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Should Flanders consider lowering its target age for colorectal cancer screening to 45–49?

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ABSTRACT

Introduction: Colorectal cancer (CRC) screening generally starts screening by the age of 50 based on guidelines. Lately however, a U.S. guideline recommended to start CRC screening from age 45 and, very recently, two studies were published that addressed young-onset in Europe (in part) (Vuik et al., 2019; Araghi et al., 2019).
Materials and Methods: Flemish CRC incidence and mortality data contextualise trend results for age groups under 50 and what the implications could be for practice.
Results: CRC incidence rates showed considerable variability over a 12-year period without a clear increase in disease burden for the age group 45–49 in Flanders. In several age groups under 39 an increasing incidence trend was visible for both genders. Data was analysed in a period where no CRC screening was present in Flanders.
Discussion: Decreasing the target age for the Flemish CRC screening does not seem to be straightforward and primary prevention should be considered more prominently.

1. Introduction

Until 2018, colorectal cancer (CRC) screening for the general population was recommended by most guidelines to start at age 50 [3–5], as from this age, people are considered to be at average risk of CRC. In May 2018, however, the American Cancer Society (ACS) published a qualified recommendation to start CRC screening for the general population from age 45 [6]. A qualified recommendation indicates clear evidence of benefits, but less certainty about the balance of the benefits or about patients' values and preferences, that could lead to different individual decisions. This recommendation was based on published Surveillance Epidemiology and End Results data [7] and microsimulation model studies [8], U.S. data only.

Since only U.S. data were involved it can be discussed if these results are useful for Europe, starting by exploring whether an increase in disease burden for CRC is present for the population aged under 50. In recent years, multiple U.S. and Asian studies showed a significant increase of annual percent change (APC) of CRC incidence for people aged under 50 [7,9–11] and only very recently for Europe [1,2]. APC is one way to characterise trends in cancer rates over time. While APC is an informative way of reporting trend data, we stress the clinical relevance by considering the absolute increase in CRC incidence combined with the CRC-related mortality trend.

To evaluate trends of CRC incidence in age groups under 50 years in Flanders (Belgian Region), Flemish CRC incidence and mortality data by age group with an age interval of 5 years between 2001–2013 are used. The Flemish population-based CRC screening programme started in October 2013, therefore data given are not influenced by screening and CRC incidence rates in younger people can only be attributed to disease burden and not to early diagnosis due to screening.

2. Comparing incidence trends

2.1. U.S. Data

Bailey et al. (2015) showed a significant CRC incidence APC increase of 2.0% (CI 95% 1.5–2.5) and 0.4% (CI 95% 0.1–0.7) for people aged 20–34 and 35–49 repectively [10]. Other U.S. studies showed similar results regarding young onset CRC with significant APC increase of CRC incidence (1.7% [9] to 2.3% [7]) for people aged 40–49 while all age groups of 55+ showed a significant APC decrease of CRC incidence [7,9].

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2.2. European data

Based on the recent publication of Vuik et al. (2019) [1], comparisons between European countries regarding increasing CRC incidence for the age groups 40–49 were possible. Out of the 20 countries considered, 11 showed no significant trend, 8 showed a significant increase in CRC incidence over the years and 1 showed a significant decrease. Unfortunately, there is no data comparing the age group 45–49 which is more relevant for policy makers when one considers to lower the target age for national CRC screening initiatives. This recent publication considered Belgium as a whole, while normally this is not done due to regional differences in CRC screening programmes and incidence. The relevance of analysing Flemish data in more detail becomes interesting when considering the fact that for example in Germany and the Netherlands significant increases in CRC incidence APC (0.7 and 2.1) were observed for the age group 40–49, while for the neighbouring country Belgium this APC is 0.0.

2.3. Flemish data

In Flanders, between 1999 and 2013 a non-significant APC for colon cancer (0.9%, CI 95% -0.1-1.8) was reported for 35–49y old males and a significant APC increase of 1.9% (CI 95% 0.1–3.7) for 35–49y old females while for rectal cancer significant APC increases were reported of 2.0% and 2.8% respectively [12]. These data show differences between APC when considering gender and tumour location, which is why they were reported in a stratified manner and highlights how individually based increased risk actually is. While the abovementioned studies do not report on the age group 45–49, this study of Flemish data does and it becomes visible that the increase in CRC incidence over the years is different between the age groups 35–39, 40–44 and 45–49 stratified by gender (Fig. 1).

The age standardised CRC incidence rates from Flanders between 2001 to 2013 (for age groups 40–44 and 45–49) show large variability over the years and no stable positive trend (Fig. 1). In contrast to the decrease of CRC incidence reported in prior studies for all age groups of 55+, the age group 50–74 in Flanders showed a significant APC increase for colon cancer incidence and a non-significant APC for rectal cancer between 1999 and 2013 (0.9% and 0.3% for males and 1.7% and 0.2% for females) [12]. This slight increase is illustrated in Fig. 2.

3. Impact on mortality

The CRC incidence, together with the CRC mortality in the U.S. were visualised neatly by Murphy et al. (2017) for several age groups under the age of 50 over the years 1992–2013 [13]. An increased CRC incidence rate was visualised for age group 40–49 together with a stable mortality rate. Regarding CRC mortality in Belgium, a decrease of CRC mortality under the age of 50 was observed between 1958 and 2013, while for the U.S. after a similar decrease, this rate stabilised since 1990 [14]. For the European data a similar decrease was observed until 2008 after which it significantly increased between 2009 and 2016 (APC 1.1) [1], while if we consider the Flemish mortality data under the age of 50 (2004–2013), for all age groups (5-year interval) the mortality is either decreasing, or stable [15].

4. International relevance

Currently, lowering the recommended target age from 50 to 45 for CRC screening is not recommended by the European guidelines. Due to the topicality of the subject an updated European recommendation is needed, in the meanwhile national policy makers need to rely on local data. In Europe, the young-onset CRC data (age 40–49) varies considerably between countries, which justifies an analyses of young-onset CRC within countries and regions based on their own data. Since decreasing the target age for CRC screening could be an added value for the one country and is deemed unnecessary for the other.

5. Recommendations for Flemish practice

Until this point, Flemish data showed no necessity of lowering the age for the target population to 45–49y as a slight highly variable increase in CRC incidence seems present for men while for women the data suggest a rather stable CRC incidence rate over the years also based on variable data points (Fig. 1). Considering the observed variability, very minimal increases could still be possible but when taking into account the absolute increase for the age group 45–49 they do not exceed a total increase 2/100,000 person years over 12 years of observations. It could therefore be discussed whether it is appropriate and cost-effective to screen 45–49-year-old people. This age group is the second largest in the Flemish population with an annual average of 465,802 people in the period 2001–2013 and a median absolute number of CRC of 130 persons respectively. When FIT screening would be applied to this population there would be an imbalance in

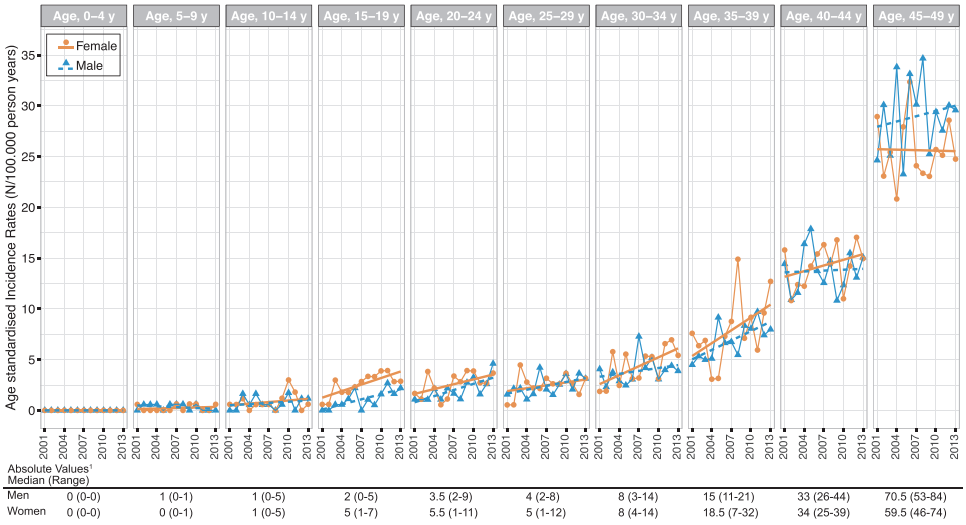
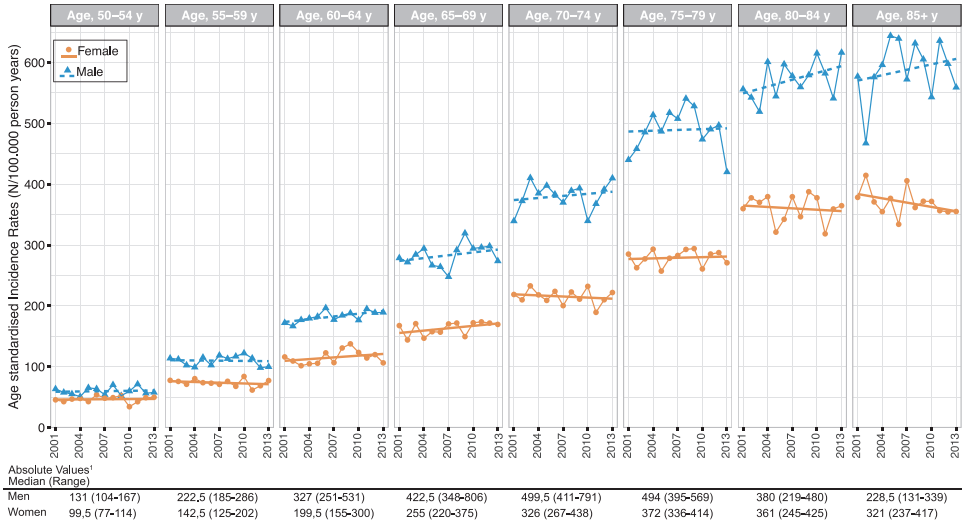


Fig. 1. Age standardised Colorectal cancer incidence rates from 2001 to 2013 stratified by gender and age group 0–49 with a 5-year interval.
1 The median incidence rate combined with the range of the lowest and highest incidence observed over the years.



Absolute Values[1]
Median (Range)

	Age, 50–54 y	Age, 55–59 y	Age, 60–64 y	Age, 65–69 y	Age, 70–74 y	Age, 75–79 y	Age, 80–84 y	Age, 85+ y
Men	131 (104-167)	222,5 (185-286)	327 (251-531)	422,5 (348-806)	499,5 (411-791)	494 (395-569)	380 (219-480)	228,5 (131-339)
Women	99,5 (77-114)	142,5 (125-202)	199,5 (155-300)	255 (220-375)	326 (267-438)	372 (336-414)	361 (245-425)	321 (237-417)

Fig. 2. Age standardised Colorectal cancer incidence rates from 2001 to 2013 stratified by gender and age group 50–85+ with a 5-year interval.
1 The median incidence rate combined with the range of the lowest and highest incidence observed over the years.

colonoscopy results (after a positive FIT) between normal or non-cancerous results and precursor lesions or CRC. Prior Flemish work reported that decreasing age (alone and in combination with other variables) is associated with an increased risk of finding a normal or non-cancerous result during colonoscopy instead of a precursor lesion or CRC [16]. It is estimated that the proportion of participants aged 45–49 with a positive FIT resulting in a normal or noncancerous result during colonoscopy over precancerous or CRC results will increase [16]. In other words, the false positive rate of FIT will increase through a higher referral rate resulting in a negative colonoscopy (for precursor lesions and CRC) in this age group. This will increase the cost of screening and the burden for society, since screening is not without risk and colonoscopy complications range from 0.04 to 8% depending on multiple factors [17–19].

Including more personalised data, based on multiple risk factors instead of age only (which is current practice) could improve screening precision. This rationale was mentioned in a recent commentary (2018) as: 'Without a personalised risk, we must live with age alone as the default determinant of when to start screening. Although convenient and simple, age is imprecise and impersonal as a risk surrogate; its use alone signifies the tension between a public health recommendation and provision of preventive care for individual patients' [20].

For most of the age groups under 40, the Flemish data shows an increase in CRC incidence of which the absolute increase is relatively marginal when considering the incidence rates of the current screening target population (Fig. 2). The increase in this age group is not tackled by incorporating them in current screening approaches as it is not evidence based to do so and will most likely introduce problems such as an unnecessary high number needed to screen. Furthermore, when CRC runs in families, people of younger ages are more likely to be afflicted with predispositions of CRC. They are considered as high-risk for CRC and should not participate in CRC screening because follow-up options should be discussed with their health professional.

Therefore, when one does not consider personalised preselection, an approach by primary prevention is a logical and feasible candidate to tackle the trend of increasing CRC incidence in the age groups under 50, as risk factors for CRC are well studied. In addition, age groups under 50 should be correctly advised by healthcare workers, especially when having familial or genetic risk.

CRC incidences in Flanders show no stable positive trend for the age group 45–49 between 2001 and 2013, considering the variability. These findings are in contrast with previously published U.S. data on which the ACSs recommendation is based to start CRC screening at age 45, but are in line with Belgian data for age group 40–49 [1]. We therefore conclude that regional evidence refutes the necessity of lowering the target age at this point for the Flemish CRC screening programme. When CRC incidence would clearly rise for 45–49 year old people, a formal modelling study in Flanders could be appropriate to estimate the effects on life years gained, needed FITs and colonoscopies when starting screening by FIT at age 45. Regarding the detected rise in CRC incidence in people below the age of 40, primary prevention and correct advise by healthcare workers regarding familial CRC risk is recommended in Flanders.

Authorship contribution statement

W.v.d.V, G.V.H, M.P and S.H, conceived and planned the research. W.v.d.V, carried out the analyses. All authors contributed to interpreting the results and provided critical feedback, helped shape the research, analysis and the manuscript. W.v.d.V wrote the manuscript and G.V.H, M.P and S.H supervised the project. All authors read the manuscript gave feedback and approved the final version for publication.

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