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**Authors:**

Agustín Albillos Martínez, Julia López Cardona, Javier Crespo García, Fernando Carballo Álvarez

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## Population screening for colorectal cancer in Spain - A public health success with remaining challenges

Agustín Albillos<sup>1</sup>, Julia López-Cardona<sup>1</sup>, Javier Crespo<sup>2</sup>, Fernando Carballo<sup>3</sup>

<sup>1</sup>Department of Gastroenterology and Hepatology. Hospital Universitario Ramón y Cajal. Instituto Ramón y Cajal de Investigación Sanitaria (IRYCIS). Centro de Investigación Biomédica en Red en Enfermedades Hepáticas y Digestivas (CIBEREHD). Universidad de Alcalá de Henares. Alcalá de Henares, Madrid. Spain. <sup>2</sup>Instituto de Investigación de Valdecilla. IDIVAL. School of Medicine. Universidad de Cantabria. Santander, Spain. <sup>3</sup>School of Medicine. Universidad de Murcia. Murcia, Spain

Colorectal cancer (CRC) is the third most common type of cancer worldwide and the second most common cause of cancer-related mortality, representing 12.6 % (1). In Europe, its incidence in 2022 was 73 per 100,000 inhabitants; it also is 30 % higher in males, with a mortality rate 32 per 100,000 inhabitants (1). In Spain the situation is more serious with incidence and mortality rates higher than the global average: 35.8 versus 19.5, and 11.5 versus 9.0, respectively. CRC represents a significant public health challenge with an estimated overall cost of € 1,900 million a year in Europe (2).

The seriousness of this issue has led to prioritize early detection by screening programs in developed countries, which has reduced incidence and mortality (3). This paper addresses two key issues in Spanish CRC screening programs: differences in participation among autonomous communities (ACs) and the need to extend screening beyond 70 years of age. These challenges are underscored in two recent articles in REED that analyze CRC incidence trends and offer strategic recommendations for screening programs (4,5).

### **Population screening for colorectal cancer: a public health priority**

The most important prognostic factor in CRC is tumor stage at diagnosis; survival at 5 years is 95 %-100 % with surgery for local tumors, and falls down to 15 % for disseminated cases. Organized screening programs for people aged 50 to 75 years are cost-effective in reducing CRC incidence and mortality whether through colonoscopy or fecal occult blood testing (FOBT) (6,7). These programs, which systematically invite all the eligible population, are more efficient and equitable than opportunistic screening, and result in higher participation rates (7). In this context, a US study showed that an organized program had doubled participation from 40 % to 85 %, and reduced CRC incidence and mortality by more than 25 % and 52 %, respectively, when compared to the values observed within five years prior to implementation (8).

In 2003, the Council of the European Union recommended member states to develop screening programs for various types of cancer, including CRC (9). Currently, 20 of the 27 countries in the European Union, including Spain, have already implemented nation-wide population screening programs (10,11). In order to cost-effectively reduce mortality, it is crucial that programs have high participation rates, this being the reason why the 2021 Europe's Beating Cancer Plan established the goal of reaching at least 65 % participation among the eligible population (12).

### **Identifying and overcoming barriers in order to increase participation**

In Spain, population screening for CRC was included in the common National Health System services portfolio in 2014, with a 5-year deadline for implementation in all ACs, and a 10-year end point for nearing 100 % coverage (13). All programs consist of biennial FOBT for people between 50 and 69 years of age, followed by colonoscopy for positive cases (14). Currently, this program has already been implemented in all ACs and reached full coverage, although significant differences in participation rates still exist.

A major challenge for population screening in Spain is low participation of the target population. Mean participation among ACs is 45 %, with some ACs showing 40 % and only two reaching above 70 % (5,14). These figures are similar to those in other European countries also relying on FOBT. In fact, an analysis of results between 2018 and 2020 revealed that participation in national full-coverage programs ranged from 29 % in Croatia to 67 % and 64 %

in Denmark and the Netherlands, respectively (15). Interestingly, as in Spain, in Italy, where the program was independently implemented in each region, up to six fold differences in participation levels are apparent among regions.

Identifying, addressing participation-limiting barriers is a major challenge for health systems dealing with population screening programs, as is the case in Spain. Barriers are diverse and should be considered collectively (Table 1). Studies indicate that participation is lower in younger people, those in rural areas, males, disadvantaged groups with lower socioeconomic and educational levels, migrants, and individuals with sparser contact with the health system (15-18). These groups usually share a reduced CRC risk perception and unawareness of the benefits of early diagnosis. Interestingly, in contrast to other countries, living in rural areas does not represent a barrier to screening in our health care model (19).

Program efficiency and quality are dependent on cooperation between citizens and healthcare professionals, as well as on logistics facilitating patient care pathways through the health system (7). Promoting knowledge about CRC and awareness of early diagnosis benefits is key for overcoming perceived barriers to screening. This requires educational campaigns with specific emphasis on vulnerable groups, and providing Primary Care with resources to inform the population. Furthermore, it is key that strategies be designed to improve access to the various screening stages —sending reminders, facilitating fecal sample delivery and collection, and regularly re-inviting those who skip screening (Table 1).

Differences in participation between ACs can only be reduced using strategies that address structural barriers to access, and foster screening demand by citizens (5,14,16) (Fig. 1). Such strategies must be adapted to local circumstances and require funding and commitment from the health system.

### **Extending the target population age range**

Age is the primary risk factor for CRC, with incidence increasing with age, particularly from 50 years on. Median age at diagnosis is 67 years and nearly 70 % of cases are diagnosed in people over 65 years (20). A recent study shows that in Spain CRC incidence increases gradually with age up to 80-84 years, although sex-related differences are present (21). From 1990 to 2014

incidence simultaneously increased in all age groups and in both sexes, albeit showing a steeper slope in males, which enlarged the incidence gap between males and females. Starting in 2014 incidence has levelled out for women and slightly decreased men, although the gap persists (21).

Population screening trials in the 1990s showed that screening reduced CRC mortality when done for the population at average risk up to 75 years of age (22). Currently, the European Union recommends screening between 50 and 74 years of age (9). In line with these recommendations, major North American societies (23) and multiple European programs, including those in Sweden, the Netherlands, France, Norway, and Belgium, include the population up to 74 years of age or at least 70 years of age (11). Therefore, it is crucial for Spanish ACs to extend screening age range to 74 years, possibly through a recommendation by the Health Ministry (Fig. 1). From 75 years on general screening is not recommended because of its questionable impact on mortality rate, although it should be considered on an individual basis according to patient comorbidities, screening history, and preferences (23).

A decrease in initial screening age to 45 years años is currently debated. Some North American societies have recommended this change after observing an increase in CRC incidence in people younger than 50, which went from 6 to 8.7 per 100.000 population between 2000 and 2019. However, this trend has not been confirmed in many European countries; in some of them, such as France or Italy, incidence has remained stable or decreased, as in Spain, while in others, including Germany and Denmark, incidence slightly increased (20,21). Furthermore, screening cost-effectiveness between 45 and 50 years of age is comparable to that for 50-55 years but much lower than for older population segments. In fact, redirecting resources in order to promote screening at older ages might reduce CRC mortality by threefold (24). Therefore, since life expectancy is on the rise, the controversy about screening age limits should be extended beyond merely reducing the lower limit to also increasing the upper one, while weighing risks against benefits on an individual basis (25).

To conclude, the implementation of the national CRC screening program represents a huge achievement for Spanish public health, aligning Spain with other European countries. In this respect, in tune with other programs, extending screening age range to an upper limit of 74

years is key according to recommendations by the European Union. A crucial aspect for improving screening in our country is increased population participation, which requires specific resources devoted to overcoming participation barriers.

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Table 1.

| Limiting factors                       |   |
|--|---|
| Patient's own                          | <p><i>Psychological:</i> fear, indifference, distrust of the health system, religion</p> <p><i>Sociodemographic:</i> younger age, male sex, rural setting, infrequent contact with the health system, no intimate partner</p> <p><i>Socioeconomic:</i> low socioeconomic level, poor education, immigrants</p> <p>Scarce awareness</p> <p>Lifestyle</p> |
| Program management's own               | <p>Poor coordination</p> <p>Insufficient communication with citizens</p> <p>Lack of follow-up</p>   |
| Health system's own                    | <p><i>Coverage:</i> invitation limitations in public systems, insurance costs in private systems</p> <p><i>Circuits:</i> difficult access, flow barriers</p> <p>Financing</p>   |
| Facilitation measures                  |   |
| In education and dissemination         | <p>General campaigns</p> <p>Specific campaigns for vulnerable groups</p>  |
| In patient-health system communication | <p>Repeated, individualized reminders</p> <p>Re-invitation of non-screened population</p> <p>Customized incidence management</p> <p>Use of novel communication channels</p> <p>Information transmission</p> <p>Support from primary care</p>  |
| In circuit logistics                   | <p>Test collection (home, pharmacy shipments)</p> <p>Test delivery (extended timetable)</p> <p>Easy colonoscopy management</p> <p>Quick clinical information feedback</p>   |



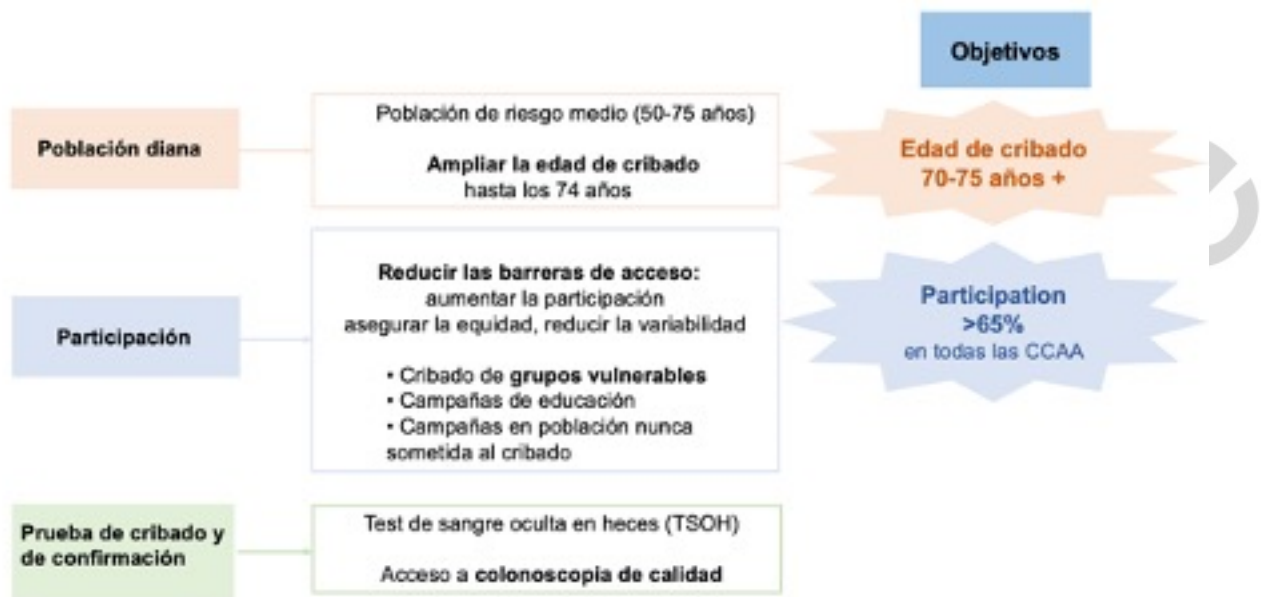


Figure 1. Strategic framework for the optimization of population CRC screening in Spain.