OBTAINING OPTIMAL PERSONALIZED SURVEILLANCE STRATEGIES FOR PATIENTS WITH SCREEN-DETECTED COLORECTAL ADENOMAS USING DISCRETE EVENT SIMULATION

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BACKGROUND

Evidence from several studies has shown that Colorectal cancer (CRC) screening is effective and cost-effective in an average-risk population. Many European countries have introduced CRC screening in recent years, although the population program coverage remains low. In Spain, CRC screening uses a fecal-occult blood test (FOBT) for screening and colonoscopy as diagnostic tool in case of a positive FOBT result (around 5.8%). Advanced and non-advanced adenomas constitute the most frequent findings of this colonoscopy (40-50%), and the removal (polypectomy) of these premalignant lesions is considered the main contributor to the reduction of not only mortality, but also incidence of CRC.

In that sense, one of the biggest challenges of CRC screening at present is postpolypectomy surveillance because of the high volume of affected individuals and the relatively reduced information regarding cost-effectiveness of the different strategies. Existing evidence is inconclusive and there is no clear agreement among the different scientific societies or collaborative initiatives regarding the risk classification of adenomas as well as the optimal surveillance strategy for each degree of risk. Current strategies and intervals are somehow arbitrary because they are not based on clinical trials and their compliance is heterogeneous among screening programs and clinical settings.

Risk stratification of patients with adenomas at baseline examination is still challenging because the existing guidelines are based only on the number, size and histological characteristics of resected and evaluated lesions. However, it is well recognized that the behavior of patients with apparently similar risk at baseline is quite heterogeneous, thus emphasizing the need for more accurate predictors of colorectal neoplasm development. Genomics may contribute to further delineate individual risk, and its characterization is crucial for improving the effectiveness of surveillance strategies by targeting individuals who would benefit the most.

OBJECTIVE

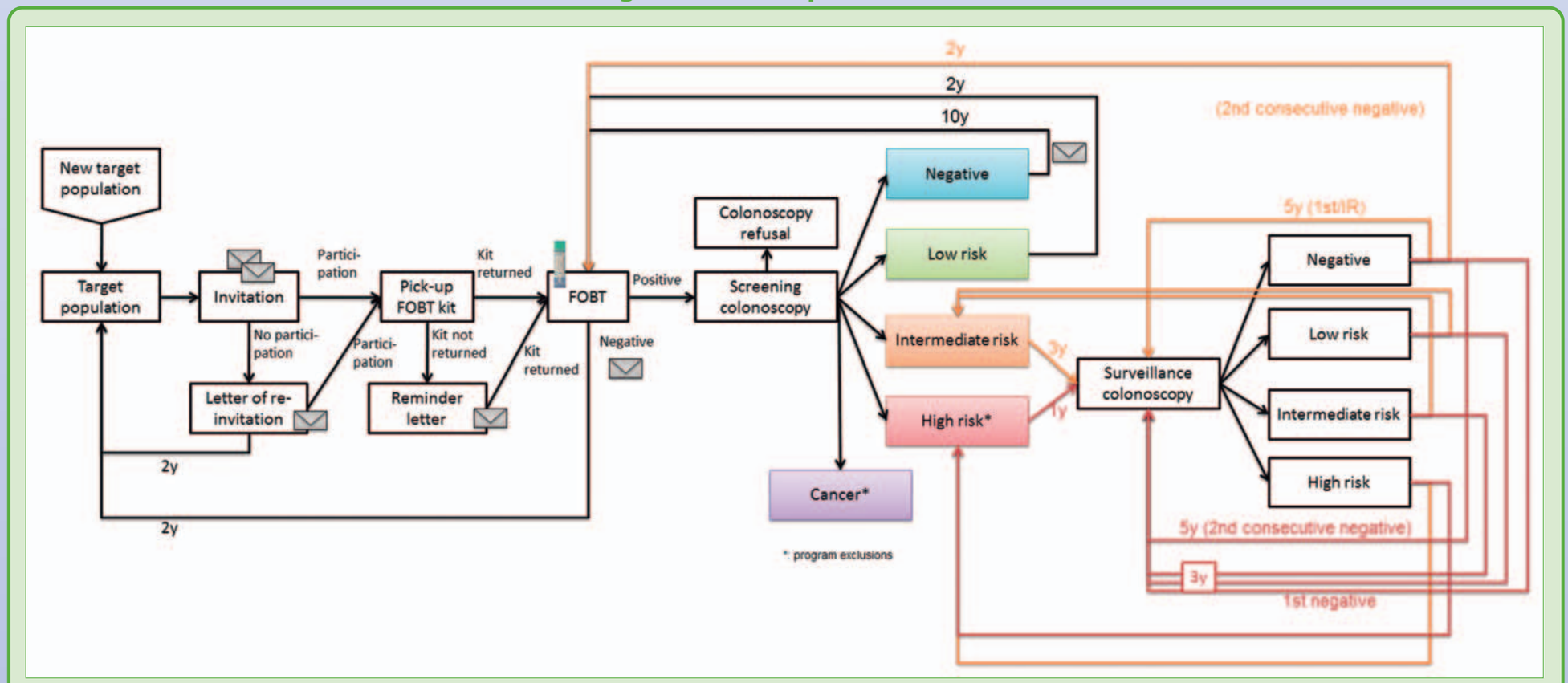
To optimize, within a CRC screening program, surveillance of premalignant lesions using individual risk-based strategies, based on genetic analysis, that take into account benefits, harms and costs.

METHODS

A discrete-event simulation model that reproduces the process of screening and takes into account the costs at every stage, from invitation to screening to surveillance of findings (figure 1) will be upgraded. The model in figure 1 shows the surveillance schedule according to European Guidelines for CRC screening. The natural history of the disease will be included, based on a review of previously published simulation models, and with special emphasis on the events after adenoma detection at screening colonoscopy.

Based on the results of an ongoing study aimed at identifying common genetic variants associated with an increased susceptibility to develop colorectal adenomas, we will evaluate whether any of these common genetic variants may influence the risk of developing metachronous neoplastic lesions in patients in whom colorectal adenomas were detected in a FOBT-based screening program. For this purpose, we will select those cases with advanced adenomas identified in the cohort and analyze the results of the surveillance colonoscopy at three years. The risk of developing cancer or recurrent adenomas according to the clinical characteristics of the patients will be included in the model. The interval between surveillance colonoscopies (orange and red arrows in figure 1) will be optimized with the objective of minimizing the number of colonoscopies while keeping the same level of effectiveness, defined as the impact on incidence of advanced adenomas and cancer over time. The necessary inputs regarding the operating characteristics of screening, such as participation, test sensitivity and specificity, and stage at diagnosis, will be obtained from two ongoing population-based CRC Screening Programs.

Figure 1: Conceptual model.



IMPLICATIONS

Simulation models can help in the design of personalized screening strategies:

- To find out more effective cancer screening strategies according to benefit-harm balance, including genetic susceptibility.
- To propose optimal cancer screening strategies to help citizens, professionals and health policy decision-makers improving the effectiveness of screening programs.

Personalizing CRC screening through adenoma surveillance strategies may improve allocation of resources under cost constraints, minimize harms and maximize benefits of population-based programs, affecting millions of people.

Funding: Fondo de Investigación Sanitaria PI07/90357 and Fundación Mútua Madrileña AP94422011.

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