Cancer Epidemiology 101 (2026) 103001

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Cancer survival in Italian patients diagnosed between 2008 and 2017

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https://doi.org/10.1016/j.canep.2026.103001
Received 2 December 2025; Received in revised form 14 January 2026; Accepted 17 January 2026
Available online 6 February 2026

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ARTICLE INFO

Keywords:
Population-based cancer registries
Cancer epidemiology
Cancer survival
Geographical disparities
Sex differences

ABSTRACT

As national cancer survival estimates in Italy date back to 2011, we provided updated figures using population-based cancer registries. Analyses by age and sex included 1.418.044 cancers diagnosed between 2013 and 2017 from 34 registries covering 48 million residents. The 2008–2017 period, with 20 registries covering 24 million residents, was used for trends and regional comparisons. Net survival was estimated by Pohar-Perme method with life tables by year, sex, residence and calculated using the international standard distribution. Five-year age-standardized net survival for all cancers combined was 66.7 % in females and 62.2 % in males. Females had better survival than males for most cancers, notably acute lymphatic leukaemia (+9 % points (pp)), upper respiratory/digestive (+9 pp), lung (+6 pp), CNS (+5 pp), and stomach (+4 pp). Males had a higher survival for bladder (+4 pp), kidney (+2 pp), and urinary cancers (+5 pp). Best outcomes (>75 %) were documented for prostate, testicular, breast, endometrial, thyroid, melanoma, Hodgkin lymphoma, bladder, and chronic lymphatic leukaemia. Poorest prognosis (<30 %) was for CNS, liver, lung, pancreas, and acute myeloid leukaemias. Survival was age-dependent, highest in younger and lowest in older patients, with > 40 % points gaps in some haematological cancers. From 2008–2017, net survival arose from 65.7 % to 70.7 % in men and from 69.9 % to 74.1 % in women. Improvements were seen for pancreas, lung, and acute leukaemias, mainly in women, while decreases affected bladder, cervical, chronic lymphatic leukaemia in men. Geographical disparities persisted, with higher survival in Northern-Central Italy (64.0 % for men and 68.3 % for women) than in Southern-Islands (58.1 % for men and 63.7 %, for women). Our findings confirmed a better prognosis for younger patients and females than male patients. Survival has continued to improve over time, even at a higher improving rate in the considered period than the past.

1. Introduction

Survival is a complex indicator of healthcare system quality and efficiency, encompassing diagnostic innovation, access to effective therapies, and adherence to guidelines [1]. Cancer survival can be influenced by multiple factors such as access to prevention, diagnosis, and treatment, as well as the quality of oncological healthcare services [2]. Screening programs and early detection may play also a crucial role in determining longer, and in some cases, truly improved survival, whereas delayed diagnosis is one of the main causes of survival gaps across countries [3]. Differences in survival often reflect variations in healthcare investment, though disparities also exist among countries with similar expenditure levels, suggesting that spending alone is not the only determinant [1].

At the global level, in the period between 2000 and 2014, the five-year survival resulted the highest in high-income countries, with survival trends improving even for aggressive cancers such as liver, pancreas, and lung [4]. In Europe, during the early 2000s, survival rose significantly, especially for prostate, rectal cancer, and non-Hodgkin lymphomas, largely due to advances in screening activities and advances in surgery, and therapies [5]. However, sharp differences remain between Western and Eastern Europe, with the highest observed survival in Nordic, Central, and Southern countries, but considerably lower in Eastern nations, where limited resources and late diagnoses still hinder outcomes [5].

The regular and prompt updating of survival estimates provided by population-based cancer registries (CRs) is of the greatest importance for the evaluation and the planning of health care services [6]. In Italy some organizational criticalities due to differing regional registration frameworks, legal difficulties related to privacy restrictions, and the impact on cancer registration of the recent Covid-19 pandemic, have hindered the optimal functioning of CRs. Accordingly, no national-based survival estimates were up to now available for patients diagnosed after the year 2011 [2], [7], [8]. The latest available systematic survival analysis from the Italian population-based cancer registries have documented continuous survival improvements, from the mid years 1990s to the end of the years 2000s, for most of the considered cancers, but with a persisting gap between different Italian areas, with a north to south negative gradient [9]. Therefore, it is important to investigate to what extent the increasing survival trend can be confirmed over time, and whether geographical disparities were eventually mitigated.

To fill this gap of knowledge, we used data from 34 population-based cancer registries. These registries covered the 84 % of the Italian resident population, being representative of all the geographical areas, while providing updated survival figures on cancer survival in patients diagnosed up to the year 2017, with closure of follow-up at the end of 2022. More in depth, we aimed at providing an overall national picture on the survival of cancer patients, analysed for 27 single cancer entities plus 3 groupings (all malignant cancers, large bowel, and all leukemias), by site, sex, age, period of diagnosis, and geographical area. A series of dedicated data sheets **(**Supplementary Figures**)** for each specific cancer entity, with a more detailed numerical and graphical format and a brief accompanying comment, was also provided.

2. Material and methods

A detailed description of the data considered for the statistical analyses and of the methods used is presented in another paper of this special issue [10]. Briefly, the data collected by population-based cancer registries on 2.807.198 cancer cases diagnosed in patients aged 15–99 between 2008 and 2017 in Italy were accessed. The statistical analyses, conducted by age and sex, were restricted to 1.418.044 cases diagnosed between 2013 and 2017 (Supplementary Table 1), the most recent available period of surveillance provided by 34 cancer registries covering in 2017 a population of 48 million Italian resident inhabitants. Their distribution by cancer site, sex, and age-groups, is reported in

Supplementary Table 1. Males were 53 % of the total sample, with a widely variable proportion, from 88 % of those with larynx to 24 % of those with thyroid cancers. The entire available ten-years period of surveillance, including 20 registries with a covered population of 24 million resident inhabitants, was considered to explore time trends and to estimate conditional survival reported in the Supplementary Figures. The same selection of 20 registries was considered to make geographical comparisons of survival estimates by macro-area (north-central versus southern-islands) for both sexes combined and the quinquennial period 2013–2017. The list of the considered cancers, including site and morphology codes, is available from a companion paper [10]. Malignant cancers only were included, with exception of non-infiltrating bladder cancers. Second and later independent primaries were also included. Instead, Death Certificate Only (DCO) cases and those with major error in the mandatory variables or with less than 5 years of potential follow-up were excluded.

Net survival, i.e. the hypothetical survival in absence of other competing causes of death, was estimated by the Pohar-Perme method [11]. The analysis was based on the general population life tables, disaggregated by year, sex, and place of residence [12]. Age-standardized net survival (ASNS) was calculated using the international standard cancer patient distribution [13]. Conditional survival, the further survival of patients that have already survived a certain number of years since diagnosis, was calculated by dividing the net survival estimates at the end by those at the beginning of the considered interval. Confidence intervals were provided at the 95 % probability level. Survival trends were assessed by the Absolute Difference (AD) of the survival between the last and the first time periods and the corresponding standard error, with statistical significances being evaluated by the z-test. Survival trends were also expressed by the Annual Percent Change (APC), calculated as exp (100*b)-1, where *b* is the slope of the linear regression of the log-survival in the four considered time periods against the mid-year of each period.

3. Results

The five-year age-standardized net survival observed in the 27 considered sites, and for all cancers combined, is represented for males and females in Fig. 1 (cancers are ranked by decreasing average survival). The net survival for all cancers (excluding non-melanoma skin

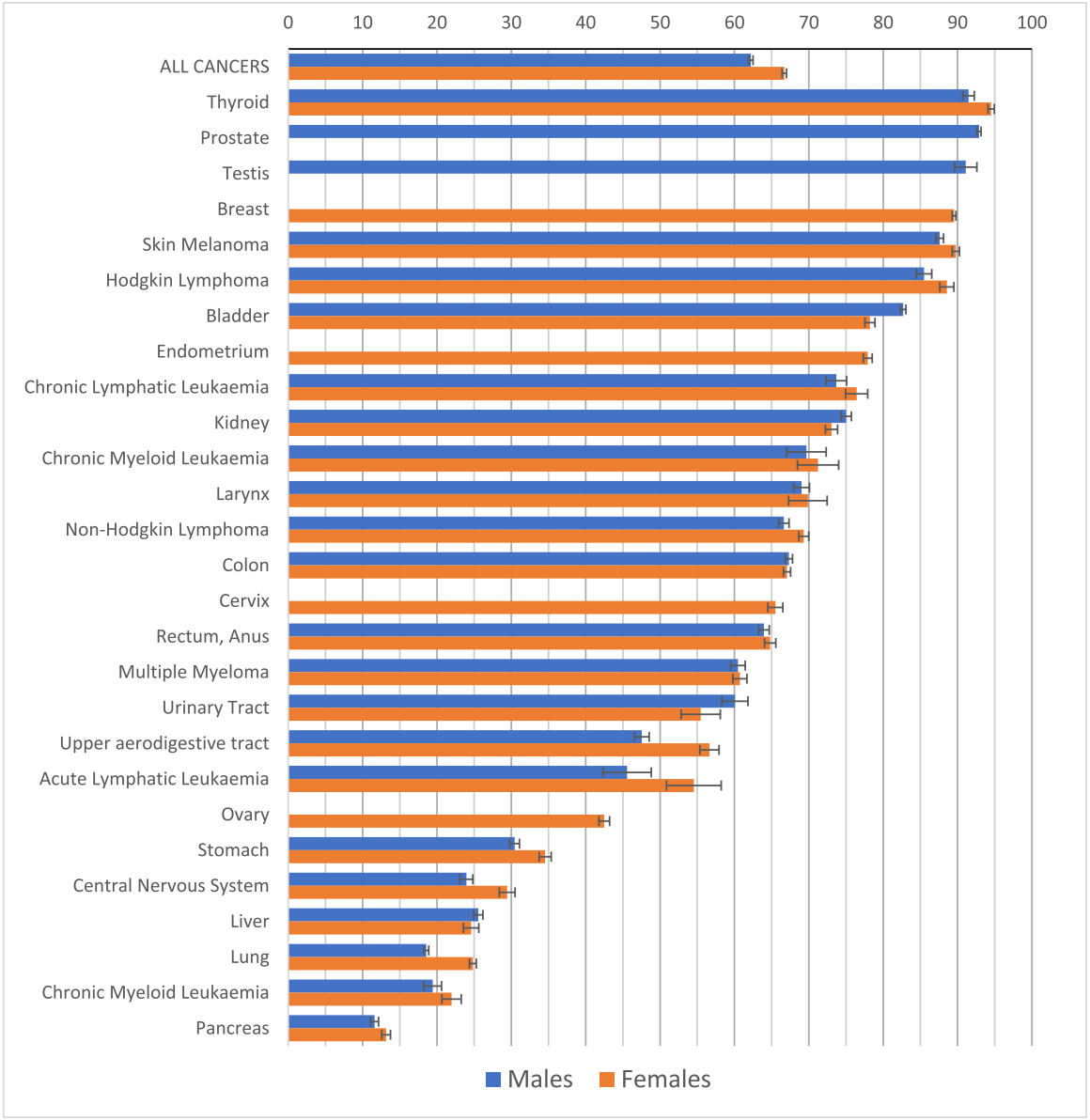

Fig. 1. Age-standardized 5-year net survival, with 95 % confidence intervals, in Italian cancer patients diagnosed between 2013 and 2017, by cancer site and sex.

cancers) was generally higher in females (5-year ASNS: 66.7 %; 95 %C.I.: 66.5–66.8) than in males (5-year ASNS: 62.2; 95 %C.I.: 62.0–62.3). More in depth, females had a better 5-year survival than males for most of the considered cancer sites (Fig. 1). As compared to males, particularly high and significant differences of + 9.0 % points (pp) were highlighted for acute lymphatic leukaemia, cancers of the upper respiratory and of digestive tract. Female survival was also higher for lung cancer (+6.0 pp), tumour of the central nervous system (+5.0 pp), and stomach cancer (+4.0 pp). By contrast, significant higher survivals were documented in males for bladder (+4.0 pp), kidney (+2.0 pp), and other urinary tract cancers (+5.0 pp).

Nine cancer sites (prostate and testis in males, breast, endometrium, and chronic lymphatic leukaemia in females, thyroid, skin melanoma, Hodgkin lymphoma, and bladder cancer in both sexes) had a 5-year net survival higher than 75 % (Fig. 1). Cancers with the worst prognosis were those of central nervous system, liver, lung, pancreas, and acute myeloid leukaemias, documenting a 5-year net survival under 30 %. Survival for the remaining cancer sites ranged between 50 % and 75 %, except for stomach cancer (30 % in males and 35 % in females), ovarian cancer (42 %), male upper aerodigestive tract (48 %) and male acute lymphocytic leukaemia (46 %).

The survival ranking by cancer site estimated at 5 years since diagnosis (Fig. 1) was similar to those observed at 1 and 10 years (Supplementary Table 2), with few exceptions. One-year survival estimates for Kidney and Non-Hodgkin Lymphoma ranked worse than 5-year estimates, while a better position was observed for rectum-anus and cervix cancers, respectively, indicating a relatively high and low death risk immediately after diagnosis.

Net survival clearly decreased by age at diagnosis, overall and for the single cancer sites, with some exceptions (Table 1). Five-year net survival by age and sex for all cancers was lower in males, decreasing from 83 % in patients aged 15–44 years old to 49 % in those aged > 75 years old, than in females, with the overall five-year cancer survival decreasing even more, from 89 % in patients aged 15–44 years old to 48 % in those aged > 75 years old, which is close to the males figure for the same age-group. The same pattern was observed for most of the considered cancer sites, whereas the lowest 5-year survival was observed for the oldest patients, while the highest survival level was found in the youngest ones, with the only exception of colon and prostate cancers in men, with the highest survival rate highlighted in patients aged 55–64 years old, and of colon-rectum, rectum, stomach, and breast cancers, in women, with the highest survival reported for the age class 45–54. Of interest, the difference in 5-year net survival between the youngest and the oldest patients was of 10 % points or more for all cancers, and up to more than 40 pp for all haematological malignancies (apart from NH lymphoma in men, with a difference of 37 pp), with peaks of over 56 pp in acute lymphocytic leukaemia and 53 pp for prostate cancer.

Age standardized 5-year net survival trends, with their 95 % confidence intervals, are reported in Table 2. For all cancers combined the ASNS regularly and significantly increased from 64.3 % (95 %CI: 64.0–64.6) in 2008–2009–67.0 % (95 %CI: 66.6–67.3) in 2016–2017 for men (Table 2.**A**), and from 69.1 % (95 % CI: 68.7–69.4) to 71.3 % (95 % CI: 71.0–71.7) during the same period for women (Table 2.**B**).

With regard to the absolute difference (AD) in 5-years standardized net survival during the considered period between the first and the last biennial subperiods (Table 2, Fig. 2), the largest survival increases were observed for acute lymphocytic leukaemia (+7.3 pp, not significant, in males, and +22.3 pp in females), for liver and lung cancers, and acute myeloid leukaemia, in women (+4.9 pp, +4.2 pp, and +4.1 pp, respectively). Substantial and significant ASNS improvements, ranging between 2.0 and 4.0 pp, were then found for pancreatic cancer and skin melanoma for both sexes, for cancers of liver, lung, Hodgkin lymphoma, acute and chronic myeloid leukaemia in males only, and for cancers of the rectum, breast, and ovary, in females only. By contrast, statistically significant survival decreases were observed for bladder cancer (around −2.0 pp), all leukaemias (around −5.0 pp), and chronic lymphatic leukaemia (-6.9 pp in men), and for cervical cancer (-5.0 pp). Even if not significant, there was also a −4.0 pp difference in survival for cancer of "other urinary organs" in men.

Table 1
Five-year net survival in Italian cancer patients diagnosed between 2013 and 2017, by cancer site, sex, and age-group.

	MALES					FEMALES				
CANCER SITES	**15–44**	**45–54**	**55–64**	**65–74**	**75 +**	**15–44**	**45–54**	**55–64**	**65–74**	**75 +**
ALL CANCERS	83.5	67.8	65.9	64.5	49.4	89.3	83.9	74.6	66.7	47.7
Upper aerodigestive tract	70.8	55.6	50.0	47.1	37.1	78.5	69.5	62.4	56.4	41.7
Stomach	36.5	35.7	34.1	32.9	21.5	38.8	39.9	37.4	39.5	24.1
Colorectal	70.2	69.5	70.8	69.4	59.6	72.8	73.2	72.8	69.7	55.6
Colon	70.2	70.1	71.0	69.8	60.1	74.1	73.0	72.4	69.4	56.4
Rectum	70.1	68.2	69.4	66.9	53.5	69.9	73.6	73.4	68.9	49.0
Liver	37.7	32.2	29.4	25.6	16.8	43.3	31.0	27.6	26.6	13.0
Pancreas	32.7	16.3	13.1	10.3	4.8	45.2	21.3	14.9	9.9	4.0
Larynx	78.3	71.9	71.6	72.6	60.0	80.0	78.1	75.5	71.2	58.3
Lung	31.7	21.0	20.7	20.2	11.1	39.0	31.2	28.3	27.4	13.5
Skin melanoma	93.0	90.4	88.6	85.9	74.3	95.8	95.4	91.4	87.7	71.5
Breast (female)	-	-	-	-	-	92.2	93.8	92.1	92.1	82.5
Cervix	-	-	-	-	-	82.3	73.3	67.7	55.2	33.9
Endometrium	-	-	-	-	-	90.0	88.1	85.5	79.8	62.9
Ovary	-	-	-	-	-	75.8	64.1	53.7	39.7	19.5
Prostate	97.5	96.6	97.9	92.6	42.5	-	-	-	-	-
Testis	97.1	96.2	91.6	80.2	60.0	-	-	-	-	-
Kidney	87.5	83.8	79.9	78.1	61.6	91.0	86.4	83.5	76.4	51.6
Urinary tract	81.9	70.7	66.2	60.1	45.6	72.1	64.8	61.8	58.5	39.5
Bladder	96.5	90.4	87.3	84.4	70.8	92.9	87.8	85.1	81.1	62.4
Central Nervous System	55.5	23.5	12.1	7.0	3.5	63.6	34.3	17.6	8.2	3.4
Thyroid	99.1	97.3	94.7	89.3	67.6	99.6	99.0	97.7	94.6	74.1
Leukaemias	71.9	71.0	63.0	47.4	25.5	73.2	68.8	61.2	46.9	23.1
Acute Lymphatic Leukaemia	58.9	43.9	27.8	22.5	8.1	69.0	56.3	43.3	24.8	6.8
Chronic Lymphatic Leukaemia	97.4	89.8	85.5	77.3	48.4	94.0	93.6	91.6	83.0	46.5
Acute Myeloid Leukaemia	58.4	40.5	29.4	10.5	2.3	60.4	47.5	32.8	13.3	2.2
Chronic Myeloid Leukaemia	94.7	94.2	82.8	70.1	42.7	94.4	91.7	91.2	71.7	41.0
Hodgkin Lymphoma	96.1	87.1	83.0	64.9	43.8	98.1	92.8	88.5	74.2	41.3
Non-Hodgkin Lymphoma	84.7	79.8	75.9	68.1	48.0	89.4	85.6	81.7	71.5	45.7
Multiple Myeloma	86.9	77.6	73.2	59.9	37.4	91.6	82.6	74.3	59.4	34.9

Table 2
Age-standardized 5-year net survival (ASNS) by cancer, diagnostic period, and sex. Annual Percent Change (APC), and Absolute Difference (AD) in 5-years standardized net survival between the first and last period of diagnosis. Italy, 2008–2017.

A) Males	2008–2009			2010–2011			2012–2013			2014–2015			2016–2017			APC	AD	s.e. (AD)	
	5-yr NS	95 % C.I.		5-yr NS	95 % C.I.		5-yr NS	95 % C.I.		5-yr NS	95 % C.I.		5-yr NS	95 % C.I.					
ALL CANCERS[1]	**64.3**	64	64.6	**65.2**	64.8	65.5	**66.7**	66.4	67	**67.3**	67	67.6	**67**	66.6	67.3	*0.54*	*2.7*	*0.2*	*
Upper aerodigestive tract	**46.4**	44.0	48.7	**44.9**	42.5	47.2	**46.8**	44.5	49.2	**48.1**	45.8	50.4	**47.8**	45.5	50.1	*0.63*	*1.4*	*1.7*	
Stomach	**30.8**	29.6	32.0	**31.0**	29.9	32.1	**29.5**	28.4	30.6	**30.3**	29.3	31.4	**31.1**	30.0	32.3	*0.07*	*0.3*	*0.8*	
Colon, Rectum, Anus	**64.7**	63.8	65.6	**66.0**	65.1	66.9	**65.4**	64.4	66.4	**66.6**	65.7	67.5	**65.9**	64.9	66.9	*0.24*	*1.2*	*0.7*	
Colon	**65.3**	64.2	66.4	**66.6**	65.5	67.7	**65.5**	64.3	66.6	**65.9**	64.8	67.1	**65.8**	64.5	67.0	*0.03*	*0.5*	*0.8*	
Rectum	**63.4**	62.1	64.7	**63.5**	62.3	64.8	**63.6**	62.4	64.7	**64.0**	62.8	65.1	**62.9**	61.7	64.1	*-0.04*	*-0.5*	*0.9*	
Liver	**22.5**	21.3	23.7	**23.4**	22.1	24.7	**24.1**	22.8	25.5	**25.1**	23.7	26.5	**24.9**	23.4	26.4	*1.33*	*2.4*	*1.0*	*
Pancreas	**7.7**	6.6	8.8	**9.4**	8.3	10.5	**11.1**	9.9	12.3	**11.7**	10.5	12.9	**11.6**	10.3	12.9	*5.00*	*3.9*	*0.9*	*
Larynx	**66.8**	64.4	69.2	**69.8**	67.4	72.1	**71.1**	68.7	73.5	**70.5**	68.0	72.5	**68.0**	65.7	70.7	*0.16*	*1.2*	*1.8*	
Lung	**15.0**	14.4	15.7	**15.4**	14.7	16.1	**16.8**	16.0	17.5	**17.4**	16.7	18.2	**18.1**	17.3	18.9	*2.42*	*3.1*	*0.5*	*
Skin melanoma	**84.4**	82.8	86.1	**83.6**	82.0	85.2	**85.8**	84.4	87.2	**87.4**	86.1	88.7	**88.3**	87.0	89.6	*0.67*	*3.9*	*1.1*	*
Prostate	**89.2**	88.5	89.9	**90.9**	90.3	91.6	**91.4**	90.8	92.1	**90.8**	90.1	91.4	**90.7**	90.0	91.3	*0.14*	*1.5*	*0.5*	*
Testis	**91.8**	86.9	95.1	**89.5**	85.4	93.7	**91.4**	87.3	95.5	**90.8**	84.6	94.2	**91.7**	88.5	94.9	*0.05*	*-0.1*	*2.7*	
Kidney	**69.8**	68.0	71.6	**71.3**	69.6	73.1	**74.0**	72.2	75.7	**74.8**	73.1	76.4	**71.2**	69.5	72.9	*0.37*	*1.4*	*1.3*	
Urinary tract	**58.9**	54.3	63.5	**64.2**	60.1	68.3	**62.5**	58.2	66.8	**56.3**	51.9	60.7	**54.9**	50.7	59.0	*-1.45*	*-4.0*	*3.2*	
Bladder	**80.3**	79.4	81.2	**79.5**	78.7	80.4	**81.0**	80.2	81.9	**80.8**	79.9	81.6	**78.2**	77.3	79.1	*-0.21*	*-2.1*	*0.6*	*
Thyroid	**89.7**	87.5	91.9	**90.1**	88.0	92.3	**91.5**	89.5	93.6	**89.5**	87.4	91.6	**89.9**	88.0	91.7	*-0.05*	*0.2*	*1.5*	
Central Nervous System	**21.2**	19.2	23.1	**21.9**	19.8	24.0	**24.2**	22.2	26.3	**23.2**	21.3	25.2	**23.1**	20.8	25.3	*0.97*	*1.9*	*1.5*	
Leukaemias	**53.1**	51.2	55.0	**54.4**	52.4	56.4	**52.0**	50.1	54.0	**52.3**	50.3	54.2	**47.6**	45.6	49.6	*-1.27*	*-5.5*	*1.4*	*
Acute Lymphatic Leukaemia	**42.1**	36.0	48.2	**42.4**	36.4	48.4	**37.0**	31.8	42.2	**46.6**	41.1	52.1	**49.4**	43.6	55.1	*2.44*	*7.3*	*4.3*	
Chronic Lymphatic Leukaemia	**78.6**	76.2	80.9	**78.5**	76.1	81.0	**76.7**	74.4	79.0	**75.5**	73.1	77.9	**71.7**	69.2	74.1	*-1.10*	*-6.9*	*1.7*	*
Acute Myeloid Leukaemia	**16.5**	14.4	18.7	**20.0**	17.7	22.3	**19.2**	17.3	21.2	**19.5**	17.5	21.5	**19.9**	17.8	21.9	*1.70*	*3.4*	*1.5*	*
Chronic Myeloid Leukaemia	**66.4**	61.5	71.2	**68.6**	64.1	73.1	**71.2**	66.9	75.4	**69.5**	64.9	74.0	**70.1**	65.2	74.9	*0.52*	*3.7*	*3.5*	
Hodgkin Lymphoma	**83.0**	80.4	85.7	**85.0**	82.5	87.5	**85.5**	83.2	87.8	**83.1**	80.7	85.5	**85.6**	83.1	88.2	*0.16*	*2.6*	*1.9*	
Non-Hodgkin Lymphoma	**62.1**	60.4	63.9	**64.3**	62.5	66.1	**65.7**	64.0	67.5	**64.9**	63.2	66.6	**63.5**	61.8	65.2	*0.20*	*1.4*	*1.2*	
Multiple Myeloma	**57.5**	55.1	59.9	**58.2**	55.8	60.3	**57.9**	55.5	60.6	**61.0**	58.7	63.4	**58.0**	55.7	60.4	*0.34*	*0.5*	*1.7*	

B) Females	2008–2009			2010–2011			2012–2013			2014–2015			2016–2017			APC	AD	s.e. (AD)	
	5-yr NS	95 % C.I.		5-yr NS	95 % C.I.		5-yr NS	95 % C.I.		5-yr NS	95 % C.I.		5-yr NS	95 % C.I.					
ALL CANCERS[1]	**69.1**	68.7	69.4	**69.7**	69.4	70	**70.5**	70.2	70.8	**71**	70.7	71.3	**71.3**	71	71.7	*0.39*	*2.2*	*0.3*	*
Upper aerodigestive tract	**56.0**	52.7	59.4	**55.4**	52.2	58.6	**58.5**	55.4	61.6	**57.1**	54.0	60.1	**52.5**	49.2	55.8	*-0.60*	*-3.5*	*2.4*	
Stomach	**33.6**	32.1	35.1	**33.4**	32.0	34.8	**35.3**	33.9	36.7	**33.4**	32.1	34.6	**34.3**	32.9	35.7	*0.11*	*0.7*	*1.0*	
Colon, Rectum, Anus	**64.1**	63.1	65.0	**65.2**	64.3	66.1	**64.8**	63.8	65.7	**65.1**	64.1	66.0	**64.6**	63.6	65.6	*0.07*	*0.5*	*0.7*	
Colon	**64.3**	63.2	65.4	**65.8**	64.7	66.9	**65.1**	64.0	66.2	**65.9**	64.7	67.0	**64.6**	63.4	65.8	*0.05*	*0.3*	*0.8*	
Rectum	**63.4**	62.0	64.8	**63.1**	61.8	64.4	**63.6**	62.3	64.9	**64.4**	63.2	65.5	**66.0**	64.7	67.3	*0.51*	*2.6*	*1.0*	*
Liver	**21.3**	19.2	23.5	**24.4**	22.2	26.6	**23.0**	20.7	25.2	**23.2**	20.9	25.5	**26.2**	23.7	28.8	*1.86*	*4.9*	*1.7*	*
Pancreas	**9.4**	8.1	10.7	**10.3**	9.1	11.6	**11.8**	10.5	13.2	**12.0**	10.6	13.3	**13.1**	11.7	14.5	*3.96*	*3.7*	*1.0*	*
Larynx	**69.9**	64.1	75.7	**69.8**	64.0	75.6	**70.0**	64.1	75.9	**65.6**	59.5	71.7	**67.6**	61.4	73.8	*-0.68*	*-2.3*	*4.3*	
Lung	**20.6**	19.4	21.7	**20.8**	19.7	21.9	**22.5**	21.4	23.7	**23.8**	22.7	24.9	**24.8**	23.6	25.9	*2.50*	*4.2*	*0.8*	*
Skin melanoma	**87.0**	85.8	88.2	**87.2**	86.2	88.2	**89.5**	88.6	90.4	**89.6**	88.5	90.7	**89.8**	88.8	90.9	*0.42*	*2.8*	*0.8*	*
Breast	**86.7**	86.2	87.2	**86.8**	86.4	87.3	**87.6**	87.2	88.0	**88.7**	88.3	89.1	**88.9**	88.4	89.3	*0.36*	*2.2*	*0.3*	*
Cervix	**69.3**	67.3	71.2	**67.2**	65.4	69.0	**67.2**	65.5	68.9	**65.9**	64.3	67.5	**64.3**	62.5	66.0	*-0.84*	*-5.0*	*1.3*	*
Endometrium	**76.8**	75.6	78.0	**77.8**	76.7	79.0	**77.8**	76.8	78.8	**78.1**	77.1	79.0	**76.8**	75.9	77.8	*0.01*	*0.0*	*0.8*	
Ovary	**40.2**	38.9	41.6	**40.7**	39.4	42.0	**43.2**	41.9	44.4	**42.0**	40.9	43.1	**43.0**	41.7	44.2	*0.74*	*2.8*	*0.9*	*
Kidney	**70.3**	68.2	72.4	**72.4**	70.3	74.5	**72.0**	69.9	74.0	**72.2**	70.1	74.2	**71.0**	69.0	73.0	*0.07*	*0.7*	*1.5*	
Urinary tract	**58.0**	51.8	64.2	**57.3**	51.9	62.7	**55.9**	49.4	62.4	**55.0**	49.2	60.7	**56.4**	50.4	62.4	*-0.45*	*-1.6*	*4.4*	
Bladder	**77.7**	76.0	79.3	**78.5**	76.9	80.2	**77.8**	76.1	79.4	**77.1**	75.5	78.7	**76.1**	74.5	77.7	*-0.30*	*-1.6*	*1.2*	
Thyroid	**93.2**	92.0	94.3	**94.0**	92.9	95.2	**94.3**	93.2	95.4	**94.4**	93.3	95.5	**93.1**	92.0	94.3	*0.00*	*-0.1*	*0.8*	
Central Nervous System	**26.9**	24.5	29.3	**29.2**	26.8	31.6	**26.9**	24.5	29.2	**28.0**	25.6	30.5	**28.5**	25.7	31.2	*0.45*	*1.6*	*1.9*	
Leukaemias	**50.8**	48.7	53.0	**50.3**	48.0	52.5	**50.5**	48.3	52.8	**49.8**	47.6	52.0	**48.7**	46.4	51.0	*-0.49*	*-2.1*	*1.6*	

(*continued on next page*)

Table 2 (*continued*)

B) Females	2008–2009			2010–2011			2012–2013			2014–2015			2016–2017			APC	AD	s.e. (AD)	
Acute Lymphatic Leukaemia	**35.2**	27.9	42.5	**45.1**	37.6	52.7	**42.8**	36.2	49.3	**58.2**	51.7	64.6	**57.5**	51.1	63.8	*6.49*	*22.3*	*4.9*	*
Chronic Lymphatic Leukaemia	**78.7**	76.0	81.3	**78.5**	75.9	81.1	**78.6**	76.2	80.9	**77.5**	75.1	79.9	**75.7**	73.2	78.2	*-0.47*	*-3.0*	*1.9*	
Acute Myeloid Leukaemia	**19.0**	16.6	21.5	**19.7**	17.3	22.0	**19.6**	17.4	21.8	**22.7**	20.5	24.9	**23.1**	20.9	25.4	*2.79*	*4.1*	*1.7*	*
Chronic Myeloid Leukaemia	**69.0**	64.2	73.8	**74.0**	69.6	78.4	**74.1**	69.2	78.9	**72.6**	67.7	77.5	**70.1**	65.2	75.0	*-0.01*	*1.1*	*3.5*	
Hodgkin Lymphoma	**87.7**	85.1	90.2	**85.9**	83.5	88.3	**88.4**	86.0	90.8	**88.5**	86.1	90.9	**88.1**	85.9	90.3	*0.17*	*0.4*	*1.7*	
Non-Hodgkin Lymphoma	**67.1**	65.4	68.7	**68.4**	66.7	70.1	**68.2**	66.6	69.9	**68.8**	67.2	70.4	**67.4**	65.7	69.1	*0.06*	*0.3*	*1.2*	
Multiple Myeloma	**58.3**	55.9	60.6	**61.3**	58.9	63.6	**60.3**	57.9	62.6	**60.2**	58.0	62.4	**60.1**	57.7	62.4	*0.20*	*1.8*	*1.7*	

1: Excluding skin non-melanoma; * Statistically significant values (p-value <0.05)

A comparison of the five-year net survival of patients diagnosed with cancer in the last available quinquennial period (2013–2017) between North-Central and South-Islands macro-areas is shown in Fig. 3. Survival for all cancers combined was significantly higher in the Northern-Central macro-area (66.4 %; 95 %CI: 66.3–66.6) compared to the one highlighted in the Southern and Islands macro-area (61.4 %; 95 %CI: 61.2–61.7). This statistically significant difference remained for all the single cancer sites, except for larynx, testis, urinary tract, and central nervous system, whose confidence intervals overlapped. Absolute differences greater than 5 % points were observed for cancers of upper aerodigestive tract (5.5 pp), stomach cancer (7.7 pp), skin melanomas (5.4 pp), cervical cancer (5.8 pp), endometrial (5.3 pp), and ovarian (5.2 pp) cancers, for NHL (8.2 pp), and for multiple myeloma (5.1 pp). The sex-specific comparisons confirmed these observations by sex both for all cancer sites (Table 3), with males and females from the Northen-Central Italy having statistical significantly higher age-standardized 5-year net survivals than the ones from South and Islands (in males: North-Centre 5-year ASSN: 64.0; 95 %CI: 63.8–64.2; South and Islands 5-year ASSN: 58.1; 95 %CI: 57.7–58.5; in females: North-Centre 5-year ASSN: 68.3; 95 %CI: 68.0–68.5; South and Islands 5-year ASSN: 63.7; 95 %CI: 63.3–64.1), and by cancer site, despite with some exceptions for testicular cancer (North-Centre 5-year ASSN: 91.1; 95 %CI: 89.8–92.3; South and Islands 5-year ASSN: 92.9; 95 %CI: 89.7–96.1), CNS tumours in males, which had a similar survival in the two macro-areas (North-Centre 5-year ASSN: 24.1; 95 %CI: 22.7–25.5; South and Islands 5-year ASSN: 23.9; 95 %CI: 21.7–26.1), and urinary tract cancers, with contrasting geographical survival differences in the two sexes: significantly higher for males in the North-Centre (5-year ASSN: 60.7; 95 %CI: 57.9–63.4) than in South and Islands (5-year ASSN: 54.5; 95 %CI: 49.6–59.3), while higher, but not significantly, for females in the South and Islands (5-year ASSN: 59.1; 95 %CI: 52.4–65.8) as compared to North-Centre (5-year ASSN: 55.6; 95 %CI: 51.7–59.5).

4. Discussion

We conducted a population-based study to update cancer survival estimates in Italy to the most recent period available, using data from the national network of population-based cancer registries. More in depth, the study aimed at verifying whether survival figures have been continuing to improve in recent years and at exploring the influence of sex, age, and geographical differences, on survival outcomes.

Our findings confirm much of the previous evidence while providing new insights at the same time [14]. Female patients consistently demonstrated a more favourable prognosis than male ones. This advantage was observed not only for all cancers combined — largely due to a lower proportion of lethal cancers such as lung, head and neck, and liver cancer, in women — but also for many specific sites. The main exceptions were kidney, bladder, and other urinary tract cancers, for which the reasons behind the lack of female advantage remains unclear. A possible explanation could be that males receive more frequent urologic diagnostic scrutiny and access to specialist care due to prevalence of lower urinary tract symptoms and prostate cancer screening. However, these cases require further investigation into histology, stage distribution, and biological prognostic factors. Several explanations have been proposed for the female survival advantage. An important consideration is the difference in the most common cancers by sex. Among women, breast cancer is the leading malignancy, whereas among men, lung cancer predominates. This distinction is clinically relevant because the two cancers have very different prognoses. Breast cancer, thanks to widespread screening programs and advances in targeted therapies, is often diagnosed at earlier stages and is associated with a relatively favourable survival. In contrast, lung cancer is frequently detected at advanced stages and continues to carry a poor prognosis despite therapeutic progress [14]. Other contributing factors include biological and hormonal differences, behaviours, and lifestyle habits [15]. Historically, men have been more exposed to work environmental carcinogens and other risk factors, such as tobacco use and alcohol consumption [16]. Moreover, Italian men consume fewer fruits and vegetables and drink larger amounts of alcohol than women [17]. A focus on this specific issue in Italy has been provided by another paper in this monographic issue, specifically devoted to address the role of gender in cancer epidemiology [18].

Cancer prognosis varied dramatically across different sites. Five-year survival rates above 75 % were observed for several cancers, such as prostate and testicular cancers in men, breast and endometrial cancers in women, as well as thyroid cancer, skin melanoma, Hodgkin lymphoma, bladder cancer, and chronic lymphatic leukaemia, in women. In these diseases, progress in early detection, widespread availability of effective treatments, and in some cases more favourable tumour biology, have translated into high probabilities of long-term survival [19].

In contrast, cancers such as those of the central nervous system, liver, lung, and pancreas, as well as acute myeloid leukaemia, presented five-year survival rates below 30 %, whereas these malignancies as of today tend to progress aggressively, are often diagnosed late, and have limited therapeutic options [14], [20], [21].

Several cancers presented intermediate survival rates, with treatments that offer partial but not complete benefit. Ovarian cancer is an exception, showing worse outcomes compared with other tumours in this group: the late-stage diagnosis and the treatment difficulties account for its particularly unfavourable prognosis, despite not being the most aggressive among gynaecological cancers from a biological point of view [22].

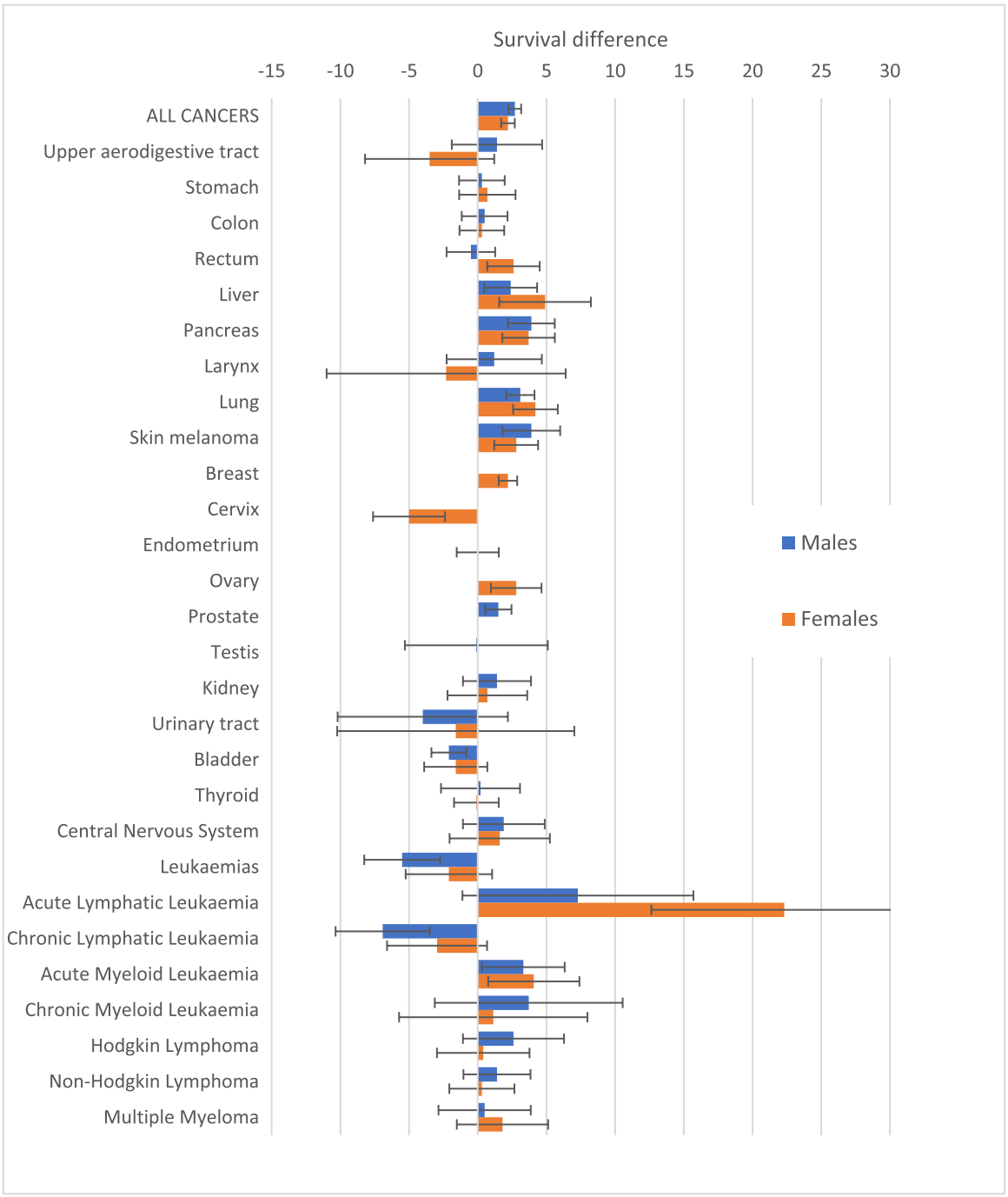

Fig. 2. Differences in age-standardized 5-year net survival, with 95 % confidence intervals, in Italian patients diagnosed with cancer between 2016 and 2017 and 2008–2009, by cancer and sex.

Short- and long-term outcomes also differed by cancer type. Kidney cancer and non-Hodgkin lymphoma are usually associated with high early mortality, reflecting late diagnosis and aggressive subtypes [23], [24]. However, those who survive the first year often benefit from new treatments — such as targeted therapies, chemotherapy, and immunotherapy — which improve long-term survival [25], [26]. In contrast, rectal and cervical cancers typically showed favourable one-year survivals thanks to an effective initial treatment, but their five-year prognosis worsen due to recurrence and progression during follow-up [27], [28]. This emphasizes that while some cancers pose their greatest threat immediately after diagnosis, others reveal challenges later on, highlighting the need for both effective early treatment and long-term monitoring.

Net survival decreased with advancing age across nearly all cancers, with the decline being particularly steep for haematological malignancies. The survival disadvantage in older age groups was greater among women, partly due to the higher proportion of very elderly women in the population [5]. The EUROCARE study suggested that comorbidities, complications, and side effects of therapies may also play a significant role in worsening prognosis for elderly patients [29]. These findings indicate that both tumour biology and patient-related factors contribute to the observed disparities by age [5].

During the study period, net survival improved for nearly all cancer types in Italy. Our estimates confirmed earlier evidence showing a

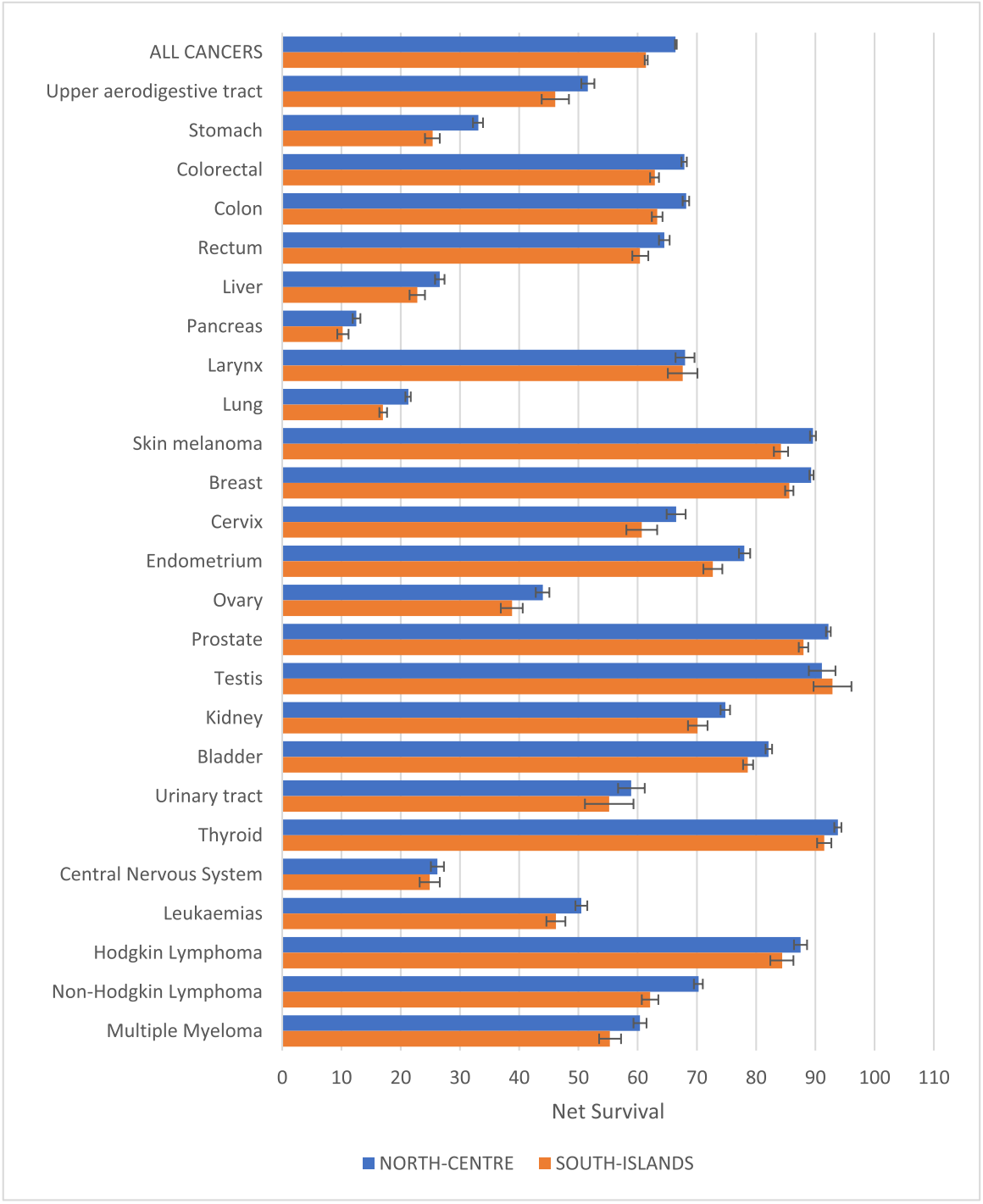

Fig. 3. Age standardized 5-year net survival, with 95 % confidence intervals, by cancer site and geographical macro-area (North-Centre versus South and Islands), in Italian patients diagnosed with cancer in 2013–2017.

regular increase in survival of about 1 % every three years for men and every four years for women, between 1994 and 2011 [9]. The new data suggested further increases in survival, likely attributable to advances in diagnostic anticipation and improvements in clinical care pathways [30].

Survival for the most common cancers, such as breast, prostate, and colorectal, remained relatively stable in Italy. However, marked progress was seen for more aggressive cancers including pancreas, lung, and acute leukaemia, with improvements especially evident in women [14, 31]. More in depth, an increasing frequency of adenocarcinoma, which has somewhat more favourable prognosis, may have contributed to the improvement in lung cancer survival trend [32].

At the same time, declines were observed for bladder cancer and chronic lymphatic leukaemia in men. The reduction in cervical cancer survival may partly reflect lower participation in screening and vaccination programs in some groups of women [33]. These results highlight the importance of maintaining attention on prevention, screening, and therapeutic innovation. Declines were also noted, though not statistically significant, for urinary tract cancers.

According to our findings, a clear north–south divide in cancer survival was confirmed in Italy. Five-year net survival was consistently higher in the North and Centre compared with the South and Islands.

Table 3
Age-standardized 5-year net survival (ASNS), with 95 % confidence intervals, by cancer site, sex, and geographical macro-area (North-Centre; South and Islands), in Italian patients diagnosed with cancer in 2013–2017.

a) MALES	NORTH-CENTER			SOUTH-ISLANDS		
CANCER SITES	5-yr Survival	Confidence Interval		5-yr Survival	Confidence Interval	
ALL CANCERS	64.0	63.8	64.2	58.1	57.7	58.5
Upper aerodigestive tract	49.2	47.7	50.6	42.6	39.8	45.5
Stomach	31.2	30.1	32.2	23.7	22.1	25.3
Colorectal	67.2	66.5	67.8	62.1	61.1	63.1
Colon	67.6	66.8	68.4	62.4	61.2	63.7
Rectum	63.6	62.4	64.8	59.8	58.0	61.6
Liver	27.4	26.4	28.3	22.4	20.8	23.9
Pancreas	12.1	11.3	13.0	9.0	7.8	10.2
Larynx	68.2	66.4	69.9	67.9	65.2	70.5
Lung	19.2	18.7	19.8	15.5	14.8	16.3
Skin melanoma	87.9	87.2	88.7	83.2	81.6	84.9
Prostate	92.2	91.8	92.6	88.0	87.2	88.8
Testis	91.1	88.9	93.4	92.9	89.7	96.1
Kidney	75.5	74.5	76.5	69.6	67.5	71.8
Bladder	82.6	82.0	83.1	78.9	78.0	79.8
Urinary tract	60.7	57.9	63.4	54.5	49.6	59.3
Thyroid	91.0	89.8	92.3	89.0	86.6	91.3
Central Nervous System	24.1	22.7	25.5	23.9	21.7	26.1
Leukaemias	51.1	49.8	52.4	47.1	45.0	49.2
Hodgkin Lymphoma	86.4	84.8	87.9	81.6	78.9	84.2
Non-Hodgkin Lymphoma	68.7	67.6	69.7	60.6	58.7	62.6
Multiple Myeloma	59.7	58.2	61.3	54.2	51.6	56.8
b) FEMALES	**NORTH-CENTER**			**SOUTH-ISLANDS**		
CANCER SITES	5-yr Survival	Confidence Interval		5-yr Survival	Confidence Interval	
ALL CANCERS	68.3	68.0	68.5	63.7	63.3	64.1
Upper aerodigestive tract	56.6	54.7	58.5	52.6	48.9	56.3
Stomach	35.7	34.4	37.1	27.9	25.9	30.0
Colorectal	67.3	66.7	68.0	62.7	61.7	63.8
Colon	67.5	66.7	68.3	63.1	61.9	64.3
Rectum	64.7	63.5	66.0	60.6	58.7	62.5
Liver	24.4	22.8	26.0	23.7	21.2	26.1
Pancreas	13.1	12.1	14.0	11.7	10.3	13.1
Larynx	66.2	62.0	70.4	62.8	55.5	70.0
Lung	24.7	23.9	25.4	20.7	19.5	21.9
Skin melanoma	90.3	89.6	91.0	84.6	82.9	86.3
Breast	89.3	89.0	89.7	85.6	84.9	86.3
Cervix	66.5	64.9	68.1	60.7	58.1	63.3
Endometrium	78.0	77.1	79.0	72.7	71.1	74.3
Ovary	44.0	42.8	45.1	38.8	36.9	40.6
Kidney	72.6	71.4	73.9	70.9	68.4	73.4
Bladder	77.8	76.7	78.8	75.7	73.9	77.5
Urinary tract	55.6	51.7	59.5	59.1	52.4	65.8
Thyroid	94.8	94.2	95.5	92.7	91.3	94.1
Central Nervous System	29.4	27.7	31.1	26.4	23.7	29.0
Leukaemias	49.2	47.7	50.7	45.0	42.6	47.3
Hodgkin Lymphoma	88.7	87.3	90.1	87.5	84.7	90.2
Non-Hodgkin Lymphoma	71.5	70.5	72.5	63.6	61.6	65.6
Multiple Myeloma	60.9	59.4	62.3	56.6	54.0	59.2

This pattern was seen across almost all cancer types, with the largest differences for upper digestive tract, stomach, skin melanoma, cervix, endometrium, ovary, testis, non-Hodgkin lymphoma, and multiple myeloma. Similar disparities were observed in the previous analyses conducted by AIRTUM for the surveillance period 2005–2009, whereas southern regions lagged by 3–4 %age points compared with the northern ones [9]. Both our results and those of AIRTUM confirmed higher survival outcomes in the North-Centre, and lowest in the South-Islands, with some improvement highlighted for liver cancer only [9]. Explanations may include differences in healthcare organization, uneven access to advanced diagnostics and treatments, delays in implementing multidisciplinary care models, and variations in regional cancer networks [34]. Participation in oncological screening programs remained also higher in the North, with opportunistic screening (e.g., prostate cancer, melanoma) further contributing to these differences, although its effectiveness is debated and may inflate survival through overdiagnosis [35]. Moreover, socio-economic inequalities may play a role in reinforcing these disparities: the economic crisis between 2008 and 2013 hit southern Italy hardest, limiting healthcare investment and widening the survival gap [36]. Unhealthy lifestyle factors — higher prevalence of smoking, together with high caloric intakes and lower physical activity, resulting in obesity — may further explain the disadvantage affecting in the South [37], [17]. Standardizing care, introducing high-quality treatments, including the use of molecular biomarkers to better address them, and ensuring equal access to early diagnosis, are essential for narrowing these inequalities [38].

Several limitations of the present study must be noted and discussed. First, there is a long delay between the diagnosis period and the availability of results, with up to eight years of lag. Thus, more recent changes in cancer epidemiology, including the impact of the COVID-19 pandemic on cancer care, were not captured by our investigation [39]. Second, differences in the cancer data timeline provided by the registries forced a trade-off between maximizing coverage and including the most recent data. Lastly, key clinical variables, such as tumour stage, grade, prognostic markers, and treatments, were not available in a sufficiently standardized form to be included in the analyses. Anyway, these gaps

are expected to be addressed through the forthcoming implementation of the national cancer registry in Italy [7].

5. Conclusions

This study is the first nationwide comprehensive survival analysis in Italy since 2016. Its strengths lie in the large population coverage, including 1.6 million cancer cases collected by 34 population-based cancer registries, approximately covering the 84 % of the Italian population. All data were standardized according to a common protocol and centrally analysed, ensuring reliability and comparability.

Of relevance, better survival was observed in women, according to the different epidemiology characterising the different genders. Overall survival continued to improve over time for nearly all cancer types, despite survival probabilities were particularly high in northern regions, similarly to those of Western Europe, but remained low in the South and Islands. Closing the north to south gap will require reinforcing screening and prevention programs, improving access to diagnostics and effective treatments, and reducing socio-economic barriers. By strengthening equity across regions, Italy could even document further improve in overall cancer survival.

Funding

None to be declared.

CRediT authorship contribution statement

Fabrizio Stracci: Writing – review & editing, Supervision, Project administration. **MAZZUCCO WALTER:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Conceptualization. **Santo Fruscione:** Writing – original draft, Conceptualization. **Maria Teresa Pesce:** Project administration, Methodology, Data curation. **Mario Fusco:** Writing – review & editing, Writing – original draft, Project administration, Methodology. **Maurizio Zarcone:** Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. **Riccardo Capocaccia:** Writing – review & editing, Writing – original draft, Software, Project administration, Methodology, Formal analysis, Data curation.

Declaration of Competing Interest

I am writing on behalf of the Authors and the AIRTUM WG. With regard to the manuscript entitled "**Cancer survival in Italian patients diagnosed between 2008 and 2017**", the declaration of interest is: none.

Acknowledgements

The authors sincerely thank all the operators and registrars working in the cancer registries belonging to the AIRTUM network for their considerable efforts in collecting and processing the high-quality data used in this manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.canep.2026.103001.

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