



## Review



## Risk factors behind the increase of early-onset cancer in Italian adolescents and young adults: An investigation from the Italian AYA Working group

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## ABSTRACT

The incidence of early-onset cancers in adolescents and young adults (AYA) has been increasing worldwide since the 1990s. In Italy, a significant increased rate of 1.6 % per year has been reported for early-onset cancers among females between 2008 and 2016. This is mainly attributable to melanoma, thyroid, breast and endometrial cancer. The aim of our work was to describe temporal trends of the main established lifestyle risk factors (tobacco use, alcohol consumption, obesity, physical inactivity, dietary westernization and reproductive factors) over the last 20 years in the Italian AYA population. Available data on behavioural risk factors, individual and household daily life have been obtained and elaborated from PASSI, ISTAT and Eurostat reports. Lowering age of smoking initiation, an increase in alcohol drinkers among young females, and an obesity and overweight epidemic, particularly among children and adolescents as a result of physical inactivity and dietary habits, may be contributing factors behind this cancer epidemic, especially among females. In-depth investigations are needed to understand the exact role of each contributing factor, the effects of exposure to nicotine-containing products and environmental factors such as endocrine disruptors that could play a role in this phenomenon.

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## 1. Introduction

Several reports indicated that the incidence of cancers diagnosed in adolescents and young adults (AYA) has been increasing worldwide since the 1990s [1–3], although caution is needed in interpreting these results due to many potential biases in the analyses. Cancer diagnosis in adolescent and young adults (AYA, i.e. people aged 15–39 years) has substantial personal and socio-economic implications. In AYA, cancers are associated with considerable mortality and morbidity in that survivors have a high risk of additional long-term health problems such as cardiovascular disease, infertility and secondary cancers [4–8].

The reasons of this epidemic are difficult to investigate since cancer is a multifactorial disease resulting from the combined influence of genetic, lifestyle and environmental factors. A significant fraction of AYA patients carries pathogenic or likely pathogenic variants in cancer predisposition genes [9], but no evidence has emerged for increased population prevalence of pathogenic variants in any cancer gene [8]. The increase of cancer incidence may be associated to changes in lifestyle and environmental factors (the so-called exposome) during childhood and adolescence. These have been reported worldwide since the end of the twentieth century [8,10–12].

In Italy, the Italian Association of Cancer Registries (AIRTUM) collects data with a cut-off of 50 years. Therefore, data on cancer trends in AYA are neither published nor available. Nevertheless, the last data on temporal trends reported a significant increase in early-onset cancer rates (EOC, i.e. diagnosed in individuals younger than 50 years). In more detail, rates were reported as increasing by 1.6 % per year in females and by 0.7 % per year in males between 2008 and 2016. The most dramatic increase was observed for melanoma in both sexes (+7.3 % per year among males and +7.6 % per year among females), followed by prostate cancer (+3.4 % per year) and thyroid (+3.5 % per year), endometrial (+2.3 % per year), and breast cancer (+1.6 % per year) in females [13]. The increased incidence of melanoma, also reported for older people, could be explained by exposure to UV radiations [14]. Moreover, the widespread use of “opportunistic screening” and an increasing use of ultrasound for thyroid dysfunctions could explain the rising incidence of clinically silent prostate and thyroid cancers in young individuals [8,15,16]. Established risk factors for premenopausal breast cancer include tobacco use, alcohol consumption, central obesity, physical inactivity, dietary westernization (diets high in animal fats, low in fruit and vegetables, and low in dairy products) and reproductive factors (younger age at menarche, nulliparity, older age at first childbirth, and never breastfeeding) [17–25]. Endometrial cancer shares some risk factors with breast cancer such as smoking, central obesity and nulliparity [26,27].

Our work aimed to describe changes in the aforementioned risk factors in Italy over the last 20 years, in order to offer a possible explanation for the registered rise of EOC in AYA, especially breast and endometrial cancer.

## 2. Data sources

PASSI is a public health surveillance system from the Italian National Institute of Health based on the Behavioural Risk Factor Surveillance model. It gathers information on health and behavioural risk factors for chronic diseases in the Italian population aged 18–69 through periodic sample surveys. From 2008 to 2022, a total of 497,000 surveys have been conducted [28]. The sample survey “Aspects of daily life” is part of an integrated system of social surveys - The Multipurpose Surveys on Households. It has collected fundamental information on individual and household daily life since 1993. Relative results are freely available on the platform IstatData [29,30]. Finally, Eurostat is the European Union’s statistical office. It provides statistics and data on Europe to enable comparisons between countries and regions [31]. Data were extracted from these sources and reported in tables and charts to describe temporal trends over the last 20 years for tobacco use, alcohol consumption,

obesity, physical inactivity, dietary habits and reproductive aspects, specifically in the Italian population aged less than 49 years.

## 3. Results

### 3.1. Tobacco use

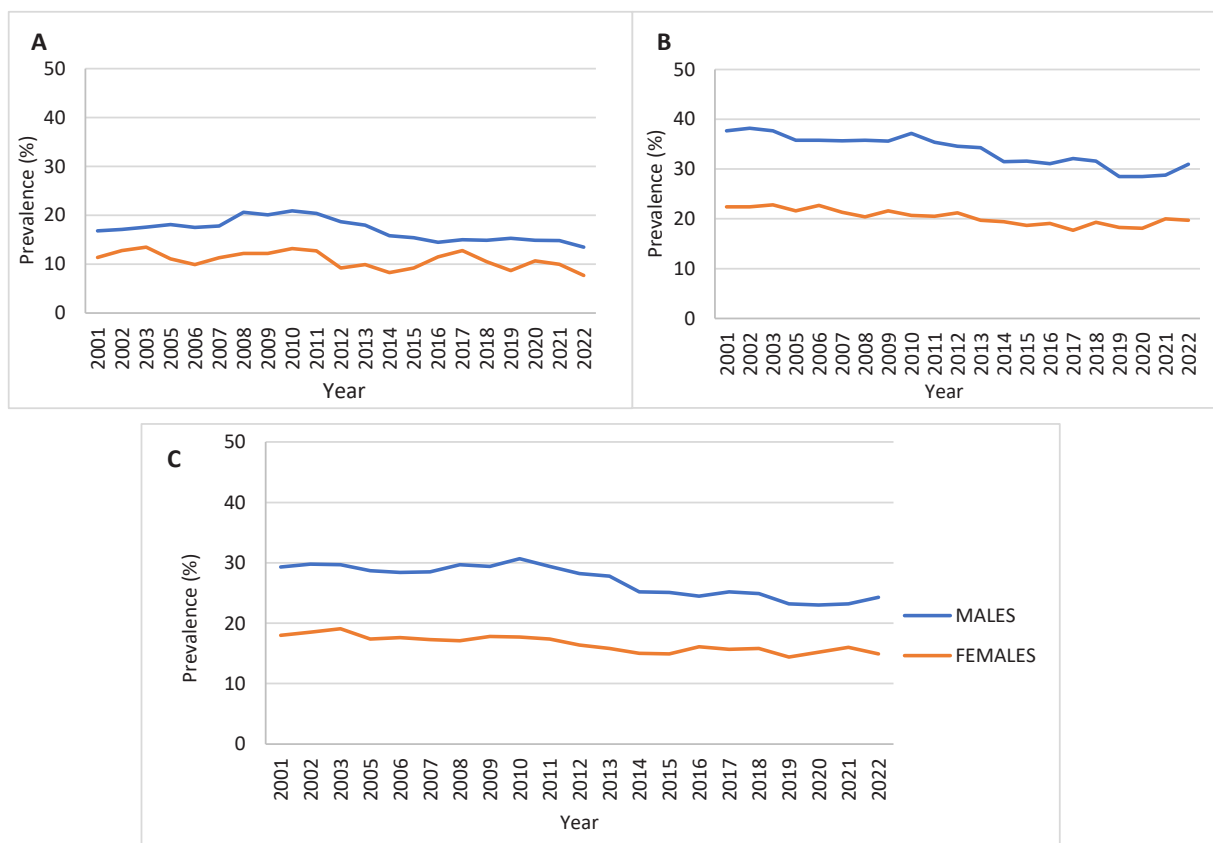
Tobacco and tobacco smoke contain more than 80 compounds considered as carcinogens [32]. Tobacco smoking significantly increases risk of many types of cancer including lung, larynx, oesophagus, oral cavity and pharynx, bladder, liver, uterine cervix, kidney, stomach, colorectum, pancreas, and myeloid leukaemia [33]. In Europe, smoking initiation rates during early adolescence (11–15 years) showed a 50 %-increase after 1990, especially in Western Europe. [34]. According to the 2021 Eurobarometer report on Europeans’ attitudes towards tobacco and electronic cigarettes, 15 % of European smokers start smoking before 15 years of age and a further 39 % begins smoking between 15 and 17 years [35]. Beyond its carcinogenetic effect, early tobacco exposure is particularly harmful because adolescents are more susceptible to tobacco effects during growth, with a consequent increased risk of developing psychiatric disorders and cognitive impairment in later life [36]. At the same time, exposure in early puberty may have an impact on future generations of offspring [37]. Moreover, young adolescents are particularly vulnerable to nicotine’s gateway effects [38].

In Italy, the prevalence of current smokers among people aged 14–44 years declined between 2001 and 2022. The reduction is more prominent in males (from 29.3 % to 24.3 %) than in females (from 18.0 % to 14.9 %) (Figure 1C), and it is especially marked among males aged 20–44 years (from 37.7 % to 31.0 %) (Figures 1A and 1B). Looking at regional variation, several regions from Southern Italy present the highest age-standardized prevalence of current tobacco use [39].

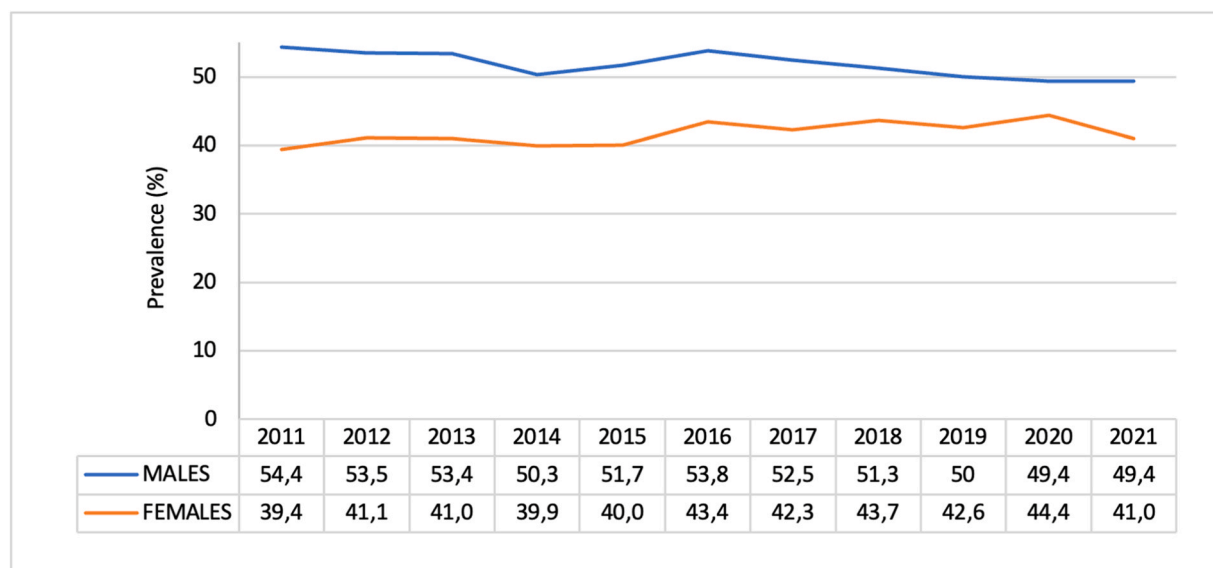
An emerging tendency is the combined use of several nicotine-containing products such as e-cigarettes (electronic nicotine-delivery systems) and heat-not-burn (HnB) tobacco products in addition to traditional cigarettes. In Italy, the use of both e-cigarettes and HnB tobacco products has doubled from 2014 to 2021 and affects 8 % of people aged 18–34 years [40]. In younger people, nearly 40 % of smokers aged 14–17 years make use of more than one product among e-cigarettes, HnB tobacco products and traditional cigarettes, while 30 % of the same group make exclusive use of e-cigarettes or HnB tobacco products [41,42].

### 3.2. Alcohol consumption

Drinking alcohol increases risk of many cancer types, including oesophagus, oral cavity and pharynx, larynx, liver, colorectum, and breast cancers [43,44]. There is no safe level of alcohol consumption: even small amounts of alcohol have a detrimental effect [45]. Consistent with what has been what reported for tobacco smoking, alcohol use during adolescence is associated with poorer cognitive functioning into adulthood [46] beyond carcinogenetic effects, especially in the development of breast cancer [47]. The National Observatory for Alcohol of the National Centre on Addictions and Doping is the official reference body of the Italian National Health Institute for research, prevention and training activities on alcohol and alcohol-related problems [48]. In Italy, 49.4 % of males and 41.0 % of females aged 11–25 years drank at least one alcoholic beverage in 2021. Between 2011 and 2021, the prevalence of alcohol drinkers in this age group decreased from 54.4 % to 49.4 % in males, while it slightly increased in females (from 39.4 % to 41.0 %) reaching a peak in 2020 (44.4 %) (Figure 2). In addition, 14.2 % of females aged 11–17 years and 65.3 % of females aged 18–49 years drank at least one alcoholic beverage in 2021 [49]. At a regional level, variability in alcohol consumption is very wide, with northern regions, particularly the North-East, at the top of the list of regions with the highest age-standardized prevalence of alcohol consumption [39].



**Fig. 1. Smoking** Annual current smoking prevalence trends in people aged (A) 14-19 years, (B) 20-44 years, and (C) 14-44 years, in Italy (2001–2022). Source: IstatData.



**Fig. 2. Alcohol consumption** Annual alcohol-drinking prevalence trends in people aged 11–25 years in Italy (2011 to 2021). Sources: National Observatory for Alcohol, ISTAT Multipurpose Surveys on Households.

3.3. Obesity

Worldwide obesity has almost tripled since 1975 [50]. According to the “Fourth Italian obesity barometer report 2022”, age-controlled overweight and obesity rates have increased in Italy by 10 % and 40 %, respectively, in the adult population since 2001. In detail, the prevalence of obese adults increased from 8.8 % in 2001 to 11.4 % in

2021. It is worth noting that the increase is more prominent among males [51]. A general trend towards obesity and overweight increase is evident in younger adults (18–34 years), while an opposite trend is reported for older adults (50–69 years) [52]. Overall, regional variability in overweight is wide, with the highest values for southern regions. In regions such as Molise, Campania or Puglia, half of the adult population is found to be overweight [39].

Focusing on younger adults (18–34 years), the analysis reveals that the increase in obesity and overweight in the last 20 years is more evident in people aged 18–24 years than in those aged 25–34. Between 2001 and 2022, obesity nearly trebled (from 1.3 % to 3.6 %) among individuals aged 18–24 years and almost doubled (from 3.5 % to 5.9 %) in those aged 25–34. In detail, a major increase was reported for obesity among females aged 18–24 years (from 0.6 % in 2001 to 2.8 % in 2022, after a 4.2 %-peak in 2021) (Figure 3).

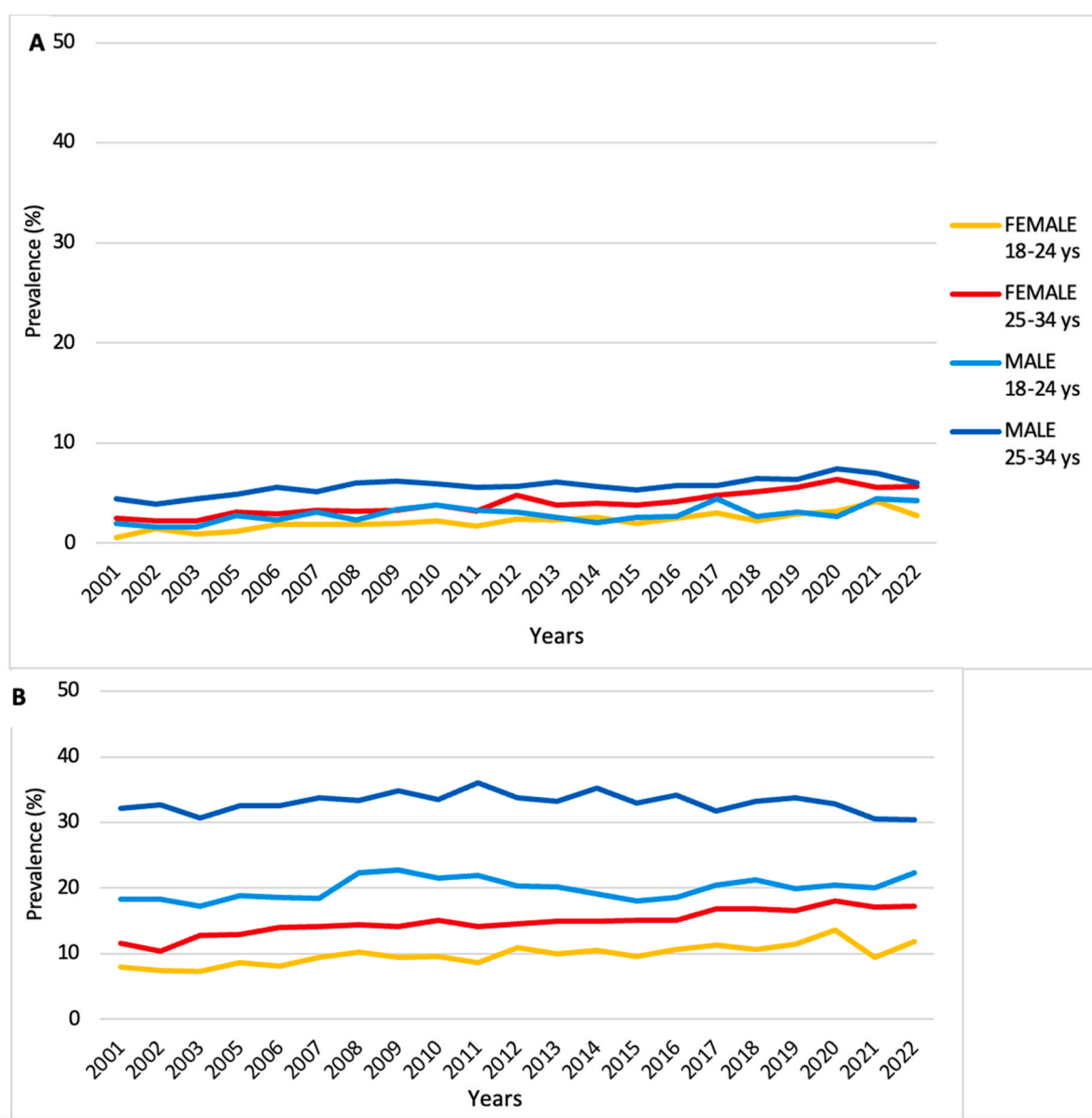
Overweight and obesity are an area of grave concern in relation to children and adolescents. In Italy, one in four minors aged 3–17 years is overweighted or obese. After a first reduction from 28.5 % in 2010–2011 to 25.5 % in 2016–2017, the prevalence of overweighted or obese minors has started to increase again in both sexes in the last few years, reaching 27 % in 2020–2021 [51] (Figure 4). Data from the “Health Behaviour in School-Aged Children 2022” survey also reports an increase in overweight and obese adolescents aged 11–17 years in the last five years: in 2022, 18.2 % of adolescents aged 11–17 was overweight (vs 16.6 % in 2018) and an additional 4.4 % was obese (vs 3.2 %

in 2018) [53].

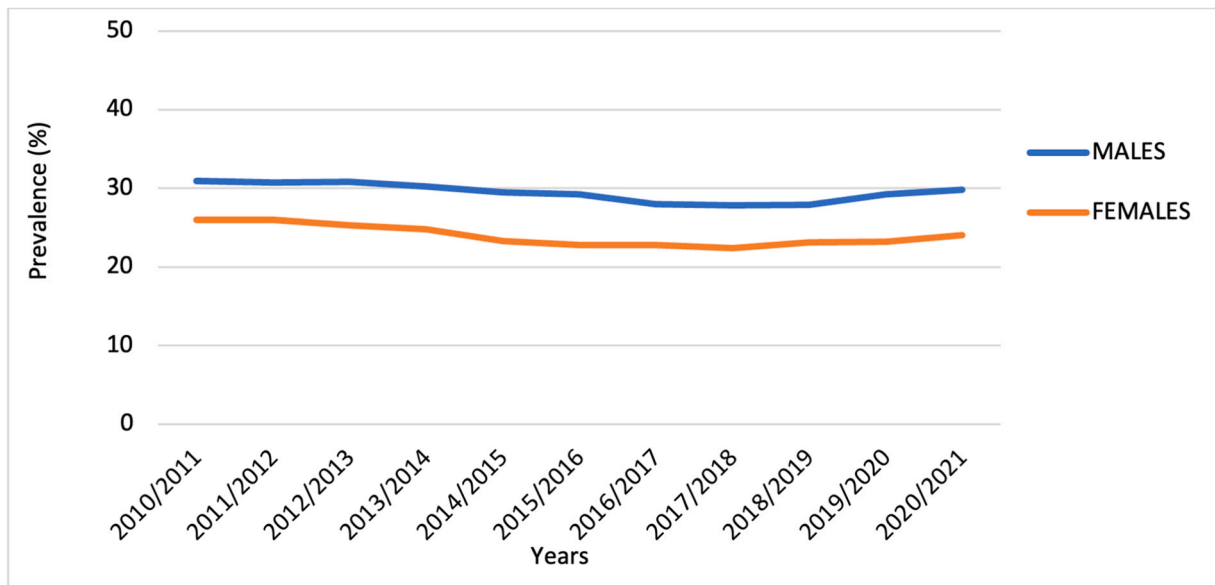
### 3.4. Physical inactivity

Physical activity is associated with a reduction in overall cancer risk as well as cardiovascular and metabolic diseases [54]. In Italy, the proportion of sedentary people (defined by the absence of physical activity during free time and by sedentary work) in the adult population aged 18–44 years significantly increased over the last four years (from 24.4 % in 2018 to 27.4 % in 2022), after a drop between 2015 and 2018. Sedentary lifestyle is more frequent among women than men (Figure 5) [28]. Across age groups, regional variability in physical activity is wide and shows a very clear North-South gradient to the detriment of southern regions, where the share of sedentary people is among the highest [39].

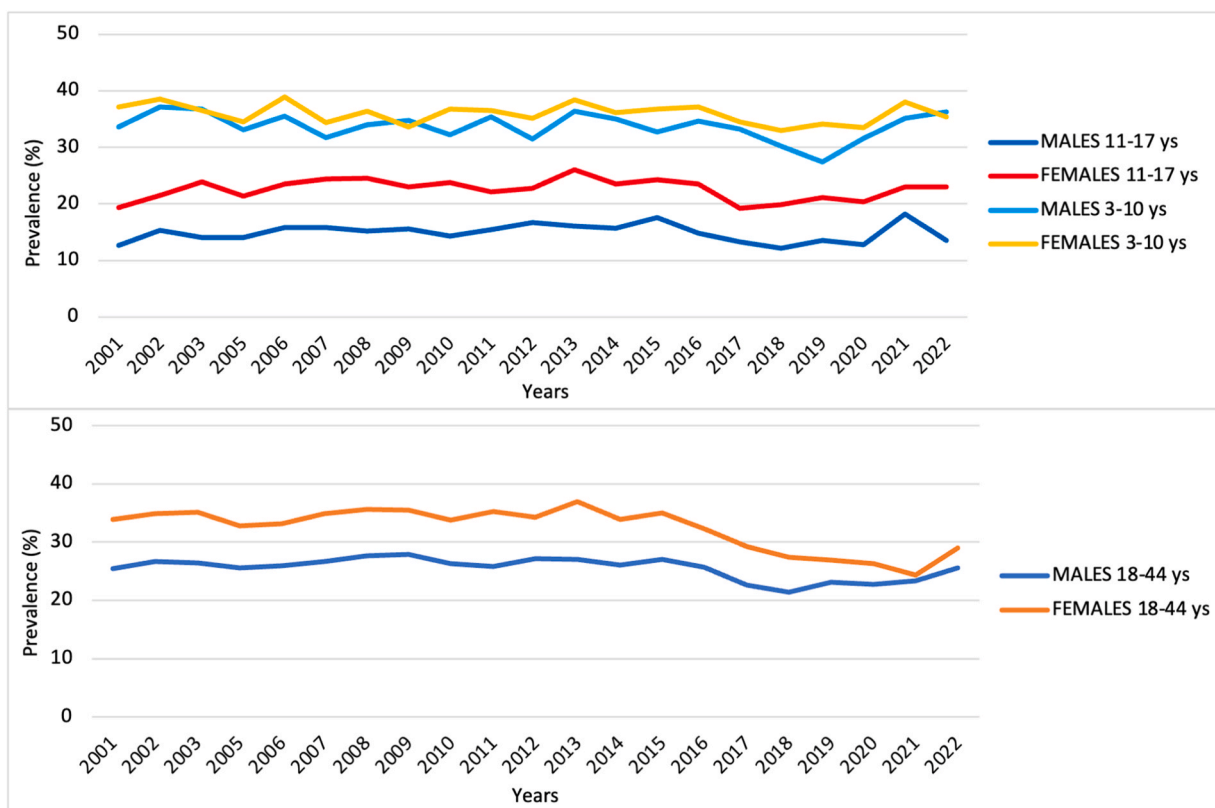
As is the case with obesity, physical inactivity among children and adolescents is an area of serious concern, with particular reference to data from the last few years. More specifically, the proportion of



**Fig. 3. Obesity and overweight in young adults** Annual prevalence trends of (A) obesity and (B) overweight among adults aged 18–24 years and 25–34 years in Italy (2001 to 2022) according to sex. Source: IstatData, Aspects of daily life.



**Fig. 4. Obesity and overweight among minors** Annual prevalence trends of overweight and obesity among minors aged 3–17 years in Italy by sex (2011–2021). Source: IstatData, Aspects of daily life.



**Fig. 5. Physical inactivity** Annual prevalence trends of sedentary people in Italy (2001–2022) by age group (3–10 years, 11–17 years, 18–44 years) and sex. Source: IstatData, Aspects of daily life.

individuals aged 3–17 years engaging in sports dramatically dropped from 51.3 % in 2019 to 36.2 % in 2021. This decline has only been partially compensated by an increase in unstructured physical activity (from 18.6 % to 26.9 %). Females are more sedentary than males during both childhood and adolescence. The proportion of sedentary individuals aged 3–10 years increased by 5 % (from 30.8 % in 2019 to 35.8 % in 2022) (Figure 5) [55], while that of adolescents engaging in

moderate-intense physical activity on at least 3 days a week (60 min a day, as recommended by the WHO [56]) diminished from 45.3 % in 2014 to 40.8 % in 2022. As such, it returned to the levels registered in 2010. Moreover, one third of females aged 17 years is sedentary compared to 12 % of their male counterparts [53].

### 3.5. Dietary westernization

The Mediterranean diet is a healthy dietary pattern based on a daily intake of cereals, vegetables, fruit, low-fat dairy products, olive oil, a weekly intake of fish and legumes, and limited meat consumption. This dietary pattern has been demonstrated to reduce risk of several types of cancers [57]. A progressive abandoning of the Mediterranean diet has been reported worldwide, but also in the populations of the Mediterranean region from the 1960s to the early twenty-first century [58]. Currently, only 13 % of the Italian population has a Mediterranean diet [59]. This is partly due to the westernization of eating habits, i.e. a tendency to live on a diet high in animal fats, low in fruit and vegetables, and low in milk and dairy products.

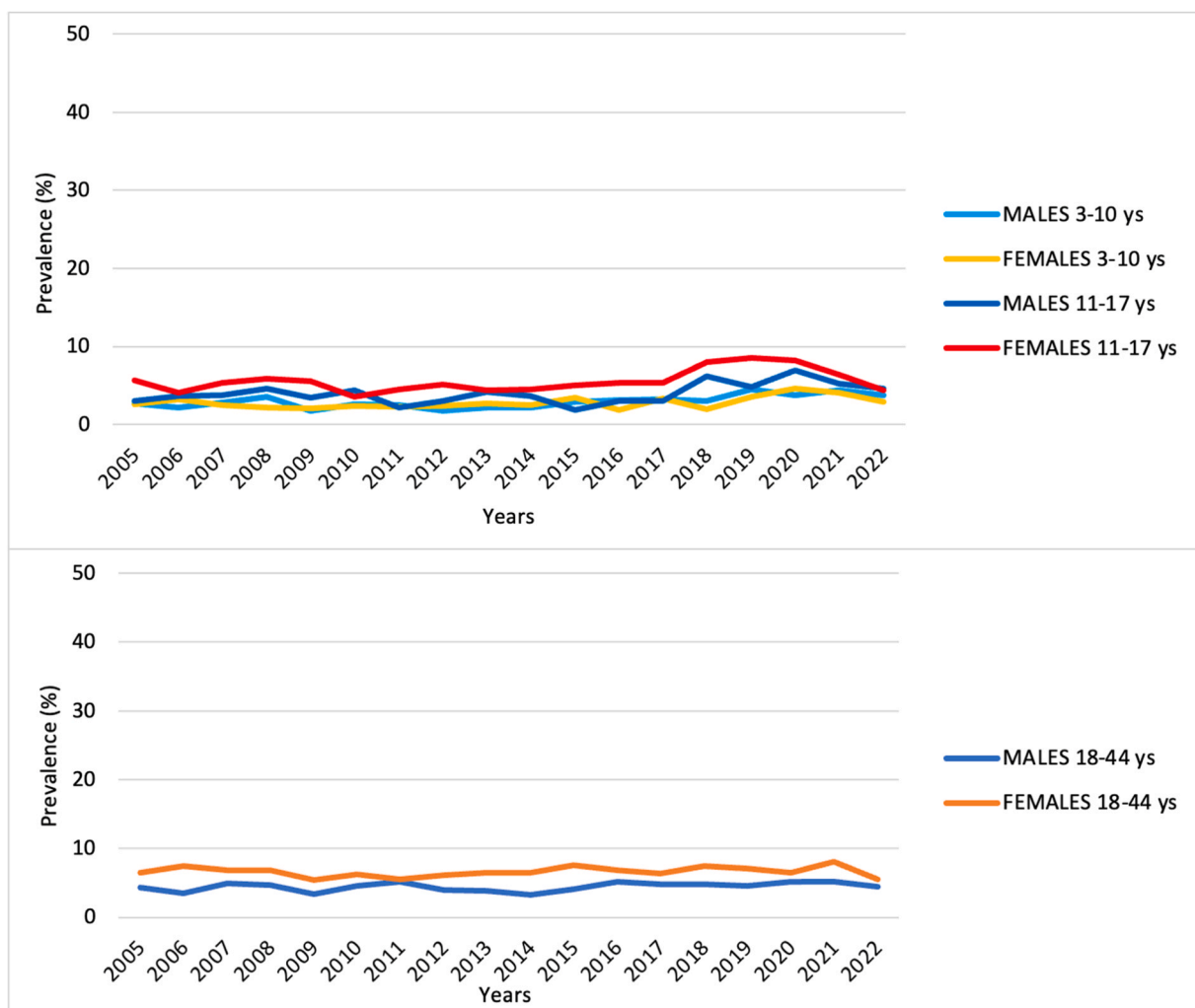
Daily consumption of at least five portions of fruit and vegetables is recommended by the WHO to lower risk of cardiovascular disease and some types of cancer [60]. In Italy, less than 9 % of females and less than 6 % of males until 44 years of age follow this recommendation [28]. In particular, regional variability in acting on WHO recommendations results in Italy being divided into two parts. Among the most virtuous regions (mostly northern regions and the two large islands of Sardinia and Sicily), the prevalence of “five a day” was shown to be still limited and not to exceed 13 %. On the other hand, this share remains below 5 % in most southern regions [39].

The percentage of children (3–10 years) and adolescent (11–17

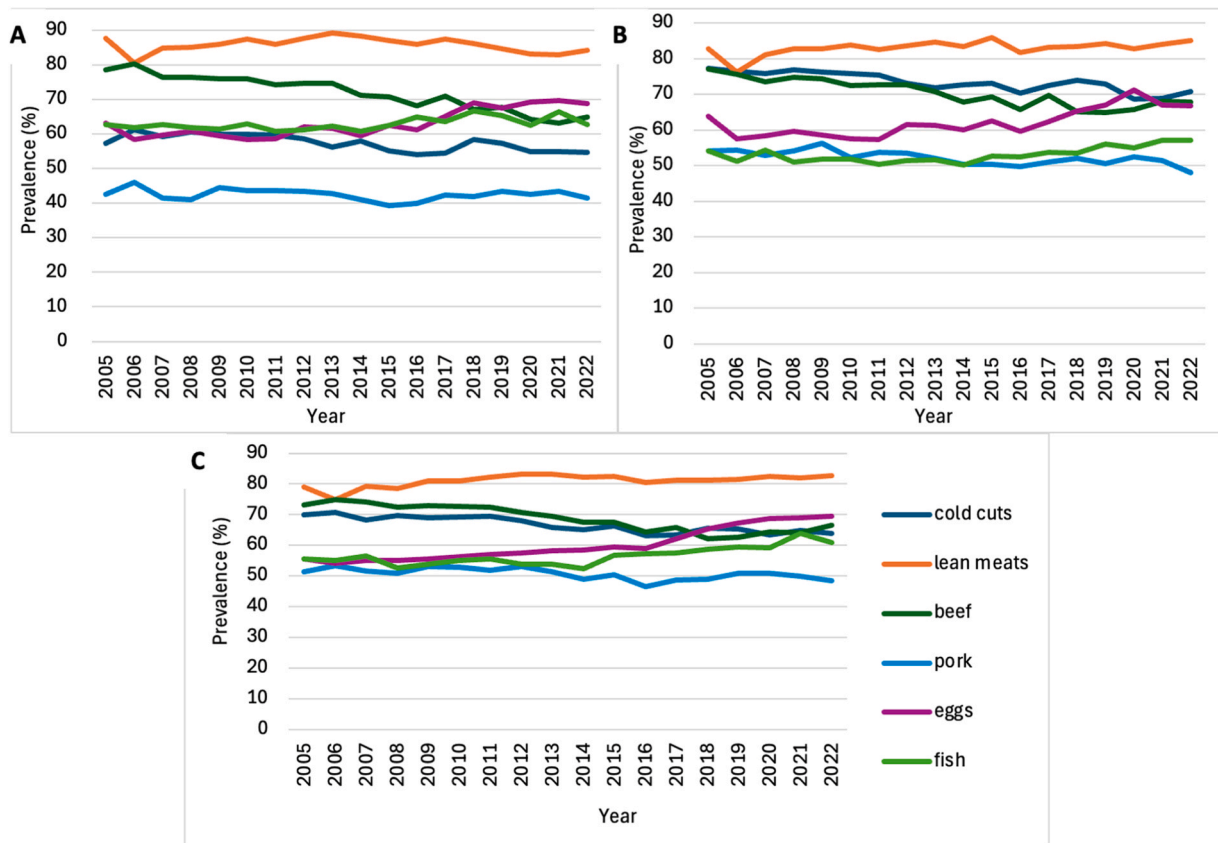
years) consuming at least five portions of fruit and vegetables per day in Italy is even lower. In 2022, only 3.3 % of children and 4.5 % of adolescents follow WHO recommendations, and this trend has grown over the last few years (Figure 6). As for the intake of protein sources (cold cuts, beef, pork, lean meats, fish and eggs), a trend has been reported since 2005 for decreasing consumption of cold cuts, beef and pork, and for increasing consumption of lean meats, fish and eggs in children and young adults (Figure 7). The percentage of individuals having milk or cheese at least once a day has decreased since 2005 in children and young adults. Drinking milk daily reportedly becomes less of a habit with increasing age (Figure 8).

### 3.6. Reproductive factors

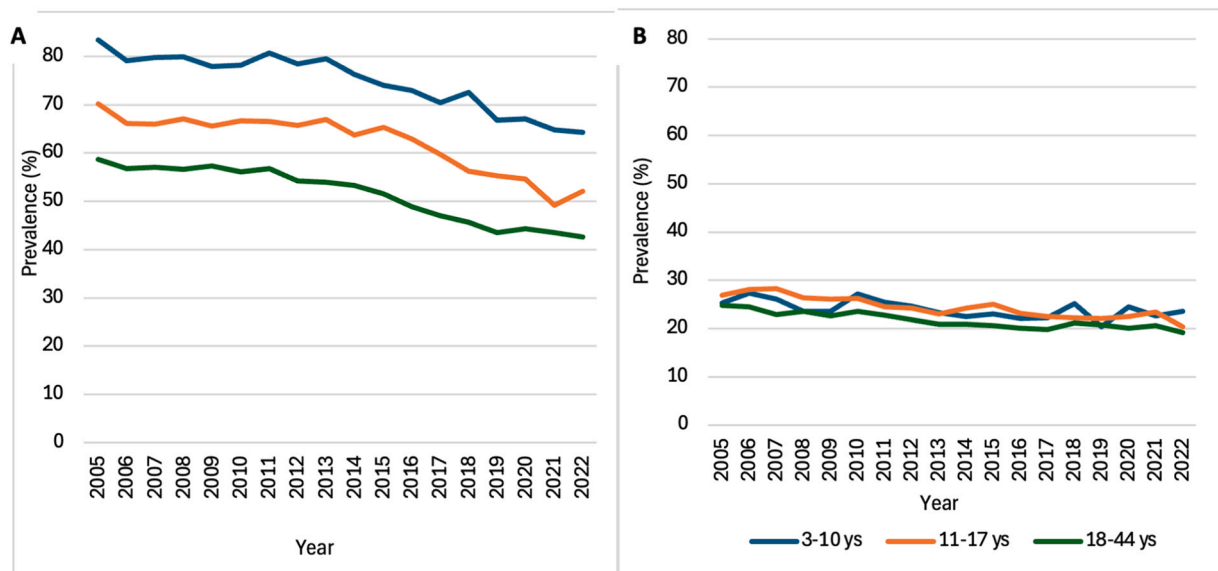
Younger age at menarche, nulliparity, older age at first childbirth, and never having breastfed are recognised risk factors for breast cancer. Moreover, nulliparity is also a risk factor for endometrial cancer [24–27, 61]. A decline in age at pubertal onset over the last century has been reported in different European populations, including Italy [62,63]. Since the COVID-19 outbreak, the incidence of central precocious puberty among girls has increased in Italy, as reported by a 4-year study [64]. A reduction of physical activity and increased overweight and obesity rates are possible determining factors. In Italy, the total fertility rate (i.e., the average number of children that a woman would give birth



**Fig. 6. Fruit and vegetables** Annual prevalence trends of individuals consuming at least five portions of fruit and vegetables per day in Italy (2005–2022) by age group (3–10 years, 11–17 years, 18–44 years) and sex. Source: IstatData, Aspects of daily life.



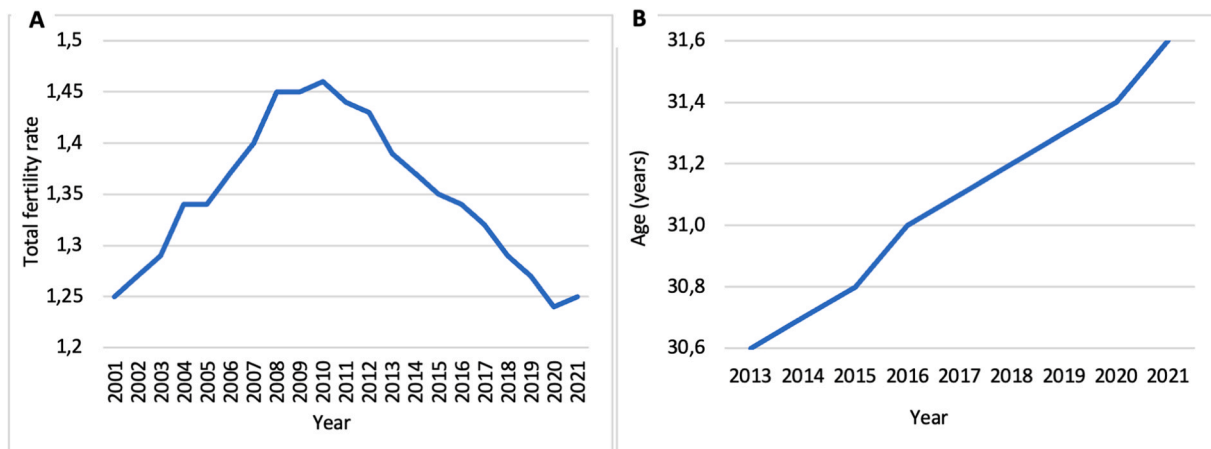
**Fig. 7. Protein sources** Annual prevalence trends of (A) children (3-10 years), (B) adolescents (11-17 years) and (C) young adults (18-44 years) consuming cold cuts, lean meats, beef, pork, eggs or fish at least a few times a week in Italy (2005-2022). Source: IstatData, Aspects of daily life.



**Fig. 8. Dairy products** Annual prevalence trends of children (3–10 years), adolescents (11–17 years) and young adults (18–44 years) consuming (A) milk or (B) cheese at least once daily in Italy (2005- 2022). Source: IstatData, Aspects of daily life.

to over her lifetime) declined in the last ten years, from 1.46 in 2010 to 1.25 in 2021 (Figure 9A). At the same time, mean age of women at birth of the first child increased by one year from 30.6 years in 2013 to 31.6 years in 2021 (Figure 9B). The last available data about breastfeeding in

Italy cover the years between 2000 and 2013. In this period, the proportion of breastfeeding women increased from 81.1 % to 85.5 %. Similarly, mean breastfeeding duration rose from 6.2 to 8.3 months [65].



**Fig. 9. Reproductive factors** (A) Annual trend of total fertility rate in Italy (2001–2021). (B) Annual mean age of women at birth of the first child in Italy (2013–2021).

Source: Eurostat.

### 3.7. Air pollution

While there is strong evidence supporting a causal link between air pollution, especially fine particulate matter (PM), and lung cancer, epidemiological evidence on air pollution and the risk of other types of cancer (such as breast cancer) is more limited [66]. A recent meta-analysis showed a clear (if loose) correlation between nitrogen dioxide (NO<sub>2</sub>) exposure, a common traffic-related air pollutant, and breast cancer risk [67]. Another meta-analysis suggested that fine PM (PM<sub>2.5</sub>) exposure may raise breast cancer mortality, but not morbidity [68].

Italy is one of the most seriously air-polluted areas in Europe, with the largest proportion of premature deaths attributable to PM<sub>2.5</sub> and NO<sub>2</sub> [69]. After a rapid growth in pollutant emissions in the 1960s and 1970s, due to the economic boom of that period, a decrease has been reported over the last 40 years thanks to the positive impact of regulations implemented to reduce air pollution [70,71]. However, according to Legambiente, Italy's biggest environmental organisation, the Italian downward trend is still too slow, with an average annual rate of NO<sub>2</sub> cutback of 3 % only [72]. As regards regional variability, it is noteworthy that the Po Valley (Northern Italy) is one of the most heavily polluted areas in Europe, particularly in terms of PM concentrations [73]. In 2022, PM<sub>10</sub> concentrations in the Po Valley were second only to those in the Balkan countries and some industrial sites in Spain [74]. A recent study reported that every year PM<sub>2.5</sub> was responsible for 72,083 deaths in Italy between 2016 and 2019 (11.7 % of national mortality for natural causes), with higher values (15.2 %) in the Northern Regions. In the Po Valley, in particular, PM<sub>2.5</sub> was responsible of 39,628 deaths every year, more than half the total cases in Italy [75].

## 4. Discussion

### 4.1. The Italian data

Cancer is a multifactorial disease resulting from the combined influence of genetic, lifestyle and environmental factors. Regardless of recognised germline genetic factors, establishing the role of each lifestyle and environmental factor is challenging in light of possible long latency periods between exposure and disease development as well as possible confounding effects. In fact, the earliest phase of carcinogenesis might start in childhood or young adulthood, and several decades could elapse before clinical cancer detection [76–78]. Even exposure during intrauterine life can trigger cellular reprogramming and a consequent increased lifetime susceptibility to certain diseases, including cancer [79–82]. As a result, the analysis of lifestyle factors predisposing to EOC

in AYA should take into account exposure since the first years of life. However, considering such long exposure periods hinders efforts to estimate the true or confounding effect of each risk factor. For example, physical inactivity and unhealthy dietary habits lead to obesity, and estimating the exact role of each of these risk factors is challenging. Childhood obesity, if associated to obesity during adulthood, can become a confounder for adulthood exposure [8]. In addition, data on prevalence and temporal trends of modifiable risk factors are available in Italy from 2001 onwards. Such a long observation period facilitates the identification of some trends. At the same time, because of the long-time lag between exposure and cancer detection, our analysis only partially elucidates the contributing role of behavioural risk factors to EOC development in the first decade of the twenty-first century.

Despite these limits, our analysis pointed out that several significant changes in lifestyle risk factors reported worldwide since the end of the twentieth century [1,34,50,58] have also occurred in Italy over the last 20 years. In detail, it seems that these changes have been more prominent among adolescents than adults, especially in young females, who are more biologically vulnerable to side effects of certain lifestyle risk factors. For instance, even if smoking has declined over the last 20 years in people aged 14–44 years, smoking initiation rates during early adolescence showed a 50 %-increase after 1990. Decline rates have been more marked for individuals aged 20–44 years and slower for adolescent girls. Women are at higher risk of smoking-related morbidity and mortality than their male peers due to an increased cancer and cardiovascular disease risk [83]. Similarly, the prevalence of alcohol drinking in females aged 11–25 years has increased over the last 20 years, reaching a 44 %-peak in 2020. With 14.2 % of females aged 11–17 years drinking at least one alcoholic beverage during 2021, any alcohol consumption in this age group poses risks according to WHO recommendations [84]. Most women are not aware that females are physiologically more sensitive and vulnerable to alcohol side effects than males, due to an increased risk of breast cancer, osteoporosis, fertility reduction, and pregnancy-related complications [85].

Overweight and obesity are an area of serious concern. Since 2001, obesity has nearly trebled in individuals aged 18–24 years and almost doubled in individuals aged 25–34, while an opposite trend has been reported for older adults. A major increase was noted for females aged 18–24 years. Moreover, overweight and obesity affect one in four children and adolescents aged 3–17 years, with a worrying rising trend over the last 5 years among adolescents. Beyond an increased risk of cardiovascular and metabolic diseases such as type 2 diabetes in adulthood, a high body mass index in childhood and adolescence is associated with an increased risk of malignancies such as leukaemia, Hodgkin's lymphoma, colorectal and breast cancer [86,87]. Overweight and obesity



are direct consequences of both sedentary lifestyles and incorrect dietary habits. In particular, sedentary lifestyles have increased since 2018 and are more prevalent in females than males starting from childhood. Surprisingly, only 13 % of the Italian population lives on a Mediterranean diet. Both physical activity and the Mediterranean diet act as protecting factors for several types of cancer. Physical activity is especially associated with a reduction in breast and colorectal cancer risk [54], while the Mediterranean diet has been shown to reduce risk of colorectal, breast, gastric, prostate, liver, and head and neck cancers [57]. Childhood obesity is also a risk factor for central precocious puberty in girls [88]. A consequent younger age at menarche, along with low and decreasing fertility rates and increasing women's age at first childbirth, may have contributed to a rise in early breast cancer cases. These factors share increased lifetime exposure to estrogen, which contributes to cancer development through both estrogen receptor-mediated and estrogen receptor-independent effects [89,90].

In-depth investigations are undoubtedly needed to understand the exact role of each contributing factor and the poorly known effects of exposure to emerging chemical compounds deriving from both lifestyle and environmental exposure. For example, the use of nicotine-containing products is becoming popular among adolescents and young adults, possibly because of a widespread belief that e-cigarettes are a less dangerous alternative to traditional cigarettes for the absence of harmful combustion products. However, available preclinical data pointed out that activation of the sympathetic nervous system by inhaled nicotine may promote cancer development and progression. Moreover, vapor from e-cigarettes contains many toxic chemicals such as acetaldehyde, formaldehyde, acetone, acrolein, chromium, N-nitrosamines and others [91]. Air pollution, particularly through exposure to NO<sub>2</sub> and PM<sub>2.5</sub>, seems to play a marginal role in increasing breast cancer risk, but current evidence is limited [66–68]. Although a decrease in air pollution has been reported over the last decades, Italy remains one of the most seriously air-polluted regions in Europe. Among emergent environmental factors, endocrine disruptors are a large, ubiquitous, heterogenous and currently not fully elucidated chemical compound group that alters endocrine system functions [92]. Levels and trends of exposure to endocrine disruptors are largely unknown, although these chemical compounds are known contributors to breast cancer development [93]. Finally, healthcare professionals should be made aware of the increasing incidence of EOC in AYA to consider the possibility of cancer diagnosis need even in patients younger than 40 years, when clinically suspected.

One final topic worth discussing is the increasing role of immigration from non-European countries. In Italy, immigrants are becoming a constituent element of the population. Nevertheless, they are much younger than Italians. In addition, migration generally selects the healthier among them as those more capable to cope with the difficulties posed by migration [94,95]. Immigrants, at least those coming from countries that are economically and culturally very different from Italy, showed a generally lower cancer incidence than Italian natives [94,96], with some exceptions for cervical and lung cancer [97–99]. On these grounds, migration flows towards Italy seem to play no significant role in the increase of EOC incidence in Italian AYAs.

#### 4.2. Healthcare policies for cancer prevention

A call for action for further research and appropriate healthcare policies is deemed necessary to heighten population awareness of cancer risks associated with unhealthy lifestyle patterns, especially for children and adolescents. As highlighted by Marmot [97], cancer prevention cannot be pursued simply by encouraging people to reinforce healthy behaviours. Rather, action on social determinants of health is required. In high-income countries, smoking and obesity follow the socio-economic gradient. In Italy, smoking habits among people of low social status did not change from 2008 to 2022, while a decrease in smoker prevalence has been observed in people without economic

difficulties during the same period. Similarly, fruit and vegetable consumption and physical activity follow a social gradient to the disadvantage of poorer and/or less educated people [39].

Previous experiences of healthcare policies for cancer prevention in high-income countries showed positive effects. A virtuous example of this approach was the Euromelanoma project, initiated in 1999. Euromelanoma was the first public screening campaign ever to be organized on a national scale in all participating Central and Eastern European countries as well as in the Baltic states [98]. The most common benefits of the campaign were an increase in population awareness of skin cancer and preventive measures, and an increase in demand for skin examinations, leading to an increase in the number of early diagnoses [99]. Another valuable experience was “The Real Cost” campaign. In February 2014, the US Food and Drug Administration (FDA) launched an anti-smoking campaign named “The Real Cost,” which initially targeted cigarette use by young people aged 12–17 years. Since then, the successful campaign has been run on TV, radio, print, web and social media and expanded to chewing tobacco and e-cigarette prevention. In young people who reported never having smoked a cigarette in the baseline survey, high campaign exposure was associated with a 30 %-decrease in risk of smoking initiation (AOR=0.70, 95 % CI=0.55, 0.91) [100]. In terms of cost effectiveness [101], “The Real Cost” was shown to reduce tobacco-related morbidity and mortality for a generation of young people from the US, while also ensuring substantial cost savings.

These experiences highlight the need for much stronger efforts to raise awareness of modifiable risk factors in future campaigns. Research in this area also requires a team science approach where, in order to reach the youngest segment of the population, expertise in social media marketing, behavioral science, public health, health communication and clinicians are needed [102].

#### 4.3. Conclusions

The current EOC epidemic in Italy, especially among females, could in part be attributed to significant changes in lifestyle risk factors such as early smoking and alcohol consumption, physical inactivity and unhealthy dietary habits leading to obesity and overweight, particularly in children and adolescents. Regional variation in risk factor exposure does not help in defining the major contributors to such an increase in cancer incidence. Some factors are more represented in the South, such as smoking habits, physical inactivity and overweight, whereas others, including alcohol intake and pollution, are more present in the North. Moreover, along with these well recognized risk factors, many other elements should be borne in mind that remain unknown, with further research needed to fully elucidate the reasons of this worrying trend.

#### Ethical approval

Not applicable.

#### Disclosure

The authors have no conflicts of interest to declare that are relevant to the content of this manuscript.

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Writing – review & editing, Investigation. **Fedro Peccatori**: Writing – review & editing, Visualization, Supervision, Conceptualization. **Angela Toss**: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Investigation, Conceptualization. **Giuseppe Maria Milano**: Writing – review & editing, Supervision. **Marco Maruzzo**: Writing – review & editing, Investigation. **Annalisa Trama**: Visualization, Supervision, Investigation, Formal analysis. **Maurizio Mascarin**: Writing – review & editing, Visualization. **Andrea Ferrari**: Writing – review & editing, Supervision, Investigation, Conceptualization. **Claudia Piombino**: Writing – review & editing, Writing – original draft, Investigation, Data curation. **Paola Quarello**: Writing – review & editing, Investigation, Data curation.

## Declaration of Competing Interest

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