

A proposal for an evidence-based model of the screening for the colorectal carcinoma in an Italian setting

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Key words

Evidence-based model • Colorectal screening • Palermo and province

Summary

Introduction. *The aim of this paper is to improve the feasibility perception of policymakers, health care workers and target population about the cost-effectiveness of the implementation of colorectal screening as Public Health strategy*

Methods. *Retrospective study by application of a three-step model designed for a local setting in Sicily (Palermo and its Province) in order to distribute Fecal Occult Blood Tests (FOBTs), offer colonoscopy and surgery, by district allocation of pharmacies, public digestive endoscopic centres and oncologic and general surgery units. Mean adherence to consolidated colorectal screening programs in Italy was applied in order to evaluate the feasibility of an operative model in our area.*

Results. *Applying the model to the target population (269,368 individuals of both sexes), it can be expected a mean percent-*

age of 79% delivered invitation and a mean participation rate of 46.3% accounting for a total of 213,070 invited individuals and 98,651 participating in the first round of the program. Furthermore, considering the national mean of 6% positive FOBT, 82% of colonoscopy adhesion and 7% CRC detection rate, it can be scheduled a burden for health care structures involved in the program accounting for 49,325 FOBTs, 2,338 colonoscopies and 141 surgeries for each year.

Discussion. *This work demonstrates the feasibility of a colorectal screening project in our area, showing a sustainable impact for local health care involved structures. Furthermore, this program may be spread as an applicative model to other areas, adapting the project to the needs of the local setting in which the colorectal screening will be organized.*

Introduction

In 2002 colorectal cancer was responsible for 12.6% of tumors in males and 13.4% in females all over the world. Colorectal carcinoma (CRC) is the fourth most common tumor, as well as the fourth cause of death for malignant neoplasm in both males and females. Moreover, it is the second cause of death in Europe and the United States, being much more widespread in industrialized countries than in developed ones [1].

Over the last few years, Italy has seen a significant rise in diagnosed cases of colorectal carcinoma which has corresponded to a slight, but nonetheless significant, decrease in the death rate and, above all, an increase in the survival rate, a phenomenon due to more timely diagnosis and a greater efficiency in surgical and post-surgical treatment [2-4].

In the oncologic field, early identification of a tumor can radically change the natural course of the disease. As far as colorectal cancer is concerned, the 2008 guidelines of the American Cancer Society recommend that tests checking for occult blood in stool (FOBT) is carried out with methodical immunochemistry at least annually in

individuals between 50 and 74 years of age and a colonoscopy every 10 years after 50 years of age [5].

In Italy, oncologic screenings are the object of a series of legislative measures in the health plan. In fact, colorectal carcinoma screening was included in the Essential Levels of Assistance [6, 7].

According to the data from the 7th report by the National Screening Observatory, most of the colorectal screening programs are based on the immunochemical FOBT test carried out every two years in the 50-70 years old people followed up by a colonoscopy in positive cases. The same report affirms that about half of the Italian Regions are still unable to guarantee an organized colorectal screening program for the public [7, 8].

The aim of this work is to apply an operative model of colorectal carcinoma screening for the population resident in the city of Palermo and its Province. It is based on both the average efficiency data obtained from similar programs carried out in other Italian regions and on information reported in medical publications, taking into account the work and economic load of the first two years.

Methods

The application area of the model and the health service The Province of Palermo covers an area of 4,992 km² and is made up of 82 town council areas and subdivided into 10 districts.

On 31.12.2006 the resident population was 1,241,241 with 269,368 inhabitants between the ages of 50 and 69 years, of which 150,553 are resident in the Palermo town council area [9].

The local epidemiological data relative to the neoplastic pathology were taken from the Tumor Registry office of the Province of Palermo which started up in 2004 in the Hygiene section of the Science Department for the promotion of Health "G. D'Alessandro" in the University of Palermo. In Palermo and its Province there are 325 pharmacies which are relatively well distributed throughout the area. There are 177 in the Palermo town council area and 148 in the towns and villages throughout the Province [10].

In the Province of Palermo, based on the data from the Epidemiological Observatory of the Sicilian Administration area, there were 20 centres (including Hospitals, Hospital Facilities and accredited Private Hospitals) which can carry out at least 300 diagnostic and therapeutic pancolonoscopies per year (15 of which are in Palermo and 5 in the Province) and 22 Operative Units of General Surgery and Oncology, all of which have carried out at least one surgical operation to remove a colorectal carcinoma (17 in Palermo and 5 in the Province) [11].

INDICATORS AND STAGES OF THE MODEL

In order to create this operative model, reference was made to the process indicator values which refer to the European Guidelines for quality assurance in colorectal cancer screening and diagnosis and to the mean values of the colorectal screening programs in Italy which were included in the seventh National Screening Observatory report [8, 12].

The indicators of process used from each of these programs are as follows:

- invitation coverage;
- uptake rate;
- rate of positive FOBT;
- rate of referral to follow-up colonoscopy after positive FOBT;
- rate of complete colonoscopy;
- rate of high grade neoplasia reported in a colonoscopy screening programme.

Moreover, the indicator of quality that should be monitored during the course of the entire screening programme are as follows [12]:

- maximum time between FOBT and receipt of result (15 days);
- maximum time between referral after positive screening (any modality) and follow-up colonoscopy (31 days);
- time interval between positive colonoscopy/FOBT and definitive management (31 days);

- endoscopists participating in CRC screening programme should perform a minimum no. of procedures per year (≥ 300);
- biopsies and lesions identified in the screening programme and the subsequent resection specimen should be reported on a proforma.

The colorectal screening programs underway in Italy last two years and have three active levels [8]:

Level I: Distribution of the kit for testing for occult blood in faeces (FOBT) every two years for members of the public between the ages of 50 and 69 years. Collection of the fecal sample from home and its delivery to the collection point at an appointed Pharmacy; the sending of the sample to the analysis laboratory taking part in the program and the carrying out of the dosage and consequent initiation of the II diagnostic level in positive cases.

Level II: Colonoscopies for those people with positive FOBT results in one of the II level centres. In the case of adenomatous lesions found during the colonoscopy, the carrying out of a polypectomy. In cases where it is not possible to carry out a total colonoscopy to the end of the blind intestine, the prescription of CT colonography [12]. If the results are positive, the patient is transferred to the III level.

Level III: Further treatment is carried out in the Operative Surgical Units of the Public Oncologic Departments or in the Operative Surgical Units specializing in oncology.

The estimation of the costs was carried out applying the program and the specific costs in the 2007 Health Service Tariff of the Region of Sicily [13].

This includes:

- the FOBT kit and its results: approximately 4 euros;
- diagnostic colonoscopy: approximately 70 euros;
- operative colonoscopy: approximately 100 euros;
- CT colonography: approximately 140 euros.

Furthermore, taking into account the cost of sending personalized invites for appointments by post costing 2 euros (the cost of envelopes, stamps and sending expenses) and of other various expenses, we can estimate that the total cost for the first level of screening as being 8 euros per person.

Results

The flow diagram explaining the procedural levels of the operative models and its application is represented in Figure 1.

The dark grey part indicates the optimal theoretical route, while the white part shows the obtainable route as an average resulting from the programs that have been carried out in Italy. The light grey part shows the possible variables on the basis of the different percentages of the planned indicators of the process [8].

The number of invites to be delivered by post in the first two years of the program, applying the observed average percentage of the extension of invites (79.1%), should be 213,070 [8].

If we allow for a participation rate which is in line with that observed in 2007, 98,651 members of the public in the rest of Italy (46,3%) should undergo the FOBT test [8].

On the other hand, as reported in the literature, it is possible that participation could be less (30%), but could subsequently increase to the average values registered in Italy [8, 14].

In this case, the number of people who will undergo the test for occult blood in faeces will be 80,810 in the first two years. If the percentage of positive results in the first FOBT is in line with the National percentage, the total number of colonoscopies performed will be 5,919 in the first two years.

Even if we were to surmise a percentage of positive results equal to that in the Lazio Region, the only Italian region which is different from the others (9%), the number of colonoscopies to be carried out would increase to 8,878 in two years [8]. The participation in the detailed diagnostic colonoscopy in the screening programs which were set up in Italy in 2007 is about 79%, corresponding to 4,676 colonoscopies [8].

Furthermore, adhering to the percentages of completed colonoscopies (92%), only 374 of them would then require a subsequent detailed diagnostic exam with a CT colonography.

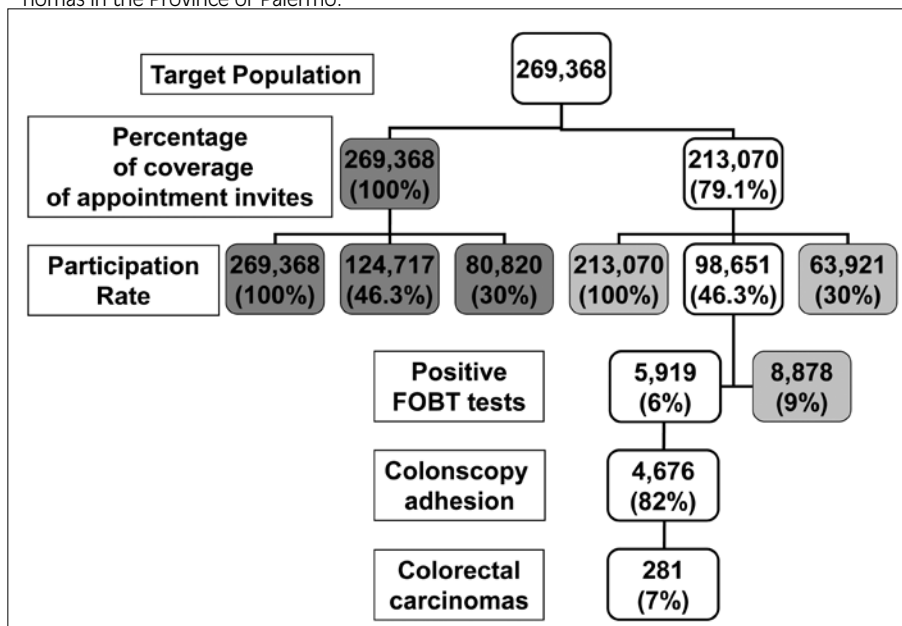
Lastly, because on average 6% of people who underwent a colonoscopy were diagnosed with a colorectal carcinoma and 30% with an advanced adenoma, in the first two years in Palermo and its Province about 300 new cases of CRC would be diagnosed and about 1,400 advanced adenomas would be found and removed [8].

In Table I, based on the route taken from the average results of the Italian programs, the number of exams was subdivided by each year and each month, even envisaging the monthly workload of the operative structures in the proposed model.

The annual workload would correspond to 106,535 invites to be sent by post (8,878 invites per month) that is 49,325 tests for occult blood in faeces (4,110 tests per month). Dividing the number of kits to be delivered each month by the number of pharmacies in the area, each pharmacy would only receive a delivery of 13 kits each month.

As far as the II level is concerned, the workload would include 2,338 diagnostic colonoscopies to be carried out each year (194 per month), and then the III level would include 141 surgical operations to remove the colorectal carcinomas (corresponding to 12 operations per month).

Fig. 1. Flow diagram of the procedure levels for the screening organization for colorectal carcinomas in the Province of Palermo.



Subdividing the workload in the II and III level structures in the Province of Palermo, each digestive endoscopic centre would have to carry out about 10 colonoscopies each month and the Operative Units of General Surgery and Oncology would have to carry out 0.55 surgical operations.

Table II shows the costs of the diagnostic surgical services envisaged in the operative model in both the first two years and the first year.

Applying the estimated costs for the sending, the collection, the testing and the reading of results of the FOBT test, the cost for the first diagnostic level would be declared to be at around 790 thousand euros in total, or 400 thousand euros per year.

The total cost for the diagnostic confirmation colonoscopy for those people with a positive FOBT result would be 200 thousand euros per year, which would become 380 thousand if the rate of positive results in the FOBT test are superposable above those recorded in the Lazio region [8]. Lastly, the cost of the CT colonography which are carried out in the first two years would only be 52 thousand euro.

Discussion

In the operative models of colorectal screening activated in Italy, there are some criticisms which should be modified, such as the low numbers of participants, the centrality of the General Practitioner's role (GP) and the definition of the target population.

Recent data have tried to explain the reasons for the low participation rate in colorectal screening [15].

A questionnaire was given to those people who had not undergone the test for FOBT and 64% of them affirmed that they did not need to do the test while 94% answered

Tab. I. Interventions to be carried out and monthly workload of the operative model.

	Level I: FOBT	Level II: Colonoscopies	Level III: Surgical interventions
N° total interventions (every two years)	98,651	4,676	281
N° annual interventions	49,325	2,338	141
N° monthly interventions	4,110	195	12
Monthly workload (each structure)*	13	10	0,55

* I level structures: Pharmacies 325; 177 in Palermo and 148 in the Province. II level structures: 20 digestive endoscopy centres; 15 in Palermo and 5 in the Province. III level structures: 22 Operative Units of General Surgery and Oncology; 17 in Palermo and 5 in the Province.

Tab. II. Operative model costs in the first two years in the first activity year based on the I and II levels of diagnostic exams according to the data in the seventh National Screening Observatory Report.

	FOBT (n = 98,651)	Diagnostic colonoscopies (n = 2,806)	Surgical diagnostic colonoscopies (n = 1,870)	CT colonography (n = 374)	Total
Two yearly cost (€)	789,208	196,420	187,000	52,360	1,224,988
Annual cost (€)	394,604	98,210	93,500	26,180	612,494

that they had not been informed about the importance of the test by their GP [15].

A questionnaire was also given to those people who had not undergone endoscopies and they were asked the reasons for their decision.

Only 1% of people had refused the option due to the pain and discomfort of the exam, 72% of these people affirmed they did not need the exams and 92% had not received adequate advice from their GPs. These results would indicate that the target population is not being informed by their "doctor" (GP) as well as by an inadequate campaign of training and information [15].

The General Practitioner has the fundamental task of managing the first level of intervention, motivating the participants, recruiting the *non responders* and excluding those people who run the highest risk of developing CRC, for example those with first grade family members with positive CRC results, colorectal inflammatory illnesses and hereditary pathologies.

On the other hand, waiting time in the GPs office could further contribute to lowering the correct percentage of people taking part in the screening programs, something which has already happened in the rest of Italy where, over the years, the number of participants has decreased from 51.3% in 2004 to 46.3% in 2007 [8].

However, even though it has been shown that there was a better response when the FOBT kits were sent by post than when they were given out directly by the GP, the advantages were not significant enough to justify the increase in cost [14].

It is for the above mentioned reasons that in our model Pharmacies have been chosen as first level structures where the kits for testing for occult fecal blood can be delivered and collected.

In this case the postal invite sent out to the target population would remain the same and the members of the public would be invited to go to the Chemist's nearest to their home to receive the kit with instructions for its use.

As far as the individualization of the target population is concerned, despite the fact that indications from the United States and Europe envisage colorectal screening

for the age group of 50-74 years old, most of the data from the experience in Italy limits the age range between 50 and 69 years old.

This kind of approach, well documented in literature, appears to be more opportune because the sustainability of the program's cost is greater, guaranteeing maximum participation from the target population [16, 17].

The involvement of the age group between 50 and 69 years old is also supported by previous experience in the remaining Italian regions where participation in the screening programs was considerably less in the over seventies [7].

Lastly, it is paramount to evaluate the sustainability of our model regarding the availability of the assistance, diagnoses and therapy within the health structures which are involved in the three levels of the program.

In particular, the number of colonoscopies to be carried out seems acceptable for the available facilities in the Digestive Endoscopy Centres in Palermo and its Province, because 4,968 colonoscopies were carried out during routine hospital work and in some day hospitals (DH) in 2006 [11]. Assuming that the number of colonoscopies carried out in health centres would be at least equivalent to those carried out during routine hospitalization and in day hospitals, the proposed screening program would represent about a quarter of the total colonoscopies carried out in the Palermo area, only relatively increasing the workload of the Digestive Endoscopy Centres.

On the contrary, in order to reduce the waiting lists and the latency in the various diagnostic-therapeutic levels as much as possible, the digestive endoscopy centres and the Operative Units of general surgery and oncology, which are distributed in the Province area, in order to cope with the overload of colonoscopies and operations deriving from the screening program, at least half of the envisaged operations will have to be redirected to the more numerous centres in the towns.

The total cost in the first year of the activity of the proposed operative model would not be more than 2 million euros after having added to the estimated expense of the three intervention levels, both the costs of the educative and informative campaign for the general public and the

payment and training of those who will carry out the screening program.

On the other hand, as shown in the literature, the onset of a colorectal carcinoma not diagnosed in time appears to be much more expensive both in terms of the hospitalization, the operation and post-operative care and in terms of the "social cost" connected with the reduction of the lifespan and the physical, psychological and social suffering [18]. In any case, our estimated expenses are much less than the management costs of about new 600 cases of colorectal cancer which are diagnosed annually in Palermo and its Province, quantified at approximately 36 million euros [19].

Conclusions

The exponential growth of incidence and death rate due to colorectal carcinomas over the last few decades, recorded both in Italy and Sicily, seems to be not balanced by an adequate prevention of this tumor in our Region. In particular there is an apparent lack of both an adequate evaluation of the phenomenon and a real policy which incites to correctly evaluate its impact on Public Health.

References

- [1] Parkin DM, Bray F, Ferlay J, et al. *Estimating the world cancer burden (GLOBOCAN 2000)*. Int J Cancer 2001;94:153-6.
- [2] AIRTum Working Group. *Italian cancer figures, Report 2006: Incidence, Mortality and estimates*. Epidemiol Prev 2006;30(Suppl 2):8-10, 12-28, 30-101.
- [3] AIRTum Working Group. *New incidence and mortality data. 2003-2005*. Epidemiol Prev 2009;33(Suppl 2):e1-3, e5-26.
- [4] Roazzi P, Capocaccia R, Santaquilani M, et al. *Eurocare Working Group. Electronic Availability of Eurocare-3 data: a tool for further analysis*. Ann Oncol 2003;14(Suppl 5):v150-5.
- [5] Levin B, Lieberman DA, McFarland B et al. *Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint Guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology*. Gastroenterology 2008;134:1570-95.
- [6] Commissione Oncologica Nazionale. *Materiale prodotto dalla Commissione Oncologica Nazionale (D.M. 26.05.2004) per un Piano Oncologico Nazionale*. http://www.salute.gov.it/imgs/C_17_pubblicazioni_655_allegato.pdf
- [7] Zorzi M, Falcini F, Grazzini G et al. *Lo screening coloretale in Italia: survey 2005 e dati preliminari 2006 (6° rapporto ONS)*. www.osservatorionazionalescreening.it/ons/pubblicazioni/rapporto6.pdf
- [8] Zorzi M, Fedato C, Naldoni C, et al. *Lo screening coloretale in Italia: survey 2007 (7° rapporto ONS)*. www.osservatorionazionalescreening.it/7rapporto/pag084-101_ONS_2008.pdf
- [9] <http://dawinci.istat.it/daWinci/jsp/MD/dawinciMD.jsp?a1=m0GG0c0I0&a2=mG0Y8048f8&n=1UH92Q07TK32R&v=1UH0JH07TK3000000>
- [10] www.geriatriaonline.com/home/farmacie/sicilia/Palermo.html
- [11] Dipartimento attività sanitarie e osservatorio epidemiologico regione Sicilia - Assessorato Regionale Sanità Regione Sicilia.
- [12] Segnan N, Patnick J, von Karsa L. *European Guidelines for quality assurance in colorectal cancer screening and diagnosis*. http://bookshop.europa.eu/is-bin/INTERSHOP.enfinity/WFS/EU-Bookshop-Site/en_GB/-/EUR/ViewPublication-Start?PublicationKey=ND3210390
- [13] Suppl. Ord. alla Gazzetta Ufficiale della Regione Siciliana (p. I) n.53 del 09-11-2007/allegato A. <http://www.gurs.regione.sicilia.it/Gazzette/g07-53o/g07-53o-a.pdf>
- [14] Segnan N, Senore C, Andreoni B, et al. *Randomized trial of different screening strategies for colorectal cancer: Patient response and detection rates*. J Natl Cancer Inst 2005;97:347-57.
- [15] Wee CC, McCarthy EP, Phillips RS. *Factors associated with colon cancer screening: the role of patient factors and physician counselling*. Prev Med 2005;41:23-9.
- [16] Grazzini G, Castiglione G, Isu A, et al. *Colorectal cancer screening by fecal occult blood testing: results of a population based experience*. Tumori 2000;86:384-8.
- [17] Zappa M, Castiglione G, Grazzini G. *Effect of FOBT on colorectal cancer mortality. Results of a population-based case-control study in a district of Florence*. Int J Cancer 1997;73:208-10.
- [18] Vijan S, Hwang EW, Hofer TP, et al. *Which colon cancer screening test? A comparison of costs, effectiveness and compliance*. Am J Med 2001;111:593-601.
- [19] Registro Tumori della Provincia di Palermo (Cancer Register Province of Palermo). *Rapporto di incidenza dei tumori maligni nella Provincia di Palermo anno 2004*. (Unpublished).

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