to the Hospital Presidium Medical Management, which provides information on the specific computer program supplied by the Health Ministry, and by the Italian National Institute of Statistics. Once the data have been entered online, the program automatically generates an internal hospital database from which we extracted, for a single year, the data taken into account through the Query System (Microsoft Office, Access, 2015) by applying specific filters for the data collection and sorting.

Statistical analyses

In relation to the presence or absence of fetal malformations, the sample was split up into two groups, *i.e.* a control group, consisting of the women who underwent VIP because of fetal malformations and case group formed by those who resorted to abortion for other causes. Statistical processing was carried out using StatSoft software (StatSoft®, version 10). We performed chi square and t-test, for categorical and continuous variables respectively, to assess the differences of the socio-demographic variables in the control and case groups. Pearson correlation test was used to evaluate the relationship between VIPs and the independent variables, *ie*. socio-demographic characteristics. The value of $P \leq 0.05$ was considered significant.

Results

We collected all VIPs data related to the period 2012-2016, of which only 4% was due to a diagnosis of fetal malformation. The analysed sample consisted of 1131 women, aged between 16 and 50 years (31.20 ± 7. 33). Table I reports the socio-demographic characteristics of the all sample split up in control group, consisting of the 45 women, and the more numerous case group formed by 1086 women.

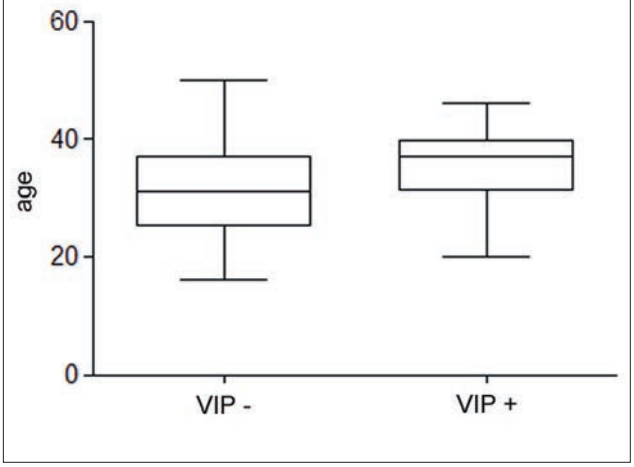
In particular, we considered the following socio-demographic factors: education level, marital status, profession, number of children, number of previous abortions and nationality.

In comparison to control group we observed that features significantly associated with VIP in the absence of malformations were age, education level, marital status, profession and number of previous children. As shown in Figure 1, highly significant differences were related to age since VIPs in the absence of malformations were associated with younger age (31.03 ± 7.33 *vs*. 35.53 ± 5.74).

Furthermore, in the case group were significantly more frequent the women with a lower educational level, unmarried, unemployed and already with children. Conversely, nationality and previous abortions were not significantly related to VIP choice in the case group (Tab. I).

Pearson test confirmed these results highlighting that the variables strongly related to VIP ($P < 0.0001$) were marital status and age. In particular, VIP in the absence of malformations (cases: enconded as 1 *vs*. controls encoded as 0) was inversely related to the continuous variable age ($r = 0.118$) and to categorical variable marital status for which unmarried, separated/divorced/widow and married were encoded as 1, 2 and 3 respectively ($r = -0.195$). Similarly, the educational level, the employment and having children already were inversely related to VIP in the absence of malformations ($P < 0.05$).

Fig. 1. Box plots of age in relation to absence versus presence of malformation.



Tab. I. Socio-demographic characteristics of the examined women divided into two groups in relation to the presence or absence of fetal malformations as possible cause of VIP.

	VIP without malformation	VIP with malformation	p
Mean age (± SD)	31.03 (± 7.33)	35.53 (± 5.74)	t = -3.79 P = 0.0002
Education level			
Graduation High school Middle/elementary school	7.73 44.22 48.04	22.50 45.00 32.50	χ^2 = 10.93 P = 0.012
Marital status			
Married Separated/divorced /widow Unmarried	34.94 4.00 61.06	85.00 2.50 12.50	χ^2 = 38.83 P = 0.00001
Profession			
Employed Housewife Unemployed Student	33.48 0.55 52.32 13.65	57.50 0.00 40.00 2.50	χ^2 = 8.81 P = 0.003
Nationality			
Non EU citizens Eastern Europe Italy	5.19 10.28 84.53	7.50 5.00 87.50	ns
Number of children			
0 ≤ 2 > 2	38.13 49.59 12.28	57.50 40.00 2.50	χ^2 = 9.14 P = 0.002
Previous VIP			
None Yes	84.53 15.47	90.00 10.00	ns

Lastly, only nationality and previous VIP were not related.

Discussion and conclusions

The collection of VIP data through the compilation and subsequent consultation of D12 forms has allowed us to obtain useful data for identifying the possible factors that induce women to undergo VIP in the absence of fetal malformations. Despite the large case group, the major limitation of our cross-sectional study was the small number of the reference sample that could reduce the power of the study.

Our survey showed that they had a lower level of education, were unemployed or unmarried, and/or had other children. In particular, the co-existence of these variables significantly increased the use of VIP. From the results obtained, we can extrapolate the influence of socio-economic factors in choosing not to carry on a pregnancy. This hypothesis is confirmed by the multivariate analysis and by the opposite characteristics presented by women who, due to the presence of fetal malformations, chose to undergo VIP.

Contrary to women who used VIP in the absence of malformations, women who chose abortion due to fetal malformations were more often graduated (22.5% *vs* 7.7%), employed (57.5 *vs* 33.5%) and married (85% *vs* 34.94%). Based on this, we can state that a higher level of education, being employed and being married are protective factors, in the absence of malformations, against the use of VIPs.

No correlation was found with nationality, probably due to the relatively small number of foreign women having a VIP on the total number of VIPs carried out in the examined Gynecology and Obstetrics Unit.

Based on our results, and in the light of the evidence indicating a constant and progressive decrease of VIPs, it is crucial to further prevent requests for VIPs, since such requests must represent in the majority of cases an "*extrema ratio*" and not the choice of election even for the induced psychological consequences [8, 9]. This aim can be obtained by a number of ways, as already indicated in the 2000 Maternal-Child Projective Objective (in Italian POMI) [6]. These ways include information and sex education programmes for adolescents in schools and consultants, and responsible procreation promotion programmes that can be implemented, for example, after a childbirth and during the prevention session of female

Tab. II. Multiple regression analysis for education level, marital status (married/unmarried), profession, age and number of sons (Adjusted R^2= .08391179).

Covariates	B value	P value
Education level	-0.018	0.575
Marital status	-0.237	0.000000
Profession	-0.050	0.113
Number of children	-0.236	0.000000
Age	0.116	0.0014

cancers [10]. Staff working within the services for family care may discuss a woman's request for VIP with her, and together assess the reasons for her choice and explore alternative solutions [11].
According to Articles 2 and 5 of the Italian law 194/1978, counselling may help women to find solutions; information should be given on financial and social support issues, and the right to give birth anonymously. It should be emphasised that family counsellors are far more competent in the provision of maternity support networks, in collaboration with the social services of municipalities and the private social sector. In the interviews, it is also important to prevent the risk of repeated abortion through an analysis of the contraceptive methods used and the failure of the same, in order to convey the correct information and to ensure the effective use of contraception [6, 12, 13]. From all these considerations, the importance of the integration of all the protagonists of these prevention programmes (schools, families, family care services) for the formulation of targeted interventions is evident [7]. These interventions could be addressed especially to the adolescents that, as showed by previous studies, are a high risk category [14, 15].
In conclusion, despite the decreasing of the phenomenon during the last 30 years, the prevention of VIPs remains a primary objective of Public Health that must engage understanding the territorial needs and all critical issues through the constant commitment of the Regions. The latter, continuing to collect data regarding VIPs in all our territory, allow the identification of the target populations on which to focus the intervention strategies in order to improve the situation.

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Conflict of interest statement

None declared.

Authors' contributions

GV, AF and RR conceived and designed the experiments; PP, OT, AD and RR performed the data collection; ADP and GV analysed the data; RR and AF wrote the paper.

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ORIGINAL ARTICLE

Correctional nursing in Liguria, Italy: examining the ethical challenges

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Keywords

Correctional nursing • Moral distress • Nursing ethics • Italy

Summary

Introduction. *Correctional nursing can involve significant ethical difficulties. This study examined ethical challenges encountered by correctional nurses in the Italian region of Liguria. Empirical data were analyzed in relation to relevant ethical standards. The former involved a study of 75 nurses and managers in the Ligurian correctional system, while the latter involved an analysis of the Italian Code of Ethics for Nurses and related standards for correctional practice.*
Methods. *Quantitative and qualitative methods were used for the empirical study. Questionnaires were administered to collect data on participants' characteristics and care settings. The Measure of Job Satisfaction (MJS) was also administered. Five focus groups were conducted.*
Results. *Quantitative Data: Respondents identified factors that mostly impacted on recruitment and retention. Unfavourable factors included: structural, organizational, and relational factors. Favourable factors included: nursing consultation, continuing education activities, and peer support. MJS results were equal to 'unsatisfied'. Qualitative Data: five themes were identified through thematic analysis of focus group data: Health needs of incarcerated persons; Negotiation of the boundaries between care and custody; Job satisfaction related to nursing in a correctional setting; Barriers to providing good care; and Security needs. Ten categories of norms were identified in the Code as areas of ethical standards relevant for the empirical data.*
Conclusions. *Our empirical findings demonstrate that these nursing standards can be systematically compromised in correctional settings. Nurses feel compelled to provide ethically-problematic nursing services, with situations of moral distress. This research informs the development of needed policy, educational, and practice changes for nurses in correctional settings.*

Introduction

The aim of this study was to examine the ethical challenges encountered by nurses practicing in correctional settings in the Italian region of Liguria. Despite the regional focus of this research, we believe that this investigation will also help advance our understanding of correctional nursing in other settings internationally. The term 'correctional nursing' is sometimes used in this article because it is widely used in the international literature, although we recognize the problematic tone of the term. For this reason, we frequently use the expression 'nursing practice in correctional settings' as an alternative.
International literature has demonstrated that nursing practice in correctional settings can involve significant ethical challenges [1-4]. These ethical challenges have been under-examined; frequently relating to dilemmas for which existing ethical standards are unclear or even contradictory. In particular, as nurses in correctional settings strive to attend to the health needs of patients and clients who are incarcerated, they are often called upon to use their clinical expertise for purposes of control or punishment.
Nurses practicing in correctional settings confront complex problems [1, 5-10]. They have a high degree of responsibility as they are required to manage emergencies and mental health problems, among other chronic conditions. Patient health information must be kept confidential and not generally shared with correctional officers unless there is a justifiable reason. Nurses practice in settings where safety is a constant workplace concern. Nurses often report to a warden, rather than a health administrator, facing difficult negotiations of care practices [1].
The number of incarcerated persons in the United States has been increasing significantly. Incarcerated men and women have increased rates of serious and chronic physical and mental illnesses [2]. Maeve and Vaughn [2] highlighted numerous ethical problems faced by nurses in correctional settings: maintaining patient confidentiality; using chemical restraint for security rather than medical purposes; working with underqualified personnel; providing care outside their scope of practice; caring for addicted prisoners; caring for the mentally ill; caring for incarcerated mothers and their newborns; managing the visitation rights of children whose parents are incarcerated; dealing with violence; coping with prolonged isolation and segregation of inmates; providing adequate planning for released detainees; and involvement of nurses and physicians in carrying out the death penalty [2].

In a critical examination of forensic psychiatric nursing in corrections, Holmes has reported that nurses are 'objects of governmental technologies' [11]. They become the body onto which processes of conforming to the correctional setting is dictated and inscribed. Nurse–patient relationships involve under-recognized power structures. Nurses frequently participate in behaviour modification programmes that involve unethical nursing approaches to mentally ill offenders [12].

An ethnographic study of twelve prisons in England highlighted the significant responsibilities borne by nurses [8]. The National Health System has recognized the importance of synergy in the role of nurses with other health professionals in prisons (e.g., psychiatrists, social workers, etc.). In new models of care, nursing roles are authorized to provide prescriptions for minor illnesses (e.g., constipation, toothache, colds), perform intake assessments (e.g., nurse-led triage), and evaluate and manage complex chronic illnesses (e.g., nurse-led clinics). Physician assessments follow from assessments performed by nurses. Nurses are central agents in rehabilitation programs for substance, psychotropic drug, or nutritional abuse; prescribing non-pharmacological treatments such as physical activity or behavioral programs that promote sleep. The health service has developed a culture that recognizes the importance of health and quality of care, limiting the abuse of control measures.

National evidence in Italy has highlighted that illness levels and health care needs are significantly more elevated among detainees than in the general population [13-15]. The most common illnesses include: tuberculosis, HIV, hepatitis, syphilis, and other sexually transmitted infections. Mental illness is significantly elevated, as well as substance abuse [14]. Nursing ethical concerns relating to correctional settings have been scarcely examined in Italy. One study was conducted with detainees and nurses to investigate the roles of nurses in these settings [16]. Most participants regarded nurses as mere treatment providers.

A number of international statements and research reports have highlighted standards that should be upheld for nursing in correctional settings. For example, the European Code for Health in Prisons recognizes the rights of detainees to have access to health care without discrimination and highlights the 'pathogenic' impact of confinement on mental health [17].

In Britain, recent increases in nursing staffing, training, and development of holistic practices and promotion of a code of ethics have demonstrated improvements in the health and social integration outcomes of detainees [14]. The National Commission on Correctional Health Care identified six ethical principles for nurses in correctional settings: a) respect for persons (autonomy and self-determination); b) beneficence (doing good); c) nonmaleficence (avoiding harm); d) justice (fairness, equitability, truthfulness); e) veracity (telling the truth); and f) fidelity (remaining faithful to one's commitment) [18].

The journal *Nursing Standard* published a theme issue in 2010 that focused on correctional nursing. Within this volume, Perry published a competency mapping and a grid for evaluating the performance of nurses in correctional settings [6]. These competencies included: prevention of communicable diseases; the management of mental disorders and chronic illnesses in an inadequate context; integration with other professionals for evaluation activities; and regional networking to ensure continuity of care.

The International Association of Forensic Nurses has highlighted guiding principles for ethical decision-making in forensic nursing, that is: a) fidelity to patients and clients; b) responsibility to the public; c) obligation to science; and d) dedication to colleagues [19].

The American Nurses Association has highlighted that correctional nurses have to balance an attitude of care while maintaining safe boundaries. Nurses should advocate for access to care. For patients that die while incarcerated, nurses should help patients die with dignity and comfort. The American Nurses Association has also argued that correctional nurses should not participate in executions [20].

There is an absence of explicit ethical standards for nursing practice in correctional settings in Italy. There have been, however, some significant structural shifts in correctional health services that imply potential improvements in nursing practice conditions [21]. Heath professionals practicing within correctional settings, including nurses, are now administratively accountable to the Public Health Branch of the National Health System; rather than the correctional services administration, as they were before. This initiative sought to bridge practice standards as well as collaborations among health professionals practicing within prisons with the broader community of practitioners in the general population. Moreover, this restructuring establishes a clearer boundary between security measures and responses to the health needs of detainees.

The principal objective of this study was to examine the ethical challenges encountered by nurses practicing in correctional settings in the Italian region of Liguria. Drawing on a framework for ethical analysis referred to as the 'is-ought problem' [22], an empirical examination of clinical practice was analyzed in relation to relevant ethical standards to highlight tensions that may exist between the a) 'is' of current practices (i.e., what nurses *are doing*); and b) 'ought' applicable to these practices (i.e., what nurses *should be doing*). The former were documented through a quantitative and qualitative investigation and the latter were examined through an analysis of the Italian Code of Ethics for Nurses [23] and related standards for correctional practice in Italy and Europe. This research was conducted to help inform the development of policy, practice change, and educational initiatives to address the ethical challenges encountered by nurses in correctional settings.

Methods

The empirical component of this study is based on a reanalysis of data collected from an earlier study conduct-

ed by three of the authors (i.e., Bagnasco A, Delogu B, Sasso L.) [24]. The study was conducted as part of one author's (Delogu B.) graduate studies. The aim of the initial study was to document occupational challenges and job satisfaction among nurses working in correctional settings in Liguria, Italy. Upon completion of the research, the authors noted significant ethical concerns that were underlying the data. They therefore recruited the remaining author (FAC), a nursing ethicist, to assist with an ethical analysis of the empirical data along with an analysis of relevant norms.

Description of participants

Participants in the study included nurses and their managers in the Ligurian correctional health system (i.e., Medicina Penitenziaria delle cinque AASSLL della Liguria) as well as nurses that worked within this system in the past. A total of 74 nurses participated in the study.
A mixed methods design was used for the study, drawing on quantitative and qualitative methods. Measurement instruments from the international literature (described below) were translated, adapted, and validated for an Italian context by the University of Genoa doctoral nursing program.

Quantitative methods

Participants were administered a questionnaire, adapted from the work of Almost et al. [25], to document the: a) demographic characteristics of the sample; b) care provision settings represented in the study context; and c) factors associated with job retention and nurses' intention to leave their jobs. To measure the latter, a validated measure of job satisfaction was attached to the questionnaire (i.e. M*easure* of J*ob Satisfaction,* MJS) [26]. Work satisfaction is an important predictor of retention and intent to leave [27]. The MJS consists of 38 items grouped into five factors: a) personal; b) workload; c) professional support; d) training; and e) economic remuneration and opportunities for career development. For each MJS item, participants responded to the following question: 'How satisfied are you with this aspect of your job?': 1) very dissatisfied; 2) dissatisfied; 3) neither satisfied nor dissatisfied; 4) satisfied; 5) very satisfied.

Qualitative methods

Focus groups were used to collect qualitative data. Five focus group meetings were conducted with nurses and nursing managers in: La Spezia, Savona, Genova Marassi, Pontedecimo, and Sanremo. Chiavari and Imperia were excluded as study settings because the number of nurses in these settings was too limited for the study.
Five principal questions were used to orient the focus groups: a) How do you identify the health needs of detainees and which prisoners do you think have the greatest health needs?; b) How would you describe the differences between working in a hospital and working in your context?; c) What are your needs today to perform this work?; d) What are the sources of satisfaction in your work activities?; e) What are the obstacles to providing good health services in your work setting? Qualitative data were analyzed with NVIVO 10 software.

Results

Empirical Analysis

Quantitative Data

Respondents identified favorable and unfavorable factors that had the most significant impact on the recruitment and retention of nurses in their setting. Unfavorable factors included: structural, organizational, and relational factors (Tab. I). Favorable factors included: nursing consultation: 35.1%; continuing education activities: 31.1%; and peer support: 16.2%.

Measure of job satisfaction

Fifty-nine participants completed the MJS to measure their level of satisfaction regarding five specific factors. None of the measures for the five factors reached a mean as high as 4.0, the level corresponding with 'satisfied'. Personal Satisfaction and Satisfaction with Professional Support were the most highly rated (i.e., 3.878 and 3.814, respectively) and Economic Remuneration and Opportunities for Career Development had the lowest rating (i.e., 3.034).
It is noteworthy that none of the means for the five factors were less than 3.0; that is, none were oriented toward a clear measure of dissatisfaction. All means were below 4.0 (satisfaction) and above 3.0 (neither satisfied or dissatisfied), which implies that despite the significant difficulties encountered by these nurses they also derived some favorable returns from their work to counter these difficulties.

Qualitative data

Five major themes were identified through a thematic analysis of data recorded during the focus groups:
(1) Health needs of incarcerated persons (detainees); (2) Negotiation of the boundaries between care and custody; (3) Job satisfaction related to nursing in a correctional setting; (4) Barriers to providing good care; and (5) Security needs.

Tab. I. Summary of quantitative results.
Themes identified within each factor are listed.

Theme I: Structural	
Distance & isolation	32.4%
Logistical	27.0%
Absence of a care setting	21.6%
Theme II: Organizational	
Insufficient staff	24.3%
Heavy workload	21.7%
Limited professional autonomy	17.6%
Excessive professional autonomy	16.2%
Resource restrictions	13.5%
Theme III: Relational	
Absence of continuing education	29.7%
Conflict with care recipients	35.2%
Conflict with correctional officers	20.3%
Conflict with the medical team	10.9%

NB: The proportion of respondents who reported each theme is indicated in parentheses.

1. Health needs of incarcerated persons (detainees)
When compared to practicing in conventional hospital settings, correctional settings entail: (a) a much greater number of patients for each nurse; (b) greater professional autonomy and therefore increased individual responsibility; (c) a particularly high proportion of health concerns related to mental health and substance abuse problems; and (d) a number of barriers for the nurse-client relationship, which require an alteration in how nurses approach patients.

2. Negotiation of the boundaries between care and custody
Correctional settings have a culture of order and disciplinary control, which overshadow concerns about the health of detainees. Participants reported that a greater proportion of their time is devoted to maintaining security rather than promoting health or managing illness.

3. Job satisfaction related to nursing in a correctional setting
Nursing practice in these settings can provide some opportunities for personal and professional enrichment, which was related to inter-professional work, detainee multiculturalism, and trust relationships that can be established with patients. On the other hand, job satisfaction can be compromised when: a) correctional officers expect nurses to collaborate with them to exert control measures on detainees; b) detainees try to manipulate nurses to obtain favors; c) there is insufficient time for nurses to develop a non-judgemental attitude with detainees; d) nursing practice requires advanced expertise in assessing health needs of detainees who are not presenting their symptoms honestly; e) working with substance abuse and mental health problems; f) personal freedom is restricted in the workplace; g) there are insufficient nursing staff, which increases workload and reduces opportunities for rest breaks; and h) there is little recognition of the specialized competence required to practice in correctional settings.

4. Barriers to providing good care
Security requirements seem to limit the professional autonomy of nurses. That is, nurses are not recognized as professionals but as mere providers of treatments without any autonomous thought. Prison administrators refer exclusively to physicians as the health care professionals. Care is also sometimes compromised by conflictual relationships with correctional officers who tend not to recognize the health needs of detainees. Some prisons draw on 'cooperatives' for nursing staffing, which results in very high nursing turnover rates. This limits nurses' ability to consolidate their competencies and compromises trust relationships between nurses and detainees as well as nurses and correctional officers.

5. Security needs
The principal priority in correctional settings is security. Consequently, nursing actions are predominantly focused on managing medications and sharps – rather than providing care.

Normative Analysis

Empirical findings helped orient an analysis of relevant ethical norms that define ethical practice for nurses in correctional settings in Italy. The principal normative source that was examined was the Code of Ethics for Nurses in Italy (referred to below as 'Code') [23].
Ten categories of norms were identified in the Code as areas of ethical concern highlighted by the empirical data. These included: General Responsibilities; General Ethical Considerations; Nursing Competence; Respect for the General Rights of Patients; Respect the Autonomy of Patients; Respect Patients' Privacy and Confidentiality; Respect for the Wellbeing of Patients; Promote Inter-Professionalism; Promote Patient Safety; Prevent Conflict of Interest. Table II lists the specific sections of the Code related to each normative category. These normative standards highlight explicit nursing standards that can be systematically compromised in a correctional setting – given the empirical findings reported above – placing nurses in situations where they feel compelled to practice against the standards of the profession.
Additional sources were examined for articulations of practice standards specifically relevant for health professionals in correctional settings; in Italy and Europe. Although these were not specifically focused on nursing practice, they provided specificity that complemented the more general norms drawn from the Code.
The Italian National Bioethics Committee prepared a Report on ethical considerations that should be applied to the health of detainees, citing relevant Italian & European norms [15]. The Report outlines health risks identified among incarcerated populations and the health-related rights of detainees that should be respected. The Report commends the shift of administrative responsibility for health services from correctional authorities to state health services administration. This will help preserve the professional autonomy of health professionals and prevent the confusion of health services with security services (i.e. dual roles) within these settings, among other merits of such a restructuring. For example, health professionals responsible for providing health care to detainees should not also be responsible for providing expert assessments of the detainees' health for the justice or security procedures of the courts or correctional systems such as prisons (e.g. assessment of detainee's capacity to endure disciplinary measures such as solitary confinement). A limitation of this Report, for the purposes of this study, is that it is predominantly focused on the practice of physicians, with occasional references to health professionals more broadly. Although the Report appears directly applicable to other health professionals, such as nurses, this is not explicitly articulated.
The Report corroborates related international standards regarding detainees. Specifically, the European Code for Health in Prisons recognized that a) detainees should have a right to health services without discrimination; and b) the restriction of personal freedom can have a harmful impact on the mental health of detainees [17]. Disciplinary measures should therefore be restricted to minimize these harms. The World Health Organization

Tab. II. Analysis of Italian Code of Ethics for Nurses (From Federazione Nazionale Collegi IPASVI, 2009 [23], mod.).
General responsibilities
Article 1: A nurse is a healthcare professional in charge of nursing care. Article 3: Nurses have the responsibility to assist, look after and take care of people in the respect for the individual's life, health, freedom and dignity.
General ethical considerations
Article 8: In situations of conflict, caused by divergent ethical opinions, nurses do their best to find a solution through dialogue. In the event of a persistent request for an action that goes against the ethical principles of the profession or personal values, nurses may avail themselves of the clause of conscience, to ensure the patient's safety and life. Article 16: Nurses should be proactive in analyzing the ethical dilemmas they experience in their everyday practice and seek ethical advice, and thus help deepen bioethical reflection. Article 43: Nurses report to their respective Nursing Council any abuse or unethical professional conduct of their colleagues. Article 50: To protect the public, nurses must report situations of unlawful practice of the nursing profession to their Nursing Council. Article 51: Nurses must report to their Nursing Council situations involving circumstances or the persistence of conditions that limit the quality of treatment and care or the dignity of professional practice.
Nursing competence
Article 2 : Nursing is service to the person, families and the community, provided through specific, autonomous and complementary interventions of intellectual, technical-scientific, managerial, relational and educational nature. Article 11: Nurses perform evidence-based practice and refresh their knowledge and competences by means of life-long education, critical reflection on experience and research, they design, carry out and take part in educational activities and promote, start and take part in research activities and disseminate the findings. Article 13: Nurses take on responsibility proportionally to their level of competence and if necessary, seek the intervention or advice of nurse practitioners or specialists. They give advice by putting their knowledge and skills at the disposal of the professional community. Article 15: Nurses should ask for training and/or supervision for practices that are new or for which they have no experience.
Respect for the general rights of patients (i.e., Detainees)
Article 4: Nurses provide care according to the principles of equity and fairness, taking into account the ethical, religious and cultural values, as well as the gender and the social conditions of the person. Article 5: The respect for the fundamental human rights and the ethical principles of the profession is an essential condition to practice nursing. Article 20: Nurses listen to, inform, and involve patients and together they assess their healthcare needs, in order to provide the proper level of care and help patients make their own choices. Article 21: Nurses, by respecting the patients' will, favour their relationships with the community and with their next of kin, by involving them in their healthcare plan. Nurses consider both the intercultural dimension and the healthcare needs linked to it. Article 30: Nurses do their best so that they resort to constraint only in exceptional cases, supported by medical prescription or by documented healthcare exams. Article 32: Nurses help protect patients who find themselves in conditions that limit their development o expressions, when their family and context are not adequate for their needs. Article 47: Nurses, according to their level of responsibility, contribute to guide the policies and the development of the healthcare system, to ensure that the patient's rights are respected, resources are sensibly and appropriately allocated and that the professional role is valued.
Respect the autonomy of patients (i.e., Detainees)
Article 5: The respect for the fundamental human rights and the ethical principles of the profession is an essential condition to practice nursing. Article 20: Nurses listen to, inform, and involve patients and together they assess their healthcare needs, in order to provide the proper level of care and help patients make their own choices. Article 30: Nurses do their best so that they resort to constraint only in exceptional cases, supported by medical prescription or by documented healthcare exams. Article 32: Nurses help protect patients who find themselves in conditions that limit their development o expressions, when their family and context are not adequate for their needs. Article 37: When patients are unable to express their will, nurses take into account what they had previously clearly declared or documented.
Respect patients' privacy and confidentiality
Article 26: Nurses do not disclose any confidential information on the patients. When gathering, handling and reporting data on patients, nurses limit themselves only to what is relevant to the nursing process. Article 28: Nurses respect professional secrecy not just because it is a legal obligation, but because they are deeply convinced that this is a concrete expression of their relation with patients built on trust.
Respect for the wellbeing of patients (i.e., Incarcerated)
Article 6: Nurses consider health as a fundamental gift for the person, as well as the best interest of the entire community and engage in protecting it through prevention, care, rehabilitation and palliation. Article 7: Nurses act in the best interest of the patient, by promoting his/her resources in order to help him/her achieve the highest possible level of autonomy, especially when the patient is disabled, disadvantaged or fragile. Article 22: Nurses know the diagnostic-therapeutic project due to its influence on the nursing process and on the relations with the patient. Article 23: Nurses understand the value of integrated multi-professional information and do their best so that patients have all the necessary information for their daily life.

continues

Tab. II. *(follows)*
Article 24: Nurses help and support patients in their choices, providing healthcare information regarding their diagnostic-therapeutic projects and adapting their communication so that they can easily understand. Article 31: With regard to healthcare, diagnostic-therapeutic and experimental decisions, nurses do their best so that the opinion of a minor is taken into consideration according to his/her age and level of maturity.
Promote inter-professionalism
Article 14: Nurses recognize that both interaction among professionals and inter-professional integration are essential conditions that allow to meet all the patient's needs.
Promote patient safety
Article 29: Nurses contribute to the promotion of better safety conditions for patients and their families and to the development of the culture of learning from errors. They take part in clinical risk management initiatives. Article 33: When nurses notice any abuse or deprivation at the expense of the patient, they use all means to protect him/her and, if required, report the case to the competent authority.
Prevent conflict of interest
Article 17: Nurses, in their professional practice refuse any conditioning, pressure or interest deriving from the patient, the family, other health workers, companies, associations or organizations. Article 49: Nurses, in the best interest of their patients, make up for the deficiencies and the disorganization that exceptionally occur in the centre they work for. They must abstain themselves from doing this, by producing documentary evidence, when the above deficiencies and disorganization are habitual or recurrent, or in any case systematically compromise their professional mandate.

Note: Some sections are cited more than once, as they correspond with multiple themes.

has outlined steps that correctional systems should take to reduce the public health risks that can result from compulsory detention, drawing on internationally recommended standards for prison health [28]. The WHO Guide for prison health states: 'People who are in prison have the same right to health care as everyone else; Prison administrations have a responsibility to ensure that prisoners receive proper health care and that prison conditions promote the well-being of both prisoners and prison staff; Health care staff must deal with prisoners primarily as patients and not prisoners; Health care staff must have the same professional independence as their professional colleagues who work in the community; Health policy in prisons should be integrated into national health policy, and the administration of public health should be closely linked to the health services administered in prisons; This applies to all health matters but is particularly important for communicable diseases; and The European Prison Rules of the Council of Europe provide important standards for prison health care.

Integration of empirical and normative analyses

Although some gaps persist in the development of ethical norms for correctional nursing in Italy, existing norms highlight major health-related rights and entitlements of incarcerated persons that correspond to the ways that non-incarcerated persons should be treated. However, the empirical evidence reported here demonstrates that nurses confront significant barriers in their attempts to respect these standards. A serious gap exists between the 'is' and the 'ought' of correctional nursing in this setting. These nurses feel systematically compelled to provide ethically-problematic nursing service.

This scenario of feeling impeded from practicing according to one's understanding of what is ethically required corresponds with situations described in the literature that lead to *moral distress*. Originally defined by Jameton [29], moral distress refers to the malaise that results when one knows how one ought to act in a situation but feels prevented from doing so by barriers presented by the situation. This phenomenon was initially described in the nursing literature and has remained a significant nursing concern. This may be attributable to a common disconnect between the professional responsibilities held by nurses in various practice contexts and the limited authority that they are granted to fulfill these responsibilities. Moral distress frequently results in strong feelings of guilt, regret, and remorse toward one's actions or inaction – while having a sense of inability to act differently. The data reported by the nurses participating in this study highlight a significant risk for moral distress among nurses practicing in Italian correctional settings.

Discussion

The prison environment has a culture characterized by order, discipline, and control [2, 4, 11, 12, 25, 30]. This culture can impede nurses' responses to the health needs of detainees. The results from our research reveal the experiences of nurses who care for detainees, which is sometimes challenging and frustrating and can lead to moral distress.

The recent 2008 shift of responsibility for prison health to the regional health system in Italy [21], has had an impact on the professional role of nurses practicing in prisons. Adjustments have had to be made for health services provided in correctional settings, to ensure that they are comparable to services provided to the non-incarcerated. The goal of this shift is to ensure that health care providers are not responsible for performing security and control measures. This will also help correctional settings with a nursing shortage to supplement staffing with nurses from the regional health care sector.

In many cases, health care professionals employed by the Ministry of Justice have asked to be transferred to settings

other than prisons. The initial lack of knowledge on the part of the regional health system about prison health regarding the specific particularities of a) this context, b) clients, and c) relational dynamics, resulted in errors of judgment in the assignment of nursing staff [14]. These nursing staff assignments were unsuitable for ensuring the performance of activities required in this setting. This has caused difficulties in nursing staff retention and increased turnover, resulting in the fragmentation of continuity of care. Consequently, most of the nurses currently working in the correctional settings of Liguria have practiced in this context for only a short time. This leads to difficulties in the assessment of detainees' health needs; as they are often not sincere about their state of health in their interactions with nurses as well as correctional officers. This highlights a need for specialized training for correctional nursing, which entails a broad scope of expertise requiring university-level education [1-6].

This is corroborated by Powell who highlighted that policies and organizational changes have an impact on professional roles and that conflict can develop between detention and health care delivery systems [8]. We support that the 'ethos of health care for prisoners', identified by Willmott [4], must be further developed and should be the object of future research.

Focus groups data in this study revealed how participants thought that the real challenge was to meet the everyday health needs of prisoners while negotiating compliance with safety requirements. This continuous bargaining caused conflict between parties that have different mandates; caregivers in prison are viewed ambivalently by those responsible for safety. Nurses were considered by correctional staff as a hindrance to the conduct of non-health-care prison activities. Correctional officers, usually with limited work experience, are led to believe that detainees do not have any illnesses or health needs. Listening to patients, by nurses, is considered a waste of time. This discounting of professional nursing practice can further contribute to moral distress among nurses.

The findings in this Italian study corroborate the findings reported in the international nursing literature. Correctional nurses have reported tremendous pressure to speed up their provision of care [9, 25, 27]. Nurses have described interference with their professional autonomy, as their practice can be severely restricted by prison rules [31]. Some studies have revealed bullying practices by correctional officers toward nurses [9]. Future research should examine the dangerous alliances that can sometimes develop between nurses and correctional officers at the expense of the patient.

Nurses in these settings are aware of being regarded by correctional officers as more directly accessible than physicians. This results in frequent and unnecessary calls that distract the nurse from other activities [32]. These calls are scarcely related to health problems; as officers solicit nurses to administer 'treatments' aimed at controlling detainees. Nurses' refusal to agree to such requests may lead to further conflict [30].

Correctional nurses seek recognition of the importance of their role. Some correctional nurses have reported feelings of marginalization [8, 9, 14, 25, 33]. Colleagues and acquaintances demonstrate pity as well as suspicion toward them. This nursing practice is often denigrated and inadequately compensated, when compared to workers in other high-risk sectors [33].

Our results have implications for nursing practice as well as nursing education. Some nurses highlighted the need for specific training in the management of conflicts, including ethical conflicts. Training initiatives should focus on the specific features of nursing practiced in correctional settings. These settings are significantly different from other practice settings.

We conclude that an important practical outcome of this research should be the development of educational programs to help nurses manage the complex ethical challenges they confront in their practice. These challenges include maintaining the integrity of nursing practice as well as the safety of both nurses and patients [10].

Conclusions

Correctional nursing operates in a particular context that is not primarily health-oriented; where the principal objectives are safety, control, and serving of prison sentences. Security requirements are commonly posed as a priority over the health needs of detainees. Recent policy and organizational changes strive to advance the professional role of nurses; recognizing the conflict between control and health care provision. Significant turnover compromises continuity of care and the therapeutic relationship between patients and nurses. Nurses need special training and adequate skills and experience to provide required care for detainees, who are often difficult and manipulative patients.

Future Developments

Future research should focus on the development of ethics-related knowledge and professional practice standards for correctional nursing. This should examine how to help nurses cope with moral distress associated with working with this difficult population and practice setting.

We also recommend further research on the development of effective strategies for improving relationships among detainees, correctional officers, and health care providers. Nurses are often considered as central agents in managing conflict and feel great a responsibility to support the needs of the different actors involved.

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Conflict of interest statement

None declared.

Authors' contributions

AB and LS supervized the study and reviewed the manuscript. FC conducted the data analysis and drafted the manuscript. BD collected the data and conducted her thesis on the topic of this manuscript.

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Overview

The history of tuberculosis: the social role of sanatoria for the treatment of tuberculosis in Italy between the end of the 19th century and the middle of the 20th

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Keywords

History of tuberculosis • History of sanatoria • Social role of sanatoria

Summary

Since ancient times, the most frequently prescribed remedy for the treatment of tuberculosis was a stay in a temperate climate. From the middle of the 19th century to the middle of the 20th, Europe saw the development of sanatoria, where patients were able to benefit from outdoor walks, physical exercise and a balanced diet. Moreover, the institutionalisation and isolation of patients deemed to be contagious remains one of the most efficacious measures for the control of this type of infection. The first sanatorium opened in Germany in 1854, while in Italy the earliest experiments were conducted at the beginning of the 20th century. At that time, it was widely believed in Italy that pulmonary tuberculosis could improve in a marine climate. By contrast, the scholar Biagio Castaldi described the salubrious effects of mountain air and documented a lower incidence of tuberculosis among mountain populations, which supported the hypothesis of a hereditary predisposition to the disease. In 1898, several local committees (Siena, Pisa, Padua) were founded to fight tuberculosis. The following year, these gave rise to the Lega Italiana (Italian League) under the patronage of the King of Italy, which helped to promote state intervention in the building of sanatoria.
The pioneer of the institution of dedicated facilities for the treatment of tuberculosis was Edoardo Maragliano in Genoa in 1896. A few years later, in 1900, the first specialised hospital, with a capacity of 100 beds, was built in Budrio in a non-mountainous area, the aim being to treat patients within their habitual climatic environment. In the following years, institutes were built in Bologna, Livorno, Rome, Turin and Venice. A large sanatorium for the treatment of working-class patients was constructed in Valtellina by the fascist government at the beginning of the century, in the wake of studies by Eugenio Morelli on the climatic conditions of the pine woods in Sortenna di Sondalo, which he deemed to be ideal. In December 1916, the Italian Red Cross inaugurated the first military sanatorium in the "Luigi Merello" maritime hospice in Bergeggi (SV) to treat soldiers affected by curable tuberculosis. In 1919, a specific law mandated a 10-fold increase in funding for the construction of dispensaries and sanatoria. As a result, the Provincial Anti-tuberculosis Committees were transformed into Consortiums of municipal and provincial authorities and anti-TB associations, with the aim of coordinating the action to be undertaken. In 1927, the constitution of an Anti-tuberculosis Consortium in every province became a legal obligation.
Despite this growth in social and healthcare measures, tuberculosis in Italy continued to constitute a major public health problem until the advent of antibiotics in the 1950s. Until that time, the sanatorium played a leading role in the treatment of tuberculosis in Italy, as in the rest of Europe.

Introduction

Since ancient times, the institutionalisation of patients who constitute a risk of contagion has been one of the most efficacious measures for the control of pulmonary infections, including tuberculosis (TB) [1].
In the second half of the 19th century, the conviction spread that particular climatic environments could contribute to curing TB. Subsequently, the most frequently prescribed remedy for pulmonary forms was a stay in a temperate climate [2].
Thus, from the middle of the 19th century to the middle of the 20th, Europe saw the development of sanatoria, where patients affected by tuberculosis, in addition to being isolated from the rest of the community, could benefit from a period of convalescence that included treatment programs and outdoor excursions on foot or on horseback. Patients were hosted in locations where they could enjoy complete rest, a balanced diet, fresh air, sunshine and moderate physical exercise under strict medical supervision. Indeed, in such places, increasing importance was attached to the role of rest in the process of treatment, as also to the implementation of particular norms of hygiene [3].

The origin of sanatoria as places for the treatment of tuberculosis

In Europe, the first sanatorium was founded in 1854 by Hermann Brehmer in Germany, in Goebersdorf in Silesia, a village on the border between Poland and the Czech Republic. Brehmer stressed the therapeutic effect

of the climate in the treatment of phthisis. His method of treatment spread throughout Germany, France and Switzerland, especially in the region of Davos, in the Engadin Valley, where the first high-altitude sanatoria were opened for paying patients [4].
The new sanatoria were designed in such a way that patients could stay in single rooms or rooms with a few beds, which usually gave onto large terraces where inmates could take so-called "sun baths". The buildings were surrounded by spacious meadows and tree-lined gardens, where guests could go for long healthy walks. Patients stayed in the institution for very long periods – from a minimum of six months to seven, eight or even 16 years [5].
In Italy, Biagio Castaldi, who was himself affected by pulmonary tuberculosis, personally experienced the positive effects of a balanced diet and a stay in the mountains at the beginning of the 20th century, supporting the theories widely held in the rest of Europe at that time. In an 1858 publication, Castaldi had first reported that the incidence of phthisis declined as altitude increased, and that the disease was very rare at altitudes above 1000 m. On the basis of the observation of a lower rate of mortality due to pulmonary TB among mountain populations, it was thought that sanatoria should be located at high altitude. Moreover, it was believed that patients had a hereditary predisposition to TB, while the possible role of isolation in limiting the spread of the disease was overlooked [6].
In the same period in Italy, it was widely believed that a maritime climate could also facilitate the healing of pulmonary tuberculosis and contribute to the resolution of cases diagnosed in an initial stage. Antonio Sciascia was the first to apply heliotherapy to the treatment of tuberculosis, claiming that the forms involving the lymphatic ganglia, joints and bones, skin, serous membranes and kidneys were those which could benefit most [7].
In the newly founded Kingdom of Italy, the first mountain "colonies" were instituted in Florence in 1853, in Prato in 1864 and in Pistoia in 1866, while the first seaside hospices were opened in Viareggio and Rimini in 1874 by the Bolognese Opera Pia Ospizi Marini [8].
In 1871, the Piedmontese Marine Hospice opened in Loano in Liguria. This was the first Italian hospice for children and young people of both sexes affected by bone, articular, cutaneous and glandular tuberculosis [9].
In the early years of the 20th century, again in Loano, the Hospice instituted summer and winter resorts for schoolchildren who were "frail, lymphatic, children of tuberculosis sufferers" in another building that it owned [10].
In the same period, another new therapeutic intervention for tuberculosis was invented by Carlo Forlanini, an Italian physician, in 1882; he created the first artificial intrapleural pneumo-thorax by collapsing the lung and filling the pleural cavity with nitrogen [11].
In Boston in 1889, the American Society of Climatology recognised the sanatorium as the best opportunity of cure for pulmonary TB, particularly for working-class patients. In Europe, the first example of such a facility was the section assigned to host persons of modest economic means, which was instituted in Göbersdorf in 1874 [12].

The fight against tuberculosis in Italy at the beginning of the 20th century

In Italy, between 1908 and 1914, an average of 84,335 people died of tuberculosis each year. The spread of the disease was facilitated by the insalubrious conditions in which much of the population lived, in which scant attention was paid to the most elementary norms of hygiene, whether in cities or in the country, at home or in the workplace [13].
In Europe, the first National League against TB was founded in France in 1891. This was followed in 1893 by the foundation of the Swiss Association, which was instituted in order to combat TB and to promote the building of sanatoria. Two years later, in Germany, the German Central Committee for the fight against tuberculosis was established.
In Italy, an organised effort to fight tuberculosis began at the end of the 19th century. This was initially conducted by circumscribed voluntary initiatives, which were, however, limited by their scant relationships with the newly constituted Anti-TB League (1899).
The pioneer of the fight against tuberculosis in Italy was Edoardo Maragliano, who, in 1896, founded the first Italian dispensary and the first ward for the diagnosis of TB in the Medical Clinic which he ran at the University of Genoa [14].
In Italy, the drive to fight TB came from below, especially from the poorer classes, who were hardest hit by the disease; in Pisa in 1899, a committee was set up with the aim of building a sanatorium to treat these people. Subsequently, this committee also organised an anti-TB propaganda conference. In Padua in the same year, the first Regional Committee of the National League against tuberculosis was founded through the unification of the first local committees (Siena, Pisa, Padua) under the patronage of the King of Italy and the guidance of the President, Guido Baccelli. In 1900, on the initiative of the Italian League, a congress on tuberculosis was held in Naples; its concluding motion cited two important objectives. The first was to institute a Chair for the experimental and clinical study of tuberculosis; the second was to enlist the aid of the state and of public authorities for the construction of sanatoria.
The very same year, the first specialised hospital institute was inaugurated in Budrio, a village in the Province of Bologna. Built with the aid of a generous private donation, it was equipped with 100 beds. The decision to build a sanatorium in a non-mountainous area was motivated by the desire to keep patients in their habitual climatic environment. This meant that patients could be supported and assisted more easily by their family members and maintain their daily habits – factors deemed conducive to achieving a more stable "cure" than would be possible if the patient were transferred to a mountain environment [15].

Contemporarily with the Bolognese sanatorium, another institute for the treatment of TB was founded in Gries, in the Province of Bolzano.
Among the staunchest advocates of the validity of this therapeutic approach in Italy was Giulio Bizzozero, who claimed that caring for underprivileged patients in ordinary hospitals or at home, where medical assistance was extremely poor, would increase the risk of contagion.
In Italy, the first large sanatorium devoted to treating the poor was built in 1903 in Valtellina, at an altitude of 1250 m, in the pine woods of Sortenna di Sondalo, where the climatic conditions were deemed to be favourable. Dedicated to the memory of Eugenio Morelli, the facility was set in this location on the recommendation of a young doctor, Ausonio Zubiani.
Subsequently, the fight against TB in Italy was carried forward around the city of Milan, first through the activities of the dispensaries, with the construction of the People's Sanatoria of the City of Milan in Prasomaso, and then through the building of the large sanatoria in Garbagnate and Pietra Ligure by the Milanese Opera Pia di Santa Corona [16].
Anti-TB dispensaries were promoted in Italy from 1904 onwards (in the city of Livorno), and in 1905 the Umberto I Hospice was inaugurated in Rome.
In Turin in 1909, the new San Luigi Hospital was founded in Mirafiori, which was then in open country. In the following year, the municipal "Preventorio" (prevention centre) was opened. Promoted by the Piedmontese Society of Hygiene, this facility was run by a general practitioner, who was aided by an assistant physician, a "healthcare educator" and 34 home health inspectors; these latter were chosen from among municipal teachers and were charged with providing hygiene advice and gathering information on social conditions. The Preventorio, the function of which was essentially educational, was open every day, including public holidays, and also acted as an intermediary for the provision of subsidies in the form of money and food [17].
In 1911, a large dispensary opened in Rome as a result of a donation by Queen Margherita, and was entirely run by the Italian Red Cross.
In Bologna in March 1914, the local Anti-tuberculosis Association opened the first anti-TB dispensary in the Region, while at the same time a phthisis ward began operating in S. Orsola Hospital. In Venice, the San Marco Hospital for the treatment of pulmonary tuberculosis was founded in the same year [18].
Thanks to the institution of these facilities for the prevention and treatment of TB in various Italian cities, a marked reduction in the epidemic of tuberculosis was seen between 1900 and 1914.

The social and healthcare role of the sanatorium in the fight against tuberculosis

The first Italian Congress for the fight against TB, which was held in Milan in 1906, dealt with subjects that were of extraordinary importance for the time, including the use of dispensaries as a means of both prophylaxis and treatment [19].
On 5 November 1910, the Italian Federation of Anti-tuberculosis Societies (FIOA) was founded in Genoa with the aims of coordinating the various initiatives that had been undertaken in Italy in the previous years and implementing a common approach in the various institutes.
In 1915, the Society for the Prevention of Infantile Tuberculosis (Mangiagalli) was founded in Milan, where it assisted the children of phthisis sufferers. Similar initiatives were undertaken in other Italian cities (Turin, Verona, Palermo, Alessandria, Trapani, Rome, Reggio Calabria), thanks to generous donations by banks and private citizens [20].
Before the First World War, the fight against tuberculosis was largely carried out by voluntary societies and spontaneous associations. During the war, however, when the TB epidemic flared up once again, it became clear that more structured intervention was urgently needed in order to tackle this re-emerging public health problem. Thus, the stage was set for the state to become directly involved in organising and planning healthcare and social solutions to the problems connected with the disease [21].
First of all, facilities for the treatment of military personnel were set up, with the aim of providing appropriate and timely treatment for combatants in the war as soon as the first symptoms of the disease appeared. In December 1916, the Directorship of Military Healthcare instituted wards for the diagnosis of TB, and the Italian Red Cross inaugurated the first military sanatorium in the "Luigi Merello" Maritime Hospice in Bergeggi (SV), to treat soldiers suffering from curable TB [22].
At the end of the war, the Army closed down its TB hospitals, with the sole exception of its sanatorium in Anzio. Similarly, the Italian Red Cross disbanded its wartime units, directing its efforts to the construction of new civilian sanatoria; these made a significant contribution to the fight against TB in the 1920s and 1930s. In addition, the Red Cross established "prevention centres" for the care of the children of tuberculosis sufferers. One of the best-known of these centres was the Fara Sabina centre; opened on 16 November 1918, it had a capacity of 100 beds. On 16 July 1919, however, it was closed down and subsequently converted into a boarding school for the children of TB sufferers [23].
In 1919, a specific law increased funding 10-fold and granted credits and subsidies for the construction of dispensaries and sanatoria. As a result, the Provincial Antituberculosis Committees were transformed into Consortiums of municipal and provincial authorities and anti-TB associations, with the aim of improving the coordination and uniformity of the action to be undertaken. The executive branch of these consortiums consisted of the Dispensaries, the tasks of which were: to identify cases of TB (even in latent forms); to provide instruction on healthcare and prevention; to offer moral and material support for the sick (particularly children, who were transferred to maritime and mountain "colonies"); and to carry out activities

of propaganda, statistical data collection and the promotion of studies and research [24].
In Italy, as in the rest of Europe, the 1920s saw the emergence of several private and state initiatives in various cities. These constituted a nationwide network for the active prevention of TB in high-risk populations, such as children, adolescents and the children of TB sufferers. Founded by the government in 1925, the National Society for Mothers and Children institutionalised and oriented these initiatives, taking charge of the prevention of tuberculosis among the children of TB sufferers through provisions and measures for primary and secondary prevention. This innovation was part of a series of dispositions and norms issued by the government, and highlighted the central role of the state in the fight against tuberculosis [25].
In 1923, provincial Prefects were granted the option to mandate the foundation of Consortiums. Subsequently, in 1927, all Provinces became legally obliged to constitute an anti-TB Consortium as a public body dedicated to managing the fight against TB, to assisting the sick, and to safeguarding healthy subjects in their respective territories. Specifically, the Decree Law of 17 October 1927 instituted obligatory insurance against tuberculosis for all workers, a veritable milestone in the fight against the disease [26].
In Naples in 1925, the National Congress on tuberculosis tackled the following issues: sanatoria in the mountains, in the plains and on the coast; preventive vaccination; and funding for the fight against tuberculosis. During this Congress, the Italian Society for Scientific Studies on Tuberculosis was founded. Thanks to the joint action of the state and private individuals, the number of beds in the sanatoria increased from 12,000 in 1923 to 32,000 in 1930 [27, 28].

Conclusions

The sanatorium regimen planned to cure tuberculosis with Galenic principles of hygiene: isolation, fresh air, exercise and good nutrition. Eminent physicians supported these remedy for the treatment of more serious forms of the disease for a few decades. Despite the growth in social and healthcare measures, tuberculosis in Italy continued to constitute a major public health problem until the advent of antibiotics in the 1950s. Until that time, the sanatorium played a leading role as an efficacious means of treating tuberculosis in Italy, as in the rest of Europe.

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Conflict of interest statement

None declared.

Authors' contributions

MM and IB conceived the study, drafted and revised the manuscript. MM, VG, IB, MB, NLB performed a search of the literature. MM and VG revised critically the manuscript. All authors read and approved the last version of the manuscript.

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Overview

The historical experience and practice of fight against tuberculosis in country which is one of the high drug resistant-tuberculosis (DR-TB) burden countries in European Union (EU)

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Keywords

Tuberculosis • Mycobacterium tuberculosis • History of tuberculosis

Summary

Despite considerable efforts and quite early initiated anti-tuberculosis (TB) actions, Lithuania still remains one of the European Union (EU) countries with the highest tuberculosis rates, especially multidrug-resistant (MDR) TB. According to the European Centre for Disease Prevention and Control, in 2016, 58 994 cases of TB were reported in 30 EU/European Economic Area (EEA) countries. MDR TB was reported for 3.7% of 36 071 cases with drug susceptibility testing results and continues to be highest in the three Baltic countries - Estonia, Latvia and Lithuania.
In this article we present the Lithuanian anti-TB action history review and comparison with other countries in this area of action. Literature review was performed by using documents available in the Martynas Mazvydas Library's resource, articles of foreign authors and archival materials.
According to archaeological studies, tuberculosis was common in Europe including Lithuania in the Middle Ages. Tuberculosis reporting started in Lithuania in 1926. The first tuberculosis sanatorium in Lithuania was opened in 1891. Patients were treated with sun bathing procedures, fresh air and sunlight. Later the treatment included pneumothorax, toracocaustic, toracoplastic, treatment with gold products and other procedures. Lithuania introduced directly observed treatment, short course therapy (DOTS) in 1999, and since 2007 it has been working in accordance with the requirements of this strategy.

The fight against tuberculosis

It is believed that mycobacterium appeared more than 150 million years ago and claimed more human lives that any other well-known pathogen [1]. Three million years ago early hominids in the East Africa might be infected with *M. tuberculosis* (MT) ancestors [2]. Presumably, approximately 35-15 thousand years ago *M. tuberculosis* complex bacteria, including *Mycobacterium africanum*, *Mycobacterium canettii*, *Mycobacterium bovis* had a common ancestor in Africa [2-4]. In Egypt tuberculosis was documented more than five thousand years ago. Skeletal abnormalities typical to tuberculosis, including Pott's deformation, were found in Egyptian mummies and clearly portrayed by the early Egyptian art [5-8]. Early humans began to migrate out of Africa more than 1.7 million years ago. These migrants were largely replaced by the subsequent wave of people over the last 35 to 89 thousand years [9]. Assumably, the migrants came with diseases, including tuberculosis. The first written documents describing TB, dating back to 3300 and 2300 years ago, were found in India and in China respectively [7, 10].
Archaeological evidence showed that tuberculosis was common in the Middle Ages in Europe. Clovis of France, who included the touch of persons with scrofula in his coronation ceremony in 496, may have been the first European monarch to touch scrofulous persons, and for many generations his descendants claimed to have inherited his healing power. The illness was known in England and France as "king's evil", and it was widely believed that persons affected could heal after a royal touch [11, 12]. Archaeological findings proved existence of tuberculosis also in Lithuania in 14-15th and 18-19th century. In Leipalingis the excavation with spine abnormalities typical to tuberculosis was found (Fig. 1) [13]. Within the framework of the Lithuanian Mummy Project, seven spontaneously mummified human bodies from a church crypt in Vilnius, dating from the 18th-19th century, were CT-scanned to assess the presence of tuberculosis or other lung diseases. Authors encountered pulmonary lesions suggestive of cases of pulmonary tuberculosis. In addition, one case might have been affected by extra-pulmonary tuberculosis [14].
The history of tuberculosis was radically changed on 24th of March 1882 when Robert Koch gave his presentation about the etiology of tuberculosis in the Berlin Physiologists Society and declared postulates. In 1905 he was awarded the Nobel Prize for tuberculosis etiology interpretation. His Nobel lecture included a number of effective anti-TB recommendations relevant today: tuberculosis patient isolation, continued treatment in

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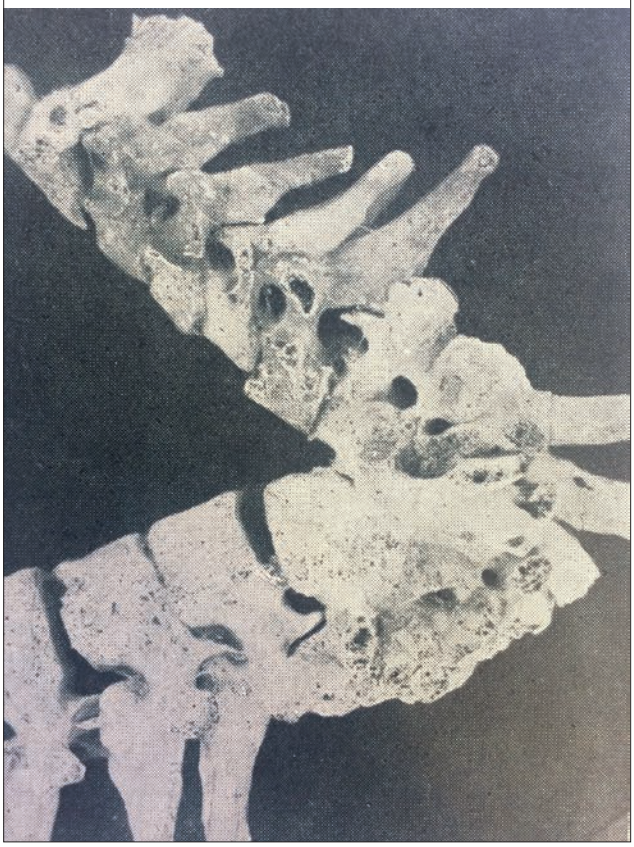
Fig. 1. Human spine deformed by tuberculosis, Leipalingis, Lithuania, 14-15th century.



specialized dispensaries, information of the population, especially the patients' next of kin, their education, the need to register all TB cases because the statistical information was necessary [15, 16].

A copy of the honorary member's diploma awarded by the Vilnius (Lithuania) Medical Society to R. Koch on the 12th of December 1895 was found in the Vilnius University Library Manuscript Department Archive Fund. R. Koch's letter of thanks for this award was also stored. The Fund maintains documents attesting correspondence of R. Koch with the Vilnius Medical Society Presidents who used his findings in combating tuberculosis [17].

More vigorous action in the fight against tuberculosis was launched in Lithuania in 1911. At that time a meeting was convened in Kaunas where it was decided to establish a division of the recently created All-Russian League for Fighting Against Tuberculosis. In 1914 Association activities were terminated due to the war. In 1921, in the first Congress of Lithuanian doctors it was decided to set up Society for Combating Tuberculosis (SCT) [18]. Doctor Kazys Grinius initiated the establishment of SCT on 31 July 1924. He was elected as a Chairman and one of the editors of the publication "The fight against phthisis". SCT purpose was to combat the spread of tuberculosis. SCT disseminated information on tuberculosis, studied the causes of the disease, treatments and outcomes, founded and maintained sanatoriums, hospitals, shelters, boarding houses, children's summer camps, tuberculosis departments in hospitals, clinics, emergency points, took care of the children's protection against tuberculosis, supported the poor patients and their families, cooperated with Lithuanian and foreign organizations. SCT in its activities followed the practice of other countries [19, 20]. In 1927 the SCT had 11 sections embracing about one thousand members. In 1934 it has expanded its activities and had 12 operating sections, 11 dispensaries, 1 sanatorium, 7 quartz lamps, 2 X-ray apparatus and 1.5 thousand members [21].

In Lithuania mortality rate from tuberculosis was counted by the City Board based on the death certificates presented by physicians. The calculations were not accurate, about 20 percent of people were buried without a death certificate. In 1926 the journal "The fight against phthisis" mentioned that the fight against tuberculosis was just beginning, while the mortality rate from tuberculosis was around 30 cases per 10000 population in Lithuania [20], in 1923 in Estonia - 25.6 cases per 10000 population, in 1925 – 22.9 cases per 10000 population [22]. In 1925 3903 people died from tuberculosis in Latvia, in 1926 - 3798 [23]. In 1920 the mortality rate from tuberculosis in Sweden reached 16.2 cases per 10000 population in the Netherlands - 14.9 cases per 10000 population, in England - 11.3 cases per 10000 population, in Denmark 10.6 cases per 10000 population [20]. In 1934 around 6 000 people died of tuberculosis in Lithuania, about 5 percent of the population had tuberculosis [18]. German and Swiss models to fight tuberculosis were considered successful. Germans maintained 17 765 beds ex gratis and nearly 3 thousand dispensaries and similar institutions [24].

In Lithuania health services were hardly available to the patients with "milder" tuberculosis (about 60 thousand). Lithuanian villages were very poor. Most of the cases remained undiagnosed. The suggested actions against tuberculosis included establishment of the outpatient departments-dispensaries, free special trainings on tuberculosis lead by doctors, school curricula about health and hygiene [20]. At the time tuberculosis was called a "disease of uneducated people", so SCT particularly focused on education: "the school must educate not only cultured but also healthy citizens" [24].

Tuberculin skin test (TST)

In 1890 R. Koch presented the work about substance isolation from the tuberculosis bacteria in the tenth International Medical Conference in Berlin. R. Koch has named this substance tuberculin, it was intended to treat tuberculosis. Soon, this substance was rejected as ineffective. R. Koch injected tuberculin himself and noticed an unset of fever up to 39.6°C and unusual tremor. After this experiment R. Koch offered to use tuberculin for disease diagnostic. The Danish veterinarians continued with further tuberculin tests [25, 26]. TST is used to diagnose persons who have been sensitized by Mycobacterium tuberculosis, a condition referred to as latent tuberculosis infection. Clemens von Pirquet was the first

scientist who mentioned and introduced the concept of latent tuberculosis in his works. In 1907 von Pirquet created the tuberculin skin test, which was used to identify the persons who previously had been in contact with TB. It made clear that the majority of people infected with tuberculosis were asymptomatic and might suffer from active tuberculosis in the future [27]. In 1908 Charles Mantoux introduced tuberculin injections into a skin. Florence Seibert developed purified protein derivative (PPD). With an availability of well-standardized PPD, careful studies of tuberculin reaction sizes became possible and such studies led to further knowledge of mycobacterial infections. In 1952 Carroll Palmer and Leroy Batt published a large-scale research work providing assessment of tuberculin reaction in TB patients. Reaction of the five tuberculin units (PPD-S) had an average of 17 mm [28]. After three years, the World Health Organization (WHO) published a report describing reaction of the healthy school children to tuberculin, which was similar to that of patients with tuberculosis - they were diagnosed with latent tuberculosis [29].

In Lithuania 1924, 59 tuberculin tests were performed in Kaunas City Municipality Tuberculosis Dispensary. In 1934 totally 483 tests were conducted. In 1925 the Pirquet tests were performed in Kaunas city Vilijampole district schools, which showed that about 80 percent of children aged 7-14 were infected with tuberculosis [22]. Tuberculin testing with Dermatubin by rubbing it into a skin was also conducted [30]. In 1938 it was decided to oblige doctors to perform tuberculin testing in all students by Dermatubin, Pirquet or Manthoux methods [31].

Sanatorium for tuberculosis treatment

In 1859 Herman Brehmer opened the first sanatorium for tuberculosis in Germany. The rest and nutrition regimen was observed in the sanatorium. Soon sanatoriums for tuberculosis treatment were opened in other countries [32].

Effects of the sanatorium care to the disease outcome were indistinct. In 1923 G. Lissant Cox published his 5 years lasting research, the aim of which was to compare the mortality of patients treated at home and in sanatorium. The research showed that case fatality rate was higher in those (about 20 per cent.), who were treated at home [33].

In Lithuania sanatorium patients received not only a high-quality food, procedures including sunbathing (Fig. 2), ultraviolet radiation, pneumothorax (Fig. 3), irradiation with quartz lamps (Fig. 4), but toracoplastic were also applied.

First child (12 years) in the pictures is also treated for neck tuberculosis. Treatment procedure with Rollier machine is carried out by stretching his head [31].

Dr. Dakinevicius performs pneumothorax procedure in the Mazeikiai Department Dispensary [34].

Room at the Panemunes sanatorium, Lithuania [18].

Fig. 2. Sunbathing procedure in the Dr. K. Grinius sanatorium, Lithuania, 1938.

Fig. 3. Pneumothorax procedure. Mazeikiai Department Dispensary, Lithuania, 1936.

Fig. 4. Irradiation with quartz lamps, Lithuania.

In 1696 Giorgio Baglivi described improvement in condition of tuberculosis patient after experiencing traumatic pneumothorax (person was injured with a sword). The first therapeutic pneumothorax procedure was performed in London by F.H. Ramadge in 1834. In 1939 Oli Hjaltested and Kjeld To described outcomes of this procedure in 191 patients. Before the procedure, all patients were MT-positive, after procedure 65 died, 11 remained MT-positive, 8 - were treated further and 107 patients discontinued treatment because of an achieved desired result [35].

In 1891 the first sanatorium-summerhouse was built in Lithuania by military doctor Paskevicius near the Kazlu Ruda railway station. Sanatorium was assigned to individuals with "weak" lungs [22]. In 1925 the Department of Health set up sanatorium also in Jurbarkas, which had 50 beds [21]. In 1927 sanatorium was opened in Varena [34]. Similarly, the Latvian SCT maintained 3 children's sanatoriums (Ogruos, Bikernuos and Rodenpoize) with 265 beds. Also, the Latvian Red Cross (RC) had 5 sanatoriums, the Patient Fund - 6 sanatoriums (320 beds). There were several private and one public sanatoriums. Latvia had 1.100 beds in total for patients with tuberculosis. At the same time, Denmark allocated 3.5 thousand beds for patients [24]. In the special inter-war tuberculosis publication it was noted that the sanatorium had modern equipment, central heating, sewer, electric light and 17-staff personnel. Since the start of sanatorium operation until 1934 322 Lithuanians, 140 Jews, 14 German, 12 Russian and 8 Poles were treated. In 1938 a school was established at the sanatorium [22, 31]. To combat tuberculosis, SCT opened a new modern sanatorium in Alytus in 1939. Construction of the Sanatorium new building costed over 170 thousand Litas (about 50 thousand Euro). It was planned to treat 50 patients in there. One of the main objectives of SCT was to isolate incurable patients. Following the Norwegian example, SCT planned to establish colonies for incurable patients. Isolation was one of the key objectives of SCT. Colonies should be established in Alytus, Utena with capacities of each for 15 patients [21]. In 1932 a four-story brick Lithuanian RC sanatorium was established in Kaunas with designated 1.75 hectare plot of land. This sanatorium was owned by the Lithuanian RC, founded in 1919. In 1933 a private sanatorium for children owned by Prof. Dr. V. Tumeniene was established in Panemune [36].

In 1936 a possibility to employ the patients in the newly opened sanatoriums was discussed to reduce the patients' maintenance costs by recruiting patients at the sanatorium. A similar example was applied in Switzerland [34].

Sanatorium patients were treated "conservatively" and "actively". Conservative treatment was applied according to the Brehmer Dettweiler's Hygiene - Dietics system, providing the patients with the peace of mind and good quality food, fresh air and sunlight [22]. Patients were recommended to consume 2.5-3 thousand calories. The treatment included respiratory gymnastic, treatment with sunlight was administered to persons with larynx tuberculosis. Sunbath positive effect on people with tuberculosis was also widely discussed. Following the Berlin's good practices, it was proposed to arrange beaches at rivers in Kaunas, Panevezys and other cities [24].

Pneumothorax, neurosurgeries, oleothorax, thoracocaustic, thoracoplastic procedures, filling of lung cavities, treatment with collapse have been applied in the sanatoriums. Heliotherapy, extension were used for bone and joint tuberculosis, X-ray therapy for glandular tuberculosis [22, 24]. The intercostal nerve alcoholisation treatment was also applied: alcohol used to be injected into nerves triggering the muscle paralysis [30].

In 1927 treatment of tuberculosis with gold preparation Sanokrisin were discussed. The Health Department put a ban on import of this preparation. In 1934 the treatment with gold preparations (Sanokrisin, Triphala) was applied in Panemune sanatorium [22, 24].

Hospitals for tuberculosis treatment

Vilnius Hospital of Infectious Diseases was founded in 1905, when two brick buildings were erected for Children Infectious Diseases Hospital in Zverynas district of Vilnius. In 1911, several one store wooden buildings were additionally erected for the treatment of adult patients next to two brick buildings for the children. Patients with typhoid fever, typhus exanthematicus, epidemic relapsing fever, dysentery, cholera, meningitis, tuberculosis and trachoma were treated in this Hospital. The Hospital had 150 beds, 6 wards, 5 physicians and one microbiologist [37].

The first tuberculosis hospital was opened in Lithuania in 1923 as division of the Kaunas State Hospital. In 1926 the hospital with functionary surgery clinic was available to tuberculosis patients, patients with bone tuberculosis were referred to this Hospital. The Polyclinic-Ambulance was open every day except Sundays and holidays. X-ray costed 20 Litas (about 6 Euro), sputum examination and testing - 3 Litas (about 0.9 Euro). Poor people with permission from the City and District Board were treated for free. The National Institute of Hygiene was also accessible where research was conducted. Pulmonary patients were treated in the Kaunas Health Centre (Dispensary) where pneumothorax and sputum examination were available. It was the first health care centre in Lithuania for patients with tuberculosis. The Lung Hospital in Jurbarkas was considered one of the best hospitals in Lithuania. The Hospital maintained 50 beds, so patients had to wait in long queues. Further 80 beds were available in Varena [21].

The patients applying to the medical institutions usually suffered from neglected tuberculosis. People from rural areas often discontinued the treatment due to a lack of money [24]. The patients had to pay for the medicine themselves; some departments had agreements with pharmacies to sell medicines at lower prices. Medication for the poorest used to be reimbursed by the municipality. The patients used to receive travel, monetary and food allowances [22].

Tuberculosis - public health problem

In 1881 doctor Herman Biggs pinpointed tuberculosis as a public health problem. In 1889 he accentuated importance of tuberculosis case reporting. In 1894 H. Biggs was able to convince the New York City Board of Health that tuberculosis must be a notifiable disease. These instructions were not required until 1897. Health care specialists opposed to these directives up to 1900 [32, 38].

Tuberculosis was attributed to the public health problems also in Lithuania. Dr. A. Domasevicius in his paper *Tuberculosis and a quest of other new ways to defeat it* in 1934 mentioned that tuberculosis was not a disease of an individual, not a family disease; tuberculosis is the disease of the general population [22].

At the beginning of the 20th century, no broader measures to combat the disease were taken in the Russian Empire. Medical Service of the Russian Ministry of Internal Affairs summoned Commission for Combating Tuberculosis, which issued a circular on measures to combat tuberculosis in 1908 and Circular on the cards for *Tuberculous disease registration* in 1909 [22]. A reporting of the tuberculosis cases started in Lithuania in 1926 [21]. A registration of tuberculosis cases and deaths was not mandatory. A consideration was given to prepare and publish a law that empowered to notify any case of open tuberculosis [24]. In the work plan/estimate for 1926, case tracing was foreseen allowing a free delivery of phlegm to the laboratory, this model was applied at the time in America. In 1933 *The law for combating contagious diseases* (CD) was passed, which enabled reporting of tuberculosis cases to the municipality, but its execution wasn't controlled [21].

Bacillus Calmette-Guérin (BCG) vaccine

Doctor bacteriologist Albert Calmette and his colleague veterinarian Camille Guerin at the French Pasteur Institute attenuated *M. bovis* in 1921. BCG vaccine was ready for testing. A newborn, whose mother died of pulmonary tuberculosis, was first vaccinated with this vaccine. The child did not develop tuberculosis. Over the next seven years, more than 100 thousand children were vaccinated with this vaccine. The vaccine was readily available in Europe [39, 40].

In 1934 the launch of BCG vaccination was discussed in Lithuania, but this was not possible due to technical problems. One of the mentioned measures was for the National Institute of Hygiene or the Veterinary Bacteriology Institute to obtain original BCG culture from the Paris Pasteur Institute, to prepare it and supply to the hospitals and shelters through dispensaries as a preventive measure. In 1935 Kaunas was the first to start the BCG vaccination. In November, three children whose mothers had tuberculosis were vaccinated at the time of delivery. The vaccine used to be obtained from the Riga University Serological Institute [34]. It was recommended to vaccinate the infants within ten days of their birth [30]. Vaccination was widely used, so in 1939 the Department of Health had planned to oblige the Dispensary Heads to perform this [22].

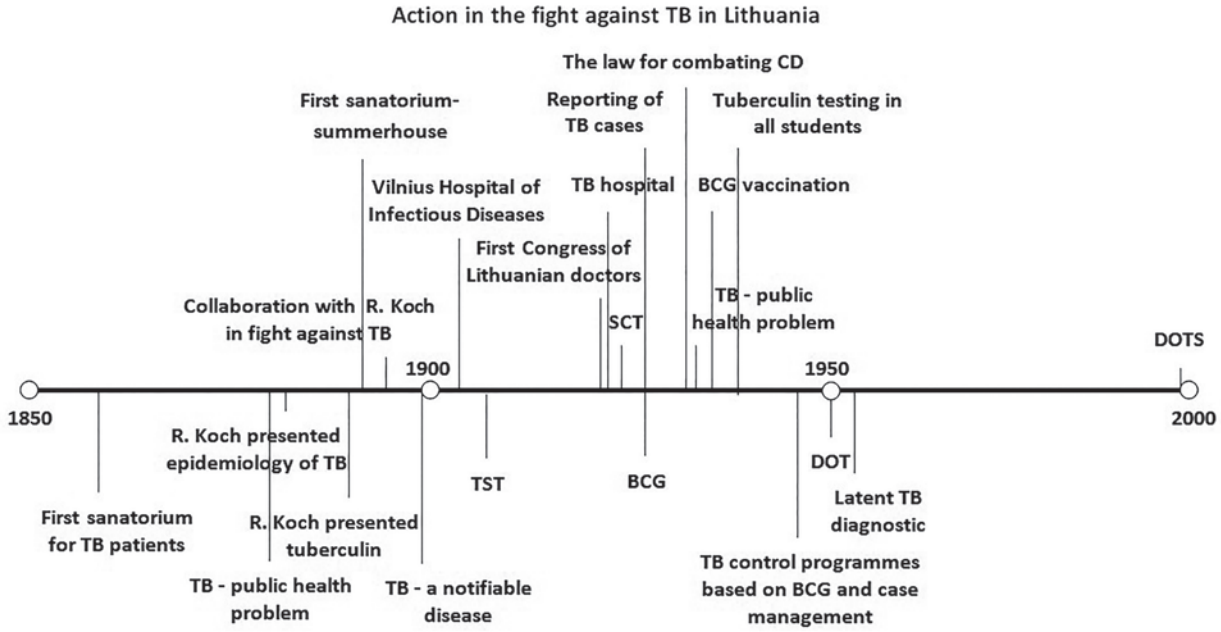
In 1947 the first WHO Expert Committee meeting took place, it was decided to assist the governments in developing effective TB control programmes based on BCG vaccination and case management. Since then, the case management has remained a major tuberculosis management strategy [41]. In 1948 United Nations International Children's Emergency Fund and the Danish RC funded campaign of tuberculin testing and BCG vaccination of those tested negative was carried out. The campaign was launched in Poland and quickly spread to other European countries. Within three years, nearly 30 million people were tested with tuberculin test, and nearly 14 million were vaccinated. This campaign was the first programme conducted by the WHO [42, 43]. In 1974 the WHO Tuberculosis Committee published the ninth report and tuberculosis control guidelines for the next two decades. The guidelines emphasized significance of the sputum microscopy and outpatient treatment calling to reach 70-80 percent vaccination coverage in the age group of less than 15-20 years [44].

In 2016 Among the Baltic States highest vaccination coverage was in Lithuania (98%), lowest in Estonia (95%) [45].

Directly observed treatment short course

With the advent of effective chemotherapy in the mid-1950s, sanatoriums began to become superfluous. By the mid-1960s most were closed. Hospital care was no longer required to provide effective treatment. A study in Madras, in which patients with tuberculosis were randomly assigned to either sanatorium or home treatment, showed no difference in either clinical outcomes or infection in the household contacts. Sanatoriums became obsolete [46, 47]. Along with the chemotherapy, a long-term patient hospitalization became a key principle of tuberculosis control. The objective was to introduce the directly observed therapy (DOT). The first similar clinic was opened in 1950. Attempts to switch to DOT were made not only in Madras, Hong Kong [48, 49] but also in London [50, 51]. Selective DOT programmes were integrated in America in 1960. They were applied only in unreliable patients [52, 53]. DOTS was an important development in global tuberculosis policy. Increasingly, poor countries began implementing the DOTS approach; many lives were saved and many new cases averted. However, for children with tuberculosis, people with both tuberculosis and advanced disease from the human immunodeficiency virus (HIV), and the increasing proportion of patients infected with strains of tuberculosis that were already drug-resistant, the DOTS strategy provided limited options for prompt diagnosis and cure [54].

Fig. 5. Essential action in the fight against TB, 1850-2000.



Lithuania introduced DOTS in 1999 and from 2007 it has been working in accordance with the requirements of this strategy [55].

Nowadays TB is still a major public health problem, for this reason a combined strategy, based on improving drug treatment, diagnostic instruments, and prevention strategy, is necessary in order to eradicate *M. Tuberculosis* by the year 2050, as committed by the WHO [56, 57]. Despite considerable efforts (Fig. 5) Lithuania is facing a number of operational problems in a fight against TB, especially in TB case management. The mechanisms for effective follow-up of patients to prevent them from defaulting are underdeveloped [58].

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Conflict of interest statement

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Authors' contributions

JK and GZ performed a search of the literature and contributed to the draft of the article. JK and PK designed and conceived the review. MM and SC revised critically the article. All authors read and approved the final version of the manuscript.

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