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Gender differences in cancer epidemiology in Italy, 2013–2017

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ABSTRACT

Gender differences in cancer burden have been consistently reported worldwide, with men exhibiting higher incidence and mortality rates for most non-sex-specific cancers. However, the extent and patterns of these disparities across cancer sites, age groups, and geographical regions in Italy remain poorly investigated. We analysed data from population-based cancer registries belonging to the AIRTUM network, including 1359,053 cancer cases diagnosed between 2013 and 2017, overall and stratified by age group (0–49, 50–69, ≥70 years) and by geographic macro-areas (North, Centre, South & Islands). Differences in five-year net survival between men and women were also assessed. Overall, cancer incidence was markedly higher in men (male-to-female incidence rate ratio [M/F IRR] 1.38; 95% confidence interval [CI]: 1.38–1.39), and this gap increased when excluding breast cancer (M/F IRR = 1.90; 95% CI: 1.89–1.90). Male predominance was observed in 29 of 30 sites, most notably laryngeal (M/F IRR = 8.74; 95% CI: 8.31–9.19), bladder (5.23; 95% CI: 5.15–5.32), mesothelioma (3.60; 95% CI: 3.40–3.82), and lung (2.92; 95% CI: 2.89–2.95) cancers, while thyroid cancer was more common in women (0.37; 95% CI: 0.36–0.38). Incidence gender gaps were greater in the South & Islands than in the North and Centre. Women showed higher five-year survival rates than men for most major cancers, including colorectal and lung. In Italy, men bear a substantially higher cancer burden than women, with significant geographical variability, while women consistently achieve better survival outcomes. Biological, behavioural, and sociocultural factors likely contribute to these differences. Addressing these disparities requires incorporating a gender perspective into cancer prevention, early detection, and treatment strategies.

1. Introduction

The vast majority of non-sex-specific cancers have higher incidence rates in males than females at most ages [1]. Many non-mutually exclusive hypotheses have been put forward to explain this, attributing the different susceptibility of males to oxidative response [2], beliefs, behaviours, different access and utilization of healthcare [3], sex chromosome complement/aneuploidy/aberrations, gene expression, hormones, viral infections [4], and occupational and environmental exposure [5]. Male predominance in lung cancer, stomach cancer, non-Hodgkin lymphoma, and bladder cancer is well recognized, with breast cancer and thyroid cancer being striking examples of female predominance [6]. Nevertheless, for malignancies other than those related to smoking, alcohol consumption, obesity, and certain occupational exposures, the sex gap remains largely unexplained.

Understanding the basic components of cancer gender disparity is essential for developing strategies to achieve comparable rates of optimal outcomes in both male and female patients with cancer.

According to the most recent estimates, in Europe in 2022, the most frequent cancers among men were prostate, lung, and colorectal cancer, while breast cancer, followed by colorectal and lung cancer, was most frequent among women [7]. The EUROCARE-5 data revealed significant gender differences in cancer survival, with women tending to have higher five-year survival rates than men for many cancer types, including colorectal and lung cancers [8]. Conversely, men showed higher survival only in a few specific cancer types, such as testicular and prostate cancer, which generally have more favourable prognoses [8]. Because the differences highlighted in cancer-specific survival between male and female cancer patients were controversial, a comprehensive understanding of this topic remains critical for cancer prevention and treatment [9]. The survival gap may be explained by a combination of biological factors influencing tumour development, differences in lifestyle and risk behaviours that affect exposure and early detection, and sex-specific variations in pharmacokinetics and pharmacodynamics, which influence treatment efficacy and toxicity [10].

In Italy, the age-standardized five-year net survival for all malignant tumours (excluding skin and bladder cancers) was 55% for men and 64% for women in the period 2005–2009, showing a significant increase compared to previous years, particularly for common cancers such as colorectal, breast, and prostate cancer [11]. The most recent national statistics documented that in 2024 about 214,500 new cases of cancer were diagnosed in men and 175,600 in women [12]. These figures were broadly stable compared to previously available evidence, with a slight decrease compared to the peak of 2023 [9]. The most frequently diagnosed cancers in Italy showed distinct patterns, with breast cancer being by far the most common (over 53,000 new cases annually) in women, followed by colorectal and lung cancer, while prostate cancer was the most frequently diagnosed cancer in men, followed by lung, colorectal, and bladder cancer [13].

The evidence of women achieving better survival outcomes than men highlights the importance of integrating a gender perspective in cancer research, prevention strategies, and post-diagnosis follow-up and care [11].

Our aim in this study was to analyse the cancer statistics in Italy according to gender predominance in order to identify unexplained disparities that could provide opportunities for both aetiological research and public health interventions. To achieve this, we used the last updated cancer dataset from the Italian Network of Cancer Registries (AIRTUM), which covers the pre-COVID19 pandemic era [14], and examined the age-adjusted male-to-female incidence rate ratios (M/F IRRs) by cancer site, age at diagnosis, and area of residence in Italy. Additionally, we explored any potential differences in cancer survival by gender and area of residence across cancer sites.

2. Materials and methods

Cancer incidence data registered between 2013 and 2017 by population-based cancer registries belonging to the AIRTUM network were used to estimate M/F IRRs, after being age-adjusted based on the 2013 European standard population. Thirty cancer sites, excluding sex-specific cancers (cervix uteri, corpus uteri, uterus NOS, ovary, vagina, vulva, other female genital organs for females and testis, penis, prostate, other male genital organs for males) were selected according to the International Classification of Diseases, Tenth Revision (ICD-10) [15], accounting for 1359,053 cancer cases. The M/F IRRs with their 95% confidence intervals (CIs) were calculated overall (all cancer sites; all cancer sites except sex-specific; all cancer sites except sex-specific and breast) and for each of the selected cancer sites, and then stratified by region of residence and age group (0–49, 50–69 and 70 + years). The Italian regions included in the study were grouped into three main areas: North, Centre, and South & Islands.

A description of the data and methods used for survival analysis is presented elsewhere [16,17]. Briefly, the analysis by age and sex [16] was limited to 1418,044 cases diagnosed during the most recent period available, from 2013 to 2017. The entire period of surveillance (2008–2017) [17], which included 20 registries covering a population of 24 million, was taken into account to compare survival estimates by macro-areas (North-Centre versus South & Islands) for both sexes combined and the more recent five-year period 2013–2017.

The SEER*Stat software (version 8.3.6) was used for statistical analyses.

3. Results

The overall incidence rate of all cancers in males was higher than that in females (M/F IRR 1.38; 95%CI 1.38–1.39), decreasing to 1.25 (95%CI 1.24–1.25) when sex-specific cancer sites were excluded, while increasing to 1.90 (95%CI 1.89–1.90) when breast cancer was also excluded. Twenty-nine out of thirty analysed cancer sites showed a male incidence predominance with M/F IRR higher than one; only thyroid cancer had an M/F IRR less than one. More in depth, the rate of laryngeal cancers was almost nine times higher in males than in females, followed by bladder cancer, Kaposi sarcoma, mesothelioma, oesophageal cancer, lung and bronchial cancers, and cancers of the liver and intrahepatic bile ducts (Table 1).

Table 1
Age-adjusted male-to-female incidence rate ratios (M/F IRR) for selected cancer sites in Italy. AIRTUM pool, period of diagnosis 2013–2017.

Tumour site	M/F IRR	95% CI	
Oral cavity and pharynx	2.40	2.33	2.47
Oesophagus	3.57	3.40	3.76
Stomach	1.91	1.87	1.94
Larynx	8.74	8.31	9.19
Colon-rectum	1.55	1.54	1.57
Colon	1.50	1.48	1.52
Rectum	1.69	1.66	1.73
Liver and intrahepatic bile ducts	2.89	2.83	2.95
Gallbladder	1.20	1.17	1.24
Pancreas	1.26	1.24	1.28
Lung and bronchus	2.92	2.89	2.95
Bone and joints	1.30	1.20	1.40
Melanoma of the skin	1.26	1.24	1.29
Mesothelioma	3.60	3.40	3.82
Kaposi sarcoma	3.38	3.11	3.67
Soft tissue	1.54	1.47	1.61
Kidney	2.29	2.25	2.34
Kidney and renal pelvis	2.38	2.33	2.43
Ureter and other urinary organs	2.93	2.78	3.08
Urinary bladder	5.23	5.15	5.32
Central nervous system	1.50	1.46	1.55
Thyroid	0.37	0.36	0.38
Hodgkin lymphoma	1.17	1.12	1.22
Non-Hodgkin lymphoma	1.43	1.40	1.46
Multiple myeloma	1.38	1.35	1.42
Acute lymphocytic leukaemia	1.31	1.22	1.41
Chronic lymphocytic leukaemia	1.90	1.82	1.99
Acute myeloid leukaemia	1.46	1.40	1.52
Chronic myeloid leukaemia	1.75	1.62	1.89
Leukaemia	1.67	1.63	1.71
All cancer sites	1.38	1.38	1.39
All cancer sites except sex-specific	1.25	1.24	1.25
All cancer sites except sex-specific and breast	1.90	1.89	1.90

Overall age-adjusted M/F IRRs were significantly higher in the South & Islands macro-area than in the North and Central areas (Table 2). With regard to individual cancer sites, the M/F IRRs for lung cancer were significantly higher in the South & Islands than in the North and Centre, as were the M/F IRRs for bladder cancer and mesothelioma. M/F IRRs in the South & Islands were also higher, but not significantly, for laryngeal and rectal cancer. In the North, significantly higher M/F IRRs were observed for oral cavity, stomach, colon, liver and intrahepatic bile duct, and kidney and renal pelvis cancers. In the same area higher, but not significantly, M/F IRRs were found for bone and joint cancers, melanomas, soft tissue sarcomas, and cancers of the central nervous system, whereas Kaposi sarcoma and gallbladder cancer showed higher M/F IRRs in the Central area of Italy. The three macro-areas were aligned in their M/F IRRs for Hodgkin lymphoma, non-Hodgkin lymphoma, multiple myeloma, and thyroid cancer, with thyroid cancer prevailing in women (Table 2).

Table 3 reports the M/F IRRs stratified by age and geographical area covered by cancer registries. Cancers showing a female predominance in incidence (M/F IRRs <1) among the 0–49 age group were colon cancer in the Central and South & Islands areas, melanoma in all three macro-areas, acute myeloid leukaemia in the Central area, and Hodgkin lymphoma in the Central and South & Islands areas. Anal cancer showed an M/F IRR < 1 in the 50–69 and > 70 age groups in the Northern and Central areas. Lung cancer showed a sharp increase in female incidence with age in all three macro-areas (from 1.16 to 3.35 in the North; 1.13–3.28 in the Centre; and 1.32–5.32 in the South & Islands), which did not result in a reduction of M/F IRRs because it was accompanied by a parallel increase in male rates (data not shown). Mesothelioma showed significantly higher M/F IRRs in the 50–60 and > 70 age groups in all Italian macro-areas. Skin melanoma M/F IRRs were below 1 for young women in all three macro-areas, but inverted to a male predominance in the 50–69 and > 70 age groups. Several tumour sites displayed in all three Italian macro-areas a statistically significant increase in M/F IRRs with age (from the youngest to the oldest age group), for example, the urinary bladder (data not shown), or between the 50–69 and > 70 age groups, for example, the larynx. In liver and intrahepatic bile duct cancers, the 50–69 age group showed statistically significantly highest M/F IRRs in the North and Central areas. When all cancers were considered together, there was a strong female predominance (M/F IRR <1) in all three macro-areas for the youngest age group. A statistically significant increase was then observed across age groups, culminating in a male predominance (M/F IRR >1) in the 50–69 and > 70 age-groups. These findings were confirmed when excluding sex-specific sites (with or without breast cancer) from the analyses.

Cancer survival figures for the period under study have been reported in another article of this special issue [17]. In the present paper we focus on age-standardized five-year net survival (NS) by cancer site (excluding sex-specific sites), gender, and geographical macro-area (North-Centre, South & Islands) (Table 4).

Analysis of the age-standardized five-year NS between geographical macro-areas showed some notable differences. Among men, the overall survival rate was significantly higher in the North-Centre macro-area (64.0%; 95%CI: 63.8–64.2) as compared to the South & Islands (58.1%; 95%CI: 57.7–58.5). With regard to individual cancer sites, the five-year NS rate was significantly higher in the North-Centre macro-area than the South & Islands for stomach, pancreatic, and lung cancer. Similarly, liver cancer showed a higher five-year NS rate in the North-Centre

Table 2
Age-adjusted male-to-female incidence rate ratios (M/F IRR) for selected cancer sites by Italian macro-areas. AIRTUM pool, period of diagnosis 2013–2017.

Cancer site		Macro-area North	Centre	South & Islands
Oral cavity and pharynx	M/F IRR	2.50	2.28	2.34
	95%CI	2.4 – 2.6	2.15 – 2.42	2.21 – 2.48
Oesophagus	M/F IRR	3.66	3.36	3.65
	95%CI	3.42 – 3.91	3.02 – 3.75	3.24 – 4.12
Stomach	M/F IRR	1.97	1.87	1.85
	95%CI	1.92 – 2.03	1.81 – 1.93	1.79 – 1.92
Larynx	M/F IRR	8.78	8.29	9.11
	95%CI	8.12 – 9.5	7.51 – 9.17	8.33 – 9.98
Colon-rectum	M/F IRR	1.58	1.52	1.56
	95%CI	1.55 – 1.6	1.49 – 1.55	1.53 – 1.59
Colon	M/F IRR	1.54	1.47	1.49
	95%CI	1.51 – 1.57	1.44 – 1.5	1.45 – 1.52
Rectum	M/F IRR	1.69	1.65	1.74
	95%CI	1.64 – 1.74	1.59 – 1.7	1.69 – 1.8
Liver and intrahepatic bile ducts	M/F IRR	3.13	2.85	2.62
	95%CI	3.04 – 3.23	2.72 – 2.98	2.52 – 2.71
Gallbladder	M/F IRR	1.22	1.25	1.15
	95%CI	1.17 – 1.28	1.18 – 1.33	1.09 – 1.21
Pancreas	M/F IRR	1.29	1.23	1.24
	95%CI	1.26 – 1.32	1.19 – 1.28	1.2 – 1.29
Lung and bronchus	M/F IRR	2.70	2.52	3.86
	95%CI	2.65 – 2.74	2.47 – 2.58	3.78 – 3.94
Bone and joints	M/F IRR	1.34	1.25	1.30
	95%CI	1.19 – 1.51	1.09 – 1.44	1.14 – 1.49
Melanoma of the skin	M/F IRR	1.29	1.25	1.22
	95%CI	1.25 – 1.32	1.21 – 1.29	1.18 – 1.27
Mesothelioma	M/F IRR	3.33	3.77	4.38
	95%CI	3.09 – 3.59	3.26 – 4.38	3.85 – 5.0
Kaposi sarcoma	M/F IRR	4.12	5.05	2.67
	95%CI	3.55 – 4.8	3.99 – 6.43	2.39 – 2.99
Soft tissue	M/F IRR	1.61	1.43	1.53
	95%CI	1.5 – 1.73	1.31 – 1.56	1.41 – 1.66
Kidney	M/F IRR	2.40	2.24	2.18
	95%CI	2.33 – 2.48	2.15 – 2.33	2.09 – 2.28
Kidney and renal pelvis	M/F IRR	2.45	2.35	2.29
	95%CI	2.38 – 2.52	2.27 – 2.44	2.21 – 2.39
Ureter and other urinary organs	M/F IRR	2.73	3.16	3.04
	95%CI	2.53 – 2.95	2.87 – 3.48	2.74 – 3.38
Urinary bladder	M/F IRR	4.94	5.04	5.87
	95%CI	4.82 – 5.06	4.89 – 5.19	5.7 – 6.03
Central nervous system	M/F IRR	1.53	1.46	1.50
	95%CI	1.47 – 1.6	1.38 – 1.54	1.43 – 1.58
Thyroid	M/F IRR	0.37	0.39	0.36
	95%CI	0.36 – 0.38	0.37 – 0.4	0.35 – 0.37
Hodgkin lymphoma	M/F IRR	1.18	1.17	1.16
	95%CI	1.11 – 1.27	1.07 – 1.27	1.08 – 1.25
Non-Hodgkin lymphoma	M/F IRR	1.41	1.48	1.42
	95%CI	1.37 – 1.45	1.43 – 1.53	1.37 – 1.47
Multiple myeloma	M/F IRR	1.38	1.38	1.40
	95%CI	1.32 – 1.43	1.31 – 1.45	1.33 – 1.47
Acute lymphocytic leukaemia	M/F IRR	1.33	1.24	1.35
	95%CI	1.18 – 1.49	1.07 – 1.45	1.19 – 1.54
Chronic lymphocytic leukaemia	M/F IRR	1.88	2.07	1.84
	95%CI	1.76 – 2	1.89 – 2.26	1.7 – 1.99
Acute myeloid leukaemia	M/F IRR	1.52	1.40	1.44
	95%CI	1.42 – 1.62	1.3 – 1.51	1.34 – 1.56
Chronic myeloid leukaemia	M/F IRR	1.95	1.96	1.46
	95%CI	1.73 – 2.19	1.66 – 2.31	1.29 – 1.65
Leukaemia	M/F IRR	1.73	1.64	1.61
	95%CI	1.67 – 1.8	1.57 – 1.72	1.55 – 1.67
All cancer sites	M/F IRR	1.38	1.33	1.44
	95%CI	1.37 – 1.39	1.32 – 1.34	1.43 – 1.45
All cancer sites except sex-specific	M/F IRR	1.22	1.20	1.33
	95%CI	1.21 – 1.23	1.19 – 1.21	1.32 – 1.34
All cancer sites except sex-specific + breast	M/F IRR	1.91	1.80	1.97
	95%CI	1.9 – 1.93	1.78 – 1.81	1.96 – 1.99

macro-area than in the South & Islands. Male survival advantages in the North-Centre macro-area compared to the South & Islands were also observed for colorectal cancer, cutaneous melanoma, kidney cancer, and bladder cancer. Further significant differences between five-year NS for males in the North-Centre and the South & Islands were found for upper aerodigestive tract cancers, leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma, and multiple myeloma (Table 4).

Among women, the overall five-year NS rate was significantly higher in the North-Centre macro-area (68.3%; 95%CI: 68.0–68.5) than in the South & Islands (63.7%; 95%CI: 63.3–64.1). The North-Centre area showed significant advantages for stomach and colorectal cancer. Geographical differences, although not significant, were also documented for upper aerodigestive tract and pancreatic cancers. Notable statistically significant geographical differences in favour of the North-Centre area also emerged for lung cancer and skin melanoma. Additional significant gaps favouring women from the North-Centre of Italy were observed for thyroid cancer, leukaemia, non-Hodgkin lymphoma, and multiple myeloma. Urinary tract tumours, on the other hand, showed better survival among women from the South & Islands, but this difference was not statistically significant (Table 4).

Women had higher survival rates overall than men in both macro-areas (North-Centre vs South & Islands). Specifically, women had an advantage for upper aerodigestive tract, stomach, lung, thyroid, and central nervous system cancers. In the South & Islands macro-area, women had a survival advantage for several cancers, including upper aerodigestive tract cancer, stomach cancer, thyroid cancer, and Hodgkin lymphoma (Table 4).

4. Discussion

The overall cancer incidence in the Italian population was found to be significantly higher in males than in females, in line with the worldwide epidemiology of cancer [18].

More in depth, cancer incidence predominated in males for all cancer sites, the only exception being thyroid cancer, which was confirmed to be more frequent in females [19,20]. Globally, thyroid cancer in women had age-standardized incidence rates three times higher than in men (10.1 per 100,000 person-years and 3.1 per 100,000 person-years) [6]. However, the mortality rates were similar (0.5 per 100,000 person-years in women and 0.3 per 100,000 in men), [6]. A study by LeClair et al. reported that in the United States women were four times more likely than men to be diagnosed with small papillary thyroid cancers confined to the thyroid, suggesting that the gender disparity in thyroid cancer diagnosis is more evident in low-risk small papillary tumours [21]. A dramatic increase in thyroid cancer incidence was observed in Italy between 1998 and 2012, largely attributable to overdiagnosis resulting from the enhanced application of diagnostic imaging and improved detection of subclinical disease [20]. Differences in thyroid cancer incidence between men and women may be explained by variations in healthcare access and utilization, as demonstrated in other countries where widespread screening significantly increased the number of diagnosed cases [22]. Biological factors (hormonal, genetic, and epigenetic) and the role of the immune system might contribute marginally [23].

Of interest, when sex-specific cancers and breast cancer were excluded from the analysis of M/F IRRs for all cancer sites, the overall M/F IRR increased significantly, confirming the epidemiological impact of breast cancer on the Italian female population [24]. Moreover, breast cancer played an important role in the cancer incidence of the 0–49-year age group: when it was excluded along with sex-specific sites, the M/F IRR increased, bringing the female cancer rates closer to those of males.

As expected, the incidence of tobacco-related cancers, such as those involving the respiratory tract, was significantly higher in males than females. Likewise, the incidence of work-related cancers, e.g., mesothelioma, was confirmed to be higher in males [25]. With regard to bladder cancer, the role of tobacco should be taken into account [26], although differences in incidence may also be due to the different metabolism of carcinogenic substances and gender differences in the timeliness and completeness of haematuria evaluation [27,28].

New cases of liver and intrahepatic bile duct cancer occurred more

Table 3
Age-adjusted male-to-female incidence rate ratios (M/F IRR) for selected cancer sites by age groups (0–49, 50–69, 70 +) and macro-areas (North, Centre, South & Islands) in Italy. AIRTUM pool, period of diagnosis 2013–2017.

Macro-area	Tumour site	Age group					
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Oral cavity and pharynx**	1.92	(1.68–2.19)	2.90	(2.73–3.09)	2.23	(2.1–2.37)
Centre		2.00	(1.69–2.39)	2.64	(2.41–2.89)	1.98	(1.81–2.18)
South & Islands		2.05	(1.77–2.37)	2.97	(2.73–3.23)	1.80	(1.64–1.98)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Oesophagus**	3.41	(2.39–4.94)	4.44	(3.96–5)	3.24	(2.98–3.52)
Centre		4.51	(2.39–9.06)	3.94	(3.27–4.78)	2.96	(2.59–3.4)
South & Islands		5.58	(3.38–9.66)	4.12	(3.41–4.99)	3.12	(2.65–3.69)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Stomach**	1.35	(1.18–1.54)	2.07	(1.96–2.18)	1.98	(1.92–2.05)
Centre		1.16	(0.99–1.37)	1.90	(1.78–2.03)	1.92	(1.84–2)
South & Islands		1.20	(1.04–1.38)	1.84	(1.74–1.96)	1.94	(1.85–2.03)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Larynx**	5.82	(4.04–8.57)	7.63	(6.82–8.55)	10.60	(9.47–11.89)
Centre		4.24	(2.84–6.48)	7.18	(6.27–8.26)	10.80	(9.27–12.65)
South & Islands		5.12	(3.81–6.97)	8.02	(7.13–9.04)	12.59	(10.73–14.86)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Colon-rectum**	1.01	(0.94–1.08)	1.48	(1.44–1.52)	1.70	(1.67–1.73)
Centre		0.98	(0.9–1.06)	1.41	(1.37–1.46)	1.65	(1.61–1.69)
South & Islands		0.94	(0.87–1.01)	1.50	(1.46–1.55)	1.67	(1.64–1.71)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Colon**	0.96	(0.88–1.04)	1.44	(1.4–1.49)	1.65	(1.62–1.69)
Centre		0.89	(0.8–0.99)	1.39	(1.33–1.44)	1.58	(1.54–1.63)
South & Islands		0.85	(0.78–0.94)	1.42	(1.37–1.47)	1.60	(1.56–1.65)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Rectum**	1.13	(1–1.27)	1.57	(1.49–1.64)	1.87	(1.79–1.94)
Centre		1.18	(1.02–1.37)	1.47	(1.38–1.55)	1.87	(1.78–1.96)
South & Islands		1.13	(0.99–1.29)	1.69	(1.61–1.78)	1.86	(1.78–1.95)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Liver and intrahepatic bile ducts**	3.12	(2.64–3.71)	4.46	(4.2–4.74)	2.60	(2.51–2.7)
Centre		2.49	(2–3.12)	4.19	(3.84–4.58)	2.30	(2.18–2.44)
South & Islands		3.85	(3.15–4.74)	3.56	(3.34–3.8)	2.18	(2.08–2.28)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Gallbladder**	1.14	(0.82–1.6)	1.12	(1.02–1.23)	1.27	(1.2–1.34)
Centre		1.35	(0.89–2.06)	1.17	(1.04–1.32)	1.29	(1.2–1.39)
South & Islands		1.29	(0.92–1.79)	1.09	(0.99–1.2)	1.17	(1.09–1.24)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Pancreas**	1.20	(1.03–1.39)	1.52	(1.45–1.6)	1.19	(1.15–1.23)
Centre		1.15	(0.96–1.38)	1.34	(1.26–1.43)	1.18	(1.13–1.24)
South & Islands		1.30	(1.1–1.53)	1.40	(1.32–1.49)	1.15	(1.1–1.21)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Lung and bronchus**	1.16	(1.06–1.28)	2.05	(1.99–2.11)	3.35	(3.28–3.43)
Centre		1.13	(1.02–1.26)	1.89	(1.83–1.95)	3.28	(3.19–3.37)
South & Islands		1.32	(1.2–1.46)	2.90	(2.8–2.99)	5.32	(5.16–5.49)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Bone and joints**	1.36	(1.14–1.62)	1.19	(0.95–1.48)	1.51	(1.2–1.92)
Centre		1.29	(1.05–1.58)	1.08	(0.82–1.42)	1.40	(1.05–1.86)
South & Islands		1.11	(0.92–1.34)	1.38	(1.05–1.8)	1.72	(1.3–2.29)
		0–49		**50–69**		**70 +**	

(continued on next page)

Table 3 (*continued*)

Macro-area	Tumour site	Age group					
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Melanoma of the skin**	0.75	(0.72–0.79)	1.35	(1.29–1.41)	2.09	(1.99–2.19)
Centre		0.77	(0.73–0.82)	1.33	(1.26–1.41)	1.97	(1.86–2.09)
South & Islands		0.74	(0.69–0.79)	1.36	(1.28–1.45)	1.86	(1.73–2)
14	**Mesothelioma**	**0–49**		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North		1.19	(0.71–2.02)	3.35	(2.89–3.89)	3.43	(3.14–3.75)
Centre		0.56	(0.23–1.32)	3.20	(2.44–4.24)	4.53	(3.78–5.47)
South & Islands		1.69	(0.89–3.29)	4.43	(3.6–5.49)	4.62	(3.88–5.52)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Kaposi sarcoma**	7.91	(4.7–14.08)	8.27	(5.48–12.97)	2.93	(2.46–3.5)
Centre		15.99	(7.23–40.94)	8.04	(4.66–14.86)	2.77	(2.06–3.75)
South & Islands		13.78	(6.71–32.79)	3.15	(2.48–4.04)	2.27	(1.99–2.59)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Soft tissue**	1.13	(0.98–1.31)	1.60	(1.42–1.81)	2.01	(1.81–2.23)
Centre		1.26	(1.04–1.52)	1.32	(1.14–1.54)	1.66	(1.45–1.9)
South & Islands		1.31	(1.12–1.53)	1.37	(1.2–1.57)	1.89	(1.65–2.17)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Kidney**	2.33	(2.11–2.58)	2.53	(2.41–2.66)	2.30	(2.21–2.41)
Centre		1.81	(1.61–2.04)	2.39	(2.24–2.54)	2.21	(2.09–2.34)
South & Islands		2.02	(1.81–2.25)	2.28	(2.14–2.43)	2.13	(1.98–2.28)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Kidney and renal pelvis**	2.27	(2.06–2.51)	2.55	(2.44–2.67)	2.39	(2.3–2.49)
Centre		1.85	(1.65–2.08)	2.44	(2.31–2.59)	2.40	(2.28–2.52)
South & Islands		2.04	(1.83–2.28)	2.40	(2.26–2.54)	2.27	(2.14–2.42)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Ureter and other urinary organs**	1.38	(0.89–2.15)	2.75	(2.39–3.17)	2.82	(2.57–3.09)
Centre		3.79	(1.78–8.62)	2.91	(2.46–3.46)	3.28	(2.92–3.7)
South & Islands		2.91	(1.57–5.65)	3.38	(2.83–4.05)	2.86	(2.51–3.27)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Urinary bladder**	3.19	(2.84–3.6)	4.32	(4.14–4.5)	5.50	(5.34–5.67)
Centre		3.23	(2.8–3.72)	4.15	(3.95–4.37)	5.91	(5.68–6.14)
South & Islands		3.34	(2.98–3.76)	5.22	(4.98–5.46)	6.68	(6.43–6.94)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**CNS**	1.42	(1.29–1.56)	1.60	(1.49–1.71)	1.53	(1.44–1.63)
Centre		1.33	(1.18–1.5)	1.52	(1.4–1.66)	1.47	(1.36–1.6)
South & Islands		1.38	(1.24–1.53)	1.71	(1.58–1.85)	1.39	(1.28–1.51)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Thyroid**	0.28	(0.27–0.3)	0.41	(0.39–0.43)	0.56	(0.52–0.62)
Centre		0.29	(0.27–0.31)	0.46	(0.43–0.48)	0.66	(0.59–0.73)
South & Islands		0.30	(0.28–0.31)	0.41	(0.39–0.43)	0.62	(0.55–0.71)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Hodgkin lymphoma**	1.01	(0.93–1.1)	1.67	(1.44–1.93)	1.59	(1.34–1.9)
Centre		0.97	(0.87–1.09)	1.63	(1.36–1.96)	1.65	(1.33–2.05)
South & Islands		0.99	(0.91–1.08)	1.78	(1.5–2.11)	1.53	(1.2–1.95)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Non-Hodgkin lymphoma**	1.30	(1.5–0)	1.29	(1.41–0)	1.41	(1.53–0)
Centre		1.31	(1.58–0)	1.30	(1.46–0)	1.51	(1.67–0)
South & Islands		1.23	(1.46–0)	1.29	(1.44–0)	1.44	(1.61–0)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Multiple myeloma**	1.30	(1.11–1.53)	1.27	(1.19–1.36)	1.46	(1.39–1.54)

(*continued on next page*)

Table 3 (*continued*)

Macro-area	Tumour site	Age group					
		0–49		**50–69**		**70 +**	
Centre		1.29	(1.07–1.56)	1.28	(1.18–1.39)	1.46	(1.37–1.56)
South & Islands		1.18	(0.99–1.42)	1.31	(1.22–1.42)	1.49	(1.4–1.6)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Acute lymphocytic leukaemia**	1.36	(1.18–1.57)	1.08	(0.82–1.43)	1.50	(1.12–2.01)
Centre		1.25	(1.03–1.5)	1.32	(0.9–1.95)	1.14	(0.8–1.64)
South & Islands		1.40	(1.2–1.63)	1.00	(0.72–1.38)	1.63	(1.12–2.38)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Chronic lymphocytic leukaemia**	1.80	(1.28–2.54)	1.87	(1.66–2.1)	1.89	(1.74–2.05)
Centre		2.14	(1.39–3.34)	2.16	(1.85–2.54)	2.00	(1.79–2.24)
South & Islands		1.67	(1.21–2.33)	1.78	(1.58–2.01)	1.90	(1.71–2.11)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Acute myeloid leukaemia**	1.09	(0.91–1.31)	1.34	(1.19–1.52)	1.80	(1.64–1.97)
Centre		0.96	(0.79–1.18)	1.29	(1.12–1.48)	1.67	(1.5–1.85)
South & Islands		1.05	(0.88–1.25)	1.30	(1.14–1.49)	1.73	(1.55–1.93)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Chronic myeloid leukaemia**	1.62	(1.25–2.09)	1.86	(1.52–2.29)	2.25	(1.88–2.7)
Centre		1.75	(1.18–2.63)	1.68	(1.24–2.29)	2.26	(1.8–2.84)
South & Islands		1.30	(1.01–1.68)	1.46	(1.2–1.79)	1.56	(1.27–1.91)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Leukaemia**	1.39	(1.28–1.51)	1.66	(1.55–1.77)	1.94	(1.85–2.03)
Centre		1.30	(1.17–1.45)	1.71	(1.58–1.86)	1.75	(1.65–1.85)
South & Islands		1.31	(1.2–1.43)	1.56	(1.45–1.67)	1.79	(1.69–1.9)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**Anal canal and anorectum**	0.93	(0.67–1.28)	0.68	(0.58–0.79)	0.80	(0.69–0.92)
Centre		0.98	(0.67–1.42)	0.58	(0.49–0.7)	0.74	(0.61–0.9)
South & Islands		1.04	(0.64–1.7)	1.04	(0.83–1.3)	0.93	(0.75–1.15)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**All cancer sites**	0.58	(0.57–0.59)	1.24	(1.23–1.25)	1.84	(1.83–1.85)
Centre		0.55	(0.54–0.56)	1.17	(1.16–1.18)	1.86	(1.84–1.88)
South & Islands		0.58	(0.57–0.59)	1.31	(1.29–1.32)	2.01	(1.99–2.03)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**All cancer sites except sex-specific**	0.53	(0.52–0.54)	1.07	(1.06–1.08)	1.64	(1.62–1.65)
Centre		0.53	(0.52–0.54)	1.06	(1.04–1.07)	1.67	(1.65–1.69)
South & Islands		0.55	(0.54–0.56)	1.24	(1.22–1.25)	1.80	(1.79–1.82)
		0–49		**50–69**		**70 +**	
		M/F IRR	95%CI	M/F IRR	95%CI	M/F IRR	95%CI
North	**All cancer sites except sex-specific and breast**	0.98	(0.96–1)	1.86	(1.84–1.88)	2.22	(2.2–2.24)
Centre		0.89	(0.87–0.91)	1.72	(1.7–1.75)	2.19	(2.17–2.22)
South & Islands		0.94	(0.92–0.96)	1.98	(1.95–2)	2.36	(2.34–2.39)

frequently in men, probably related to HBV and HCV infections and alcohol consumption, while oestrogens may have played a protective role in women [29,30]. With regard to gallbladder cancer, epidemiological studies have identified striking geographic and ethnic disparities, and a marked predominance of women over men worldwide [31]. In our analysis, however, gallbladder cancer was more prevalent among men in all three geographical areas, suggesting that we may be facing an epidemiological transition towards malignancies associated with metabolic dysfunction, obesity, and other contemporary risk factors (for example, genetic predisposition and exposure to environmental agents) [32].

Most of the exposures underlying variations in M/F IRR remain to be clarified and are speculative for many of the remaining tumour sites. Additionally, examining the differences in M/F IRRs between tumour sites in different age groups and geographical areas provided insights into cancer pathogenesis theories.

Our findings confirmed a clear male predominance in the incidence of several types of cancer, with statistically significant differences across the Italian regions. The geographical variations – which were most evident for cancers of the larynx, lung, bladder, liver, and certain haematological malignancies – reflected the complex interaction between behavioural, environmental, occupational, and sociocultural factors [33]. A more pronounced gender gap was observed in Southern Italy, particularly for non-sex-specific cancers, compared to the North and Centre areas. This pattern suggests that, although men's and women's lifestyles have gradually converged over recent decades, substantial differences persist in the distribution of risk factors between the sexes and among different areas of the country.

Table 4
Age-standardized five-year net survival (NS) rates and corresponding 95% confidence intervals (CIs) by cancer, gender, and geographical macro-area (North-Centre versus South & Islands). AIRTUM pool, period of diagnosis 2013–2017.

	MALES						FEMALES					
	NORTH-CENTRE			SOUTH-ISLANDS			NORTH-CENTRE			SOUTH-ISLANDS		
Cancer site	5-year NS	95%CI		5-year NS	95%CI		5-year NS	95%CI		5-year NS	95%CI	
All sites	64.0	63.8	64.2	58.1	57.7	58.5	68.3	68.0	68.5	63.7	63.3	64.1
Upper aerodigestive tract	49.2	47.7	50.6	42.6	39.8	45.5	56.6	54.7	58.5	52.6	48.9	56.3
Stomach	31.2	30.1	32.2	23.7	22.1	25.3	35.7	34.4	37.1	27.9	25.9	30.0
Colon-rectum	67.2	66.5	67.8	62.1	61.1	63.1	67.3	66.7	68.0	62.7	61.7	63.8
Colon	67.6	66.8	68.4	62.4	61.2	63.7	67.5	66.7	68.3	63.1	61.9	64.3
Rectum	63.6	62.4	64.8	59.8	58.0	61.6	64.7	63.5	66.0	60.6	58.7	62.5
Liver	27.4	26.4	28.3	22.4	20.8	23.9	24.4	22.8	26.0	23.7	21.2	26.1
Pancreas	12.1	11.3	13.0	9.0	7.8	10.2	13.1	12.1	14.0	11.7	10.3	13.1
Larynx	68.2	66.4	69.9	67.9	65.2	70.5	66.2	62.0	70.4	62.8	55.5	70.0
Lung	19.2	18.7	19.8	15.5	14.8	16.3	24.7	23.9	25.4	20.7	19.5	21.9
Skin melanoma	87.9	87.2	88.7	83.2	81.6	84.9	90.3	89.6	91.0	84.6	82.9	86.3
Kidney	75.5	74.5	76.5	69.6	67.5	71.8	72.6	71.4	73.9	70.9	68.4	73.4
Bladder	82.6	82.0	83.1	78.9	78.0	79.8	77.8	76.7	78.8	75.7	73.9	77.5
Urinary tract	60.7	57.9	63.4	54.5	49.6	59.3	55.6	51.7	59.5	59.1	52.4	65.8
Thyroid	91.0	89.8	92.3	89.0	86.6	91.3	94.8	94.2	95.5	92.7	91.3	94.1
Central nervous system	24.1	22.7	25.5	23.9	21.7	26.1	29.4	27.7	31.1	26.4	23.7	29.0
Leukaemia	51.1	49.8	52.4	47.1	45.0	49.2	49.2	47.7	50.7	45.0	42.6	47.3
Hodgkin lymphoma	86.4	84.8	87.9	81.6	78.9	84.2	88.7	87.3	90.1	87.5	84.7	90.2
Non-Hodgkin lymphoma	68.7	67.6	69.7	60.6	58.7	62.6	71.5	70.5	72.5	63.6	61.6	65.6
Multiple myeloma	59.7	58.2	61.3	54.2	51.6	56.8	60.9	59.4	62.3	56.6	54.0	59.2

Lung and laryngeal cancers, which show the most evident male predominance in the South, mirror the long-standing pattern of a higher smoking prevalence among men in this area and a delayed increase in smoking among women [34]. In addition, possible underdiagnosis among women – linked to lower risk awareness and later access to diagnostic services – may have further contributed to the observed gender imbalance in respiratory tract cancer incidence [35].

A different trend emerged for liver cancer, where the male predominance was more marked in the North. This finding may be related to the higher frequency of chronic liver diseases in men, often associated with alcohol use, metabolic disorders, and non-alcoholic fatty liver disease, which are more widespread in the northern regions of Italy [36]. In contrast, the greater burden of chronic viral hepatitis infections in the South has led to a more balanced distribution of liver cancer between the sexes. For mesothelioma, the higher male predominance observed in Southern Italy might seem unexpected, considering the historical concentration of asbestos exposure in the industrial areas of the North. However, this pattern is consistent with the lower incidence among women in the South, where women have traditionally been less involved in high-risk occupational sectors such as shipbuilding, construction, and mechanical industries [37]. This suggests that a stronger occupational segregation may have contributed to the observed difference.

Bladder cancer also showed a greater gender imbalance in the South than in the rest of the country. This is likely related to the persistence of male-dominated occupational exposures – such as those involving aromatic amines and polycyclic hydrocarbons – combined with a higher prevalence of smoking and historically weaker environmental regulations [38]. These findings underline the importance of reinforcing occupational health surveillance in high-risk industries and promoting prevention policies that are both gender and region specific.

The lower male incidence predominance observed for Kaposi sarcoma in the South can be attributed to differences in the prevalence of HIV infection and in the extent of screening and treatment programmes, which have traditionally been more widespread in Central and Northern Italy [39]. This evidence highlights the role of social and healthcare determinants, in addition to biological ones, in shaping gender disparities in cancer incidence.

The greater incidence of haematological malignancies found in males from both Northern and Central Italy, particularly chronic myeloid leukaemia, may reflect the influence of environmental and industrial exposure to carcinogens (benzene, solvents, etc.) as well as regional differences in diagnostic and registry capacity [40].

The analysis of M/F IRRs provided insights into the evolving nature of gender differences in cancer epidemiology. The incidence of AIDS-defining cancers, such as Kaposi sarcoma and non-Hodgkin lymphomas, was higher in males in all macro-areas and age classes [41]. Anal cancer showed a female incidence predominance in the 50–69 and >70 age groups in the Northern and Central areas, a finding consistent with the aetiological role of human papillomavirus in combination with HIV co-infection and a history of cervical or vulvar high-grade squamous epithelial lesions or cancer [42].

A clear female cancer incidence predominance was identified in the youngest age group (0–49 years) for several sites, including colon cancer and melanoma across all geographical macro-areas, acute myeloid leukaemia in the Central area, and Hodgkin lymphoma in both the Central and South & Islands areas. These findings are consistent with previous evidence indicating that hormonal influences, lifestyle factors, and genetic susceptibility may contribute to a greater vulnerability in younger women [43]. Skin melanoma was the most frequent cancer among females aged 25–29 and those under 40 overall, with women exhibiting a higher incidence of melanoma than men. This suggests that its aetiology may be partly related to excessive and repeated exposure to unnaturally high levels of ultraviolet (UV) A light from UVA-rich lamps, along with a biological gender predisposition [44].

In our analysis we found a female incidence predominance at younger ages not only for melanoma but also Hodgkin lymphoma and colon cancer, as previously reported [45]. Hodgkin lymphoma, a cancer that has been associated not only with genetic susceptibility but also environmental factors, particularly infection with Epstein-Barr virus, showed a higher incidence among young women [46]. A rise in the incidence of lung cancer with age was observed among women across macro-areas; however, it was paralleled by a similar rise in men, preventing an M/F IRR reduction. This trend reflected the historical convergence of smoking patterns, particularly among post-WWII female cohorts [47].

Mesothelioma showed significantly higher M/F IRRs among men aged 50–69 and >70 years in all macro-areas, consistent with occupational asbestos exposure. A similar male predominance was observed for bladder and laryngeal cancers, reflecting cumulative lifestyle and occupational risks, notably tobacco and alcohol use. Skin melanoma presented an age-related inversion: women under 50 showed a higher incidence, while in the older age groups the incidence was higher in men, likely reflecting occupational UV exposure and differences in preventive screening [48].

When all cancer sites were considered, the female cancer incidence predominance at younger ages shifted progressively to a male predominance in older groups, persisting even after the exclusion of sex-specific and breast cancers. These findings underscored that gender differences in cancer incidence are dynamic, shaped by biological, behavioural, and environmental factors across the lifespan.

The geographical disparities highlighted in the five-year age-standardized net survival suggested complex and sometimes contrasting patterns between men and women. In our analyses, men consistently showed lower survival rates for all cancer sites combined compared to women, both in the North-Centre and South & Islands macro-areas.

Among males, survival was higher in the North-Centre macro-area overall, with advantages observed for cancers of the stomach, pancreas, lung, liver, colon-rectum, melanoma, kidney and bladder, upper aerodigestive tract, leukaemia, Hodgkin lymphoma, non-Hodgkin lymphoma, and myeloma. These findings may reflect differences in diagnostic intensity, accessibility of treatment, or possibly lifestyle-related risk factors that influence tumour biology at presentation [49]. In the North-Centre macro-area we also documented clear advantages for liver, kidney, and urinary tract cancers, which could be associated with earlier detection or greater availability of specialized care in these areas [50,51].

In females, the geographical discrepancies were even more pronounced, with women in the North-Centre macro-area showing better survival outcomes than those in the South & Islands for many cancer sites, including stomach, colorectal, lung, kidney, urinary tract, and thyroid cancers as well as skin melanoma and haematological malignancies (excluding Hodgkin lymphoma) [52]. These findings highlight the specific disadvantages faced by women in the South & Islands macro-area, indicating inequalities in access to oncology services and differences in health behaviours [53]. Gender-targeted interventions are required to foster early diagnosis, improve equity of care, and reduce the gaps between different communities [54].

Multiple hypotheses have been put forward to account for the female advantage in survival. A key factor is the gender-specific distribution of the most common cancers, breast cancer in women and lung cancer in men. These diseases differ substantially in prognosis, with breast cancer generally being associated with much better outcomes [12]. This factor alone might partially account for the higher overall cancer mortality observed in men. Other contributing elements include biological and hormonal aspects, as well as lifestyle choices and behavioural patterns [43]. Historically, men have been more frequently exposed to environmental risk factors such as tobacco use, alcohol consumption, and UV radiation [6]. In addition, they have often worked in occupations associated with greater exposure to carcinogens. Moreover, data from surveys like PASSI indicate that Italian men tend to consume fewer fruits and vegetables and drink more alcohol than women [47].

The main strengths of this study included the use of the high-quality population-based AIRTUM registry database and the adoption of the M/F IRR indicator, which is less influenced by variations in diagnostic practices or coding. A key limitation, however, is the lack of adjustment for individual confounders such as smoking, BMI, and occupation, which may have contributed to the differences in cancer incidence between the two sexes [17].

5. Conclusions

Our findings, confirming the gender differences in cancer survival in Italy, with women showing higher five-year survival rates than men, are consistent with European figures [8]. The female survival advantage may be partly explained by cancer type distribution, biological, and hormonal factors as well as greater female participation in screening programmes, although it was not uniform across tumour sites, as men had better outcomes in lung and urinary tract cancers in the South & Islands macro-area [55]. The highlighted geographical disparities indicated potential differences in healthcare access, lifestyle, and environmental exposure, while minimal variations in M/F IRRs across regions suggested an additional influence of genetic and immunological factors [56,57]. Overall, despite improvements in survival, the persisting gender- and region-related gradients suggested the need for targeted prevention, equitable early detection, and uniform access to quality treatment [58].

CRediT authorship contribution statement

Maria Teresa Pesce: Visualization, Validation, Project administration, Methodology, Formal analysis, Data curation. **Viviana Perotti:** Data curation. **Santo Fruscione:** Writing – review & editing, Writing – original draft. **Rosalba Amodio:** Writing – original draft, Validation. **Fabrizio Stracci:** Writing – review & editing, Writing – original draft, Supervision, Project administration, Conceptualization. **Paolo Contiero:** Writing – review & editing, Writing – original draft, Supervision, Conceptualization. **Sabrina Fabiano:** Writing – original draft, Validation, Software, Methodology, Formal analysis, Data curation. **Maurizio Zarcone:** Methodology, Formal analysis, Data curation. **Andrea Tittarelli:** Methodology, Formal analysis, Data curation. **Giovanna Tagliabue:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Mazzucco Walter:** Writing – review & editing, Writing – original draft, Project administration, Conceptualization.

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Declaration of Competing Interest

I am writing on behalf of the Authors and the AIRTUM WG. With regard to the manuscript entitled "**Gender differences in cancer epidemiology in Italy, 2013–2017**", the declarations of interest is: none.

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