Decreasing Incidence of Colorectal Cancer in young adults in Italy

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Abstract

BACKGROUND Recent evidence has shown that although the incidence rate (IR) of colorectal cancer (CRC) is decreasing among older adults in several high-income countries, rates have increased in adults younger than 50 years.

AIM To determine recent incidence trends of CRC in Italy up to 2014 by sex, age, and area.

DESIGN, SETTING, AND PARTICIPANTS This study estimated the incidence of CRC using data from 48 Cancer Registry (2003-2014), including 60% of Italian population.

MAIN OUTCOMES Annualized percentage changes and incidence rate ratios of CRC.

RESULTS From 2003 to 2014, the incidence of CRC decreased both for men (Annual Percent Change -1.6, 95%CI -2.1 to -1.0) and for women (APC -1.2, 95%CI -1.8 to -0.6). Notably, men-female ratio is 1 below age 50 years while it is approximately 1.5 over 50 years of age.

A significant decrease of incidence emerged in Northern Italy (from 11.1 per 100,000 in 2003 to 8.5 in 2014, APC -2.4), while stable rates were observed in Southern Italy (from 8.6 in 2003 to 8.8 in 2014; APC 0.05).

CONCLUSIONS Leveling of CRC incidence in young adults among Italian areas strongly supports the need to reinforce research on specific risk factors and lifestyles possibly affecting these younger cohorts.

Introduction

Colorectal cancer is the second most frequent cancer type in Italy, with an estimated 50.000 cases per year at all ages in 2018, 14% of all cancer cases [AIOM, AIRTUM]. In people below age 50 years, it represents 7% of all cases in men and 4% in women. [mono Trend]

Increasing trends in the incidence rates of colorectal cancer (CRC) in the young adults (i.e., people aged 20-49 years) have been recently reported in many Western Countries [Møller, Lui 2019, Brenner 2017, Araghi 2019, Vuik 2019, Bhandari 2017, Troeung 2017].

Instead, Italy was among the few Countries where such trend was not confirmed [Vuik 2019] or where it was less marked [Lui 2019], while a slight decrease of incidence in men and women emerged [Zorzi 2019].

The majority of CRC cases in young adults appear to arise sporadically and risk factors in this population seem similar to those identified in older adults [Potter 2019, Rosato 2013], i.e., worsening diet, obesity, and lack of exercise.

In addition, in Italy a cut-off for starting of colorectal screening program was adopted, as in most countries, and people below age 50 years cannot benefit from screening programs [Zorzi 2006].

The aim of the present study is to investigate more recent trends of CRC incidence in young Italian adults until 2014. Herein we present an update of CRC incident cases collected by the Italian Association of Cancer Registries (AIRTUM), by sex, age group, area, and subsite.

Methods

The dataset and the methods used in this paper have been described in detail in a previous paper [Buzzoni 2019, Zorzi 2019]. In brief, we used the AIRTUM dataset of CRC incident cases, as recorded by all Italian cancer registries (CRs) according to a common protocol [Ferretti 2010]. Data were available from 48 CRs located in 17 out of the 20 Italian regions. The study period went from 2003 to 2014. The age range considered for analysis was 20 to 49 years. CRC diagnosed at older ages in the same period were also presented, for the sake of comparison.

As incidence data were not available for the whole study period for all CRs, the data matrix was completed by estimating the numbers of incident cases for calendar years with missing information [Buzzoni 2019, Zorzi 2019].

Table 1 describes the number of cases used in the analysis and the main features of population covered by cancer registration, according to region and macro-area.

Please insert Table 1 here

Overall, in 2012 the study Registries covered a resident population of almost 36 million subjects (35,799,991 as of December 31, 2012), corresponding to 60% of the whole Italian population (Table 1). Coverage of cancer registration was high in the North (71%) and South/Islands (65%), and lowest in the Centre (25%) of Italy.

Statistics

Incidence rates were calculated overall and stratified by gender, age class (20-29, 30-39, and 40-49 years), anatomic site (colon: ICD-10 code C18, and rectum: ICD-10 codes C19-C20), and geographic area (North, Centre, and South and Islands). Age adjusted rates were calculated using the European 2013 standard population.

Time trends were assessed by log-linear models and expressed as annual percent change in rates (APC) with 95% confidence intervals (95%CI); significant changes in time trends were investigated through the permutation test carried out using the Joinpoint Regression Program 4.6 version [Joinpoint].

Results

Between 2003 and 2014, a total of 17,204 CRC incident cases in 20-49 year olds contributed to the present study. Approximately two thirds of CRC cases were diagnosed in the colon (standardised incidence rate 6.0 x 100,000) and one third in the rectum (3.4 x 100,000) (Figure 1, panel a). In the overall period 2003-2014, incidence rates were similar in men (9.3 x 100,000) and women (9.4 x 100,000) (Figure 1, panel b).

Please insert Figure 1 here

Over the study period, CRC incidence rates decreased both for men (APC -1.6, 95%CI -2.1 to -1.0) and for women (APC -1.2, 95%CI -1.8 to -0.6). For both sexes combined the APC was -1.5 (95%CI -1.9 to -1.0).

The APC was -1.4 (95%CI -1.9 to -0.9) for colon cancer and -1.5 (95%CI -2.2 to -0.7) for rectum cancer. Incidence rates by site were similar in men and women (data not shown).

Please insert Figure 2 here

Figure 2 shows the trends in incidence rates over the study period by age, including the 50- to 69-year and the 70+ year old classes. The three young adult classes (20-29, 30-39 and 40-49 years) showed a similar decrease in CRC incidence rates, with annual variations of -2.6% (95%CI -6.5 to 1.4) in people aged 20 to 29 years, -1.3% (95%CI -2.3 to -0.2) in the 30 to 39 year olds and -1.4% (95%CI -1.9 to -0.9) in people aged 40 to 49 years.

Incidence rates in the 50- to 69-year age range showed a 3-phase pattern. The first period was characterized by a 1.6% annual increase until 2007; the second phase showed a 5.4% annual decrease until 2010, while the rates stabilized during 2010–2014.

In the older age class (70+ years), CRC incidence rates decreased by 1.2% per year over the whole study period.

Please insert Figure 3 here

At the beginning of the study period CRC incidence rates at ages 20-49 were more than 20% higher in the North (11.1 x 100,000), than in the South and Islands (8.6 x 100,000), with intermediate rates in the Centre (10 x 100,000) (Figure 3). During 2003-2014, incidence rates significantly decreased in the North (APC -2.4, 95%CI -3.0 to -1.7) and in the Centre (APC -1.1, 95%CI -2.0 to -0.1) while they were stable in South and Islands (APC 0.05, 95%CI -0.8 to 0.9). As a consequence, by the end of the study period, the differences in incidence rates among macro-areas had disappeared (North: 8.5 x 100,000; Centre: 8.9 x 100,000; South and Islands: 8.8 x 100,000).

Discussion

The present results show evidence of a slight decrease(~ -1% per year) in CRC incidence rates in the young Italian adults from 2003 and 2014, consistent in in men and women or in colon and rectum. Notably, a slightly diverging trend emerged in the North (-2.4%) and Centre (-1.1%) in comparison with Southern Italy (+0.0)%.

Our results confirm that the epidemiology of colorectal cancer in the young adults in Italy is somehow different from that reported for most Western Countries [Bhandari, Brenner 2017, Troeung, Moller, Lui]. For instance, the Annual Percent Change from 1988 to 2007 was 1.98 in the US, 3.33 in the United Kingdom, 2.60 in Canada and 0.87 in the Netherlands [Lui]. In fact, two recent papers on CRC incidence rates in different Countries reported increasing [Lui] and decreasing [Vuik] trends among young adults in Italy.

However, they analysed different periods (1988-2007 and 1996-2009, respectively) and covered a much lower proportion (15%) of the national population.

The underlying causes of the rise in CRC incidence observed in many Countries have not been elucidated yet. Several lifestyle behaviours have been associated with the risk of colorectal cancer, including weight gain, overweight and obesity, physical activity, tobacco smoking and alcohol consumption [Wei, Karahalios, Secretan, Turati 2017].

Compared with other European Countries, the Italian population ranks among those at a lower prevalence of obesity, and has been estimated to have one of the lowest increases in the projections up to 2025 (NCD Risk Factor Collaboration).

Of note, we found diverging figures between Italian macro-areas, similar to that observed for all ages [Zorzi 2019]. The stable incidence rates in the South and Islands, coupled with a decreasing trend in the North, deeply modified the initial geographic pattern, characterized by highest rates in the latter area. Such figures could be partly attributable to changes in lifestyle and dietary factors that begun in the previous decades. In particular, in the typical Mediterranean areas of Italy (i.e., southern regions) the reference Italian–Mediterranean diet has been progressively abandoned over the last decades [Alberti-Fidanza] and an increased consumption of meat and refined sugars has been reported [Cialfa]. A recent Italian study demonstrated a poor adherence in Italy to the Mediterranean diet and to the WCRF/AICR recommendations to prevent CRC [Turati 2017]. Authors showed also that the incidence of CRC would be reduced by 18% (95% CI: 9-28%) if all subjects shifted to the highest category of adherence, with a relevant effect also at younger ages.

Southern regions showed a higher proportion of physically inactive population too (48% vs. 23% in the North and 32% in the Centre) [PASSI attività]. Statistics about overweight in children and adolescents confirm a higher prevalence in southern Italian regions in comparison with northern and central Italy [Gargiulo], with possible further negative effects on future trends of colorectal cancer.

An increased uptake of endoscopic examinations for early diagnosis or prevention could represent an alternative explanation of the observed trends. However, it is unlikely that such effect is significantly more widespread in southern regions and that it is relevant overall, Italian CRC screening programmes targeting subjects aged 50-69 years.

Similarly, it is unlikely that our results could be associated with a different completeness in cancer registration over time [Buzzoni 2019].

The major limitation of this study is that the analysed period is relatively short (2003-2014). Indeed, as the population coverage of Cancer Registries in Italy has been much increasing during the last 15 years, we limited our analysis to the most recent years, when coverage with cancer registration was

sufficiently widespread over all Italian macro-areas. The number of available cases is also too small to provide reliable estimation of trends in specific strata of age, area and site. The absolute number of covered population and the proportion of registration coverage make unlikely a selection bias [Buzzoni 2019].

In conclusion, strategies for adopting healthy lifestyles, contrasting overweight and obesity in children and adolescents, and favouring physical activity should be reinforced in Italy, particularly in the Southern regions. These strategies may also have an impact on the prevention of several other cancer types, in young and older adults, and of cardiovascular diseases [WCRF].

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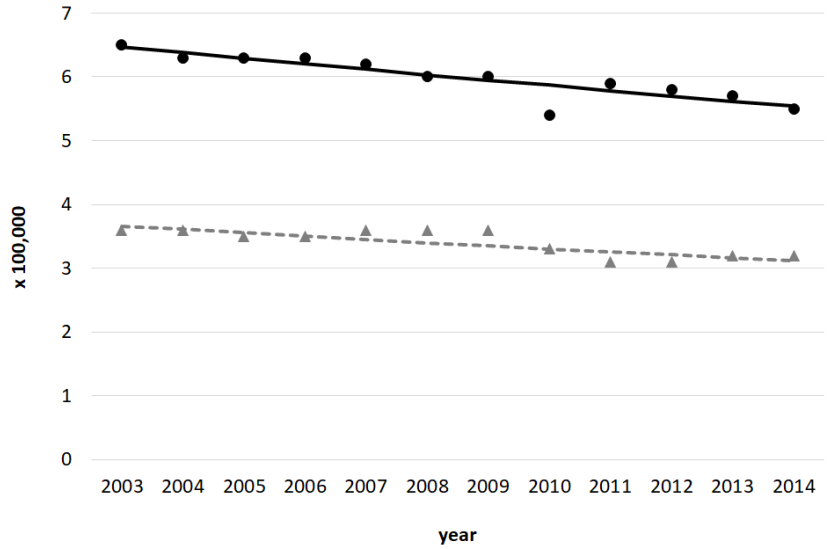
Table 1. Total number of analysed incident cases and main characteristics of the study population, by region / macro-area

Macro-area / Region	Resident population x 1,000 (as of December 31, 2012) (All ages)	Coverage with cancer registration (%)	Analyzed incident cases (n) (20-49 years)	Average incidence rate 2003-2014 x 100,000 (20-49 years)	Average annual number of cases 2003-2014 (20-49 years)	Average annual number of cases 2003-2014 (all ages)
North	**15,862**	**71**	**9,846**	**10.3**	**1,122**	**24,633**
Piemonte	4,374	30	557	9.7	159	4,317
Val d'Aosta	128	100	38	6.0	3	99
Liguria	1,565	55	425	11.0	62	1,767
Lombardia	9,795	92	4,563	10.2	406	8,267
Trentino Alto Adige	1,035	100	404	8.0	34	734
Veneto	4,882	53	1,402	11.0	218	4,218
Friuli Venezia Giulia	1,222	100	624	10.7	50	1,235
Emilia-Romagna	4,377	80	1,833	10.9	190	3,996
Centre	**11,681**	**25**	**1,412**	**9.9**	**453**	**10,074**
Toscana	3,693	33	577	10.0	144	3,346
Umbria	886	100	436	10.5	36	894
Marche	1,545	0	0	-	60*	1,400
Lazio	5,557	15	399	9.3	213	4,434
South and Islands	**20,621**	**65**	**5,946**	**8.7**	**746**	**12,641**
Abruzzo	1,313	0	0	-	46*	805
Molise	313	0	0	-	11*	192
Campania	5,770	71	1,974	9.1	223	3,122
Puglia	4,051	54	910	8.3	139	2,564
Basilicata	576	100	225	7.7	18	426
Calabria	1,958	64	548	8.6	70	1,222
Sicilia	5,000	91	1,962	8.6	177	3,190
Sardegna	1,640	42	327	9.1	62	1,120
Italy	**59,680**	**60**	**17,204**	**9.6**	**2,321**	**47,348**

* the macro-area average incidence rate was used to estimate the number of expected cases for regions not covered by cancer registration

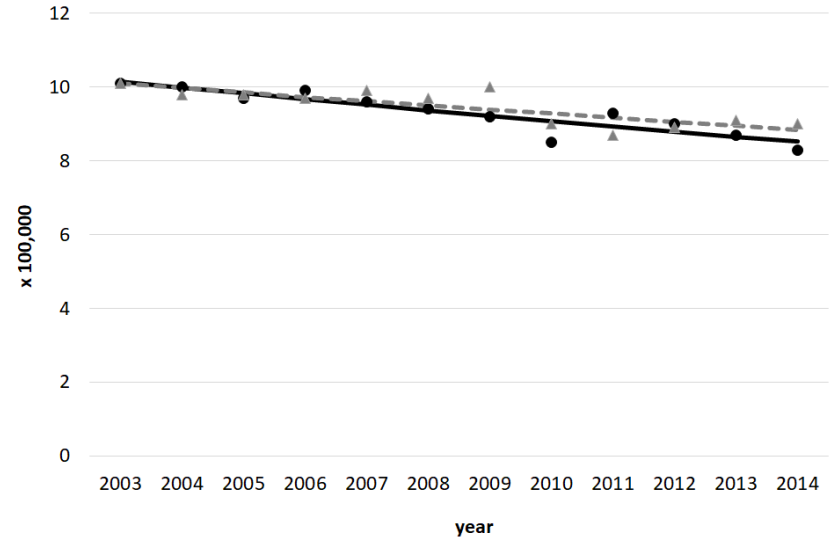
Figure 1. Standardised (Eu 2013) colorectal cancer incidence rates (IR) x 100,000 and Annual Percent Change (APC), with 95% Confidence Intervals (95% CI) in Italy from 2003 to 2014, by site (Panel A) and sex (Panel B). Age 20-49 years

Panel A



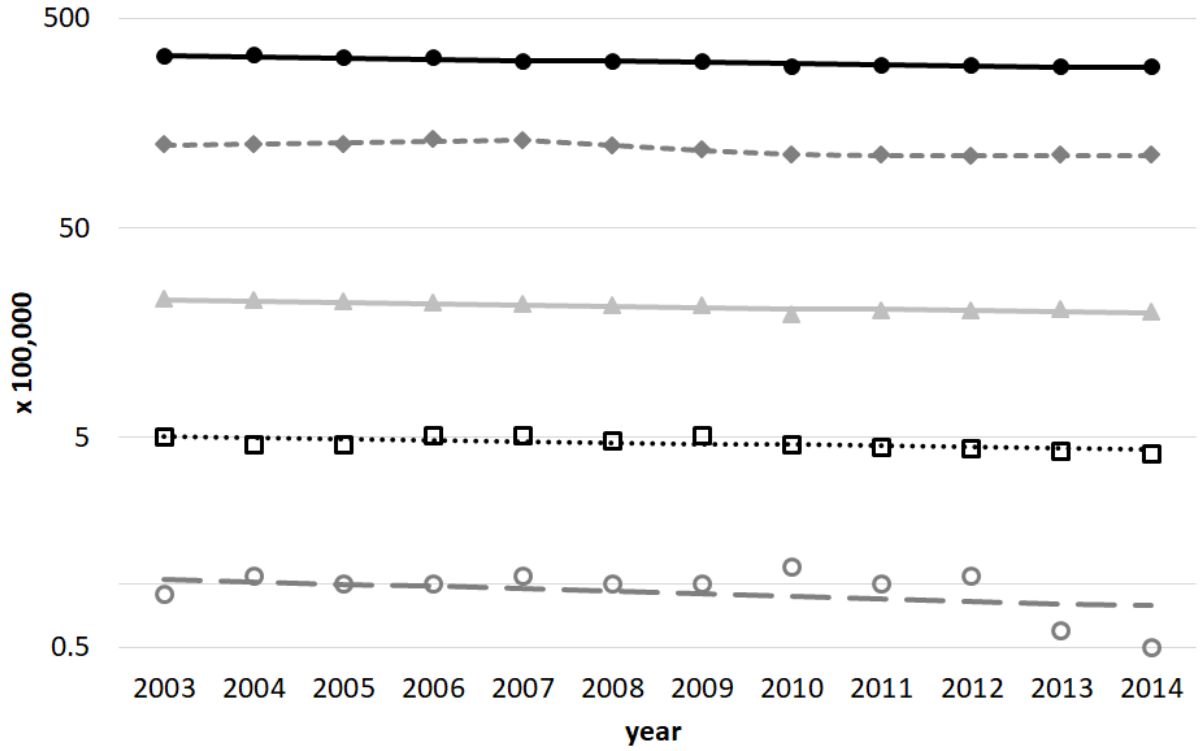
SITE	PERIOD	IR	APC	(95% CI)
colon	2003-2014	6.0	-1.4	(-1.9 ; -0.9)
rectum	2003-2014	3.4	-1.5	(-2.2 ; -0.7)

Panel B



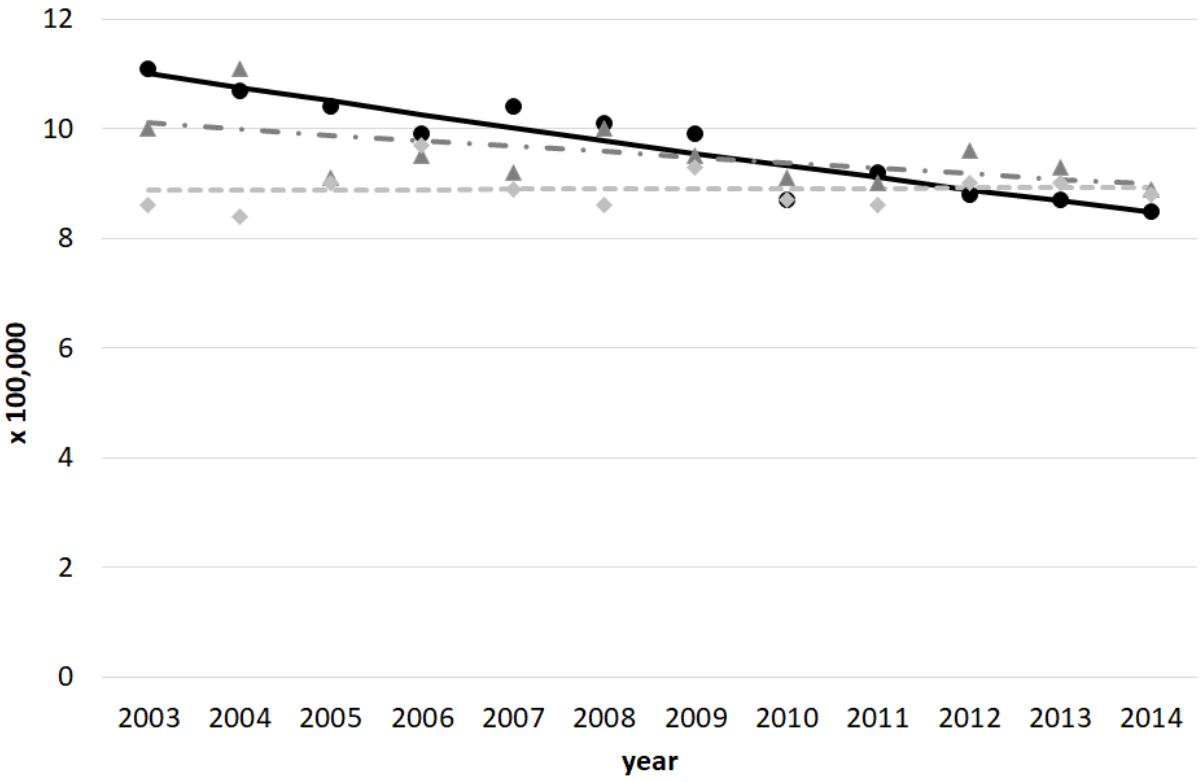
SEX	PERIOD	IR	APC	(95% CI)
male	2003-2014	9.3	-1.6	(-2.1 ; -1.0)
female	2003-2014	9.4	-1.2	(-1.8 ; -0.6)

Figure 2. Standardised (Eu 2013) colorectal cancer incidence rates (IR) x 100,000 and Annual Percent Change (APC), with 95% Confidence Intervals (95% CI) in Italy from 2003 to 2014, by age class. Men and women together. Y-axis on logarithmic scale



AGE	PERIOD	IR	APC	(95% CI)
20-29	2003-2014	1.0	-2.6	(-6.5 ; 1.4)
30-39	2003-2014	4.7	-1.3	(-2.3 ; -0.2)
40-49	2003-2014	21.0	-1.4	(-1.9 ; -0.9)
50-69	2003-2014	119.5	-1.0	(-2.5 ; 0.5)
	2003-2007		+1.6	(-0.5 ; 3.7)
	2007-2010		-5.4	(-11.7 ; 1.3)
	2010-2014		-0.2	(-2.3 ; 2.0)
70+	2003-2014		-1.2	(-1.5 ; -0.9)

Figure 3. Standardised (Eu 2013) colorectal cancer incidence rates (IR) x 100,000 and Annual Percent Change (APC), with 95% Confidence Intervals (95% CI) in Italy from 2003 to 2014, according to geographic area. Age 20-49 years, men and women together



AREA	PERIOD	IR	APC	(95% CI)
North	2003-2014	9.7	-2.4	(-3.0 ; -1.7)
Centre	2003-2014	9.5	-1.1	(-2.0 ; -0.1)
South and Islands	2003-2014	8.9	0.05	(-0.8 ; 0.9)