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ORIGINAL ARTICLE

Evaluating incidence and mortality trends of early-onset colorectal cancer and adenoma in Belgium

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Background: Colorectal cancer (CRC) incidence is rising among young adults globally, yet European data remain inconclusive. This study evaluated age- and sex-specific trends in CRC incidence, adenoma detection, and mortality in Belgium, with a focus on individuals aged 20-49 years. Diagnostic procedure trends in the 40-49 years age group were also analyzed to contextualize epidemiological patterns.

Materials and methods: Data from the Belgian Cancer Registry and diagnostic records from health insurance organizations were used to analyze trends in invasive CRC, *in situ* CRC, and adenomas and related diagnostic procedures. Mortality data were also included. Age-specific incidence rates and annual percentage changes were calculated using joinpoint regression analysis.

Results: Invasive CRC incidence remained stable in individuals aged 40-49 years between 2004 and 2023, whereas adenoma and *in situ* CRC rates increased, coinciding with increased use of fecal immunochemical tests and colonoscopy. Mortality in this age group was stable or declined. Conversely, individuals aged 30-39 years showed increasing trends in adenomas, *in situ* tumors, and both early- and advanced-stage CRC. Stages I-IV CRC incidence rose significantly in the 30-34 and 35-39 years age groups, with stage IV increasing by 9% and 5% annually, respectively. Adenoma incidence increased in nearly all age groups $<$50 years, except for males aged 20-24 years and individuals aged 25-29 years. Diagnostic activity, particularly between 2010 and 2014, likely contributed to early lesion detection.

Conclusions: Enhanced diagnostic activity in individuals aged 40-49 years appears to have led to earlier detection rather than increased advanced disease. These observations do not provide evidence that would support lowering the current starting age of organized screening. Rising CRC incidence in individuals aged 30-39 years warrants increasing clinical vigilance in younger adults with symptoms or elevated risk and requires further investigation into underlying drivers. Epidemiologic surveillance should preferably include precursor lesions and diagnostic activity.

Key words: colon cancer, colorectal cancer, early-onset colorectal cancer, epidemiology, population-based cancer registry, rectal cancer

INTRODUCTION

In 2023, ∼7800 people were diagnosed with colorectal cancer (CRC) in Belgium, representing 10% of all newly reported cancer cases. CRC ranks as the third most common cancer in both males (55%) and females (45%).[1] Its risk increases with age, peaking around the age of 85 years. The median age at diagnosis is 72 years for males and 74 years for females with colon cancer, and 69 and 68.8 years, respectively, for rectal cancer.

Recent epidemiological data indicate a rising incidence of CRC among young adults, a population not routinely included in screening programs.[2-11] A comprehensive analysis of 40 studies across 12 countries revealed a global increase of nearly 30% in CRC incidence in young adults over the past two decades, with the most pronounced rise observed in high-income countries such as the USA, Australia, and Canada. Emerging trends are also noted in low- and middle-income regions of Asia, Latin America, and the Caribbean. These cases of CRC are disproportionately located in the distal colon and rectum.[3,12-14] European data remain limited and heterogeneous. For example, Dutch registry data reported an average annual percentage increase of 1.41% in CRC incidence among individuals aged 15-49 years between 1998 and 2023, with projections

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indicating continued growth in all age groups except those aged 15-29 years.[10,12,15] Similarly, the UK has reported rising CRC incidence among individuals aged 18-49 years between 2000 and 2021, primarily driven by those aged 35-44 years, with stability observed in those aged 45-50 years.[16]

Despite consensus on the increased burden of CRC in young adults, data on adenoma prevalence in younger populations are sparse. Given that most CRCs develop from adenomatous polyps over a latency period of 5-15 years, early detection through screening is critical.[17] Adenomas are considered precursor lesions, and their identification is essential for cancer prevention.

In Belgium, regionally organized CRC screening programs started in 2009 in Brussels and Wallonia—with a switch from guaiac-based fecal occult blood testing to immunochemical fecal occult blood testing [fecal immunochemical test (FIT)] in 2016—and in 2013 with FIT in Flanders. The current protocol invites individuals aged 50-74 years for biennial FIT testing, with colonoscopy recommended after a positive result. Evidence from Cardoso et al.[18] suggests that countries with long-standing population-based screening programs targeting average-risk individuals (typically aged 50-74 years) have experienced declining CRC incidence, in contrast to countries lacking such initiatives. Belgium has similarly observed reductions in both CRC incidence and mortality, likely attributable to enhanced screening coverage and therapeutic advances.[19] In response to trends in CRC in young adults, some jurisdictions, including the USA, have lowered the screening initiation age to 45 years.

A retrospective study by van de Veerdonk et al.[20] examined Flemish CRC incidence from 2001-2013, before the implementation of screening programs. Although no significant increase was observed in the 45-49 years age cohort, rising trends were evident in individuals $<$40 years. In the age group 16-35 years, CRC incidence increased among males between 2004 and 2022; for females, incidence rose until 2017 and subsequently plateaued.[21]

This study aims to evaluate age- and sex-specific trends in CRC incidence, adenoma detection, and mortality in Belgium, with a particular focus on the early-onset population. Ancillary analyses include population-wide comparisons and assessments of diagnostic procedures, including FIT and colonoscopy utilization.

MATERIALS AND METHODS

Data sources

Colorectal tumors (invasive and *in situ*) were identified based on the cancer registration database available at the Belgian Cancer Registry (BCR), which contains validated cancer diagnoses based on data provided by both the oncological care programs (hospitals) and the laboratories for pathological anatomy. Because registration is mandatory, the BCR database is estimated to be at least 99% complete from 2004 onward.[22] For cases with a diagnosis of both an *in situ* and an invasive tumor in the same year, they were registered separately if the *in situ* diagnosis occurred before the invasive tumor with an interval of at least 3 months. For cases in which multiple tumors are diagnosed with different *International Classification of Diseases for Oncology, Third Edition* topography codes in the colon, they were registered as different tumors. Tumors of the appendix [*International Classification of Diseases, Tenth Revision* (ICD-10): C18.1] were excluded. Tumors of the colon (ICD-10: C18.0; C18.2-19.9; D01.0-D01.1) and of the rectum (ICD-10: C20.0-20.9; D01.2) were analyzed separately.

Staging was performed using the applicable TNM (tumor-node-metastasis) edition at the time of diagnosis (TNM 6th edition for incidence years 2004-2009; TNM 7th edition for incidence years 2010-2016; TNM 8th edition starting from incidence year 2017). The reported stage is a combination of both clinical and pathological stage, with priority given to the pathological stage except in case of neoadjuvant therapy. Clinical information about distant metastases always takes priority. *In situ* tumors are classified as being stage 0, whereas invasive tumors are stage I, II, III, or IV.

Colorectal adenomas were identified based on the cyto-histopathological database of BCR, which covers information on all colorectal samples, whether or not they are abnormal, as provided by the laboratories for pathological anatomy. This is also a mandatory registration; the data can be considered complete from 2013 onward. For the incidence of adenoma, only one adenoma per person per year is retained, with a preference for villous over nonvillous adenomas. If the detection of an adenoma coincided with the detection of an *in situ* or invasive colorectal tumor, the adenoma is not included.

Information regarding diagnostic procedures (FITs and colonoscopy) was derived from health insurance reimbursement data provided by the InterMutualistic Agency (IMA-AIM). IMA-AIM collects the data of all Belgian health insurance companies, and because health insurance is mandatory, 98% of the population is captured. These data are provided to BCR in the context of the organization and evaluation of the organized CRC screening programs. BCR has access to the data for people aged $\geq$40 years for the period 2002/2010-2023. If a person has multiple procedures (of the same type) in a year, only the first procedure per year and per person was considered. Only information concerning reimbursed FITs was included in the IMA-AIM data, that is, no data are available on FITs that are distributed without prescription through the pharmacies.

Data on mortality in Belgium are collected and managed by the three regions. The combined mortality data provided by Statbel encompass the period 2004-2021.

Study population

All Belgian residents with a Social Security Identification Number at the time of diagnosis were selected from both the BCR cancer database and the cyto-histopathological database. CRC incidence was evaluated by 5-year age group between 2004 and 2023 for the entire population

>20 years of age (given the small number of cases in people <20 years of age).

Due to the higher incidence of CRC in males, a sex-stratified analysis was performed for the early-onset population. Additionally, a subdivision was made for the three Belgian regions (Flanders compared with Brussels compared with Wallonia) based on the place of residence at incidence. This is because colorectal screening programs are organized by region, with considerable differences in screening coverage.

Statistics

Age-specific incidence rates were calculated by 5-year age group and expressed per 100 000 person-years. This was calculated by dividing the number of new cases observed during a given period by the corresponding population in that period. For time trends in these incidence rates, joinpoint regression was used to determine both age-specific annual percentage change (APC) and the average APC (AAPC) over the entire period with the 95% confidence interval (CI).[23] The AAPC represents a weighted average of the APC across the study period. If a single APC cannot describe the entire period, the timeline is divided into linear segments joined at specific points (joinpoints). The AAPC is then computed by averaging the APCs of each segment, weighted by the length of each segment. Estimates were made using Joinpoint Regression Software (v5.2.0.0, National Cancer Institute). Trends were considered to be increasing or decreasing when the APC was statistically significant ($P < 0.05$); otherwise, they were described as stable.

RESULTS

Age-specific CRC incidence

In 2023, there were 7837 new CRC diagnoses in Belgium (total population: 11 697 557); the majority were in the age groups targeted for screening (50-74 years; $n = 4058$; 51.8%), followed by those aged ≥75 years ($n = 3234$; 41.3%) and those between 20 and 49 years old ($n = 525$; 6.7%). Only 20 cases were diagnosed in people <20 years old.

Between 2004 and 2023, there was a significant increase in the age-specific incidence rates of invasive CRC in people between 30 and 34 years old (AAPC male 4.9%, 95% CI 2.4% to 8.4%; AAPC female 5.7%, 95% CI 2.2% to 10.3%) and 35 and 39 years old (AAPC male 2.2%, 95% CI 0.4% to 4.2%; AAPC female 2.1%, 95% CI 0.4% to 3.8%). For both males and females between 20 and 29 years old and between 40 and 54 years old, the incidence rates remained stable. Starting from the age of 55 years, a decrease was seen in the age-specific incidence rates in both males and females, which is the result of population screening for CRC that started in Brussels/Wallonia and Flanders in 2009 and 2013, respectively. A decrease was also seen in the age group ≥75 years (Figure 1). These graphs also clearly show the difference in age-specific incidence rates between the different age groups. For the ages 20-49 years, each 5-year age group had about half the crude CRC incidence level of its respective older 5-year age group.

When looking at early-onset invasive CRC in the different regions in Belgium (combined data for males and females), an increase was seen in Flanders for the 30-34 years age group (AAPC 4.1%, 95% CI 2.0% to 6.6%), 35-39 years age group (AAPC 1.9%, 95% CI 0.3% to 3.6%), and 40-44 years age group (AAPC 1.0%, 95% CI 0.1% to 1.9%). For the 30-34 years age group, a significant increase was also seen in Wallonia (AAPC 6.5%, 95% CI 3.8% to 10.2%). In contrast, Brussels showed a stable trend in all these age groups (Supplementary Figure S1, available at https://doi.org/10.1016/j.esmogo.2026.100340).

For colon cancer, the incidence significantly increased in people in the 30-34 years age group (AAPC 5.5%, 95% CI 3.0% to 8.7%). An increase in rectal cancer was seen in the 30-34 years age group (AAPC 4.6%, 95% CI 1.4% to 9.0%) and the 35-39 years age group (AAPC 3.6%, 95% CI 1.7% to 5.9%; Supplementary Figure S2, available at https://doi.org/10.1016/j.esmogo.2026.100340).

Stage-specific incidence in early-onset CRC

The incidence of *in situ* colorectal tumors increased in all age groups. Although the increase was 5.9% in the youngest age group, the increase was much larger in the older age groups (ranging from 11.0% in the 45-49 years old to 16.9% in the 35-39 years old). This steep increase is mainly the result of an increase in the period between 2004 and 2011-2014.

Stage I tumors increased in the 30-34 years age group (AAPC 7.4%, 95% CI 3.1% to 15.0%), 35-39 years age group (AAPC 3.9%, 95% CI 0.8% to 7.8%), and 45-49 years age group (AAPC 4.2%, 95% CI 2.3% to 5.5%), whereas stage II tumors only increased in the 30-34 years age group (AAPC 4.5%, 95% CI 1.5% to 8.6%) and even decreased in the 45-49 years age group (AAPC −1.5%, 95% CI −2.9% to −0.2%). In addition, stage III tumors increased in the 30-34 years old group (AAPC 4.8%, 95% CI 0.9% to 9.8%) and the 35-39 years old group (AAPC 2.4%, 95% CI 1.1% to 3.8%), while stage IV tumors increased in the same age groups: 30-34 years (AAPC 8.7%, 95% CI 5.3% to 14.3%) and 35-39 years (AAPC 4.6%, 95% CI 1.8% to 8.2%; Figure 2). In the age group 30-34 years old, about 36% of all invasive tumors were stage III and stage IV in 2023. In the age groups 35-39 years old and 40-44 years old, 46% and 42%, respectively, were stage III CRC cancers and 23% and 21%, respectively, were stage IV. In the age group 45-49 years old, most of the tumors were stage III (29%) followed by stage I (28%).

Early-onset CRC mortality

The mortality rates in individuals <50 years remained constant for the period 2004-2021 in all age groups except for those 45-49 years old, for whom mortality decreased between 2004 and 2021 (AAPC −1.7%, 95% CI −3.1% to −0.4%; Figure 3).

Figure 1. Age-specific incidence rates (N/100 000 person-years) for invasive colorectal cancer per 5-year age group for males (blue) and females (red arrow). The percentage indicates a statistically significant increase or decrease. Note the markedly different scale of the vertical axis across the rows of graphs.

Incidence of early-onset colorectal adenomas

An increase was observed in the incidence of adenoma in both males and females for all age groups <50 years except in the age groups 20-24 (males) and 25-29 (males and females) years old between 2013 and 2023 (Figure 4).

Diagnostic procedures (40-49 years old)

Females in the age groups 40-44 and 45-49 years were more likely to undergo a complete colonoscopy and FIT than males. Trends in diagnostic procedures are similar for males and females. Between 2010 and 2023, there was an increase in the number of reimbursed FITs in both age groups (AAPC 40-44

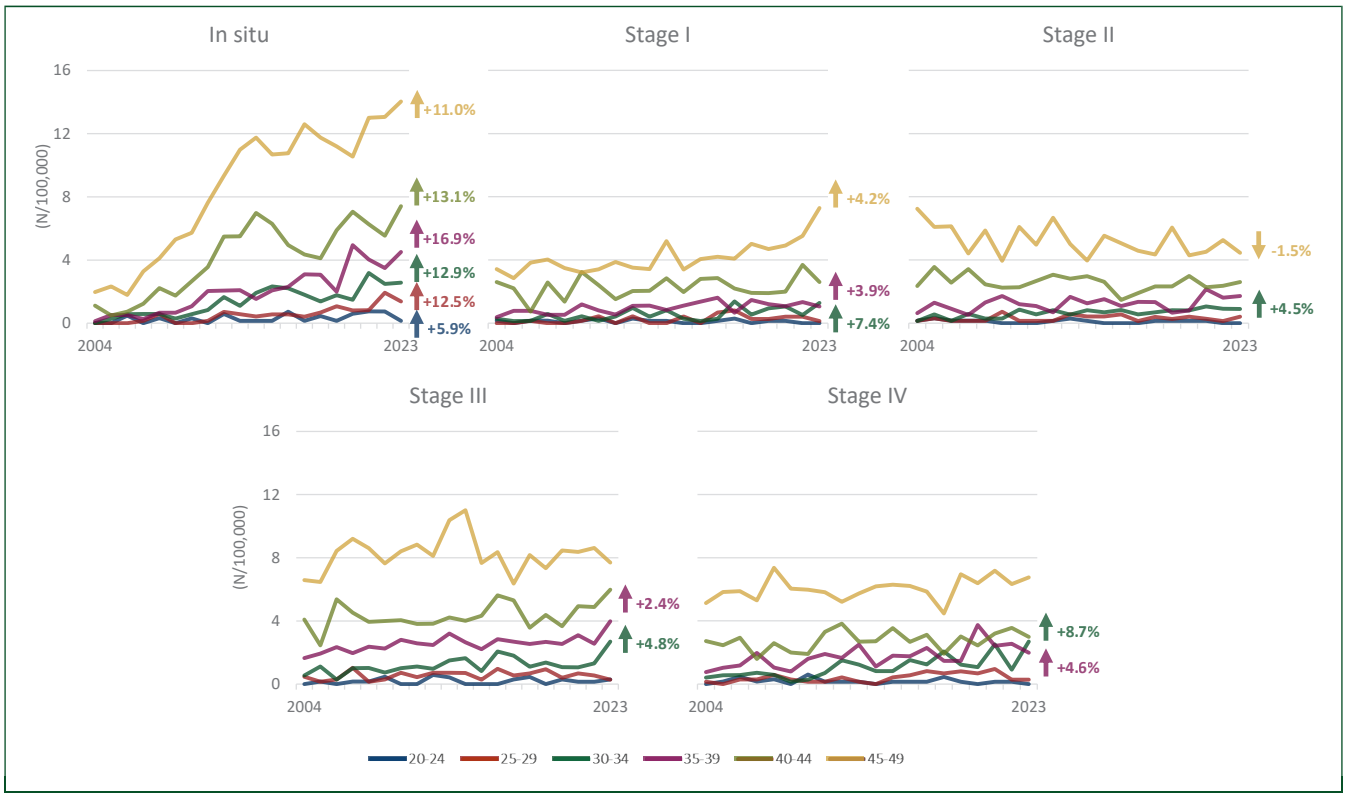

Figure 2. Age-specific incidence rates (N/100 000 person-years) for different stages of early-onset colorectal cancer per 5-year age group. The percentage indicates a statistically significant increase or decrease.

years 5.7%, 95% CI 4.0% to 7.7%; AAPC for ages 45-49 years 5.7%, 95% CI 4.4% to 7.2%). For both age groups, the increase was mainly the result of a steep increase between 2010 and 2014 (Figure 5A). For complete colonoscopy, an increase was also observed in both age groups (AAPC 40-44 years 9.2%, 95% CI 8.0% to 11.3%; AAPC 45-49 years 8.5%, 95% CI 7.3% to

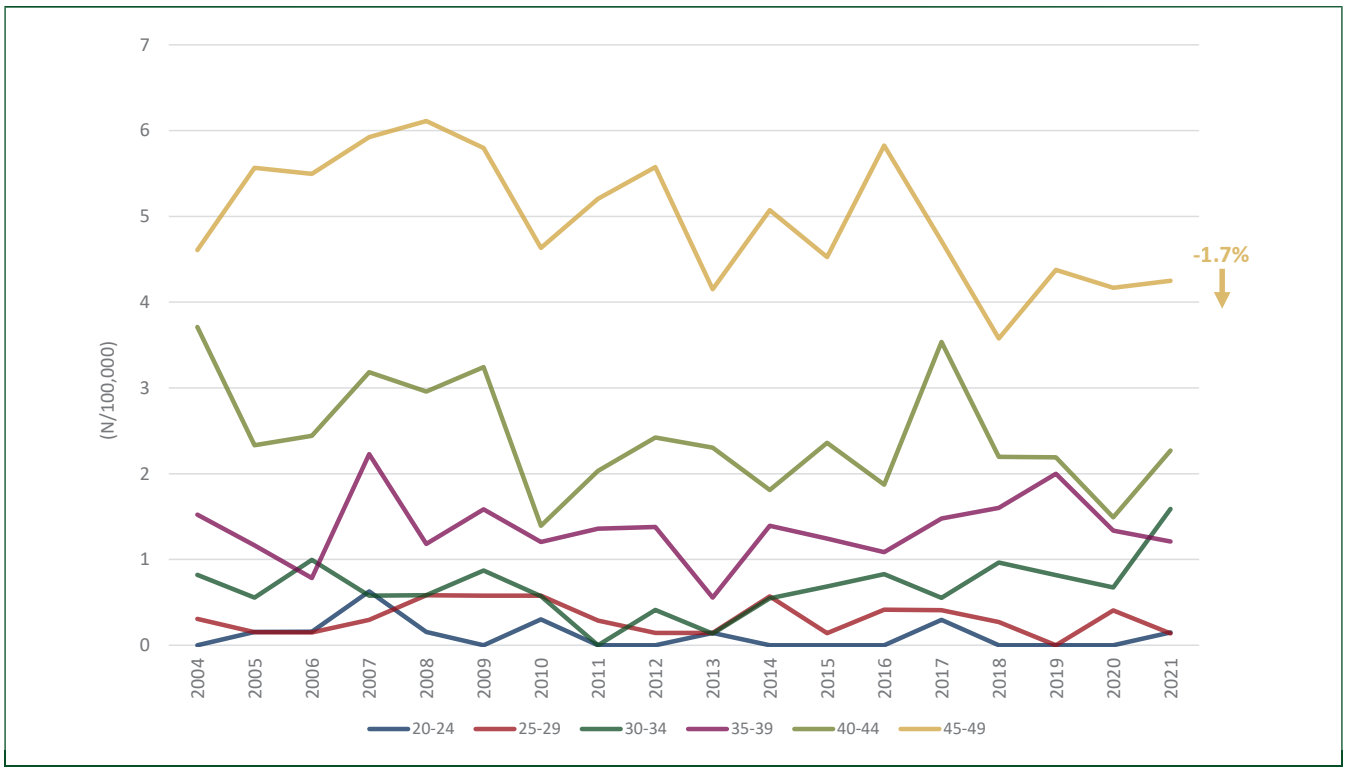

Figure 3. Age-specific mortality rates (N/100 000 person-years) of invasive colorectal cancer per 5-year age group for individuals <50 years old. The percentage indicates a statistically significant increase or decrease.

Figure 4. Age-specific incidence rates (N/100 000 person-years) for colorectal adenoma per 5-year age group for individuals <50 years for males (blue) and females (red arrow). The percentage indicates a statistically significant increase or decrease. Note the markedly different scale of the vertical axis for each of the rows with graphs.

10.5%), mainly caused by a steep increase between 2002 and 2007-2008 (Figure 5B). The temporary decrease seen in both diagnostic procedures in 2020 is almost certainly due to the COVID-19 pandemic and the related suspension of non-essential care in Belgium.

DISCUSSION

This study aimed to evaluate age-specific trends in CRC incidence in Belgium, with a particular focus on early-onset CRC and adenoma prevalence among individuals aged 20-49 years. Additionally, diagnostic procedure trends in the 40-49 years age group were analyzed to contextualize observed epidemiological changes.

In Belgium, ∼6% of CRC cases occur in individuals aged <50 years, comparable to the Netherlands (5%). These proportions are markedly lower than in the USA, where 13%-15% of cases are early onset and where projections suggest that by 2030, 25% of rectal and 10% of colon cancers in the USA will affect individuals <50 years.[15,24]

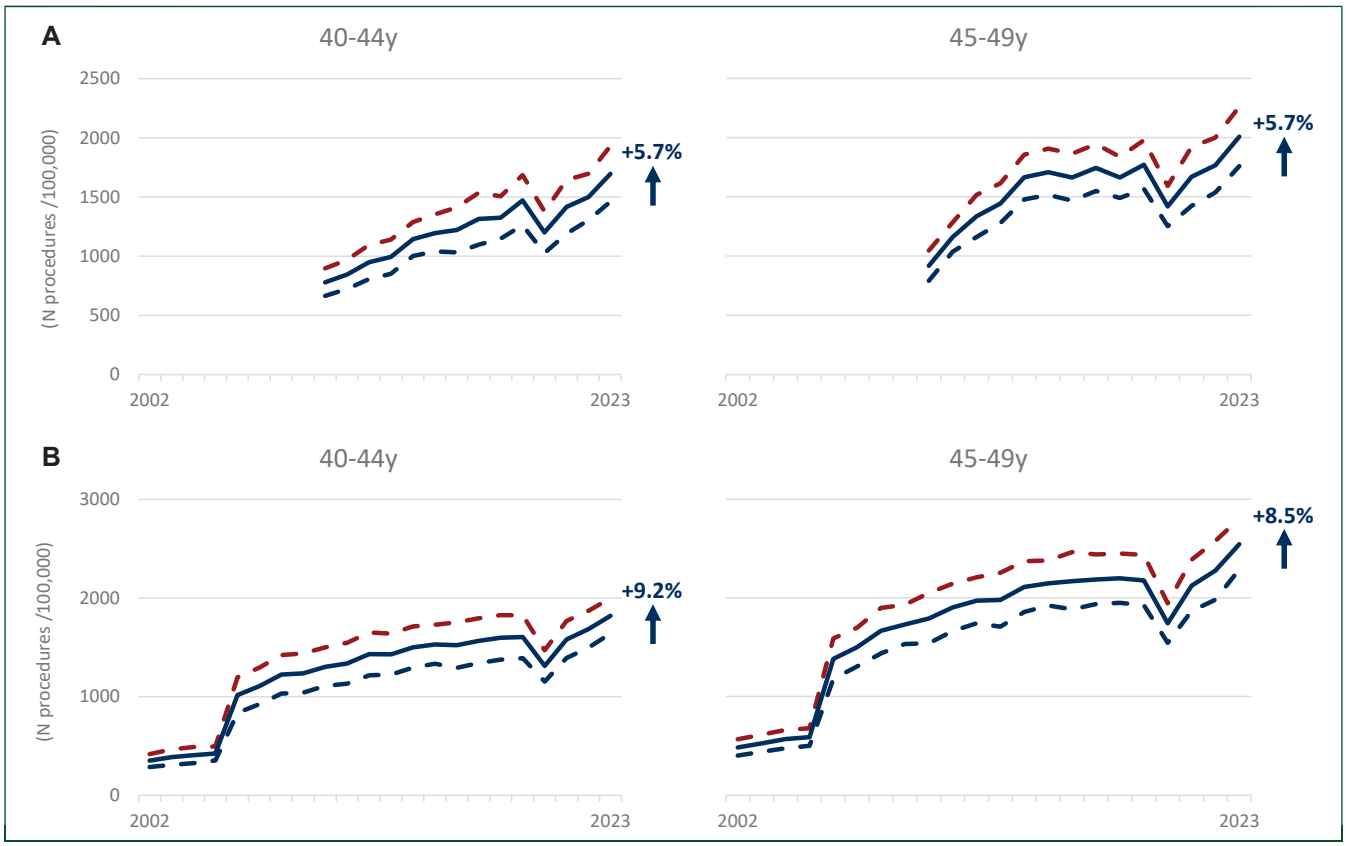

Figure 5. Age-specific incidence rates (N procedures/100 000 person-years) for the 40-44 and 45-49 years age groups for fecal immunochemical testing (A) and complete colonoscopy (B) for males (dotted blue), and females (dotted red) and both sexes combined (solid blue). The percentage indicates a statistically significant increase or decrease.

Between 2004 and 2023, CRC incidence increased among Belgian adults aged 30-39 years, while rates remained stable in the 40-49 years age group. These findings align with those of van de Veerdonk et al.,[20] who reported rising CRC incidence in Flemish adults aged <40 years between 1999 and 2013, and with international studies showing similar trends in Ireland,[25] Austria, and Italy.[26] However, this previously reported increase among people <40 years is not visible in the period 2014-2023 in the 40-49 years age group. Vuik et al.[27] also reported consistent increases in CRC among 20-29 year olds across 20 European registries. In the Netherlands, CRC incidence is projected to rise through 2035 in most age groups <50 years, except for those aged 25-29 years.[15] In England, increased incidence between 1974 and 2015 among 20-29 years old was primarily driven by distal tumors.[13] German data revealed rising CRC rates in individuals aged 15-19 years between 2003 and 2017, with rectal cancer trends more pronounced than colon cancer, except in the 40-49 years age group.[28] Similar rectal cancer increases have been observed in the USA since the mid-1990s.[29] However, many of these studies lack data on diagnostic procedures, limiting the interpretation of detection-related influences. In Belgium, both colon and rectal cancer incidence rose in the 30-34 years age group, with rectal cancer also increasing in the 35-39 years age group.

In Belgium, between 2004 and 2023, the AAPC in overall CRC incidence was ∼5% in the 30-34 years age group and 2% in the 35-39 years age group. Stage-specific incidence increased similarly for stages II and III CRC, while stage IV CRC rose more sharply: 9% annually in 30-34 years old and 5% in 35-39 years old. No significant trends were observed in stages II-IV CRC among 20-29 or 40-49 years age groups, except for a slight decline in stage II incidence in 45-49 years old. Previous studies have shown that individuals aged 30-49 years are more likely to present with late-stage CRC compared with those aged 50-74 years,[3,30-33] consistent with our findings in the 30-39 years age group. Waldmann et al.[28] reported increases in early-stage CRC between 2003 and 2017 (stages I and II) across all age groups <50 years, with late-stage increases only in 15-34 years old. Stage migration, particularly from stage II to stage III, may indicate that some of these shifts are due to improved lymph node examination over time.[34]

Despite rising advanced-stage CRC in 30-39 years old, mortality rates among individuals aged <50 years in Belgium remained stable, with a decline observed in the 45-49 years age group. This contrasts with the study by Santucci et al.,[35] who predicted unfavorable CRC mortality trends in several European countries, although more recent data show declining mortality in France, Italy, Poland, and Spain, with increases only in the UK. Data from the USA also show

a 0.5%-3% annual increase in CRC mortality among individuals aged <50 years.[36]

Our study also found rising stage I CRC incidence in the 30-34, 35-39, and 45-49 years age groups, alongside a marked increase in *in situ* tumors across all age groups between 2004 and 2023. This increase is much faster compared with invasive CRC (>10% compared with 2%-8% in other stages). These trends were most pronounced between 2004 and 2011-2014. This contrasts with the study by Ullah et al.,[25] who reported declining stage I and rising stage IV CRC in Irish patients <50 years. Between 2013 and 2023, adenoma incidence increased in nearly all age groups <50 years, except for individuals aged 25-29 years and males aged 20-24 years (and again at a faster rate compared with invasive CRC). These findings align with those of Rundle et al.,[37] who found similar adenoma prevalence in males aged 40-49 and 50-59 years, and slightly higher prevalence in females aged 50-59 than 40-49 years. Kim et al.[38] also reported a sharp age-related rise in conventional adenomas. The increase in adenomas in our study coincided with rising FIT use from 2010 to 2014, suggesting a link between diagnostic activity and early lesion detection.

CRC incidence in registry data reflects both disease risk and diagnostic activity. Increased awareness of early-onset CRC may influence physicians' testing behavior, symptomatic patient health-seeking, and opportunistic screening in asymptomatic individuals. Due to data limitations, diagnostic procedure trends were only analyzed in the 40-49 years age group. FIT and colonoscopy rates rose significantly in Belgium, with colonoscopy rates surging between 2002 and 2008 and increasing 2% annually thereafter, and FIT rates rising markedly between 2010 and 2023. These trends correspond with increased adenoma and *in situ* tumor detection in these age groups, particularly stage I CRC in 45-49 years old. No significant trends were observed in stages II-IV CRC, suggesting that increased testing primarily identifies early-stage lesions, likely due to heightened awareness and opportunistic screening rather than symptom-driven diagnostics.

Belgium's organized CRC screening program offers biennial FIT to individuals aged 50-74 years, with colonoscopy recommended after a positive result.[39,40] Regional implementation varies; in Flanders, FIT kits are mailed directly to eligible individuals, while in Wallonia and Brussels, recipients must request the test. In 2023, screening coverage was 62% in Flanders, 33% in Wallonia, and 29% in Brussels. Males and individuals aged 50-60 years consistently show lower participation. Consequently, 25% of the target population in Flanders, 47% in Wallonia, and 44% in Brussels have never been screened.[40] These disparities underscore the impact of socioeconomic and contextual factors. Rather than lowering the screening age to 45 years, our data suggest that efforts should prioritize increasing uptake among under-screened groups.[41-46]

To improve the detection of early-onset CRC, public health strategies must enhance symptom awareness and clinical recognition. Young adults often present with rectal and left-sided tumors, manifesting as rectal bleeding, altered stool frequency, and bowel obstruction. These nonspecific symptoms overlap with benign conditions, necessitating greater clinical vigilance. Physicians should routinely assess personal and family history of CRC or related conditions during evaluations.[47-51]

The strengths of this study include comprehensive population-based data from the BCR and near-complete diagnostic procedure data from IMA-AIM, enabled by Belgium's mandatory cancer reporting and health insurance systems. Mortality data were derived from official death certificates, ensuring robust population coverage.

Limitations include the absence of individual-level screening histories and clinical data, such as symptom onset or colonoscopy indications, which restricts causal inference. Additionally, data on lifestyle, diet, and genetic predispositions were unavailable, limiting interpretation of underlying risk factors.[52-54]

In conclusion, among individuals aged 40-49 years, invasive CRC incidence remained stable over the study period, and we observed no epidemiologic signal suggesting an emerging increase in advanced disease in this age group. The increase in diagnostic activity through greater use of FIT and colonoscopy together with rising rates of adenomas and *in situ* CRC appears consistent with earlier detection rather than a shift toward more invasive tumors. The mortality in this age group also remained stable or declined. Taken together, these patterns do not provide evidence of a growing early-onset disease burden that would support lowering the current starting age of organized screening in Belgium.

Increasing screening coverage among the already eligible population and maintaining clinical vigilance for symptomatic or high-risk younger adults remain important priorities. In contrast, individuals aged 30-39 years showed rising trends in adenomas, *in situ* tumors, and both early- and advanced-stage CRC, potentially driven by increased diagnostic testing, including among asymptomatic individuals, although the underlying causes require further investigation. Overall, these findings highlight the need to broaden surveillance to include precursor lesions and to consider diagnostic practices when interpreting epidemiological patterns.

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DISCLOSURE

The authors have declared no conflicts of interest.

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