

Youth-Onset Cancer and Modifiable Risk: Quantifying the Combined Impact of Obesity and Alcohol on Breast and Colorectal Cancer in Italy (18-34 Years)

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Abstract

Background

Rising rates of cancers diagnosed before the age of 50 have been reported worldwide, including in Italy. Among modifiable risk factors, obesity and alcohol consumption independently and synergistically increase the risk of breast and colorectal cancers, including early-onset disease. However, the population-level burden attributable to these exposures among adolescents and young adults (AYA) remains poorly quantified.

Methods

We integrated a narrative review with a quantitative Population Attributable Fraction (PAF) analysis to estimate the proportion of early-onset breast and colorectal cancers attributable to overweight/obesity, high-risk alcohol consumption, and their combined exposure in the Italian population aged 18–34 years. Sex- and age-specific prevalence data were derived from the national surveillance systems (“PASSI”), while relative risks were obtained from meta-analyses and large cohort studies. Combined PAFs were estimated assuming independence between exposures and tested through sensitivity analyses varying prevalence and relative risk assumptions.

Results

Among young adults aged 18–34 years, overweight and obesity together accounted for a substantial proportion of early-onset colorectal cancer cases, while high-risk alcohol consumption showed the largest individual attributable fraction. The combined contribution of excess body weight and alcohol consumption reached 12.2% of early-onset colorectal cancer cases. For early-onset breast cancer in young women, obesity and high-risk alcohol consumption were associated with PAFs of 2.8% and 4.6%, respectively. Sensitivity analyses confirmed the robustness of the estimates and indicated that uncertainty in relative risk assumptions represented the main source of variability.

Conclusions

Obesity and alcohol consumption contribute meaningfully to the burden of early-onset breast and colorectal cancers in Italy. Integrating weight management and alcohol risk assessment into clinical practice and public health strategies targeting young adults could prevent a measurable proportion of these cancers and help counteract the rising incidence of malignancies at young ages.

1. Background

1.1 Context and Rationale

Early-onset cancers, defined as malignancies diagnosed before the age of 50 years, are increasing worldwide across multiple cancer sites (1). In Italy, population-based cancer registry data indicate that cancer incidence among young adults aged 20–49 years shows site specific trends, with breast cancer representing the most frequently diagnosed malignancy in young women aged 20–49 years and colorectal cancer remaining among the most common solid tumors in both sexes (2). Over the same period, obesity has remained highly prevalent among adults in Italy, including younger age groups, with national “PASSI” surveillance system data documenting widespread excess body weight among individuals aged 18–49 years, reflecting exposure patterns that often originate early in life (3). Evidence from longitudinal and cohort studies suggests that excess adiposity in early adulthood may have long term effects on colorectal carcinogenesis, supporting a life course perspective in cancer development (4). Similarly, alcohol consumption is common among adults aged 18–49 years in Italy, and a substantial proportion report drinking patterns classified as potentially risk for health according to national data “PASSI” (5). Excess body fatness is a recognized carcinogenic exposure and has been linked to colorectal cancer and breast cancer (6). Alcohol consumption is classified as a carcinogenic exposure and has been consistently associated with increased risk of both breast and colorectal cancers (7). Obesity may promote carcinogenesis by accelerating tumor development and shifting cancer occurrence toward younger ages through biological mechanisms including chronic inflammation, insulin resistance, and hormonal dysregulation (6). In parallel, population level analyses indicate that increases in early-onset incidence of selected cancers, including colon and rectal cancer, are positively correlated with rising prevalence of overweight and obesity, supporting a potential contributory role of excess body weight in early-onset carcinogenesis (1). Recent pooled analyses have also reported a positive association between alcohol consumption and the risk of early-onset colorectal cancer (8). Although multiple modifiable lifestyle related risk factors frequently co-occur, evidence on their combined association with cancer risk has been relatively limited, as most epidemiological studies have traditionally focused on single exposures (9). To the best of our knowledge, only few studies have investigated the burden of excess body weight and alcohol intake as cancer risk factors in adolescents and young adults (AYA, 15–39 years) as defined by the AYA Working Group of the European Society for Medical Oncology and the European Society for Paediatric Oncology (10). The population attributable fraction (PAF) captures this preventive potential by estimating the proportion of cancer cases in a population that could theoretically be prevented if exposure to the risk factor were reduced to a minimum-risk level (11). Quantifying the combined population level contribution of modifiable lifestyle related risk factors, including excess body weight and alcohol consumption, is therefore critical to bridge etiological evidence with actionable cancer prevention strategies and to inform public health interventions (9).

The present study aims to:

1) Describe trends of obesity and alcohol use among Italian young adults (18–34 years);

2) Summarize key biological mechanisms linking these exposures to breast and colorectal cancer;

3) Quantify the Population Attributable Fraction (PAF) for overweight, obesity, high-risk alcohol use, and their combination in early-onset breast and colorectal cancer;

4) Derive actionable implications for clinical practice and public health.

1.2 Epidemiology of Obesity and Alcohol in Italian Youth

Overweight and obesity are concerning issues among Italians. Overweight and obesity are here defined based on BMI (Body Mass Index, kg/m^2) according to WHO definitions (12), i.e. overweight as BMI over 25 kg/m^2 and obesity as BMI over 30 kg/m^2 . According to the Italian “PASSI” surveillance system for public health, trends of both these conditions have been constantly increasing since 2008. The growing trend in obesity prevalence is small but statistically significant and has been supported especially by the younger age groups (18–34 years old) (3). In 2023–2024, 5.5% of Italians aged 18–34 were affected by obesity, while 21.5% were affected by overweight. Among Italians, overweight and obesity are more common in men and in individuals with low socioeconomic status and low level of education.

Also alcohol consumption among Italians younger generations represents a public health concern, as risky alcohol consumption is reported by about 36% of young adults aged 18–24 years (5). Risky consumption is defined as any intake different from moderate, i.e. habitual high intake (> 2 units/day for men, > 1 units/day for women), alcohol intake outside meals, and binge drinking (for each single occasion > 4 units for men, or > 3 units for women). Different from overweight and obesity, alcohol consumption is more frequent among people with high socioeconomic status and high educational level, and has increased especially among young women (13). In both sexes, drinking patterns among young people are characterized by binge drinking and alcohol intake outside meals.

Body weight and drinking habits in Italian youths reflect global data from high-income countries, where boys have higher obesity rates, and girls follow higher quality diets but engage more in risky behaviors such as drinking (14).

The early exposures to these two risk factors - overweight/obesity and alcohol consumption - often track into adulthood and are associated with increased risk of Non-Communicable Disease, including cancer. In Italy, in 2020, excess body weight accounted for 3.6% of all male cancers and for 4.0% of female ones, corresponding to nearly 7,000 and 7,200 cases, respectively (15). Although the onset of many obesity-

related and alcohol-related cancers mainly occurs in adulthood, early exposures during adolescence and young adulthood could significantly be responsible for the growing incidence before age 50 (6).

1.3 Biological and Epidemiological Evidence

1.3.1 Breast Cancer

Breast cancer risk and progression are strongly influenced by both alcohol consumption and obesity through interconnected hormonal, metabolic, and inflammatory mechanisms. Alcohol intake enhances the invasive and metastatic potential of breast cancer cells, particularly those overexpressing Human Epidermal Growth Factor Receptor 2 (HER2) (16). A key mechanism involves estrogen metabolism: alcohol consumption is associated with higher circulating estrogen levels and increased mammographic breast density, both recognized risk factors for breast cancer (17). Experimental evidence shows that ethanol enhances estrogen receptor α (ER α) expression and signaling in breast cancer cells, thereby promoting tumor growth and metastatic behavior (18). Additionally, alcohol-induced estrogen signaling may increase matrix metalloproteinase (MMP) expression, facilitating extracellular matrix degradation and tumor dissemination (19). Oxidative stress represents another central pathway linking alcohol to breast carcinogenesis. Ethanol metabolism generates reactive oxygen species (ROS), particularly through cytochrome P450 2E1 (CYP2E1) induction, leading to lipid peroxidation, DNA damage, and mutagenesis (20). Ethanol exposure also enhances epidermal growth factor receptor (EGFR) phosphorylation, stimulating mammary epithelial cell proliferation via ROS-dependent pathways (21). Obesity further amplifies breast cancer risk by altering the adipose tissue microenvironment. Obese adipose tissue is characterized by hypoxia, chronic inflammation, and a shift toward pro-tumorigenic adipokines such as leptin, while protective adiponectin levels are reduced (22). Pro-inflammatory cytokines (e.g., IL-6, TNF- α) and free fatty acids increase aromatase expression via nuclear factor-kappa B (NF- κ B) signaling, enhancing local estrogen biosynthesis and driving estrogen receptor-positive breast cancer, particularly in postmenopausal women (23).

1.3.2 Colorectal Cancer

Alcohol intake and obesity significantly contribute to colorectal cancer (CRC) development, particularly in younger populations. Ethanol exerts carcinogenic effects in the colon through both oxidative and non-oxidative metabolic pathways, promoting epithelial cell proliferation and exposure to acetaldehyde (24). Alcohol-induced dysbiosis alters gut microbiota composition, favoring acetaldehyde-producing bacteria and biofilm formation, which prolongs epithelial exposure to carcinogenic metabolites (25, 26). Additionally, alcohol increases intestinal permeability, facilitating microbial translocation and triggering chronic inflammation that enhances susceptibility to neoplastic transformation (27). Obesity promotes CRC through insulin resistance, hyperinsulinemia, and chronic inflammation. Elevated insulin and insulin-like growth factor 1 (IGF-1) levels stimulate colorectal cell proliferation and inhibit apoptosis, while hyperglycemia and lipid abnormalities increase oxidative stress and DNA damage (28). Pro-inflammatory cytokines such as IL-6 sustain tumor-promoting signaling pathways in the intestinal epithelium (29).

1.3.3 Synergistic Effects

Alcohol consumption and obesity interact synergistically to amplify cancer risk through shared mechanisms including chronic inflammation, oxidative stress, insulin resistance, and hormonal dysregulation. Experimental and observational studies indicate that obesity-related metabolic and hormonal alterations enhance alcohol-induced sensitivity to insulin and estrogens, increasing breast cancer risk, particularly in postmenopausal women (30). This synergism is also evident in hepatocellular carcinoma, where the coexistence of obesity-related fatty liver disease and alcohol-induced liver injury markedly increases long-term cancer risk compared to either factor alone (31). Evidence from a large cohort study indicates that unhealthy lifestyle factors, including alcohol consumption, interact with genetic predisposition to increase the risk of early-onset breast cancer (32). These findings highlight the importance of integrated lifestyle interventions, as sustained reductions in body weight and alcohol consumption may substantially reduce cancer risk across multiple organs (33).

2. Methods

For colorectal and breast cancers, PAFs were estimated using Levin's formula (34):

$$\text{PAF} = p \times (\text{RR} - 1) / [1 + p \times (\text{RR} - 1)]$$

where p = prevalence of each risk factor (i.e. overweight/ obesity and risky alcohol consumption as previously defined), and RR = relative risk.

Combined PAFs were calculated as:

$$\text{PAF}_{\text{combined}} = 1 - (1 - \text{PAF}_1)(1 - \text{PAF}_2)(1 - \text{PAF}_3),$$

assuming statistical independence between overweight/obesity and high-risk alcohol consumption. We acknowledge that these exposures are likely correlated in real populations; therefore, our estimates may under- or overestimate the true combined attributable fraction.

Confidence intervals for PAF were based on approximate propagation of imprecision (35), and sensitivity analyses explored alternative prevalence and RR assumptions to assess robustness. Sex-specific prevalence of overweight, obesity and risky alcohol consumption was extracted for the Italian young adults population (18–34 years) from the national “PASSI” surveillance system (3, 5). RRs with 95% confidence intervals (CIs) for the association between overweight, obesity, alcohol consumption and cancer sites were derived from recent meta-analyses (4, 36–38). Sex-specific estimates were extracted, when available.

Sensitivity analyses were conducted to assess the robustness of PAF estimates to uncertainty in both prevalence and relative risk parameters. Specifically, PAFs were recalculated across plausible ranges of prevalence and RR values, informed by the variability observed in national surveillance data and by the 95% confidence intervals reported in the literature. Results of the sensitivity analysis were visualized using contour plots, in which PAF values are represented as a topographic surface: color bands identify intervals of similar PAF magnitude, with higher intensity colors corresponding to larger attributable

fractions. This approach allows the joint influence of prevalence and RR on PAF estimates to be explored allowing the identification of parameter regions associated with higher or lower population-attributable burden.

3. Results

PAFs for overweight, obesity and high-risk alcohol consumption were estimated for early-onset colorectal and breast cancers using age and sex specific prevalence data and relative risk. Results are reported by cancer site, exposure, age group and sex (Table 1, Table 2, Figure 1). Primary analyses were conducted for the overall 18–34 age group, with additional stratified analyses for 18–24 and 25–34 years limited to alcohol exposure.

Early-onset colorectal cancer: Among young Italian adults aged 18-34 years, overweight accounted for 3.6% (95% CI: 1.7, 5.6) of early onset colorectal cancer cases, while obesity accounted for 1.7% (95% CI: 0.6, 3). Among men, PAF for colorectal cancer was 9.8% (95% CI: 6.5, 13.1) and 4.2% (95% CI: 2, 6.8) in relation to overweight and obesity, respectively. Among women, a PAF of 4.4 (95% CI: 2.2, 6.7) for overweight and a PAF of 3.7% (95% CI: 1.7, 5.9) for obesity were estimated. High-risk alcohol consumption showed a larger attributable fraction with a PAF of 8.2% (95% CI: 0.3, 16.4) in individuals aged 18-24 years and 10.7% (95% CI: 8.9, 12.5) in those aged 25-34 years. For early-onset CRC, the combined estimated contribution of excess body weight and alcohol consumption reached 12.2%.

Early-onset breast cancer: In young Italian women (18-34y), obesity accounted for 2.8% (95% CI: 1.7, 3.9) of early onset breast cancer cases, while high-risk alcohol consumption was associated with a PAF of 4.6% (95% CI: 3.8, 5.5). The negative lower confidence bound reflects statistical imprecision rather than a protective effect.

Sensitivity analyses showed that PAF estimates increased with higher values of both prevalence and relative risk. Variations in RR produced larger changes in PAFs value compared with equivalent variations in prevalence, indicating a greater sensitivity of PAF to uncertainty in risk estimates. Across the full range of plausible assumptions, however, the relative contribution of overweight, obesity and high-risk alcohol consumption to early-onset colorectal and breast cancer remained consistent. Figure 2 illustrates the results of the sensitivity analyses for selected exposure–outcome associations.

Table 1. Prevalence and Relative Risks (RRs) of Selected Exposures. Relative risks were primarily derived from studies in adult populations due to the limited availability of age-specific estimates for early-onset cancer.

Exposure	Group	Prevalence (95% CI)	Cancer RR (95% CI)			
			Colon and Rectum	Ref	Breast	Ref
Overweight	18-34 y	21.5 (20.28, 22.3)	1.18 (1.08, 1.28)	(4)		
	Men	40.7 (40.0, 41.3)	1.27 (1.17, 1.37)	(4)		
	Women	24.6 (24.0, 25.2)	1.19 (1.09, 1.29)	(4)		
Obesity	18-34 y	5.5 (5.1, 6.0)	1.32 (1.11, 1.56)	(4)		
	Men	11.2 (10.7, 11.6)	1.39 (1.18, 1.65)	(4)		
	Women	9.6 (9.3, 10)	1.22 (0.99, 1.51)	(4)	1.29 (1.18, 1.42)	(36)
High risk Alcohol Drinking	18-24 y	14.9 (13.9, 15.9)	1.26 (1.01, 1.58)	(38)		
	25-34 y	12.6 (11.9, 13.4)	1.49 (1.40, 1.58)	(38)		
	Men	21.9 (21.4, 22.4)	1.55 (1.46, 1.66)	(37)		
	Women	13.9 (13.5, 14.4)	1.09 (0.79, 1.50)	(37)	1.35 (1.28, 1.42)	(37)

Abbreviations: RR, relative risk; CI, confidence interval.

Table 2. Estimated Population Attributable Fractions (PAF) for Overweight, Obesity, and Alcohol

		PAF (95% CI), %	
Exposure	Group	Colon and Rectum	Breast
Overweight	18-34 y	3.6 (1.7, 5.6)	
	Men	9.8 (6.5, 13.1)	
	Women	4.4 (2.2, 6.7)	
Obesity	18-34 y	1.7 (0.6, 3)	
	Men	4.2 (2, 6.8)	
	Women	3.7 (1.7, 5.9)	2.8 (1.7, 3.9)
High risk Alcohol Drinking	18-24 y	8.2 (0.3, 16.4)	
	25-34 y	10.7 (8.9, 12.5)	
	Men	10.9 (9.1, 12.6)	
	Women	1.2 (-3, 6.5)	4.6 (3.8, 5.5)

Abbreviations: PAF, Population Attributable Fractions; CI, confidence interval.

4. Discussion

These findings underscore the significant, yet preventable, contribution of obesity and alcohol consumption to early-onset cancers in Italy.

Taken together, these exposures may explain up to 12.2% of early-onset CRC cases among young adults aged 18-34 years. This proportion is consistent with international evidence linking early-life adiposity and alcohol intake with increasing cancer risk.

The study's main strengths include the use of nationally representative surveillance data ("PASSI") and age-specific prevalence estimates. However, several limitations should be acknowledged: RRs were derived primarily from adult populations, and the assumption of independence between risk factors may underestimate potential synergistic effects. Additionally, prevalence estimates were limited to available national datasets, which may not fully capture temporal or regional variability among adolescents and young adults.

Despite these caveats, our analysis underscores the importance of early, integrated prevention strategies. Combining interventions on weight management and alcohol reduction could prevent a measurable proportion of early-onset colorectal and breast cancer cases. These results are particularly relevant given the rising incidence of malignancies before age 50 and the shifting distribution of modifiable exposures towards younger cohorts.

Findings from the sensitivity analyses provide additional insight into the robustness of the estimated PAFs. Although uncertainty in both prevalence and relative risk affects the magnitude of attributable fractions, the analysis indicates that relative risk assumptions represent the main driver of variability. After all, in the calculation, the RR has an exponential impact, whereas prevalence has a linear effect, making the PAF more sensitive to imprecise RR estimates. This highlights the importance of high-quality, age-specific risk estimates when quantifying the population-level impact of modifiable exposures in young adults. Importantly, even under conservative assumptions, the combined contribution of obesity and alcohol consumption to early-onset cancers remained substantial.

Clinical and Policy Implications

Our results highlight how moderate relative risks, when coupled with a high prevalence of exposure in young adults, may translate into a meaningful population-level burden, reinforcing the relevance of early preventive strategies.

From a clinical perspective, routine BMI and alcohol use screening should become an integral part of both oncology and primary care settings, ensuring that early preventive interventions are systematically offered to young adults. In this context, brief motivational counselling, following the 5A model (Ask, Advise, Assess, Assist, Arrange) as described in the WHO primary care toolkit (39), together with referral to structured weight management and alcohol reduction programs, should be established as standard components of care pathways.

At the policy level, population-wide interventions are equally crucial. Measures such as alcohol pricing regulation, warning labels, and restrictions on alcohol availability near educational environments could substantially reduce exposure among younger age groups and reinforce individual-level efforts.

Finally, key research gaps must be addressed to strengthen the evidence base. There remains an urgent need for joint prevalence studies assessing the co-occurrence of obesity and alcohol use in youth, as well as for age-stratified relative risk estimates and longitudinal analyses exploring the combined effects of these modifiable risk factors on cancer incidence.

These considerations are summarised in Box 1, which outlines key action points for clinicians, multidisciplinary teams, public health stakeholders, and researchers.

Box 1. Recommendations and call to action

Domain	Recommended Actions
Oncology Practice	Screen BMI and alcohol use at first visit; integrate brief lifestyle counselling within “Percorsi Diagnostico-Terapeutici Assistenziali” for early-onset breast and colorectal cancer.
Multidisciplinary Teams	Include dietitians, psychologists, and health educators in care pathways to deliver personalized prevention strategies.
Public Health and Policy	Implement youth-targeted information campaigns in schools and universities, strengthen alcohol taxation and labelling regulations.
Research	Promote longitudinal cohort studies exploring combined exposure trajectories and cancer outcomes in young adults.

5. Conclusion

Obesity and alcohol are preventable and measurable determinants of youth-onset cancers. Integrating lifestyle assessment and behavioral counselling into oncology and preventive pathways could substantially reduce the future burden of early-onset cancers in Italy. From a broader public health perspective, policies addressing weight control and alcohol misuse in younger populations represent a strategic opportunity to reverse current cancer trends and mitigate long-term disease risk.

Abbreviations

- AYA
- Adolescents and Young Adults
- BMI
- Body Mass Index
- CI
- Confidence Interval
- CRC
- Colorectal Cancer
- CYP2E1
- Cytochrome P450 2E1
- EGFR
- Epidermal Growth Factor Receptor
- HER2
- Human Epidermal Growth Factor Receptor 2
- ERα
- Estrogen Receptor alpha
- IGF-1
- Insulin-like Growth Factor 1
- IL-6

Interleukin 6
MMP
Matrix Metalloproteinase
NF-κB
Nuclear Factor kappa B
PAF
Population Attributable Fraction
PASSI
Progressi delle Aziende Sanitarie per la Salute in Italia
RR
Relative Risk
ROS
Reactive Oxygen Species
TNF-α
Tumor Necrosis Factor alpha
WHO
World Health Organization

Declarations

Ethics approval and consent to participate: Not applicable. This study is based on analyses of aggregated data derived from publicly available national surveillance systems and published literature.

Consent for publication: Not applicable.

Availability of data and materials: All data used in this study are derived from publicly available sources, including the Italian national surveillance system PASSI and published scientific literature. No individual-level data were used.

Competing interests: The authors declare that they have no competing interests.

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Figures

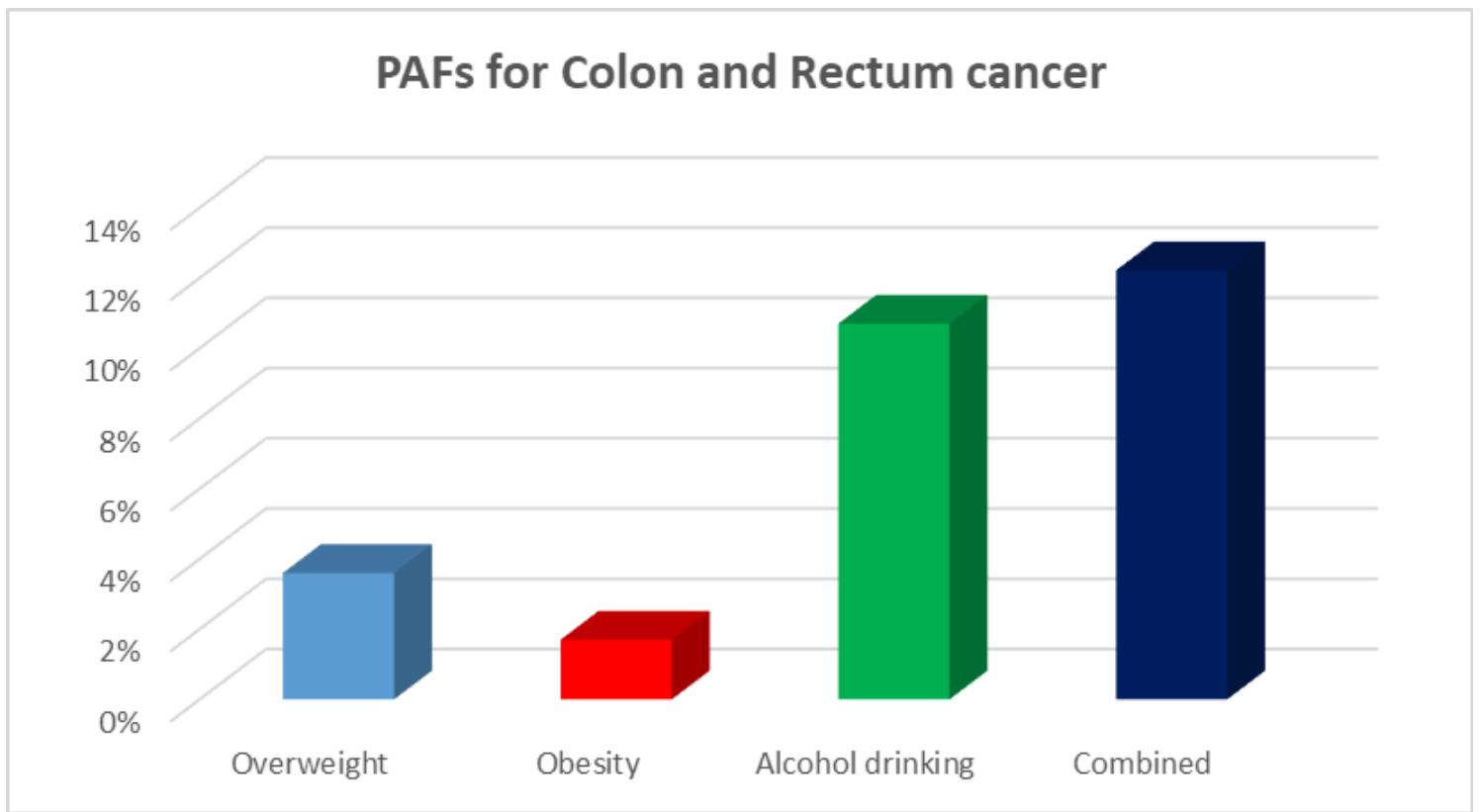
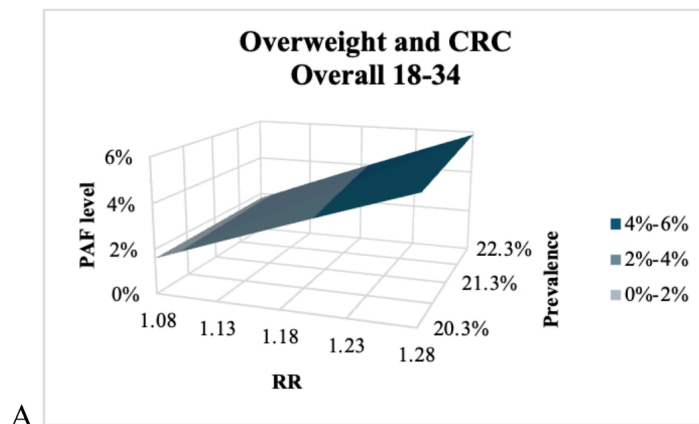
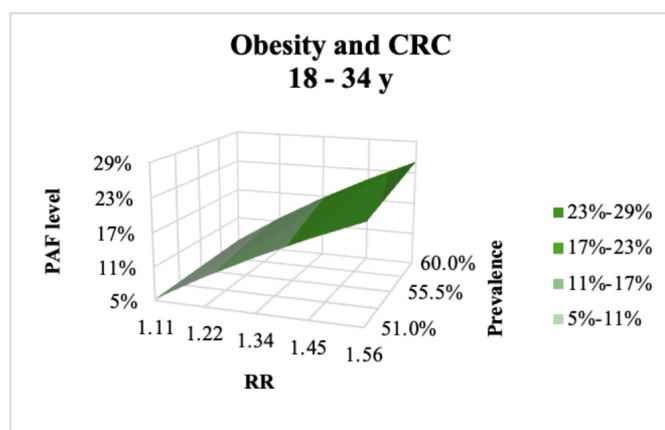


Figure 1

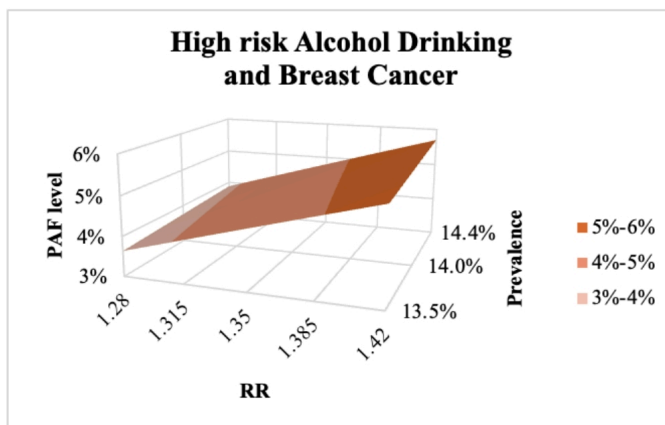
Bar chart showing combined PAF highest among joint exposure.



A



B



C

Figure 2

Sensitivity analysis of PAFs for selected exposure-cancer associations. Three-dimensional surface plots display estimated PAFs as a function of exposure prevalence (Pr) and relative risk (RR). Panel A shows overweight and early-onset colorectal cancer among young adults aged 18-34 years; Panel B shows obesity and early-onset colorectal cancer in the same age group; Panel C shows high-risk alcohol consumption and early-onset breast cancer among women aged 18-34 years. PAF values increase along

both the prevalence and relative risk axes, reflecting the combined influence of exposure frequency and strength of association on population-level cancer burden.