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A cost analysis of inherited colorectal cancer care in Varese Province

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ABSTRACT

Aim: Little scientific evidence is available on the costs of targeted genetic testing and surveillance programmes for the identification of hereditary colorectal cancers (HCRC). The present study is a cost analysis of an intensive surveillance programme with and without the use of genetic testing, carried out in a province of northern Italy. Additionally, cancer care using an intensive surveillance programme for gene carrier subjects was compared to cancer care in subjects not selected for genetic testing who followed unselective clinical surveillance.
Methods: A model based on epidemiological factors was developed to estimate the incidence of gene carriers for Lynch Syndrome. A hypothetical cohort of 98 healthy people with a high cancer risk (due to being carriers of a pathogenetic MMR mutation) was followed over a period of ten years. To evaluate the economic burden of using genetic testing, a cost analysis was performed.
Results: Despite genetic testing causing an initial increase in costs, their use within an intensive surveillance programme generated a saving of 24%, thanks to a better selection of individuals at high risk of colorectal cancers (CRC). This resulted in reduced resource consumption and in an overall saving of 36%, when considering the treatment of patients developing a genetic cancer, as compared to an unselective clinical surveillance.
Conclusions: Identification of HCRC led to surveillance that is more effective and could prevent premature death of patients affected by the most common hereditary forms of CRC. This, in the long-term, could result in an overall reduction of cancer care costs.

1. Introduction

Over the last few decades, several cancer susceptibility genes have been identified. Colorectal cancers are frequently involved in cancer syndromes and Lynch syndrome (LS) is the most common heritable cause of colorectal and endometrial cancers (EC) [1].

LS is caused by a mutation in one of the mismatch repair (MMR) genes: MLH1, MSH2, MSH6 or PMS2. Carriers of MMR mutations, have a high lifetime risk of developing specific cancer types and it is well known that intensive and specific programmes of surveillance in accordance with national and international cancer screening guidelines can prevent premature death of patients affected by LS [2].

Genetic testing has been advocated, over the last few decades, for the identification of high-risk patients affected by LS. Knowledge of the causative mutation in LS enables the identification of entire families at risk of developing cancers in the future. Thus, accurate predictive genetic testing of family members at risk of LS would allow individualised management including intensive surveillance and prophylactic surgical resection of an organ at risk of developing cancer as a risk-reduction strategy, based on established genotypic risk stratification. In addition, non-carriers could be relieved from continuous anxiety and dismissed from lifelong intensive

Abbreviations: LS, Lynch syndrome; CRC, colorectal cancer; HCRC, hereditary colorectal cancer; MMR, mismatch repair.

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surveillance, sparing them psychological burden and reducing health care costs.

Many cost-effectiveness studies have been previously conducted, in particular for HCRC syndromes such as LS, in order to compare different strategies in selecting high-risk patients. A recent study by Dinh et al. [3] showed that primary screening by genetic testing for risk assessment in unaffected individuals could be cost-effective compared to current practice, based on clinical risk criteria. Other relevant studies [4,5] evaluated the cost-effectiveness of different surveillance programmes in high risk patients, or focused the cost-effectiveness of genetic testing and surveillance programmes including moderate risk families.

Considering the long-term perspective, little scientific data is available on the costs of targeted genetic testing and surveillance programmes in Italy.

The present study aimed to fill this gap by developing a cost analysis for LS management in an epidemiologically selected area comparing:

(i) an intensive surveillance programme, with the use of genetic testing versus an intensive surveillance without the use of genetic testing.
(ii) cancer care, using an intensive surveillance programme in gene carrier subjects versus cancer care for individuals not selected with genetic testing and who follow an unselective clinical surveillance.

2. Materials and methods

2.1. Design of the study and assumptions

To investigate the economic burden of genetic identification and management of LS patients we constructed a model based on epidemiological data from the province of Varese, in northern Italy, in order to evaluate the incidence of gene carriers.

This model was established using the colorectal cancers incidence data from the Varese Cancer Registry, created in 2007. The number of inherited cancers in the province of Varese was estimated, assuming that 6% of colorectal cancers (CRC) are inherited cancers [6,7]. Regarding LS incidence, the literature report a varied range from 2% to 6% [8] and it was decided to use the higher incidence reported.

The territory of the province of Varese includes 139 municipalities with more than 855.000 residents (51,4% are women—ISTAT 2007) and twelve districts, as shown in Fig. 1, with a low population density in the northern part of the province (hilly and mountainous, with a less developed road network) and a higher population density in the southern part.

From these data, it was estimated that around 3.500 subjects would have a diagnosis of colorectal cancer, and that 210 of these may have inherited a genetic mutation (6%).

However, based on data from the Varese Cancer Registry, the crude incidence rate of colorectal cancer is, respectively, 121.4 per 100,000 inhabitants (male N = 505 cases) and 73.7 per 100,000 inhabitants (female N = 324 cases). Therefore, from epidemiological estimates, it would be expected that 49 cases affected by CRC per year including 30 males and 19 females, are carriers of a genetic mutation that predisposes them to colorectal cancers.

Each carrier can transmit a cancer predisposing genetic mutation to his/her children. In these autosomal dominant conditions (ORPHA 144), each individual has a 50% chance of being a mutation carrier for LS.

Starting from these assumptions, and based on experience of the Cancer Genetic Counseling Service in the province of Varese, we estimated an average of four kindreds within each family and, therefore, two individuals for each family would inherit the mutation.

Fig. 1. Map of social and health districts of Varese province.
The Figure gives a representation of the twelve districts of Varese province.

Over a 10-year period, the model followed a hypothetical cohort of 98 healthy people comprising 49 males and 49 females at high risk of cancer due to being carriers of the pathogenetic MMR mutation.

It should be pointed out that patients carrying predisposing mutations have a high lifetime risk of cancers and often develop multiple cancers during their life. Specifically, as reported in the literature [9], it was assumed that in the absence of intensive surveillance, male gene carriers have a lifetime risk of 80% of developing colorectal cancer and female gene carriers have a lifetime risk of 60% of developing colorectal and endometrial cancers.

On the contrary, when intensive surveillance was carried out, the lifetime cancer risks (80% for male and 60% for female) were reduced by 62% both for colorectal and endometrial cancers according to the literature [7,10]. Thus, it was expected that male gene carriers have a 30% risk of developing CRC whilst female gene carriers have a 23% risk of developing colon and/or endometrial cancer.

For the first comparison, the following assumptions were made.

I In the genetic testing strategy, we assumed that all individuals underwent genetic testing, and thus half of them (98 subjects), as proven mutation carriers, entered the intensive surveillance programme;
II In the other strategy, without genetic testing, all individuals (196) with unknown mutation status based on their family history entered the intensive surveillance programme from the outset. For this strategy, in fact, it is not possible to make any discrimination between carrier subjects and non-carriers of LS mutations.