

North-south disparity in cancer control progress in Italy: a joint analysis of incidence, mortality and survival time trends by geographical area

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ABSTRACT

In the last five decades, the epidemiology of cancer in Italy has been characterised by a north–south gradient in cancer incidence, mortality, and survival. Recently, this pattern has been changing, making it important to analyse the three indicators together to understand the underlying dynamics and to identify successes and failures in cancer control. Herein, data from 20 accredited Italian population-based cancer registries were used to examine age-standardised trends in incidence, five-year net survival, and mortality rates, for all cancers and 18 major cancer types, between 2008 and 2017. Data from the national pool were compared with macro-areas ones from north–centre and south–islands. We classified trends according to a 5-category model, ranging from 'Optimal Progress' (decreasing incidence and mortality, increasing survival) to 'Worsening' (increase of both incidence and mortality). At the national level we found progress in all indicators for all cancers combined: incidence and mortality rates declined, on average, by 2.5% and 5.5% annually, while survival increased by 2.5 % points. Similar optimal progress was shown, in men, by all cancers and lung cancer and, in both sexes, by liver cancer, and non-Hodgkin lymphoma. Conversely, evidence of worsening emerged for lung cancer in women, with incidence and mortality rates increasing, on average, by 6.5% and 4% annually. Contrasting trends emerged from north to south for colorectal, pancreatic, and kidney cancers. Trends were homogeneous, but improvements were stronger in the north–centre for all cancers, all cancers in men, male lung, prostate and bladder cancers, non-Hodgkin lymphoma, and for breast cancer mortality. For female lung cancer and breast cancer incidence, we documented a stronger burden increase in the south–islands. The advantage in cancer incidence and mortality risk shown decades ago by the south–islands macro area is being lost, and, if these trends remain stable, in near future the north–south gradient is expected to be reversed for many cancers.

1. Introduction

Cancer is the second leading cause of death in Italy. Despite having a cancer incidence rate in line with the EU average, Italy's age-standardised cancer mortality is comparatively lower. From 2011 to 2021, it fell by 15%, outpacing the EU average decline [1]. Mortality decrease may reflect progress in reducing cancer incidence, thanks to a decreasing prevalence of key risk factors, as well as advances in early detection and cancer care. Early detection, by improving timeliness and efficacy of treatments, contributes significantly to increase cancer survival and reduce cancer death risk. However, increased diagnostic intensity can also artificially inflate cancer survival without affecting mortality if diagnoses are anticipated without postponing death, or if non-aggressive lesions are over diagnosed [2,3]. Given their strong interdependency, time trends in mortality should be assessed jointly with incidence and survival time trends, to gain a comprehensive and coherent understanding of the underlying dynamics [4–6].

In Italy, it is also crucial to assess whether cancer trends observed at national level are homogeneous across the country. Despite universal National Health Service and free organised screening programmes for breast, colorectal and cervical cancers running for decades, marked regional disparities persist in Italy, particularly between southern regions (south and islands) and the rest of the country (north and centre), both in adhesion to screening programmes [7–9] and in cancer survival [10]. More deprived socioeconomic conditions further penalise cancer incidence and mortality rates in southern-islands areas [11,12], since many cancer risk factors are associated to low income and education

level [13].

Reducing cancer inequalities between, and within, the European Union countries is a flagship initiative of the Europe's Beating Cancer Plan (EBCP), launched in 2021 [14,15], and is also targeted by the Italian National Cancer Plan 2023–2027 [16]. To this end, specific interventions have been launched to reduce health inequalities and improve cancer screening uptake in southern-islands regions [17].

In this context, population-based data on cancer mortality and on its determinants (incidence and survival) provide essential information to highlight progress and sub-national disparities in cancer burden and outcome.

In the present study we aimed at comparing time trends of cancer mortality, incidence and 5-year survival for all cancers combined and for 18 major index cancers, by using high-quality data from 20 Italian population-based cancer registries accredited by the Italian Association of Cancer Registries [18]. We present results at national level, at macro-area level (north–center versus south–islands) and by sex, when relevant (lung cancer). By analysing the trends in these three interrelated indicators together, we identify patterns that reflect progress in cancer control in Italy, which vary by cancer type and geographical area.

2. Materials and methods

2.1. Study design and data selections

This observational study jointly assessed time trends in cancer incidence, mortality, and 5-year net survival, across Italy in the period

2008–2017, using incidence and survival data from population-based cancer registries, as part of a special issue on cancer epidemiology in Italy [19,20]. To ensure temporal and geographical consistency in trends' estimation, we included 20 cancer registries with incidence data in the period 2008–2017 and follow-up at least to 2021 (Supplementary Table 1). The selected registries covered 41% of the national population (45% of centre and north and 33% of south and islands). These registries represented 6 out of 9 northern administrative regions, 1 out of 4 central regions and 3 out of 8 southern-islands regions. Data on cause-specific mortality, population and lifetables for the resident population in the regions or provinces covered by the 20 registries were derived from official statistics [11,21]. Cancer diagnoses were coded according to ICD-O-3 classification and were analysed using ICD-10 groupings. We assessed trends over time of all cancers combined and of 18 major index cancers, namely, head & neck, stomach, lung, colon-rectum, colon, rectum, liver, pancreas, kidney, urinary bladder, female breast, ovary, prostate, skin melanoma, thyroid, Hodgkin and non-Hodgkin lymphoma, leukaemias (Supplementary Table 2).

The ten-year study period was divided in three intervals (2008–2011, 2012–2014, and 2015–2017) to allow for balanced comparisons of incidence, mortality, and net survival, over time and reduce random variability across all the considered categories (sex, cancer type, macro-area).

Due to the north-south gradient in cancer risk profiles documented in Italy during the last decades, epidemiological indicators were also analysed by macro-area of residence, i.e. for North-Centre (N/C) versus South-Islands (S/I).

Both national and sub-national pooled estimates for all the indicators presented were derived by pooling registry-specific individual-level data.

2.1.1. Indicators and estimation methods

Incidence and mortality rates were computed as age-standardized rates (ASR) per 100,000 person-year using the direct method and the 2013 European Standard Population. Average annual percent changes (APCs) and corresponding 95% CI were computed for incidence and mortality rates using joinpoint regression via the software distributed by the US National Cancer Institute [22].

Net survival (NS) and corresponding 95% CI were estimated using the Pohar-Perme estimator, implemented in R via the "relSurv" package [23]. The "joinrate" function was used to link individual observed survival data with provincial life tables provided by ISTAT (Italian National Institute of Statistics), stratified by calendar year, age, sex, and province of residence. The period approach was adopted to estimate 5-year survival in the three periods of follow-up (2008–2011, 2012–2014, 2015–2017), to include the most recent data (with incomplete 5-year follow up) and maximize comparability across periods [24]. Age-standardized NS estimates were calculated using the International Cancer Survival Standard (ICSS) weights [25] allowing for meaningful comparisons across geographical areas and time periods.

Trends in 5-year age-standardized net survival were evaluated by estimating the Absolute Difference (AD) between the first and last period, using the Z test for absolute differences [26]. This corresponds to apply a linear contrast with weights (−1, 0, +1). Expressing survival changes in absolute percentage points, facilitates direct interpretation in public health terms.

Trends were classified as increasing or decreasing only if statistically significant, based on p-value lower than 0.05.

To summarize progress in cancer control, pattern of each cancer site was classified according to the combined trends in incidence, mortality, and 5-year net survival. The classification scheme follows a 5-category model adapted from established frameworks [5], ranging from 'Optimal Progress' (decreasing incidence and mortality, increasing survival) to 'Worsening' (worsening of both incidence and mortality). In brief, progress is unambiguously achieved for a specific cancer when incidence and mortality rates are both reducing over time in a given

population. This reduction can be accompanied by improved survival over time (*optimal progress - pattern A*) or by no survival improvements (*good progress - pattern B*). Progress is achieved even when at least one between incidence and mortality rate is declining and the other is stable, in presence of improved or stable survival (*patterns C*). A *limited progress* is associated to unfavourable incidence trends that are compensated by survival improvements and that result in stable or even declining mortality trends (*pattern D*). Lastly, the most critical scenario of *worsening* is associated to unfavourable trends in cancer burden, i.e. when both incidence and mortality risks are rising (*pattern E*).

3. Results

Changes in age-adjusted incidence, mortality, and 5-year net survival, between 2008–2011 and 2015–2017 in Italy for the selected index cancers are presented in Table 1.

A scenario of optimal progress (**pattern A**) was observed, in both sexes, for *all cancers, liver cancer and non-Hodgkin lymphomas, and, in men, for all cancers and lung cancer* (Table 1). More in depth, between 2008 and 2017, incidence rate of all cancers declined from 581 to 552.4 per 100,000 in the Italian pool (APC = −2.5% per year) and mortality decreased even more, passing from 280.1 to 250.3 per 100,000 (APC = −5.52% per year), thanks also to a parallel increase in 5-year net survival (AD = +2.49 absolute percentage points). The highest progresses were observed in liver and male lung cancers, whose incidence declined annually by −8.8% and −7.9%, and mortality by 6.8% and 9.56%, respectively.

Significant reductions in both incidence and mortality, although not accompanied by increasing survival, were observed for *colorectal, prostate, ovary, stomach, head & neck, cancers (pattern B)*. For colorectal cancers incidence rate declined from 75.7 to 64.5 per 100,000 and mortality rate from 31.02 to 27.38. The highest decreases were observed for rectal and stomach cancer incidence (−9.92% and −8.78% per year, respectively) and for prostate and stomach cancer mortality (−8.84% and −8.74%, respectively).

All female cancers, Hodgkin lymphoma and urinary bladder cancers showed progress in at least one burden indicator (**pattern C**). Mortality rate for all female cancers decreased significantly from 207.91 to 192.08 per 100,000 (−3.94% per year), thanks to improved survival (+2.36 absolute percentage points) and stable incidence risk. For urinary bladder cancer, incidence decrease and not improving survival resulted in a mortality decline, although not strong enough to reach statistical significance.

A limited progress (**pattern D**) was found for *pancreatic cancer, skin melanoma, breast, kidney, and thyroid cancers*. For breast cancer, despite incidence increased by 2.35% per year, mortality decreased from 36.44 to 33.01 (−5% per year), in a context of slightly improved survival. Incidence of *skin melanoma* continued to rise steeply (+14.32%), but mortality didn't increase significantly over the same period, thanks also to prognostic advances (AD = +2.73%).

Lastly, the most critical scenario of *worsening (pattern E)* was highlighted for *female lung cancer*, whose incidence rates raised by 6.5% annually (from 29.4 to 33.3 per 100,000). The corresponding increase in mortality was lower (+4.01%) and was possibly mitigated by a parallel significant survival improvement (from 20.7 to 24.3).

These national patterns are the result of underlying regional patterns that are not homogeneous from North to South. Comparisons between North/Centre and South/Islands for selected cancers are shown in Figs. 1–4 (results for the remaining index cancers are plotted in Supplementary Figures 1–4). Geographical variations in the time trends of all index cancers are available in Supplementary Table 3. For all cancers and for most cancer types, excess risks, and higher survival rates persisted in N/C compared to S/I, but the magnitude, and in some cases, the direction of the trends in incidence, mortality and survival appeared quite different in the two areas.

In the period analysed incidence and mortality for *all cancers (M+F)*,

Table 1

Classification of cancer incidence, survival, and mortality trends, in Italy according to progress scenario for major index cancers, and all cancers combined. Time trends 2008–2017 of age-adjusted incidence and mortality rates per 100,000 with corresponding estimated Annual Percent Change (APC). Age adjusted period estimate of 5-year net survival (%proportions) and corresponding Absolute Difference (AD) between 2015–2017 and 2008–2011. Pool of 20 Italian cancer registries. Statistically significant changes in APC and AD values are marked with an asterisk.

Cancer entity	Sex	Incidence				5-year Net Survival				Mortality				Progress against cancer
		2008-11	2015-17	APC (%)	Trend description	2008-11	2015-17	Absolute Difference	Trend description	2008-11	2015-17	APC (%)	Trend description	
All cancers	M+F	581.0	552.4	-2.49*	dec	63.0	65.4	+2.49*	inc	280.1	250.3	-5.52*	dec	A. OPTIMAL PROGRESS - decreasing incidence and mortality, increasing survival
All cancers	M	727.1	656.5	-4.99*	dec	60.4	62.7	+2.28*	inc	389.2	334.7	-7.31*	dec	
Liver	M+F	21.7	18.0	-8.85*	dec	22.8	26.3	+3.42*	inc	18.0	15.6	-6.80*	dec	
Lung	M	110.2	93.5	-7.94*	dec	15.3	18.5	+3.29*	inc	102.9	84.3	-9.56*	dec	
Non Hodgkin lymphoma	M+F	19.7	19.5	-0.58*	dec	66.4	68.2	+1.86*	inc	7.9	7.1	-5.23*	dec	B. GOOD PROGRESS - decreasing incidence and mortality, not increasing survival
Head & Neck	M+F	9.4	9.1	-1.59*	dec	57.9	58.0	+0.11	stable	4.4	4.2	-1.61*	dec	
Stomach	M+F	22.3	18.5	-8.78*	dec	32.1	30.6	-1.49*	dec	15.9	13.3	-8.74*	dec	
Colon rectum	M+F	75.7	64.5	-7.76*	dec	66.4	66.5	+0.09	stable	31.0	27.4	-6.17*	dec	
Colon	M+F	53.3	46.4	-6.73*	dec	66.8	66.6	-0.22	stable	23.9	21.0	-6.40*	dec	
Rectum	M+F	22.4	18.1	-9.92*	dec	64.2	63.3	-0.92	stable	7.2	6.4	-5.39*	dec	
Ovary	F	15.7	14.6	-3.60*	dec	41.2	41.6	+0.43	stable	9.5	8.7	-4.73*	dec	
Prostate	M	141.0	122.9	-6.65*	dec	91.7	91.3	-0.39	stable	32.6	27.2	-8.84*	dec	
Leukaemias	M+F	14.3	12.9	-4.99*	dec	51.7	48.7	-3.01*	dec	9.4	8.6	-4.64*	dec	C. PROGRESS - Decreasing incidence, stable mortality and survival
Urinary bladder	M+F	43.6	40.6	-3.49*	dec	80.9	80.8	-0.15	stable	10.4	9.9	-2.93	stable	
All cancers	F	480.0	479.1	-0.09	stable	65.1	67.5	+2.36*	inc	207.9	192.1	-3.94*	dec	C. PROGRESS - Decreasing mortality, stable incidence and not decreasing survival
Hodgkin lymphoma	M+F	3.7	3.8	1.31	stable	85.4	86.6	+1.18	stable	0.7	0.6	-3.29*	dec	
Pancreas	M+F	18.6	19.6	2.66*	inc	9.4	12.3	+2.81*	inc	17.8	17.8	0.14	stable	D. LIMITED PROGRESS - Increasing incidence, not increasing mortality, increasing survival
Skin melanoma	M+F	15.5	20.1	14.32*	inc	86.1	88.8	+2.73*	inc	2.9	3.0	1.95	stable	
Breast	F	147.7	154.6	2.35*	inc	87.2	88.8	+1.53*	inc	36.4	33.0	-4.96*	dec	
Kidney	M+F	15.5	16.2	2.23*	inc	72.1	73.9	+1.84*	inc	5.4	5.3	-0.74	stable	
Thyroid	M+F	15.0	16.9	6.00*	inc	92.3	93.3	+1.07*	inc	0.9	0.8	-7.87*	dec	
Lung	F	29.4	33.3	6.50*	inc	20.7	24.3	+3.60*	inc	24.20	26.18	4.01*	inc	E. WORSENING - Increasing incidence and mortality, increasing survival.

declined much faster in N/C (APC: -3.32% , -6.73% , respectively) than in S/I (-0.80% , -2.80%) and survival improved also faster in N/C ($+2.43$ vs $+2.10$ % absolute percentage points) (Fig. 1.a). As a consequence, the North to South gap in the most recent period (2015–2017) was shrunk for incidence (568.7 vs 508.3), disappeared for mortality, and slightly increased for survival (66.6% vs 61.3%), compared to ten years before.

A similar pattern was observed for *all cancers in men*, but the incidence gap between the two areas was much smaller and on 2015–2017 mortality rate in S/I already exceeded that in N/C (338.4 vs 332.5) (Fig. 1.b).

Contrasting trends between N/C (optimal progress) and S/I (limited progress) emerged for *all female cancers* (Fig. 1.c): incidence decreased in N/C (APC = -0.91%) while increased in S/I ($+1.56\%$), and survival improved more in N/C. Therefore, the annual reduction of mortality rates was much higher in N/C (-5.0%) than in the S/I (-1.43%) and the gap between the two areas was narrowing.

Less favourable trends in S/I were observed for cancers in good/optimal progress scenario (Fig. 2). Incidence and mortality for *male lung cancer* declined much faster in N/C and in 2015–2017 S/I became the area at higher risk (Fig. 2.a). Incidence and mortality for *colorectal cancer* decreased steeply only in N/C (-10.58% and -8.82% per year, respectively), while no decrease was observed in S/I, and the survival gap was also not negligible (67.3% in N/C vs 62% in S/I in the most recent period) (Fig. 2.b). Similarly, mortality decline for *non-Hodgkin lymphoma* was more limited in S/I and the survival gap was even bigger (62.8 in S/I vs 69.5 in N/C) (Fig. 2.c).

For *prostatic cancer* the good progress scenario was confirmed in both macro-areas; however, mortality rates in S/I were higher than in N/C, despite lower incidence rates in S/I (Fig. 3.a). More advanced progress was observed in N/C compared to S/I for *urinary bladder cancer* (Fig. 3.b). In N/C incidence and mortality rates were lower and both significantly decreasing (-3.47% and -4.71% , respectively), whereas mortality was stable in S/I.

Age-standardised incidence and mortality rates were higher in N/C for *pancreatic cancer* (Fig. 3.c). However, S/I showed a *Worsening* pattern – both incidence and mortality increased significantly (6.12% and

4.15%, respectively) – rather than a *limited progress* as in N/C, thus North to South mortality gap was narrowing.

A limited progress characterized both areas for *breast cancer* but, again, with better perspectives in N/C (Fig. 4.a). Incidence was higher in N/C than in S/I (163.6 vs 131.9) but increased less fast (1.14% vs 4.67% per year). Mortality was slightly higher in N/C (33.59 vs 31.46) but declined slower in S/I (-2.52%) compared to N/C (-6.01%). Survival trends were stable in both areas thus the North to South gap persisted in 2015–2017 (89.0% vs 84.9%).

Two distinct patterns emerged for incidence and mortality of *kidney cancer* (Fig. 4.b): worsening in S/I (increasing trends) and limited progress in N/C (stable trends), consistently with a constant 5 % absolute percentage points difference between 5-y survival in N/C (74.5%) and S/I (69.8%).

Worsening scenario resulted for *female lung cancer* in both areas (Fig. 4.c): incidence and mortality were still higher in N/C, but the annual increase was much stronger in S/I (14.09% and 10.05%, respectively) than in N/C (3.81%, 1.86%), and the North to South gap was close to revert in 2015–2017.

4. Discussion

Our findings highlighted relevant advancements in cancer control at national level between 2008 and 2017, but also significant disparities between the North/Centre and South/Islands macro-areas and, sometimes, between men and women.

The optimal progress scenario for all cancers in men reflected the positive trends observed for many common tumours in the male population (prostate, lung, colon, rectum, stomach, liver, head and neck, non-Hodgkin lymphoma). Conversely, the limited or null progress observed for breast, thyroid, and female lung cancers contributed to explain the less positive pattern found for all cancers trends in women compared to men.

The national trends observed are the result of contrasting trends between the North/Centre and South/Islands areas of the country (e.g. for all cancers in females, colon-rectum, pancreas and kidney). Even when trends are similar, improvements are stronger in the north (all

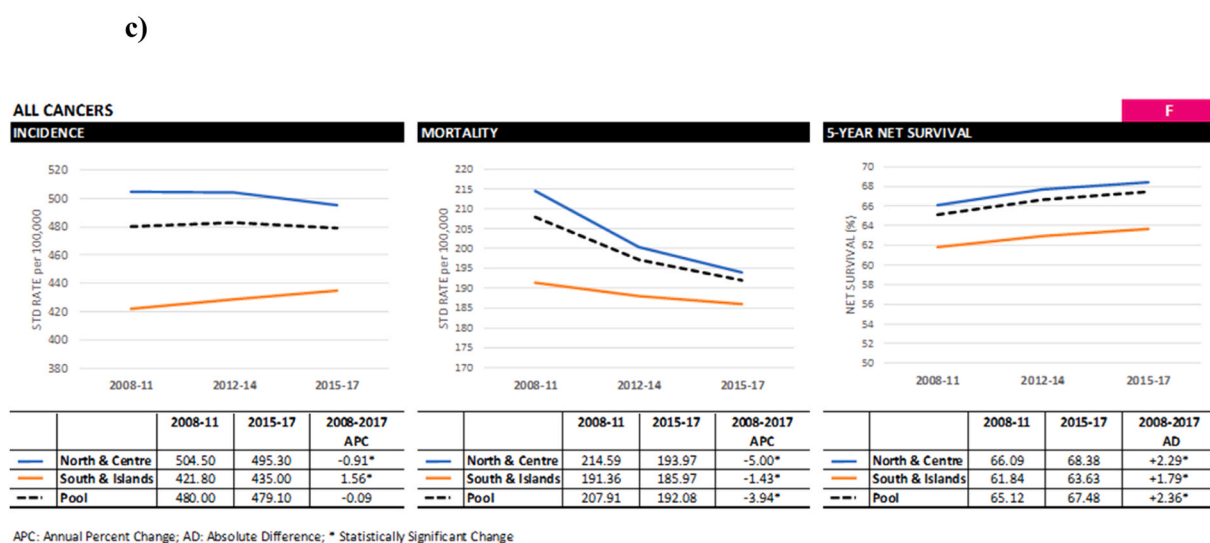
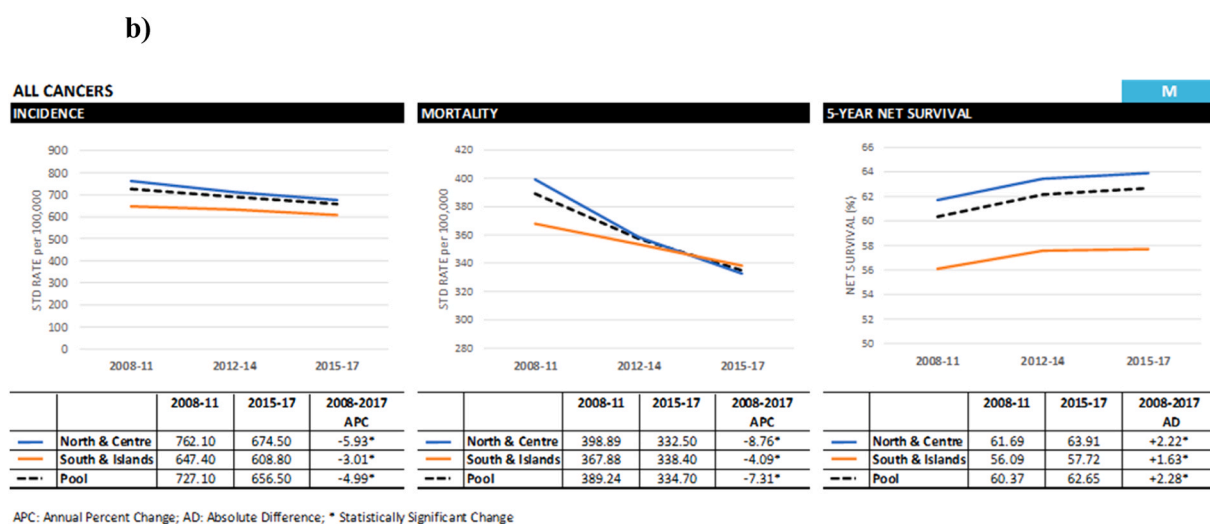
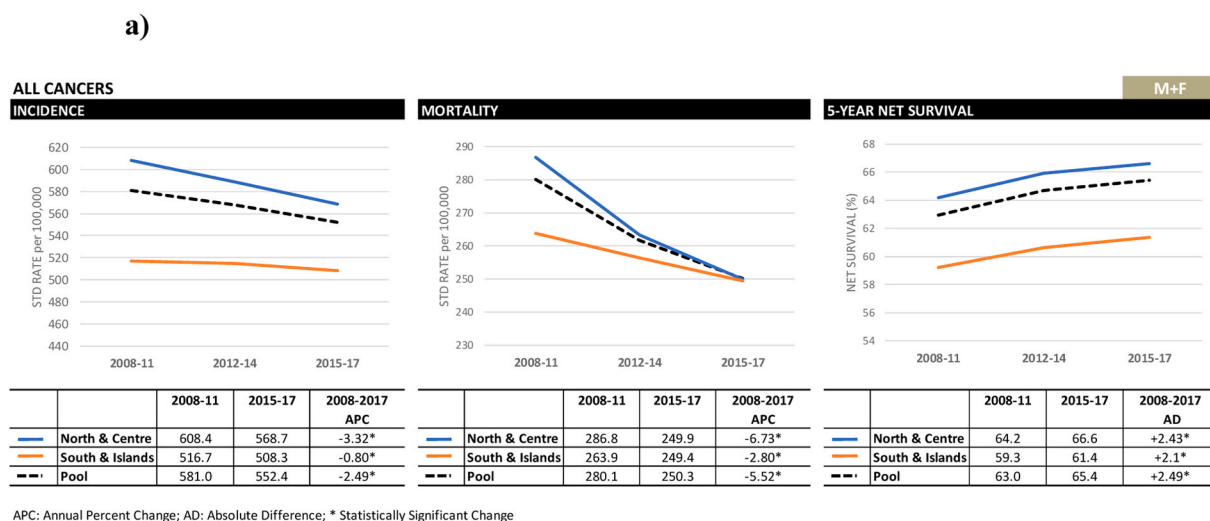
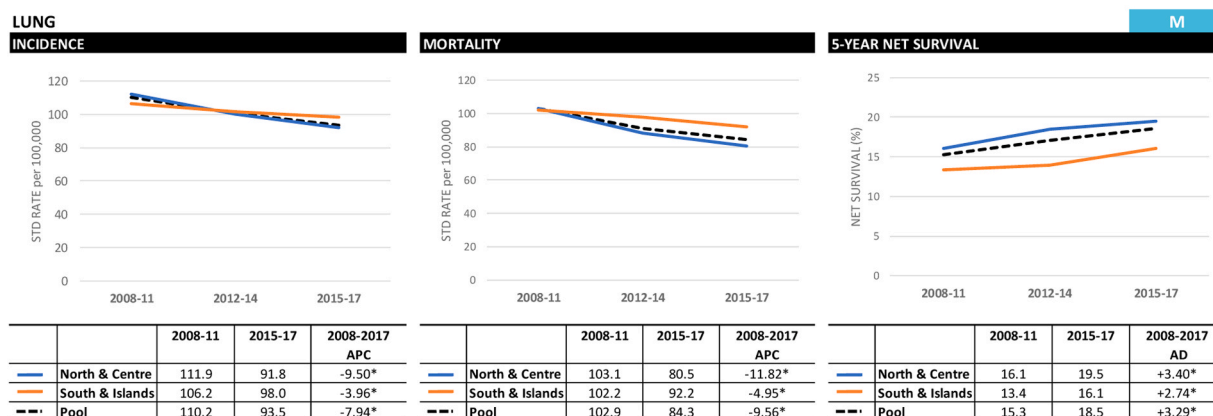


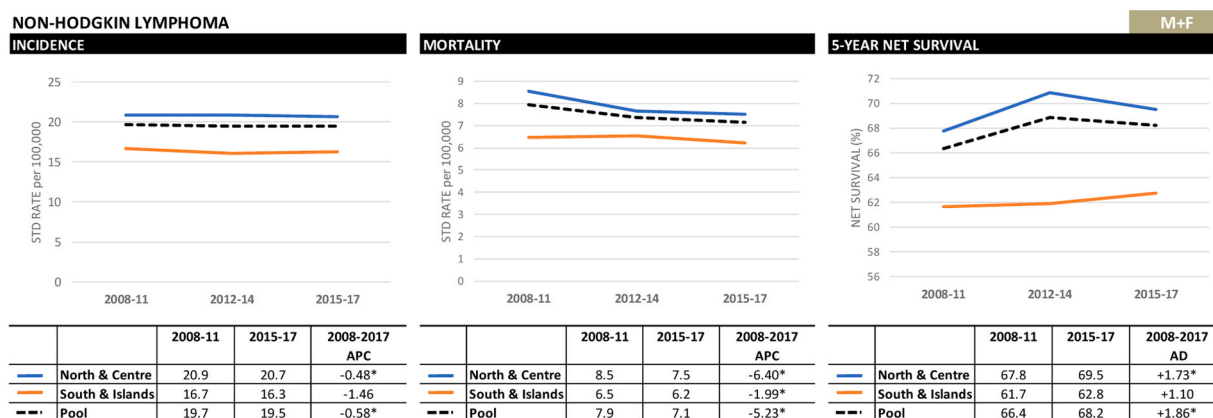
Fig. 1. All cancers by sex. Cancer incidence, survival and mortality trends in Italy (Pool of 20 cancer registries), North/Centre and South/Islands according to progress scenario for all cancers in both sexes (a), all cancers in men (b), all cancers in women (c). Time trends 2008–2017 of age-adjusted incidence and mortality rates per 100,000 with corresponding estimated Annual Percent Change (APC). Age adjusted period estimate of 5-year net survival (% proportions) and corresponding Absolute Difference (AD) between 2015–2017 and 2008–2011.

a)



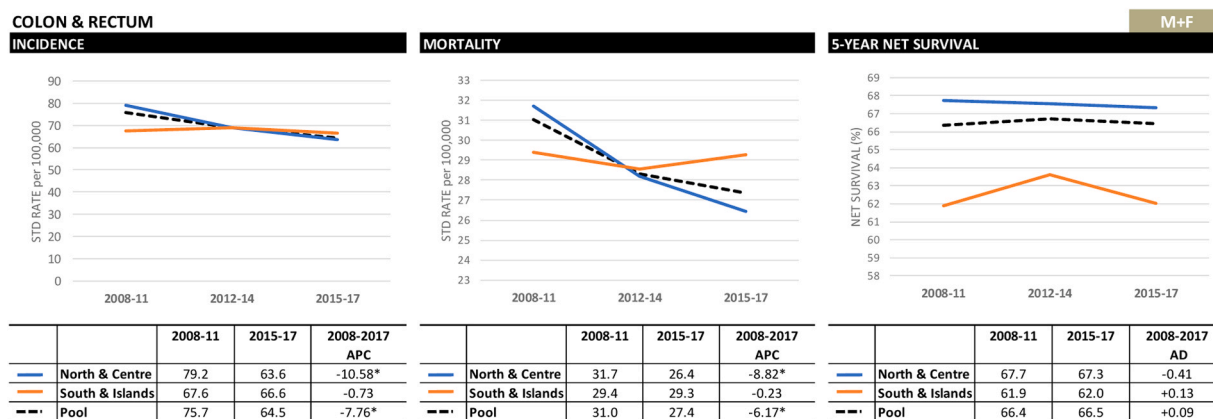
APC: Annual Percent Change; AD: Absolute Difference; * Statistically Significant Change

b)



APC: Annual Percent Change; AD: Absolute Difference; * Statistically Significant Change

c)



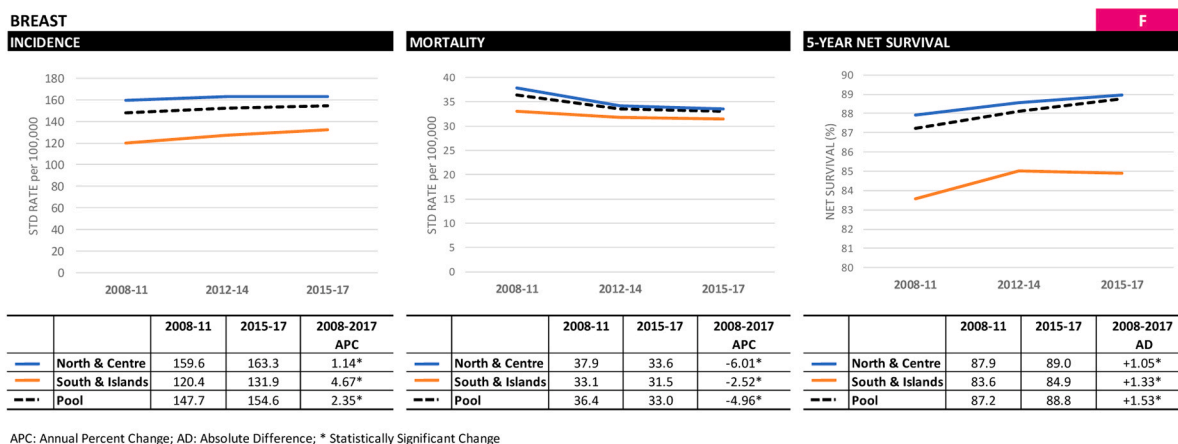
APC: Annual Percent Change; AD: Absolute Difference; * Statistically Significant Change

Fig. 2. Cancers with optimal to good progress at national level: lung cancer in men (a), non-Hodgkin lymphoma (b) and colorectal cancer (c). Cancer incidence, survival and mortality trends in Italy (Pool of 20 cancer registries), North/Centre and South/Islands according to progress scenario. Time trends 2008–2017 of age-adjusted incidence and mortality rates per 100,000 with corresponding estimated Annual Percent Change (APC). Age adjusted period estimate of 5-year net survival (% proportions) and corresponding Absolute Difference (AD) between 2015–2017 and 2008–2011.

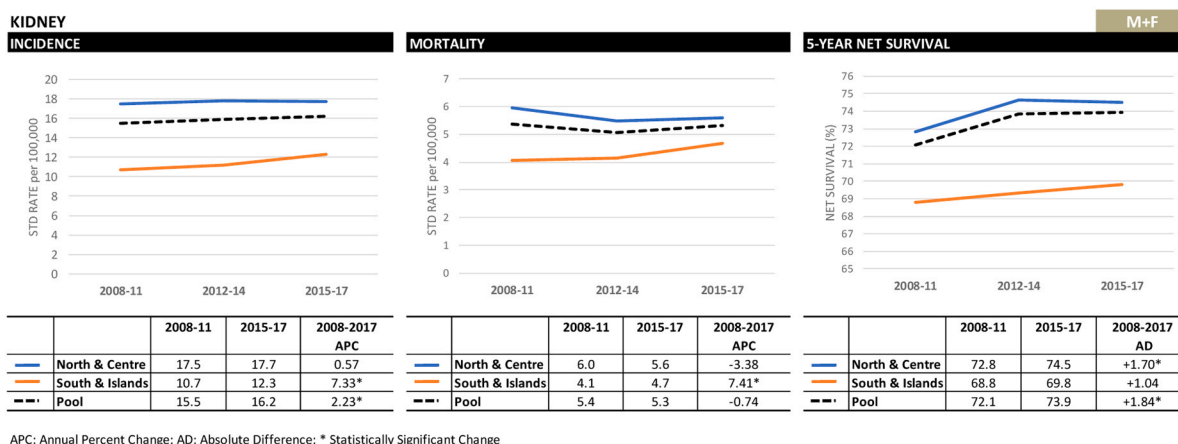


Fig. 3. Cancers showing good progress at national level (a, prostate) progress (b, urinary bladder) or limited progress (c, pancreas). Cancer incidence, survival and mortality trends in Italy (Pool of 20 cancer registries), North/Centre and South/Islands according to progress scenario. Time trends 2008–2017 of age-adjusted incidence and mortality rates per 100,000 with corresponding estimated Annual Percent Change (APC). Age adjusted period estimate of 5-year net survival (% proportions) and corresponding Absolute Difference (AD) between 2015–2017 and 2008–2011.

a)



b)



c)

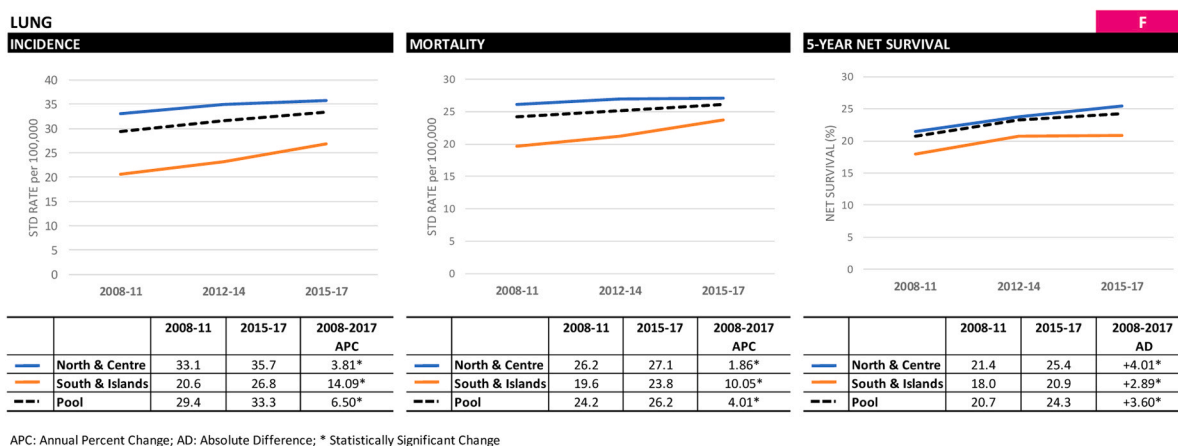


Fig. 4. Cancers showing limited progress at national level (a, breast; b, kidney) or worsening trend (c, female lung cancer). Cancer incidence, survival and mortality trends in Italy (Pool of 20 cancer registries), North/Centre and South/Islands according to progress scenario. Time trends 2008–2017 of age-adjusted incidence and mortality rates per 100,000 with corresponding estimated Annual Percent Change (APC). Age adjusted period estimate of 5-year net survival (% proportions) and corresponding Absolute Difference (AD) between 2015–2017 and 2008–2011.

cancers in both sexes, all cancers in men, lung cancer in men, non-Hodgkin lymphoma, prostate cancer, bladder cancer and breast cancer mortality) and worsening is stronger in the south (lung cancer in women, breast cancer incidence). The health advantage of the south observed in the past (low incidence and mortality) is going to be lost, and the data suggest that, in future, the southern regions and islands will be the areas at the greatest cancer risk. Considering all cancers, the progressive reduction in the north-south gradient was already well advanced in the examined period, and cancer mortality in the southern male population already exceeded that in the northern and central regions. This is the result of more favourable trends in the north and centre, and less favourable trends in the south and islands. If these trends remain stable, data from the 2020–2030 decade will likely show the reversal of the north-south gradient for many cancers.

The disadvantage of the S/I area in terms of cancer survival is systematic. It is likely that the more limited access to early diagnosis and effective treatment is influenced by a mix of individual factors (socio-economic status) and contextual factors (quality and accessibility of services in the area).

The contrasting trends in colorectal and breast cancer between northern and southern Italy are consistent with the fact that screening coverage is still lower in the south/islands today than in the northern and central regions [27] and was even lower during the period covered by the study. Referring to FIT (Fecal Immunochemical Test) tests performed on people aged 50–69, both within and outside organized screening programmes, the PASSI surveillance system reported participation rates ranging from 57.9% in 2010 to 68.4% in 2018 in northern Italy, from 36.2% to 53.9% in central Italy, and from 14.2% to 26.4% in southern Italy and the islands [8,9].

The same report referring to mammograms performed by women aged 50–69, both inside and outside organised screening programmes, highlighted an adherence varying from 80.1% in 2008 to 83.6% in 2018 in Northern Italy, from 75.4% to 80.8% in Central Italy and from 49.6% to 61.1% in the South/Islands. In addition to lower mammographic screening uptake, the dynamics of breast cancer reproductive risk factors, such as breastfeeding and parity, are more favourable in northern and central areas than in southern Italy [7].

The faster increase in female lung cancer incidence in S/I compared with N/C is consistent with the reported trends in smoking prevalence among women between 1995 and 2020, which declined in N/C and increased in S/I [28]. Similarly, with regard to male lung cancer, the disadvantage observed in S/I is coherent with the higher prevalence of smokers reported in men (36.4% and 33.4% for S/I and N/C, respectively in 1995). Smoking prevalence is higher in low socioeconomic groups [29,30] and the observed patterns are consistent with north to south socioeconomic and educational inequalities.

Results for pancreatic cancer may be partly determined by a greater prevalence in southern regions of dysmetabolic risk factors, such as diabetes and excess weight (overweight and obese) [31,32]. Regarding diabetes, the PASSI surveillance system highlighted a significant north-south gradient with percentages, in 2008, of 3.9% in North, 5.1% in Centre and 5.7% in South/Islands, with no substantial changes in subsequent years [33]. A similar geographical gradient is reported for excess weight in adults, with percentages, in 2008, of 38.8% in North, 40.7% in Centre and 46.5% in South/Islands [34].

Trends presented here are not directly comparable with previous AIRTUM studies on incidence and mortality [12] and on net survival [35] because they had different reference targets (time periods, involved cancer registries and geographical comparisons) and objectives. However, these studies confirmed the two key elements highlighted in this study: the undoubted progress in cancer control achieved in Italy and the persistent inequalities between macro-areas.

The study has some limitations. Our analysis refers to a period that is not recent. The frequency with which Italian cancer registry data are updated varies considerably across the country and this criticality has been accentuated by difficulties linked to the restrictions on privacy as

well as by the impact of Covid pandemic on cancer registration [19]. The period 2008–2017 represented the best possible compromise between data updating and broadest geographical coverage. Nevertheless, the study provides a valid foundation for future comparisons, once more current information is available.

Given the partial population coverage, the results presented may not be fully representative of the situation in Italy, although the proportion of the population covered is fairly balanced between the North-Centre and the South-Islands.

Unfortunately, not all Italian cancer registries collect systematic information on stage at diagnosis, thus we could not assess the impact of early diagnosis on the survival inequalities we observed very often between N/C and S/I areas.

For some cancers, the intensity of diagnostic activity has a mixed impact: positive association with incidence and survival, accompanied by no or negligible impact on mortality. In particular, overdiagnosis due to increased diagnostic intensity vary across the country and this heterogeneity may have affected the geographical variations observed for skin melanoma, prostatic, thyroid and breast cancers [36–39]. Misclassification of official statistics on uterine cancer mortality in Italy impaired meaningful assessment of mortality trends for cervical and corpus uteri cancers. In the period considered, the proportion of deaths for uterine cancer coded with unspecified sub-site (ICD-10 code C55) exceeded 50%, resulting in a substantial underestimation of mortality for both cancer entities. This issue was not confined to Italy [40] and has not yet been resolved in recent years [41].

5. Conclusions

The findings from this comprehensive analysis suggest that a major transition is ongoing in Italy. The north-south gradient that has characterised cancer epidemiology over the last 50 years is expected to disappear and progressively revert due to changes in individual lifestyle that, together with social and economic disparities, contributed to homogenising the risk factors and penalising southern areas. Of relevance, lower coverage and delayed implementation of breast, colorectal and cervical cancers screenings in the south and islands - where socioeconomic deprivation is more prevalent - reduces the ability of organised programmes to promote better cancer care in the most vulnerable populations.

The persistent socioeconomic gap in southern areas can only exacerbate the less favourable trends in the south in all aspects of the cancer pathway, from primary prevention to access to treatment.

Our findings point to the need to strengthen primary prevention measures (smoking cessation, nutritional education, promotion of a healthier lifestyle, reducing pollution) and to remove the obstacles to implementing cancer screening programmes fully in southern Italy [42]. In this respect, a major initiative to be monitored in the future is the National Program for Health Equity (PNES), which includes among its scopes the promotion of cancer screening in seven southern Italian regions that are particularly behind in the organization and implementation of such programmes [17].

Furthermore, a radical overhaul of the organization of the system for taking charge and managing patients with cancer throughout the entire diagnostic, therapeutic, and care pathway, should be considered. The activation of oncology networks in some regions of southern Italy, starting in 2016, is a step in this direction, but results may only be seen in the coming years.

CRedit authorship contribution statement

Mario Fusco: Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Conceptualization. **Gemma Gatta:** Writing – review & editing. **Luigino Dal Maso:** Writing – review & editing, Validation. **Walter Mazzucco:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project

administration. **Maurizio Zarcone:** Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Roberta De Angelis:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Fabrizio Stracci:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration. **Diego Serraino:** Writing – review & editing, Validation. **Maria Teresa Pesce:** Writing – review & editing, Project administration, Methodology, Data curation. **Viviana Perotti:** Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation. **Sabrina Fabiano:** Writing – review & editing, Writing – original draft, Software, Methodology, Formal analysis, Data curation. **AIRTUM Working Group:** Writing – review & editing. Data curation.

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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 “North-south disparity in cancer control progress in Italy: a joint analysis of incidence, mortality and survival time trends by geographical area”, the declaration of interest is: none.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.canep.2026.103142](https://doi.org/10.1016/j.canep.2026.103142).

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