Young-Onset Colorectal Cancer: Earlier Diagnoses or Increasing Disease Burden?

Colorectal cancer (CRC) incidence and mortality in the United States have changed strikingly in recent decades. Overall, CRC incidence decreased by >30% from 1975 (59.5 per 100,000) to 2013 (37.9 per 100,000).[1] CRC mortality similarly declined from 28.1 per 100,000 in 1975 to 14.5 per 100,000 in 2013—nearly a 50% decrease.[1] Screen-eligible populations, particularly those over age 65, have experienced the largest declines in incidence and mortality.[2,3]

In marked contrast with populations >50 years of age, the CRC incidence is increasing in younger adults.[4,5] Starting in the early 1990s, incidence rates have increased in this population (ages 20-49 years), from 8.5 per 100,000 in 1992 to 10.7 per 100,000 in 2013, a 26% increase.[1] The largest absolute increases have occurred in the 40- to 49-year age group, from 18.2 per 100,000 in 1992 to 22.3 per 100,000 in 2013 (Figure 1*A*). Mortality rates have remained stable during the same period (around 2.4 per 100,000), ranging from 2.1 per 100,000 in 1998 to 2.7 per 100,000 in 2012 (Figure 1*B*).

The increasing incidence of young-onset CRC has prompted discussion of the relative contribution of risk factors (eg, obesity, dietary patterns) and diagnostic factors (eg, screening, case ascertainment, practice patterns) to these observed patterns. Screening can influence incidence trends.[6] For example, as evidence accumulated supporting the effectiveness of stool-based screening tests and sigmoidoscopy,[7,8] the overall CRC incidence increased from 59.3 per 100,000 in 1975 to 66.3 per 100,000 in 1985 and subsequently decreased through 2013.[1] CRC screening in the United States has gradually increased after it was first formally recommended[9] in the late 1980s, particularly screening with colonoscopy.[10] Although guidelines recommend average-risk CRC screening starting at age 50,[11] younger adults may undergo colonoscopy for many reasons, including diagnostic evaluation (ie, for bleeding), family history of CRC and/or polyps, and inflammatory bowel disease. Colonoscopy in this setting may facilitate

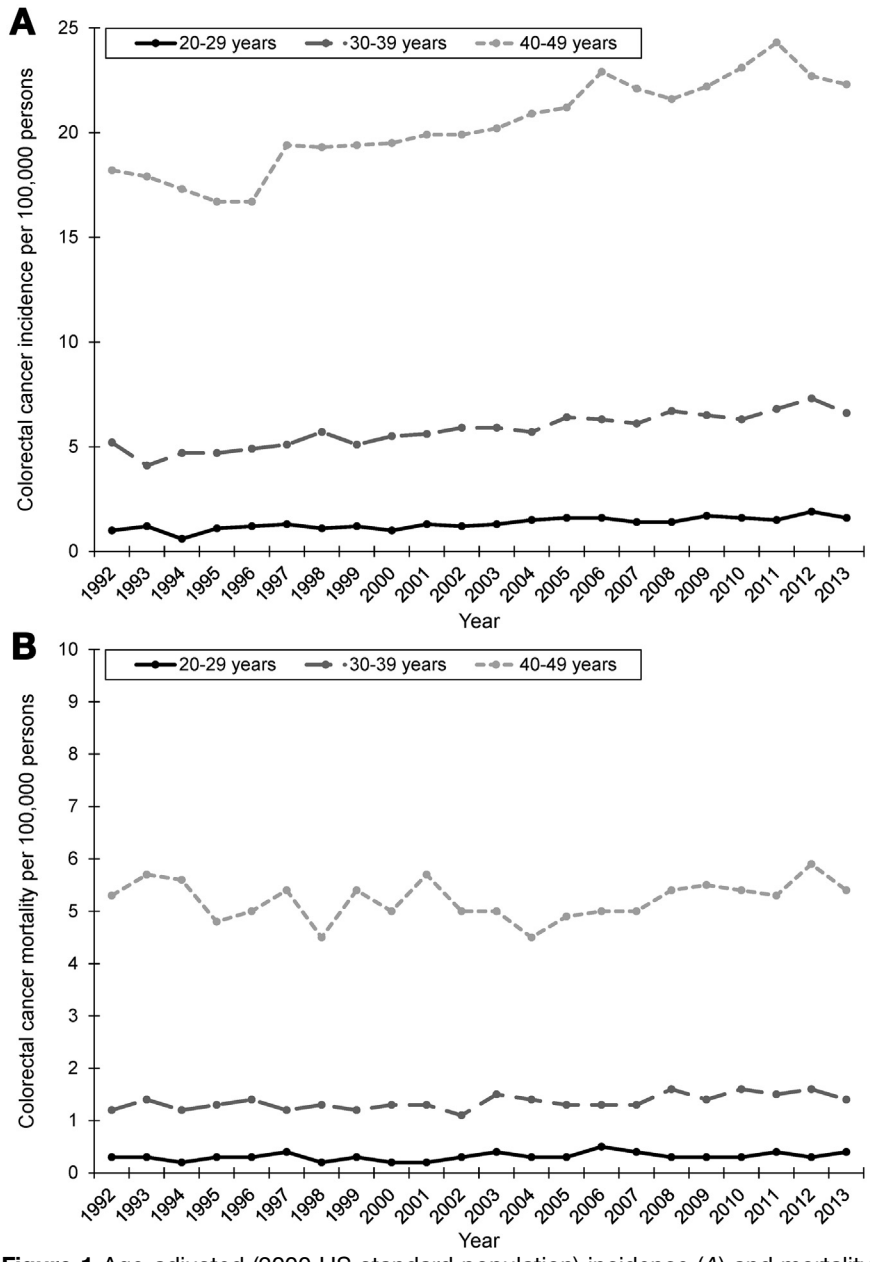

Figure 1. Age-adjusted (2000 US standard population) incidence (*A*) and mortality (*B*) of young-onset colorectal cancer by 10-year age group, Surveillance, Epidemiology, and End Results (SEER) 13, 1992–2013. Colorectal cancer (CRC) incidence and mortality were derived from the National Cancer Institute's SEER program during 1992–2013. SEER 13 registries include Atlanta, Connecticut, Detroit, Hawaii, Iowa, New Mexico, San Francisco-Oakland, Seattle-Puget Sound, Utah, Los Angeles, San Jose-Monterey, Rural Georgia, and Alaska Native Tumor Registry. Age-adjusted incidence and mortality (by using the 2000 US standard population) were obtained by using SEER*Stat version 8.3.2 as rates per 100,000 persons.

earlier detection of small tumors that increase incidence and survival without changing mortality.

Trends in young-onset CRC and diffusion of colonoscopy as a screening test raise the question of whether increasing incidence rates are an artifact of earlier diagnoses or increasing disease burden. To clarify the extent to which colonoscopy is performed in younger populations, we examined patterns of colonoscopy use in a commercially insured population of adults younger than age 50 and variation in use by age, sex, and geographic region.

Patterns of Colonoscopy Use

Using MarketScan Commercial Claims and Encounters data (Truven Health Analytics, Ann Arbor, MI), we examined patterns of colonoscopy use in younger adults (age <50 years) from 2001 to 2014. MarketScan is a large, employer-based claims database that includes 77 contributing employers and 12 contributing health plans, with 126 unique carriers and 8 Medicaid states. We summed the total number of months individuals aged 18–49 years were enrolled in their insurance plan in each calendar year as standardized denominators of "enrollee-time." We then described time trends in colonoscopy by calculating a rate of colonoscopy per 1000 enrollee-years in each calendar year, assuming constant rates within each calendar year. We also examined colonoscopy rates by sex (male vs female), age group (20-29, 30-39, and 40-49 years), and geographic region (northeast, north central, west, south).

A total of 3,216,798 colonoscopies were performed in 181,665,189 enrollee-years from 2001 to 2014. Overall colonoscopy rate increased from 15.2 per 1000 in 2001 to 19.7 per 1000 in 2009 and subsequently decreased to 16.0 per 1000 in 2014 (Figure 2). Detailed colonoscopy rates by age group, sex, and geographic region are available in Supplementary Table 1.

Colonoscopy rates were highest in the 40- to 49-year age group and lowest in the 20- to 29-year age group in all calendar years (Figure 2). Within each age group, rates generally increased from 2001 to 2009, with slight decreases through 2014 (Figure 2). For example, among 40- to 49-year-olds, the colonoscopy rate increased from 25.0 per 1000 in 2001 to 32.1 per 1000 in 2009 and decreased to 26.9 per 1000 in 2014. Women more frequently received colonoscopy in all years compared with men (Supplementary Figure 1). At its peak in 2009, the colonoscopy rate among women was 21.6 per 1000 and 17.6 per 1000 among men, with smaller decreases among women after 2010 than men. Colonoscopy rates were similar in the north central and southern regions but remained consistently higher in the northeast and lower in the west (Supplementary Figure 2).

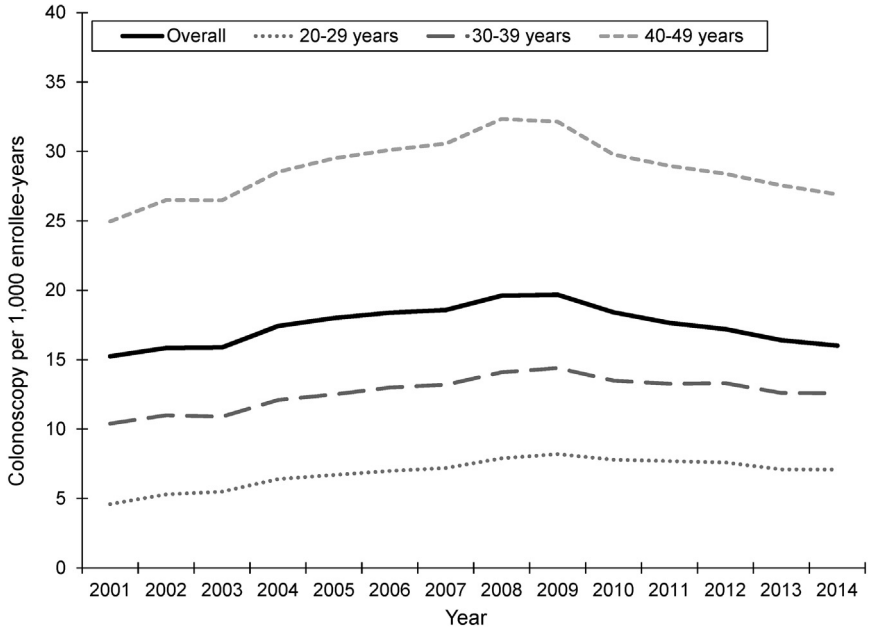

Figure 2. Colonoscopies performed per 1000 enrollee-years, overall and by 10-year age group, MarketScan Commercial Claims and Encounters Data, 2001–2014.

Colonoscopy Rates in Younger Adults Parallel Increases in CRC Incidence

Colonoscopy rates in younger adults increased by 30% from 2001 (15.2 per 1000) to 2009 (19.7 per 1000), which parallels increases in young-onset CRC adults during the same period (Figure 1*A*). Although it is unclear whether colonoscopy at younger ages represents overuse, symptomatic assessment, or high-risk screening, this increase occurred consistently across age group, sex, and geographic region. Many ambulatory surgery centers opened in the late 1990s and early 2000s after colonoscopy was endorsed as a preferred screening strategy,[12] and Medicare expanded reimbursement to include screening colonoscopy for average-risk persons,[13] increasing endoscopy capacity and efficiency.[14] This diffusion of colonoscopy into clinical practice may have had "spillover" effects, lowering thresholds for performing colonoscopy in younger patients.

Colonoscopies were most frequently performed in this commercially insured population among the oldest age group (40–49 years), where absolute increases in CRC incidence were also greatest (Figure 1*A*). Roughly 1 in every 30 adults in this age group underwent colonoscopy, suggesting colonoscopy close to age 50, when guidelines recommend average-risk screening, has become increasingly common.[15] Providers may be more apt to recommend colonoscopy in clinically nuanced situations, anticipating need for CRC screening in coming years. Or they may offer patients colonoscopy as part of preventive care, based on the small body of evidence suggesting similar prevalence