

# Cancer trends in women in Italy

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**Summary.** Cancer trends in Italy are traced and studied through population-based Cancer Registries (CRs): data is used to support the planning of health interventions but, so far, attention to gender differences has been relatively limited. The aim of this work is to describe time trends in cancer incidence and the prevalence of the main risk and protective factors in females in Italy, by geographic areas. The data produced and published by the CRs and the National Health Interview Survey (The Italian National Institute of Statistics – Istat) were analyzed by sex. In Italy, an estimated 377,000 new cancer cases were diagnosed in 2020 (52% in males and 48% in females), while 173,000 deaths from malignant cancer (55% in males and 45% in females) were registered. Breast cancer alone accounts for 30% of all neoplasms in women, followed by colorectal cancer (11%) and lung cancer (7%). Overall, the 5-year female survival in all three cancers was 63%; however, in older women and in those living in the Southern regions this percentage was lower for all three cancers. In women, the trend in all cancers was substantially heterogeneous across the Italian regions, with the Southern ones experiencing stable incidence and a slight decrease in mortality, and the Northern ones showing a marked decreasing trend in both incidence and mortality. Obesity and low levels of physical activity are more prevalent among women in the South than in the North, and screening coverage remains lower in the South. The prevalence of smoking is similar in young and middle-aged women throughout Italy, but is lower among older women in the Southern regions. A late implementation of oncological screening and a limited awareness of the most correct lifestyles still constitute health disadvantages for women living in Southern regions.

**Keywords.** Cancer, female, incidence, mortality, risk factors, trend.

## *Andamento temporale delle patologie oncologiche nella popolazione femminile in Italia.*

**Riassunto.** L'andamento temporale delle patologie oncologiche in Italia è tracciato e studiato attraverso i Registri Tumori basati sulla popolazione: i dati sono utilizzati per supportare la pianificazione degli interventi sanitari, ma finora l'attenzione alle differenze di genere è stata relativamente limitata. Lo scopo di questo lavoro è descrivere l'andamento temporale dell'incidenza del cancro e la pre-

valenza dei principali fattori di rischio e di protezione nelle donne in Italia, per aree geografiche. I dati prodotti e pubblicati dai Registri Tumori e dall'Istituto Nazionale di Statistica sono stati analizzati per sesso. In Italia si stima che nel 2020 siano stati diagnosticati 377.000 nuovi casi di cancro (52% nei maschi e 48% nelle femmine), mentre sono stati registrati 173.000 decessi per cancro maligno (55% nei maschi e 45% nelle femmine). Il cancro al seno da solo rappresenta il 30% di tutte le neoplasie nelle donne, seguito dal cancro del colon-retto (11%) e dal cancro del polmone (7%). Nel complesso, la sopravvivenza femminile a 5 anni in tutti e tre i tumori è stata del 63%; tuttavia, nelle donne anziane e in quelle che vivono nelle regioni meridionali questa percentuale era inferiore per tutti e tre i tumori. Nelle donne l'andamento di tutti i tumori è stato sostanzialmente eterogeneo nelle regioni italiane, con quelle meridionali che hanno registrato un'incidenza stabile e una leggera diminuzione della mortalità, e quelle settentrionali che hanno mostrato un marcato trend decrescente sia dell'incidenza che della mortalità. L'obesità e i bassi livelli di attività fisica sono più diffusi tra le donne al Sud che al Nord e la copertura dello screening rimane più bassa al Sud. La prevalenza del fumo è simile nelle donne giovani e di mezza età in tutta Italia, ma è inferiore tra le donne anziane delle regioni meridionali. Un'implementazione tardiva dello screening oncologico e una scarsa consapevolezza degli stili di vita più corretti costituiscono ancora svantaggi per la salute delle donne che vivono nelle regioni meridionali.

**Parole chiave.** Cancro, femmina, incidenza, mortalità, fattore di rischio, trend.

## Introduction and objectives

Cancer trends in Italy are tracked and studied through population-based Cancer Registries (CRs), which systematically record neoplasms occurring in a given population.<sup>1</sup> CRs use standard national and international rules for the registration of cancers, which makes the data comparable at global level.<sup>2,3</sup> Incidence, mortality, survival and prevalence are the main oncological indicators that make it possible to describe the disease, plan health interventions and assess the impact of cancer.

Although CRs data are presented annually to support the planning of health interventions in Italy,<sup>4</sup> until now the attention to gender differences has mostly been limited to the publication of separate incidence and mortality rates for males and females. In addition, so far cancer registries provide information only on sex at birth.

Studies confirm that the incidence of tumours is higher in males, and that survival is better in females.<sup>5,6</sup> However, the latter continue to be less represented in cancer clinical trials, despite the presence of more serious adverse events, greater toxicity and sometimes poorer response to treatments.<sup>7</sup>

In Italy, cancer incidence and mortality have shown significant differences between macro-regions, with the Southern ones at a lower risk of cancer, particularly among women. This difference has been explained by a combination of behavioural and environmental factors favoring women living in South Italy: a diet based on vegetables and olive oil – i.e., the Mediterranean diet<sup>8,9</sup> – instead of butter and other animal fats, a lower prevalence of smoking, higher viviparity, and lower levels of air pollution and occupational exposure. Some of these advantages have been observed and measured,<sup>10,11</sup> while others are only hypotheses, for example in the case of occupational exposure. On the other hand, however, health, prevention and care services in South Italy have historically been penalized by organizational problems.<sup>12,13</sup>

Recently, lifestyle has rapidly changed among the Italian population, particularly in terms of diet and physical activity. The prevalence of obesity has increased over recent decades,<sup>14</sup> while opposite trends occurred in smoking among both sexes.<sup>15</sup> Therefore, women's health status has probably changed across geographic areas as well.

The aim of this work is to describe – by age and geographic area – the trends in tumour incidence, lifestyle and adherence to cancer screening among women in Italy.

## Materials and methods

### Study design

Incidence data was taken from the essay *I numeri del cancro 2020*, which reports – both in absolute numbers and percentages – the estimates of the most frequent cancers in Italy. To estimate the expected number of cancer cases at national level in 2020, a method based on the calculation of the trends for the periods available in the AIRTUM database was used.<sup>4</sup> For the purposes of this study, the Country was divided into 4 macro-regions based on the criteria defined by the Italian National Institute of Statistics (Istat): Northwest (Piemonte, Valle d'Aosta, Lombardia, Liguria), Northeast (Trentino-Alto Adige, Veneto, Friuli-Venezia Giulia, Emilia Romagna), Centre (Toscana,

Umbria, Lazio) and South and Islands (Campania, Puglia, Basilicata, Calabria, Sicilia, Sardegna).\*

For each of these four macro-regions, incidence rates – standardized on the European population in 2013 – were calculated by year of diagnosis, cancer site, sex and age group (0-49, 50-59 and 70+). To calculate the trends, the incidence for all the years from 2003 to 2014 for each CR were used.<sup>16</sup> For each model, the trend was expressed as the annual percentage change (APC), with its corresponding 95% confidence interval (CI).

In addition, thanks to the National Health Interview Survey (conducted by Istat),<sup>17</sup> the distribution by macro-region of the main risk factors associated with the onset of cancer – i.e., smoking, physical activity and overweight and obesity – is reported. Screening test uptake data were taken from the PASSI health interview<sup>18</sup>.

Survival data, taken from the aforementioned essay, refer to cancers registered in Italy in the period 2005-2009, with a follow-up up to 2014.<sup>19</sup>

## Results

It is estimated that in 2020, in Italy, approximately 377,000 new cases of malignant tumour will be diagnosed: 195,000 (52%) in males and 182,000 (48%) in females (see Appendices).<sup>4</sup> Breast cancer alone accounts for 30% of neoplasms, followed by colorectal cancer (11%) and lung cancer (7%) (Figure 1).

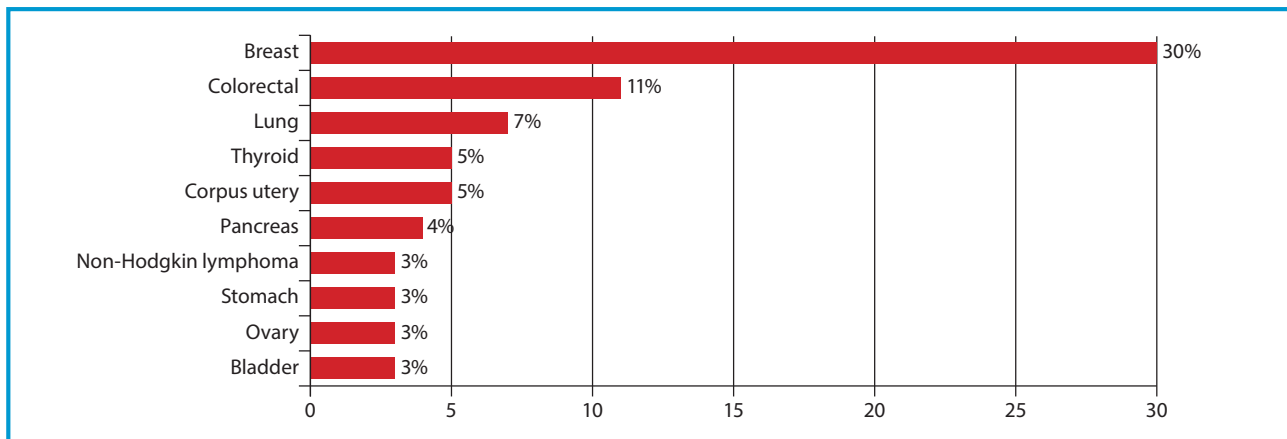
Breast cancer is the most frequent malignancy among females in all age groups, although with different percentages (41% in women <50 years of age *vs* 35% in women aged 50-69 and 22% in women aged 70+). The three age groups vary considerably in terms of frequency for the other cancer sites (Table 1).

Variations in cancer rate are also observed according to the geographic area. In Italy, a North-South gradient is still present: the incidence rate among females is 512, 494 and 423 (standardized per 100,000 residents) in the North, Centre and the South, respectively, although incidence trends are starting to show changes.<sup>4</sup>

In fact, the incidence trend for all sites is decreasing in the North and increasing in the Centre-South. Mortality is decreasing throughout the Centre-North, although the trend now appears to have stabilized, despite having increased in the South until 2007 (Figure 2, Table 2).

For the three most frequent cancer sites, the incidence of breast cancer is stable in the Centre-North and is increasing slightly in the South. Colorectal cancer is decreasing in the North, is stable in the Centre and is in-

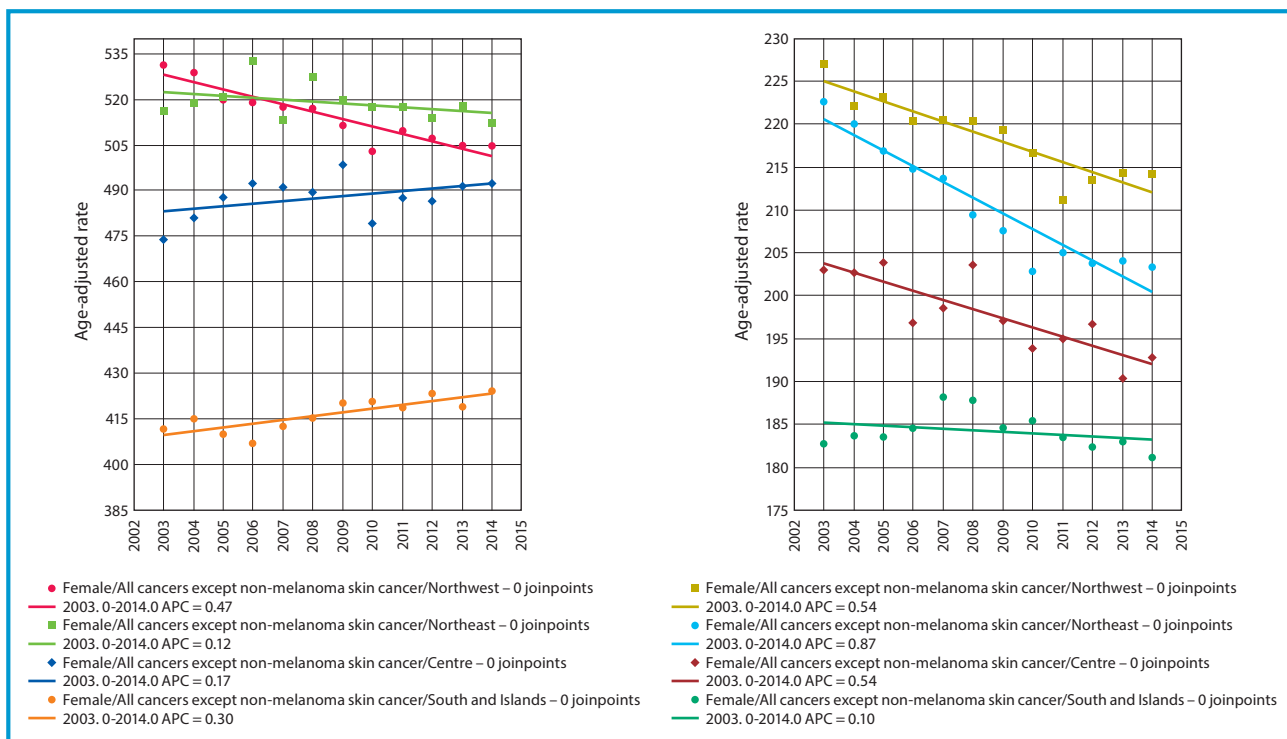
\* Marche, Abruzzo and Molise do not appear in the list above, since they had not activated their Cancer Registries in the years taken into consideration in order to calculate the trend.



**Figure 1.** Italian data estimated for 2020. The 10 most frequent cancers in women (% values out of total, except non-melanoma skin cancer).

**Table 1.** Five leading tumours in terms of frequency and proportion of the total number of incident cases (except skin cancer), by age group

Range	Age		
	0-49	50-69	70+
1 <sup>st</sup>	Breast (41%)	Breast (35%)	Breast (22%)
2 <sup>nd</sup>	Thyroid (15%)	Colorectal (11%)	Colorectal (16%)
3 <sup>rd</sup>	Melanoma (8%)	Endometrium (7%)	Lung (8%)
4 <sup>th</sup>	Colorectal (4%)	Lung (7%)	Pancreas (6%)
5 <sup>th</sup>	Uterine cervix (4%)	Thyroid (5%)	Stomach (5%)



**Figure 2.** Incidence and mortality trends for female cancers in Italy, by macro-region. All cancers except non-melanoma skin cancer.

creasing in the South. Conversely, lung cancer is increasing slightly throughout Italy (Table 2).

Figure 3 and Table 3 illustrate the trends of the main risk factors in Italy according to the geographic area. With regard to smoking (Figure 3), women <50 years of age and those aged 50-69 smoke more than women over 70, with no significant difference between North and South; among older women, those living in the South smoke less.

Overweight and obesity are more frequent in women residing in the Southern regions, where there is also

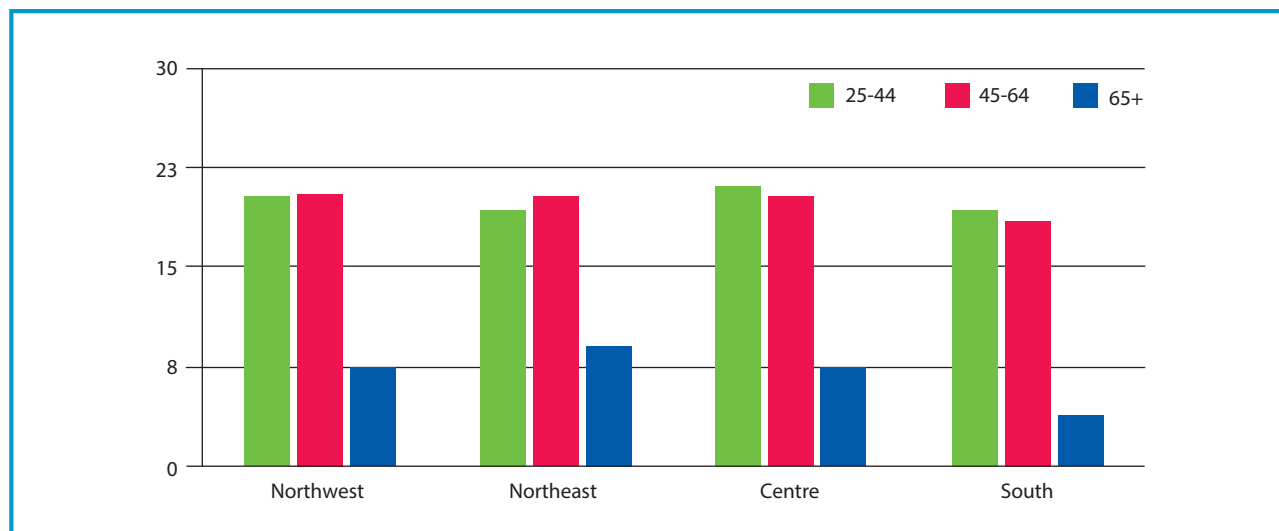
the highest percentage of women who exercise inadequately, while very few practice adequate amounts of physical activity (Table 3). With regard to the coverage of and the participation in cancer screening programs, there remains a profound gap between the women living in the Centre-North and those living in the South, for both breast cancer and colorectal cancer.

Furthermore, there is a considerable difference in the 5-year survival from the diagnosis between northern and Southern regions, the latter appearing to be at a disadvantage (Table 4).

**Table 2.** Variations in the incidence and mortality rates (APC) for female cancers in Italy by macro-region. All cancers (except non-melanoma skin cancer) and the 3 main cancer sites

	Incidence				Mortality			
		Rate	APC	95% CI		Rate	APC	95% CI
All cancers								
Northwest	2003-2014	514.6	-0.5	-0.6;-0.3	2003-2014	218.6	-0.5	-0.7;-0.4
Northeast	2003-2014	519.0	-0.1	-0.3;0.1	2003-2010	213.6	-1.2	-1.3;-1.1
					2010-2014	203.5	-0.3	-0.5;0.0
Centre	2003-2014	487.7	0.2	-0.1;0.4	2003-2014	197.9	-0.5	-0.8;-0.3
South	2003-2014	416.5	0.3	0.2;0.4	2003-2007	184.6	0.7	0.2;1.2
					2007-2014	184.5	-0.5	-0.6;0.3
Breast								
Northwest	2003-2014	161.8	-0.1	-0.3;0.1	2003-2014	39.3	-0.4	-0.9;0.0
Northeast	2003-2014	162.1	0.4	0.0;0.8	2003-2014	35.8	-1.4	-1.8;-1.0
Centre	2003-2014	143.8	0.4	0.1;0.7	2003-2014	32.0	-0.3	-1.1;0.4
South	2003-2006	116.3	-0.9	-2.5;0.8	2007-2014	33.6	-0.1	-0.6;0.4
	2006-2009	118.3	2.0	-1.2;5.4				
	2009-2014	122.7	0.3	-0.4;1.0				
Colorectal								
Northwest	2003-2014	65.3	-2.9	-3.3;-2.5	2003-2014	24.8	-1.5	-2.1;-0.9
Northeast	2003-2014	63.8	-0.9	-1.5;-0.2	2003-2014	24.2	-1.1	-1.5;-0.6
Centre	2003-2014	66.2	-0.6	-1.2;0.1	2003-2014	24.4	-1.0	-1.6;-0.3
South	2003-2014	54.7	0.5	0.2;0.9	2003-2014	23.3	-0.1	-0.5;0.4
Lung								
Northwest	2003-2014	33.5	2.4	2.1;2.7	2003-2014	26.0	0.6	0.2;1.1
Northeast	2003-2014	33.3	1.8	1.3;2.3	2003-2014	26.0	1.0	0.7;1.3
Centre	2003-2007	28.0	3.8	2.0;5.6	2003-2014	23.6	1.8	0.9;2.6
Centre	2007-2014	32.0	1.8	1.1;2.5				
South	2003-2014	19.0	1.8	1.3;2.3	2003-2014	15.6	1.0	0.1;1.8

APC: annual percent change. Data from Marche, Abruzzo and Molise do not appear, since these regions had not activated their Cancer Registries in the years taken into consideration.



**Figure 3.** Istat survey in Italy. Women. Smoking habit in Italy by macro-region and age group.

**Table 3.** Istat Survey in Italy. Women. Percentage values of overweight, obesity and adequate/inadequate physical activity (Istat data). Coverage and participation in screening by macro-region (PASSI data)

	Northwest	Northeast	Centre	South
Overweight	26.4	27.1	27.5	31.6
Obesity	9.9	10.9	10.7	12.7
Inadequate physical activity	83.4	79.5	83.7	90.5
Adequate physical activity	16.6	20.5	16.3	9.5
<b>Breast screening</b>				
Coverage	98		96	59
Participation	62		56	47
<b>Colorectal screening</b>				
Coverage	98		95	44
Participation	50		36	30

**Table 4.** Five-year survival, for all sites and for the main cancer sites, by macro-region. Women. Percentage values. Pooled 2005-2009 data

	Northwest	Northeast	Centre	South
All sites	63	64	63	60
Breast	87	88	87	85
Colorectal	66	67	66	61
Lung	20	19	19	18

## Remarks and analytical discussion of the results

In Italy, a slightly higher incidence of cancer has been confirmed in males versus females, with a M/F ratio of 1.1. In particular, incidence is higher in oesophagus, stomach, colorectal, liver, lung, bladder and haematological cancer, though not in gallbladder and biliary tract, pancreas and thyroid cancer. Similar excesses in males have been confirmed by Kim<sup>5</sup> for colon, stomach, liver and bladder cancer (due to smoking, genetic profile and occupational exposures) and for leukaemia (the risk being probably linked to hormonal factors). The M/F ratio recorded in Italy is comparable to those reported by SEER<sup>6</sup> for liver, gallbladder and thyroid, but is lower for the oesophagus. For the bladder, instead, the situation is different (4.1 in Italy versus 3.4 in SEER). Costa et al. also document how testosterone increases the risk of cancer in males (oesophagus, stomach, colon, bladder and lung), while estrogen and progesterone seem to be protective in females (for oesophagus, stomach, colon and thyroid).<sup>20</sup> Mortality in Italy shows an M/F ratio of 1.2 because cancers with a good prognosis are more represented in females, and women show a better survival rate than men for many sites.

Geographic differences in mortality and in the prevalence of risk factor are diminishing, with the South losing all of its historical advantage in cancer mortality. Both lifestyle changes and the slow implementation of cancer screening programs in the Southern regions have contributed to this loss of advantage in breast cancer mortality, as already noted in a recent analysis of the causes of death.<sup>10</sup> In addition, any advantage in terms of incidence and mortality of colorectal cancer is also decreasing, as shown by the trends in Table 2.

Differences in the organization of healthcare, which can affect early diagnosis and care, are also probably responsible for the differences in survival rates: the Southern regions show a lower survival rate for all causes, and in particular for colorectal and breast cancer.

In general, the lung is the third most frequent cancer site in Italy, in both sexes. Although in recent years the prevalence of smokers has decreased among males and increased among females,<sup>15</sup> the effects of smoking on cancer incidence is still much greater among males. Lung cancer continues to decrease among males and to increase among females; forms of adenocarcinoma are increasing in both sexes, while squamous cell forms are stable in females and decreasing in males.<sup>21</sup> Stapelfeld emphasized that, in terms of lung cancer, for an equal number of cigarettes smoked, females have a 70% higher risk of having squamous cell cancer and a 50% higher risk of adenocarcinoma, possibly due to hormonal factors.<sup>22</sup>

In general, females have fewer cancers than males, and die less from cancer, but are 1.5/1.7 times more likely to show treatment-related adverse events, greater

toxicity and a poorer response to treatments.<sup>7</sup> Moreover, females continue to be underrepresented in clinical trials: a recent study showed that, out of 5,147 patients participating in FDA-approved trials for 17 new drugs in 2018, only 38% were females.<sup>23</sup>

As for primary prevention, females have biological agents associated with cancer (e.g., papillomavirus and HIV in cervical cancer). In addition, smoking is generally not only responsible for lung cancer, but is carcinogenic (albeit with limited evidence) also for breast cancer.<sup>24</sup> Since some drugs, hormone replacement therapy and contraceptives are also risk factors for endometrial, breast, cervical and ovarian cancers – and since alcohol is a certain carcinogen for breast cancer, as well as for colorectal cancer – primary prevention measures should also include recommendations concerning these factors.

It has been estimated that the removal of the behavioural and environmental risk factors would reduce cancer deaths in females in Italy by over 20,000;<sup>25</sup> in particular, the removal of the risk factors would reduce tumours of the larynx by 94%, of the oesophagus by 75%, of the nasopharynx by 73%, of the oral cavity by 72%, of the lung by 68%, of the pharynx by 55% and of the uterus by 42%.

In this work, we report data from several sources: each refers to slightly different time periods, and has different limitations in coverage and accuracy. Italy is not entirely covered by Cancer Registries, and the areas that are covered may not be representative of the entire geographic zone. Behavioural surveillance is based on large national representative samples, but relies on self-reported habits, and desirability biases may affect the comparisons between sexes and between areas. Nevertheless, the trends for the cancer burden reported here are confirmed with regard to both mortality and incidence, because Cancer Registries have independent sources, while behavioural trends are consistent with the two available national health interviews, i.e. the survey conducted by Istat<sup>17</sup> and that conducted by the Italian National Institute of Health (ISS).<sup>18</sup>

### Key messages

- In Italy, breast cancer alone accounts for 30% of tumours in females, followed by colorectal cancer (11%) and lung cancer (7%).
- Breast cancer represents 41% of all tumours in females under 50 years of age, 35% in females aged 50-69 and 22% in females over 70.
- The 5-year survival rate is 63% in females, with significant differences between North, Centre and South.
- Women residing in the South suffer from the greatest disadvantages in terms of primary and secondary prevention.

In conclusion, in Italy women over 70 and those residing in the Southern regions have the greatest disadvantages in terms of primary and secondary prevention. The slow implementation of cancer screening and the lack of awareness of a correct lifestyle result in a disadvantage for women in the regions of Southern Italy.

## Appendices

Number of new cancer cases (total and main sites) estimated for 2020

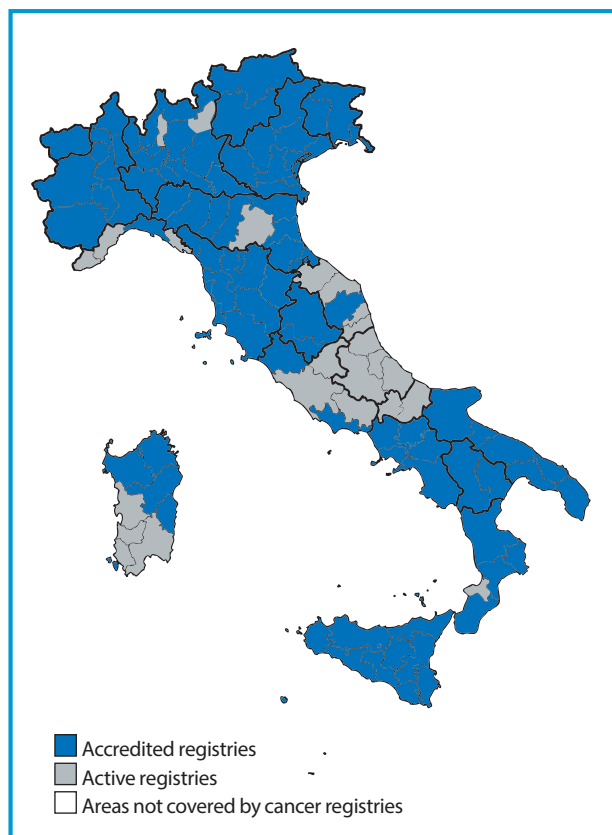
Site	Females	Males
Upper aero-digestive tract <sup>1</sup>	2,580	7,276
Oesophagus	684	1,710
Stomach	6,098	8,458
Colorectal	20,282	23,420
Liver	4,034	8,978
Gallbladder and biliary tract	3,000	2,400
Pancreas	7,416	6,847
Lung	13,328	27,554
Melanoma	6,716	8,147
Breast	54,976	589
Uterine cervix	2,365	
Endometrium	8,335	
Ovary	5,179	
Prostate		36,074
Testicle		2,289
Kidney, urinary tract <sup>2</sup>	4,472	9,049
Bladder <sup>3</sup>	5,015	20,477
Central nervous system	2,589	3,533
Thyroid	9,850	3,333
Hodgkin's lymphoma	929	1,222
Non-Hodgkin lymphoma	6,171	7,011
Myeloma	2,740	3,019
Leukaemia	3,229	4,738
All cancers except skin cancer <sup>4</sup>	181,857	194,754

<sup>1</sup>Upper aero-digestive tract includes tongue, mouth, oropharynx, nasopharynx, hypopharynx, pharynx NAS, larynx.

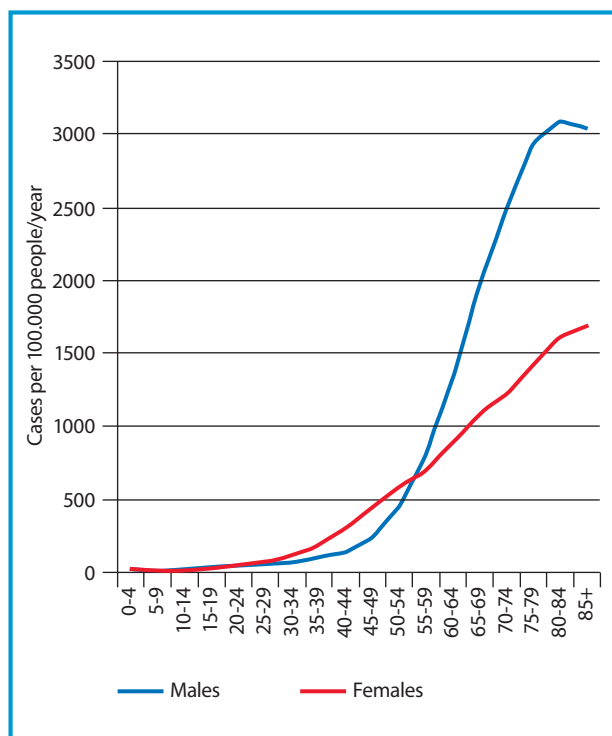
<sup>2</sup>Urinary tract includes pelvis and ureter.

<sup>3</sup>Bladder includes infiltrating and non-infiltrating.

<sup>4</sup>The total number of cases estimated for 2020 was calculated using a statistical model different from that used for each single site.



Areas of Italy covered by population-based Cancer Registries.



Incidence. Age-specific rates (x 100,000) by sex. All tumours except non-melanoma skin cancer.

Number of female cancer patients still alive in 2020, by site and sex	
	<b>Females</b>
All tumours	1,922,086
Upper aero-digestive tract	21,831
Oesophagus	2,014
Stomach	32,033
Colon, rectum and anus	233,245
Liver	8,531
Biliary tract	6,846
Pancreas	10,111
Larynx	6,006
Lung	40,657
Skin melanoma	89,831
Female breast	834,154
Uterus and cervix	51,136
Endometrium	122,553
Ovary	49,807
Prostate	
Testicle	
Kidney and urinary tract	47,151
Bladder	58,608
Brain and nervous central system	29,314
Thyroid	166,914
Hodgkin lymphoma	29,314
Non-Hodgkin lymphoma	73,584
Leukaemia	39,100
Myeloma	17,159

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