Received: 26 October 2023 | Revised: 15 January 2024 | Accepted: 20 February 2024

DOI: 10.1002/ijc.34923

RESEARCH ARTICLE

Cancer Epidemiology

IJC INTERNATIONAL JOURNAL of CANCER | UICC

Cure indicators and prevalence by stage at diagnosis for breast and colorectal cancer patients: A population-based study in Italy

Luigino Dal Maso[1] | Federica Toffolutti[1] | Angela De Paoli[2] | Fabiola Giudici[1] | Silvia Francisci[3] | Lauro Bucchi[4] | Manuel Zorzi[2] | Mario Fusco[5] | Adele Caldarella[6] | Silvia Rossi[7] | Roberta De Angelis[7] | Laura Botta[8] | Alessandra Ravaioli[4] | Claudia Casella[9] | Antonino Musolino[10] | Maria Francesca Vitale[5] | Lucia Mangone[11] | Anna Clara Fanetti[12] | Eva Carpin[2] | Maria Giovanna Burgio Lo Monaco[13] | Enrica Migliore[14] | Maria Letizia Gambino[15] | Margherita Ferrante[16] | Fabrizio Stracci[17] | Cinzia Gasparotti[18] | Giuliano Carrozzi[19] | Rossella Cavallo[20] | Walter Mazzucco[21] | Paola Ballotari[22] | Stefano Ferretti[23] | Giuseppe Sampietro[24] | Roberto Vito Rizzello[25] | Lorenza Boschetti[26] | Giuseppe Cascone[27] | Michael Mian[28] | Maria Teresa Pesce[29] | Daniela Piras[30] | Rocco Galasso[31] | Francesca Bella[32] | Pietro Seghini[33] | Pasquala Pinna[34] | Emanuele Crocetti[1] | Diego Serraino[1] | Stefano Guzzinati[2] | AIRTUM Working Group

Correspondence
Luigino Dal Maso, Cancer Epidemiology Unit, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Via Franco Gallini 2, 33081 Aviano (PN), Italy.
Email: dalmaso@cro.it

Stefano Guzzinati, Veneto Tumour Registry, Azienda Zero, Via Jacopo Avanzo 35, 35132 Padova, Italy.
Email: stefano.guzzinati@azero.veneto.it

Abstract

People alive many years after breast (BC) or colorectal cancer (CRC) diagnoses are increasing. This paper aimed to estimate the indicators of cancer cure and complete prevalence for Italian patients with BC and CRC by stage and age. A total of 31 Italian Cancer Registries (47% of the population) data until 2017 were included. Mixture cure models allowed estimation of net survival (NS); cure fraction (CF); time to cure (TTC, 5-year conditional NS >95%); cure prevalence (who will not die of cancer); and

Members of the AIRTUM WG: Elena Demuru, Sandra Mallone, Andrea Tavilla (ISS Roma), Gemma Gatta, Paolo Contiero, Giovanna Tagliabue (Fondazione IRCCS Istituto Nazionale Tumori Milano), Riccardo Capocaccia (E&P), Fabio Falcini (Romagna Cancer Registry–CR), Antonella Puppo (Liguria CR), Maria Michiara (Parma CR), Isabella Bisceglia (Reggio Emilia CR), Paola Giumelli (Sondrio-ATS Montagna CR), Massimo Rugge (Veneto CR), Gianfranco Manneschi (Tuscany CR), Martina Taborelli (FVG CR), Simona Carone (Puglia CR), Stefano Rosso (Piedmont CR), Monica Lanzoni (Insubria CR), Antonietta Alfia Torrisi (Catania-Messina-Enna CR), Fortunato Bianconi (Umbria CR), Giovanni Maifredi (Brescia CR), Claudia Cirilli (Modena CR), Giuseppe Frasci (Salerno CR), Maurizio Zarcone (Palermo CR), Erica Giacomazzi (Mantova-Cremona CR), Andreina Zanchi (Bergamo CR), Maria Adalgisa Gentilini (Trento CR), Stefano Marguati (Pavia CR), Eugenia Spata (Ragusa-Caltanissetta CR), Fabio Vittadello (Bolzano SABES-ASDAA CR), Maddalena Merola (Caserta CR), Giovanna Biddau (Nord Sardegna CR), Luciana Del Riccio (Basilicata CR), Antonino Ziino Colanino (Siracusa CR), Rita Prazzoli (Piacenza CR), Luisa Canu (Nuoro CR).

For affiliations refer to page 278

Funding information
Associazione Italiana per la Ricerca sul Cancro, Grant/Award Numbers: 28893, 21879; Italian Ministry of Health (Ricerca Corrente), Grant/Award Number: [nograntnumber]

already cured (prevalent patients living longer than TTC). 2.6% of all Italian women (806,410) were alive in 2018 after BC and 88% will not die of BC. For those diagnosed in 2010, CF was 73%, 99% when diagnosed at stage I, 81% at stage II, and 36% at stages III–IV. For all stages combined, TTC was >10 years under 45 and over 65 years and for women with advanced stages, but ≤1 year for all BC patients at stage I. The proportion of already cured prevalent BC women was 75% (94% at stage I). Prevalent CRC cases were 422,407 (0.7% of the Italian population), 90% will not die of CRC. For CRC patients, CF was 56%, 92% at stage I, 71% at stage II, and 35% at stages III–IV. TTC was ≤10 years for all age groups and stages. Already cured were 59% of all prevalent CRC patients (93% at stage I). Cancer cure indicators by stage may contribute to appropriate follow-up in the years after diagnosis, thus avoiding patients' discrimination.

KEYWORDS
breast cancer, cancer prevalence, colorectal cancer, cure fraction, stage at diagnosis, time to cure

What's New?

Organized population screening and improvements in therapies for patients with breast and colorectal cancers mean people are living longer after diagnosis and treatment. Here, the authors evaluated indicators of cure by stage at diagnosis. These indicators included time to cure, cure prevalence, and residual risk of death. Availability of these indicators can help to more accurately identify patients who have already been cured. For patients, being classified as "cured" will improve quality of life, reduce stigma and discrimination, and support a return to work, social life, and reproductive choices.

1 | INTRODUCTION

Breast cancer (BC) and colorectal cancer (CRC) are the first and second most frequent types of cancer in Italy. BC accounts for 55,100 new diagnoses and 12,600 deaths each year, while CRC for 48,600 new diagnoses and 21,800 deaths.[1] In recent decades, improved survival has been demonstrated for patients with these tumors.[2,3] The large difference between the number of diagnoses and deaths (incidence/mortality ratio >4 for BC and >2 for CRC) suggests that many people diagnosed with these two cancers may be cured and die several years after diagnosis from causes unrelated to primary cancer. Accordingly, in 2010 in Italy, it was estimated that 600,000 women diagnosed with BC and 357,000 people with CRC were alive (i.e., prevalent cases), with an expected 40% increase for the following decade.[4] For BC and CRC, the observed trends in the incidence (slightly increasing), mortality (decreasing) and prevalence (increasing) are the result of the combined effect of preventive measures, increased participation in organized population screening aimed at detecting cancer at an early stage when they can be treated and cured, and advances in treatments.[5]

The stage at diagnosis is the most important prognostic factor for patients with BC and CRC, and several studies have reported estimates of incidence and 5-year (i.e., short-term) net survival (NS) after BC[6,7] and CRC[8,9] by stage at diagnosis in high-income countries. However, information on survival beyond 5 years after diagnosis or "cure" of these cancer patients according to the stage at diagnosis is limited[6] and still lacking in Italy.

This paper aimed to describe long-term survival, the complete cancer prevalence, and four indicators of cancer cure (besides the residual risk of death) for Italian patients with BC and CRC according to the stage and age at diagnosis. A number of different indicators have been estimated to represent distinct aspects of survivorship.

2 | MATERIALS AND METHODS

2.1 | Study population

The study population included three cohorts. Cohort 1 was used to calculate the complete prevalence of BC and CRC overall (i.e., all stages). It included 31 cancer registries with at least 9 years of registration until 2017 and patient vital status ascertainment at least 1 year after the last incidence date (i.e., December 31, 2017). These 31 registries have a duration of registration ranging from 9 to 40 years, with a median of 22 years, and cover more than

28 million people of all ages (47% of the Italian population) with comparable geographical representativeness in the North Centre (43%) and South-Islands (55%). This cohort included 443,901 incident malignant BC cases diagnosed in women until January 1, 2018, and 420,726 CRC cases (Supplementary Table S1). Cohort 2 included 22 registries (covering 35% of the Italian population) with at least 15 years of registration. It was used to estimate long-term survival and all cure indicators for BC and CRC cancer overall (i.e., all stages combined). Cohort 3 included six registries for BC and five for CRC (covering 6% of the Italian population) providing stage information for at least two-thirds (67%) of the patients in each calendar year of registration, and at least 15 consecutive years in the period 1997–2017. This cohort was used to estimate long-term survival and all cure indicators according to the stage at diagnosis, available for 52,111 BC cases and 39,092 CRC cases (Supplementary Table S1).

The ICD-10 was used to identify cancer types (C18–C21 for CRC, C50 for BC), and the TNM (7th edition) to define the stage at diagnosis. According to the Italian and international rules, TNM staging was based on histopathological examination (pTNM) if available, on the clinical examinations which led to diagnosis otherwise. Stages III and IV were grouped because of the limited number of metastatic cases (stage IV) with long-term survival and, consequently, the instability of cure estimates for these patients. For each individual we considered only the first primary cancer occurring in that specific anatomic site.

2.2 | Methods

The following indicators were estimated for BC women and CRC patients, stratified by age (0–44, 45–54, 55–64, 65–74, 75+ years) and stage at diagnosis. Indicators were also estimated by sex and subtypes (i.e., colon, rectum) for CRC. The methodological details on the study population, definitions, models used and assumptions, and their validation can be found in a recent paper.[10] All models are specific for each cancer type, stage, and sex, and include period of diagnosis and age group as covariates.

The crude probability of death measures the mortality/survival patterns experienced in a cohort of cancer patients on which many possible causes of death are acting simultaneously. The NS measures the survival probability after a diagnosis of cancer (i.e., as if the disease under study was the only possible cause of death) by eliminating the chance of dying from other causes. This indicator is particularly suitable from a public health perspective (i.e., the one used in population-based studies) since allows comparison among populations or periods preventing (adjusting) major differences from being attributed to changes in the risk of dying from causes other than cancer. NS was calculated for BC and CRC cases of all ages diagnosed in the period 1991–2017 and followed up until December 31, 2018 (Cohort 2), using the cohort method and the Pohar Perme approach, as implemented by SEER*Stat software.[11] NS estimation was calculated in the period 1997–2017 for the subset of registries (Cohort 3) with information on the cancer stage. Model-based NS was calculated using mixture cure models as a combination of two models that estimate both the cure fraction (CF), that is, the proportion of cured patients reaching the same death rates as the general population, and the survival function of the remaining "not-cured" patients (i.e., fatal cases, 1-CF). Five-year conditional net survival (CNS) was calculated as the probability of surviving five additional years, given that patients already survived a certain number of years. For any cancer type and sex, the model that best fits NS and CNS was explored starting from an age-stratified Weibull model. When this model did not converge, alternative models were explored, that is, Weibull without age stratification, age-stratified exponential, or exponential without age stratification. Parameters were estimated using the SAS NLIN procedure. The goodness of fit of "model-based" NS to "observed" NS was evaluated by likelihood ratio tests and by visual comparison, for each cancer type and stage, period of diagnosis, sex, and age group (i.e., covariates).[10]

The complete prevalence represents all previously diagnosed cancer survivors, regardless of the time elapsed since diagnosis, and was calculated as of January 1, 2018 by adjusting the observed prevalence in each registry (Cohort 1) using the completeness index method. The absolute number of prevalent cases in Italy for each cancer type and stage was obtained as the sum of proportions calculated by pooling cancer registries, multiplied by the corresponding Italian population on January 1, 2018.

The CF is the proportion of newly diagnosed cases who will not die from cancer (i.e., cured patients), calculated by the mixture-cure model as the NS value corresponding to the attained age of 100, the maximum reasonable age a person in the population can reach.

The time to cure (TTC) is defined as the time to reach a 5-year CNS of more than 95%, thus assuming the excess mortality due to cancer becomes negligible. CF and TTC were centered on 2010 as the year of diagnosis (approximately the median year of diagnosis of BC and CRC Italian patients prevalent in 2018). CF and TTC were not presented for CRC <45 years by stage due to the small number of cases (Supplementary Table S1).

The cure prevalence (CurePrev) is the proportion of all prevalent patients who will not die of cancer. CurePrev was also calculated for prevalent patients who have already survived 5, 10, and 15 years after a cancer diagnosis. The complement of this quantity (i.e., 1-CurePrev) can be read as the residual excess risk of death for cancer patients, that is, those who are expected to die because of cancer.

The already cured are the number and proportion of all prevalent patients who live longer than the TTC, as described above. Already cured patients in 2018 were estimated as the sum, by age and stage at diagnosis, of patients living longer than TTC.

3 | RESULTS

3.1 | Breast cancer women

Figure 1 presents the 10-year NS of cancer patients in Italy in 3-year periods of diagnosis from 1997 to 2008. For BC women, 10-year NS for all stages combined showed a consistent increase from

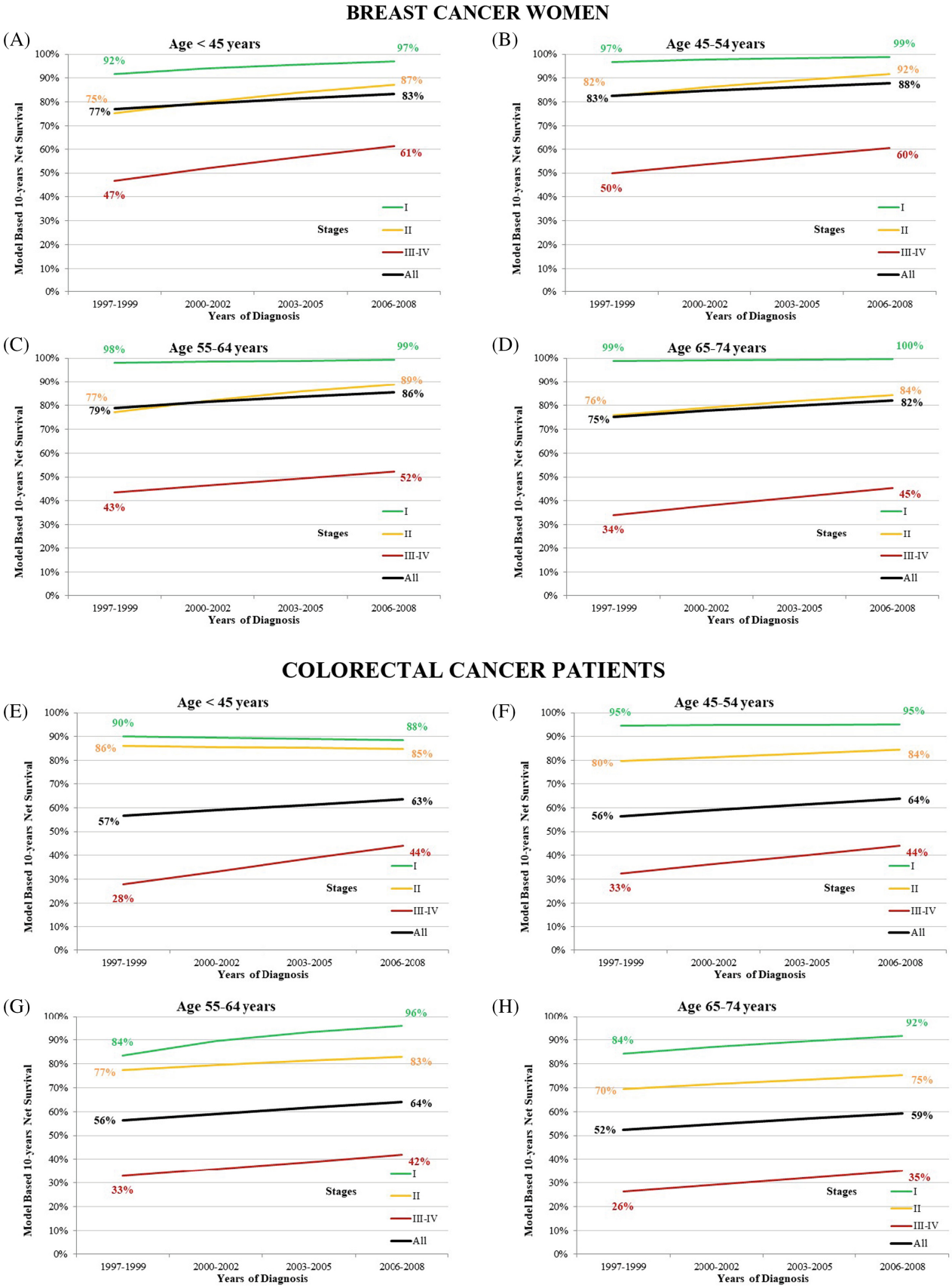

FIGURE 1 Ten-year net survival (NS; NS estimates for all stages included also those with unknown stages) (Estimates are based on the 10-year NS function for each cancer site and age parameterized using mixture cure models.) for breast (A)–(D) and colorectal (E)–(H) cancer patients diagnosed in 1997–2008 and followed up until 2018, by age and stage at diagnosis. (A) Breast cancer women, age <45 years. (B) Age 45–54 years. (C) Age 55–64 years. (D) Age 65–74 years. (E) Colorectal cancer patients, age <45 years. (F) Age 45–54 years. (G) Age 55–64 years. (H) Age 65–74 years.

TABLE 1 Complete cancer prevalence[a] (cases and proportion per 100,000) for breast and colorectal cancer patients by stage at diagnosis and age at prevalence. Italy, January 1, 2018.

		Proportion per 100,000					
		Age at prevalence (years)					
Cancer site, stage	Prevalent cases	All ages	0–44	45–54	55–64	65–74	75+
Breast, all stages	806,410	2620	185	2122	3781	6062	7355
Breast, stage I	364,715	1185	67	958	1759	3047	3085
Breast, stage II	249,173	809	58	689	1216	1823	2225
Breast, stage III–IV	67,833	220	24	199	366	481	542
Breast, stage missing	124,690	405	36	276	441	711	1503
Colorectal, all stages	422,407	705	19	191	647	1673	3397
Colorectal, stage I	98,387	164	2	34	143	427	790
Colorectal, stage II	135,237	226	3	44	171	500	1204
Colorectal, stage III–IV	111,686	186	6	67	189	468	825
Colorectal, stage missing	77,097	129	7	47	144	279	579

[a]The absolute number of prevalent cases in Italy was obtained as the sum of proportions of prevalence estimates (age-, sex-, and cancer-specific, obtained pooling cancer registries in the north-central area and the South-Islands included in this study) multiplied by the corresponding Italian population (restricted to women for breast cancer) in the same areas at the index date.

TABLE 2 Cure fraction (%)[a] for breast and colorectal cancer patients by stage and age at diagnosis. Italy.

	Age at diagnosis (years)					
Cancer site, stage	All ages[b]	0–44[c]	45–54	55–64	65–74	75+
Breast, all stages	73%	77%	82%	77%	72%	60%
Breast, stage I	99%	97%	98%	99%	99%	100%
Breast, stage II	81%	85%	89%	86%	78%	70%
Breast, stage III–IV	36%	59%	50%	40%	27%	23%
Breast, stage missing	37%	69%	61%	47%	42%	25%
Colorectal, all stages	56%	65%	65%	65%	59%	49%
Colorectal, stage I	92%		89%	95%	90%	95%
Colorectal, stage II	71%		78%	78%	70%	69%
Colorectal, stage III–IV	35%		47%	44%	36%	27%
Colorectal, stage missing	34%		57%	56%	43%	19%

[a]Cure fraction was estimated as NS until the age of 100 years for patients diagnosed in 2010[10].
[b]Estimates for all ages were calculated as the average of age-specific cure fractions, weighted by the proportion of incident cases in the corresponding age group.
[c]Estimates for CRC by stage cannot be calculated for the age group 0–44 years.

1997–1999 to 2006–2008, by about 6 percentage points in all age groups <75 years. Stage I women aged <45 years showed a 10-year NS of 97% in 2006–2008 (Figure 1A) and ≥99% in cases when aged 45 years or more (Figure 1B–D). From 1997–1999 to 2006–2008, a 10 percentage point increase of 10-years NS was observed for women with advanced disease (stage III-IV), showing in 2006–2008 a 10-years NS of about 60% at age <55 years, 52% at age 55–64 years, and 45% at age 65–74 years.

As of January 1, 2018, 806,410 women were alive after BC, representing 2.6% (i.e., 2620 per 100,000) of all Italian women, 2.1% at the age 45–54 and >6% at age ≥65 years (Table 1). About half (364,715, 1.2% of Italian women) had stage I BC, and 67,833 (0.2%) advanced BC. Thirty percent of women living after a BC had been diagnosed from <5 years and 48% from ≥10 years (31% for ≥15 years), with similar percentages for all stages at diagnosis and, in particular, 38% of stage III–IV women had been diagnosed from ≥10 years, data not shown in Tables.

Table 2 illustrates the CF of newly diagnosed BC women and CRC cancer patients by stage and age at diagnosis. The CF was 73% for women diagnosed with BC in 2010 and 77% for all those under 75 years (data not shown); ranging from 82% for those aged 45–54 years to 72% for those aged 65–74 years. For BC women diagnosed at stage I, CF was 99% for all ages combined, and 97% when diagnosed before the age of 45. CF was 81% at stage II and 36% at

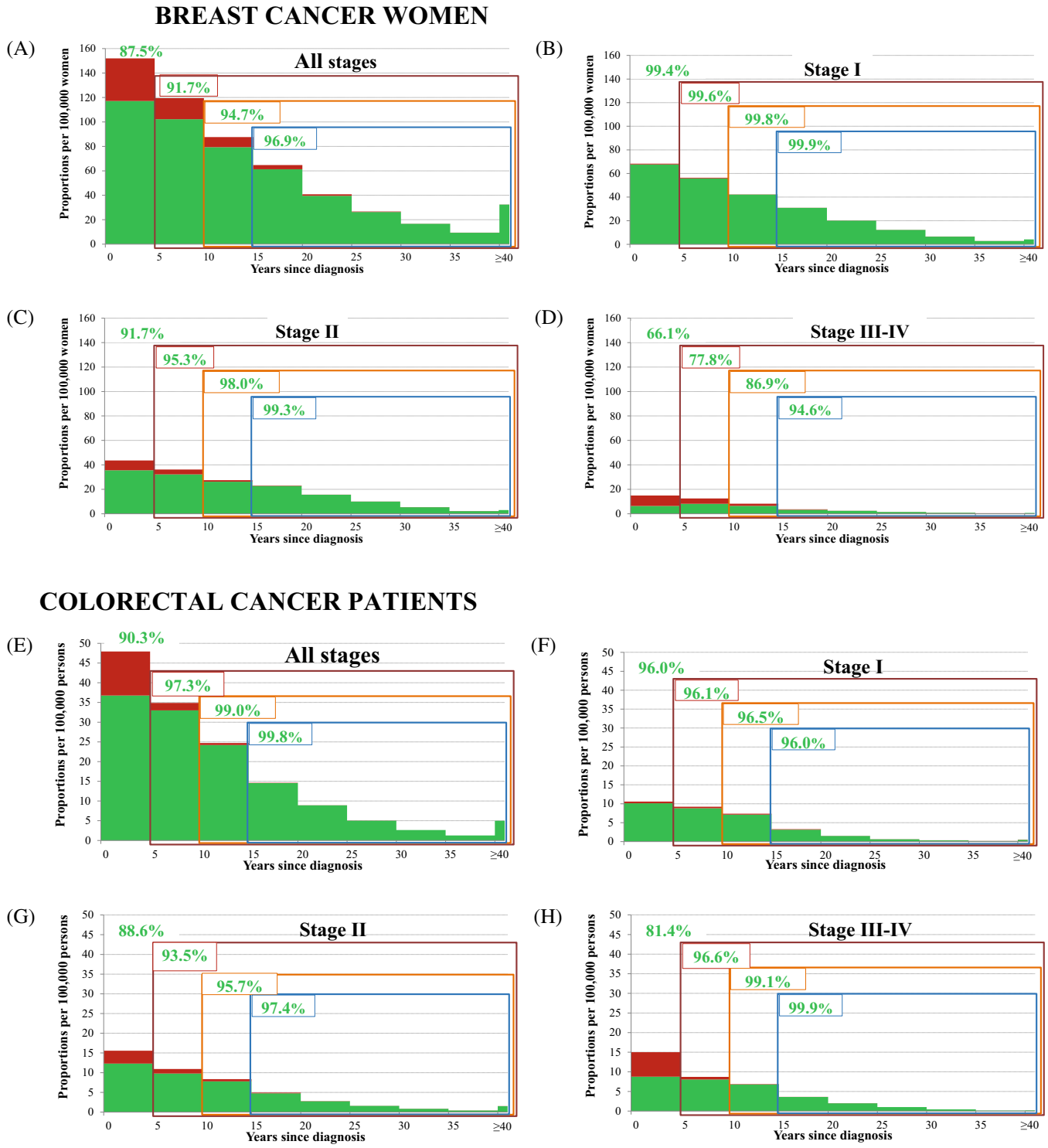

FIGURE 2 Cure prevalence (Each bar of the Figure represents the proportions of prevalent cases per 100,000 persons by time since diagnosis in 5-year periods, at all ages at January 1, 2018. For each time interval, the green part of the bars refers to those who have the same life expectancy as their peers in the general population. The cure prevalence is the proportion of these patients, expected not to die as a result of cancer, out of the total prevalent cases (i.e., 99.4% for breast cancer, stage I, all ages). Focusing on patients alive ≥5, ≥10, or ≥15 years after diagnosis (included in the red, orange, and blue boxes, respectively), the cure prevalence is the probability of being cured, conditioned to survive at least 5, 10, or 15 years after diagnosis. The complement of these probabilities (i.e., 1 − CurePrev) can be read as a residual excess risk of death for cancer patients.) (CurePrev, proportion per 100,000) for breast (A)–(D) and colorectal (E)–(H) cancer patients by stage and years since diagnosis. Italy, January 1, 2018. (A) Breast cancer women, all stages. (B) Stage I. (C) Stage II. (D) Stage III–IV. (E) Colorectal cancer patients, all stages. (F) Stage I. (G) Stage II. (H) Stage III–IV.

TABLE 3 Time to cure (TTC)[a] and already cured[b] for breast and colorectal cancer patients by stage and age at diagnosis. Italy.

	Age at diagnosis (years)					All ages	
	0–44[c]	45–54	55–64	65–74	75+	Already cured	
Cancer site, stage	TTC (years)					%	Cases
Breast, all stages	11	5	8	12	>15	75	606,235
Breast, stage I	1	1	1	1	1	94	348,081
Breast, stage II	1	1	1	12	1	84	212,537
Breast, stage III–IV	12	>15	>15	>15	>15	7	5022
Breast, stage missing	11	15	>15	>15	>15	32	40,595
Colorectal, all stages	6	7	7	8	6	59	248,414
Colorectal, stage I		1	1	1	1	93	92,501
Colorectal, stage II		7	7	10	7	48	65,700
Colorectal, stage III–IV		7	8	9	9	46	52,446
Colorectal, stage missing		10	8	9	9	48	37,767

[a]Time to cure (TTC) is calculated for patients diagnosed in 2010 as the time to reach a 5-year conditional net survival of more than 95%, for each cancer site and age. When the estimated TTC is <1 year, the TTC is set as 1 year.
[b]Calculated as the number and proportion of prevalent patients who already reached the site- and age at diagnosis- specific TTC at January 1, 2018. Already cured for all stages combined were obtained as the sum of already cured by stage. If TTC >15 years, prevalent cases were never considered already cured.
[c]Estimates of TTC for CRC patients by stage cannot be calculated for the age group 0–44 years.

stages III-IV, with a wider variation according to age for advanced stages (i.e., ≥50% under 55 years, 40% at age 55–64 years, and 27% at age 65–74 years).

The proportion of prevalent patients that will be cured by stage for all patients and by years since diagnosis is shown in Figure 2, while the corresponding numbers and proportions for BC women and CRC patients are in Supplementary Table S2. Out of 806,410 prevalent BC women, 87.5% or 705,481 women will be cured (i.e., will not die) from BC (Figure 2A). The proportion becomes 91.7% for women diagnosed since ≥5 years and 94.7% ≥10 years (i.e., the residual proportion of deaths due to BC was 8.3% for those alive for ≥5 years and 5.3% for those ≥10 years). Specifically, the CurePrev was 99.4% for prevalent women with BC at stage I (i.e., 0.6% will die from BC, Figure 2B), 91.7% at stage II (Figure 2C), and 66.1% at stages III–IV (Figure 2D), who experienced a residual risk of death of 13.1% after 10 years and 5.4% after 15 years since diagnosis.

TTC and patients that had reached TTC (i.e., already cured) for Italian cancer patients by stage and age are shown in Table 3. TTC for all BC stages combined was less than 10 years after diagnosis for women diagnosed with BC at ages 45–54 and 55–64 years, 11 years at age <45, and 12 years at age 65–74. In particular, the TTC was ≤1 year after diagnosis of stage I or stage II in BC women aged <65 years, whereas TTC was longer than 10 years for women with advanced BC. Almost all (94%) of stage I BC women and 84% of those diagnosed with stage II have already reached TTC. This percentage dramatically drops to 7% among women diagnosed at an advanced stage. Adding up women in all stages, 75% of BC women can be considered already cured.

3.2 | Colorectal cancer patients

Between 1997–1999 and 2006–2008, a 6–8 percentage points increase in 10-year NS was estimated for CRC patients below age 75 years, with proportions >60% and a particularly marked increase (about 10 percentage points) for advanced stages (Figure 1E–H).

People living after CRC were 422,407 in 2018, 0.7% (705 per 100,000) of the Italian population with a noticeable increase with age compared to BC (Table 1). These numbers were increasing by age, reaching 1.7% (110,711) at age 65–74, and 3.4% (235,981) of those aged 75 years or older. For prevalent CRC patients, 34% were diagnosed within 5 years and 42% after 10 years or more, with similar proportions for all stages at diagnosis (data not shown in tables).

CF for all CRC patients was 56%, 62% for all those <75 years of age (data not shown), and 65% for ages <65 years. CF was 92% for CRC patients diagnosed at stage I; 71% at stage II; 35% at stages III–IV; and 34% at stage missing (Table 2). A four percentage points advantage was observed across all age groups for women (CF = 64% vs. 60% in men), and a similar difference was observed for colon vs. rectal cancer patients (63% and 59%, respectively, data not shown in tables).

In CRC patients, the TTC was between 6 and 8 years in age groups. For patients with CRC at stage I, a TTC ≤1 year was observed, whereas, for patients diagnosed at stages II–IV, the TTC was reached in ≤10 years in all age groups (Table 3). The proportion of already cured CRC patients was 59%, 93% for those diagnosed at stage I, 48% at stage II, and 46% at advanced stages.

For all the 422,407 Italian CRC prevalent patients, the cure prevalence was 90.3% (i.e., 381,496 will not die from CRC), it became

97.3% for those alive at least 5 years after diagnosis and 99.0% for those alive 10 years or more after diagnosis (Figure 2E). Among prevalent CRC patients diagnosed at stage I (Figure 2F), those who will not die of CRC were 96.0%, 88.6% at stage II (Figure 2G), and 81.4% at stages III–IV (Figure 2H). Interestingly, for CRC patients at all stages, the residual risk of death for patients living at least 5 years after diagnosis was 3.9% at stage I, 6.5% at stage II, and 3.4% at stages III–IV (Supplementary Table S2).

4 | DISCUSSION

This study estimates, for the first time in Italy, population-based indicators of cure by stage at diagnosis, for patients with the two most frequent neoplasms: female breast and colorectal cancers. In particular, this study presents complete prevalence, CF, TTC, cure prevalence, the residual risk of death, and the number of patients already cured, which allows for the identification of patients who have negligible excess mortality (5-year CNS > 95%) compared with their peers in the general population.[12–14] Such cases represent 75% of women with BC and 59% of patients with CRC.

According to our results, women living after a diagnosis of stage I BC (half of all patients) have a risk of death from BC of less than 1% and can be considered "cured" immediately after diagnosis and treatment. In addition, when all stages combined are considered, almost 90% of women with BC and patients with CRC will not die for the malignancies.

Some authors have reported comparable CF and TTC estimates for BC and CRC over the past decades, but only a few studies have presented such estimates by stage at diagnosis at the population level for some European countries and in the US.[15–17] CF for all BC women diagnosed in 2010 in this study was almost 80% in all age groups, as in France,[18,19] more than 10 percentage points higher than those estimated for Italian women diagnosed with BC in 2000.[20] A population study in the United States indicated that CF, estimated for women diagnosed in 2018, was 73% in the case of localized BC, 37% in the case of regional disease, and 3% when distant metastasis was present at diagnosis.[21]

Current results on TTC for women with BC at all stages vary with age, from 5 years (at age 45–54 years) to >10 years (under 45 and over 65 years), in agreement with other studies in Europe[18,20,22,23] and elsewhere.[24,25] However, TTC is achieved immediately after treatment when the diagnosis was stage I (or localized)[21,26] with an improvement in CNS at 5 years of about 5 percentage points, compared to estimates for women diagnosed in the period 1998–2008 in the Netherlands.[27]

For CRC patients aged <65 years, CF in the present study was above 60% (5–7 percentage points higher than in 2000),[20] slightly lower at older ages and in men, but ~10% higher than in France.[18] TTC for Italian CRC patients is consistent with previous studies,[18,20,22,23] which do not show excess risk at 8–10 years after diagnosis. Our results on TTC by stage are also in line with comparable studies,[17,28] which show that TTC is achieved in less than 10 years even if CRC is diagnosed at advanced stages.[21] The Dutch study also showed that long-term survival and CF increased substantially over the years, with a greater increase in the more advanced stages of the disease.[16]

Regarding the survival gains observed over time in Italy, the results of the present study are likely attributable to improved treatment options,[29] particularly for women diagnosed with BC after 2000, including those with metastatic disease.[30] The increased prevalence of mammography screening with its down-staging effect is a concurrent explanation for the pattern of survival trend and cure observed for women with BC.[31,32] In Italy, organized BC screening during the study period of observation was largely limited to the age group 50–69 years. Consequently, the result that the 10-year NS of women younger than 45 years is only 2% lower than that of older women indicates that spontaneous use of mammography and access to effective treatment BC balanced the disadvantage of unscreened younger women. In particular, BC women aged <45 years showed higher CF than patients aged 45–64 only for stage III–IV BC, and this should be entirely attributed to effective systemic treatment.

Also for CRC patients, the progressive spread of screening programmes in the Italian regions since the early 2000s.[33] has led to earlier diagnosis, downstaging (including intra-stage downstaging),[34] and lower treatment-related mortality and morbidity. Furthermore, a proportion of BC and CRC (probably to a much lower extent) cancers detected in screening programmes are overdiagnosed[35–37] and are cured by definition.[38]

4.1 | Strengths and limitations

The completeness, accuracy, and representativeness of the cancer registries' data on incidence and survival in Italy represent an important strength of the study.[2,3,10,14] The size of the study population and the duration of follow-up (≥15 years for all CRs used in the modeling) both contributed to the reliability of the estimation of long-term survival, prevalence, and cure indicators. Another strength of the study is the comprehensive presentation, for BC and CRC, of the indicators of long-term survival, prevalence, and cure. Discussion of the links between the different indicators helps to map distinct aspects of survivorship and can answer questions from patients and clinicians in subsequent phases of illness and life. Lastly, the methodology for calculating the cure indicators presented (in particular CF and TTC) is reproducible and feasible[39] and can be applied in other countries.

This study has some limitations. Notably, complete stage information for ≥15 consecutive years was available for a subset of registries, which covered only 6% of the Italian population. This limited coverage does not invalidate the generalization of estimates of cure indicators by stage at diagnosis, since stage-specific survival showed no appreciable geographical difference throughout Italy.[40] Stages III and IV were grouped due to the relatively small number of patients, which led to unstable estimates in some patient groups, particularly those under 45 years of age (too sparse data to calculate CF for younger CRC patients). Patients with unknown stages had slightly higher CF

than stages III–IV, suggesting unstaged patients as a combination of patients with different severity of the disease with a non-negligible proportion of missing stages due to incomplete registration.

International comparisons are also questionable because of the different TNM staging systems.[21,26,41,42] The study, like most population-based studies, also suffers from a lack of individual data on important prognostic factors such as molecular profile, treatment, adherence of patients to screening programmes, and mode of diagnosis (screen-detected).

The cure models we used may have potential limitations as well. The lack of standardized and widely accepted methods for estimating cancer cure indicators[21,43,44] suggests the need for caution in the international comparisons and interpretation of results for cancer cure indicators.[10] In particular, our mixture cure model includes only two patient groups, while non-oncological mortality in cancer patients may be higher than the overall mortality in the general population[3,43] due to a combination of factors, such as long-term adverse effects of treatments and genetic, environmental or lifestyle influences. To disentangle the excess risk of death due to cancer and other associated reasons (lifestyle, treatments), more complex mixture models were proposed[44] showing asymptotic CF for colon cancer patients in France from 0% to 5% higher than the conventional model. These models should be extended and replicated elsewhere. In addition, TTC is inevitably arbitrary and susceptible to the choice of the CNS threshold to fix a low risk of recurrence, death, or the margin of clinical relevance, and the methodological approach used, in particular for cancer types such as BC, which have a non-negligible long-term excess mortality rate. Nevertheless, the threshold used (i.e., the 5-year CNS >95%) is clinically relevant and widely reproducible, as well as the CF estimated using "standard" mixture cure models, allowing comparability between countries.[10,21–23,39] It should be emphasized that, as NS estimates, CF and TTC are considerably less reliable for older patients (e.g., ≥75 years).[45] Finally, no confidence intervals have been presented for cancer cure indicators to avoid misleading interpretations of precision measures related to our results, this issue has been widely discussed elsewhere.[46]

4.2 | Relevance for patients and oncologists

The estimates of indicators of cancer cure by stage may be important for patients and the same applies to oncologists who have an additional element that brings population estimates closer to clinical practice. Our estimates of the CF and TTC for BC and CRC patients can contribute to outlining an appropriate follow-up schedule that changes in the years following diagnosis, reducing unnecessary medicalisation and focusing on the management of late effects.

The continuing increase in the population living after BC or CRC represents an enormous burden on the health care system.[47] Our data on the distribution of total prevalence by tumor stage and the residual risk of death are of considerable practical interest for planning follow-up services. This is especially the case for BC women because there is no consensus on the duration of surveillance.[48]

Estimates of the time to cure, cure prevalence, and the residual risk of death, decreasing with time since diagnosis, may help to recognize several patients as (already) cured ones. These findings may improve the patient's quality of life, avoiding stigma (e.g., discrimination and exclusion from access to life insurance and life insurance-related loans or credit services)[49] and supporting their reproductive life, full rehabilitation, and social life, including the return to work.

4.3 | Conclusions

The findings of this study can be generalized to other countries with comparable healthcare systems.[17,43] This study provides new insights into various aspects of cancer care of patients with BC and CRC, including detailed and highly relevant information on survival and cure, for patients themselves, healthcare policymakers, and stakeholders.[50]

AUTHOR CONTRIBUTIONS

Luigino Dal Maso and Stefano Guzzinati drafted the study protocol. The other authors revised the study protocol, collected the data, and prepared the cleaned data for the study database (Federica Toffolutti, Angela De Paoli, Fabiola Giudici, Silvia Francisci, Roberta De Angelis, Manuel Zorzi, Mario Fusco, Adele Caldarella, Alessandra Ravaioli, Claudia Casella, Antonino Musolino, Maria Francesca Vitale, Lucia Mangone, Anna Clara Fanetti, Eva Carpin, Maria Giovanna Burgio Lo Monaco, Enrica Migliore, Maria Letizia Gambino, Margherita Ferrante, Fabrizio Stracci, Cinzia Gasparotti, Giuliano Carrozzi, Rossella Cavallo, Walter Mazzucco, Paola Ballotari, Stefano Ferretti, Giuseppe Sampietro, Roberto Vito Rizzello, Lorenza Boschetti, Giuseppe Cascone, Michael Mian, Maria Teresa Pesce, Daniela Piras, Rocco Galasso, Francesca Bella, Pietro Seghini, Pasquala Pinna, and Diego Serraino). Luigino Dal Maso, Stefano Guzzinati, Federica Toffolutti, Angela De Paoli, and Fabiola Giudici designed the study and did the statistical analyses. Silvia Francisci, Silvia Rossi, Roberta De Angelis, and Laura Botta contributed to the validation of statistical models and revised the statistical analyses. Lauro Bucchi, Manuel Zorzi, Emanuele Crocetti, and Diego Serraino specifically discussed the assumptions and clinical implications of the indicators of cancer cure by stage. All authors contributed to the interpretation of the study results and approved the submitted version. The work reported in the paper has been performed by the authors unless clearly specified in the text.

AFFILIATIONS

[1]Cancer Epidemiology Unit, Centro di Riferimento Oncologico di Aviano (CRO) IRCCS, Aviano, Italy
[2]Epidemiological Department, Azienda Zero, Padua, Italy
[3]National Centre for Disease Prevention and Health Promotion, National Institute of Health, Rome, Italy
[4]Emilia-Romagna Cancer Registry, Romagna Unit, IRCCS Istituto Romagnolo per lo Studio dei Tumori (IRST) Dino Amadori, Meldola, Forlì, Italy
[5]Registro Tumori ASL Napoli 3 Sud, Napoli, Italy
[6]Tuscany Cancer Registry, Institute for Cancer Research, Prevention and Clinical Network, Florence, Italy

[7]Department of Oncology and Molecular Medicine, National Institute of Health, Rome, Italy
[8]Evaluative Epidemiology Unit, Department of Epidemiology and Data Science, Fondazione IRCCS Istituto Nazionale dei Tumori, Milan, Italy
[9]Liguria Cancer Registry, IRCCS Ospedale Policlinico San Martino, Genova, Italy
[10]Emilia-Romagna Cancer Registry, Parma Unit, Medical Oncology Unit, University Hospital of Parma, Parma, Italy
[11]Emilia-Romagna Cancer Registry, Reggio Emilia Unit, Epidemiology Unit, Azienda Unità Sanitaria Locale—IRCCS di Reggio Emilia, Reggio Emilia, Italy
[12]Sondrio Cancer Registry, Agenzia di Tutela della Salute della Montagna, Sondrio, Italy
[13]Coordination Centre of the Cancer Registry of Puglia—Strategic Regional Agency for Health and Social Care (AReSS), Bari, Italy
[14]Piedmont Cancer Registry, Centro di Riferimento per l'Epidemiologia e la Prevenzione Oncologica (CPO) Piemonte and University of Turin, Turin, Italy
[15]Registro tumori ATS Insubria (Provincia di Como e Varese) S.S. Epidemiologia Registri Specializzati e Reti di Patologia, Varese, Italy
[16]Registro Tumori Integrato di Catania-Messina-Enna, Igiene Ospedaliera, Azienda Ospedaliero-Universitaria Policlinico G. Rodolico-San Marco, Catania, Italy
[17]Umbria Cancer Registry, Public Health Section, Department of Medicine and Surgery, University of Perugia, Perugia, Italy
[18]Registro tumori ATS Brescia, Struttura Semplice Epidemiologia, ATS, Brescia, Italy
[19]Emilia-Romagna Cancer Registry, Modena Unit, Public Health Department, Local Health Authority, Modena, Italy
[20]Cancer Registry Azienda Sanitaria Locale (ASL) Salerno, Dipartimento di Prevenzione, Salerno, Italy
[21]Clinical Epidemiology and Cancer Registry Unit, Azienda Ospedaliera Universitaria Policlinico (AOUP) di Palermo, Palermo, Italy
[22]Osservatorio Epidemiologico, ATS Val Padana, Mantova, Italy
[23]Emilia-Romagna Cancer Registry, Ferrara Unit, Local Health Authority, Ferrara, University of Ferrara, Ferrara, Italy
[24]Bergamo Cancer Registry, Epidemiological Service, Agenzia di Tutela della Salute, Bergamo, Italy
[25]Trento Province Cancer Registry, Unit of Clinical Epidemiology, Trento, Italy
[26]Cancer Registry of the Province of Pavia, Pavia, Italy
[27]Azienda Sanitaria Provinciale (ASP) Ragusa—Dipartimento di Prevenzione—Registro Tumori, Ragusa, Italy
[28]Innovation, Research and Teaching Service (SABES-ASDAA), Lehrkrankenhaus der Paracelsus Medizinischen Privatuniversität, Bolzano-Bozen, Italy
[29]Monitoraggio Rischio Ambientale e Registro Tumori ASL Caserta, Caserta, Italy
[30]Nord Sardegna Cancer Registry, ASL, Sassari, Italy
[31]Unit of Regional Cancer Registry, Clinical Epidemiology and Biostatistics, IRCCS Centro di Riferimento Oncologico di Basilicata (CROB), Rionero in Vulture, Italy
[32]Siracusa Cancer Registry, Provincial Health Authority of Siracusa, Siracusa, Italy
[33]Emilia-Romagna Cancer Registry, Piacenza Unit, Public Health Department, AUSL Piacenza, Piacenza, Italy
[34]Nuoro Cancer Registry, RT Nuoro, Servizio Igiene e Sanità Pubblica, ASL Nuoro, Nuoro, Italy

ACKNOWLEDGEMENTS

This study is dedicated to the memory of Andrea Micheli. The authors thank Mrs Ilaria Calderan for the editorial assistance. Open access funding provided by BIBLIOSAN.

FUNDING INFORMATION

This work was supported by the Italian Association for Cancer Research (AIRC) (Grant no. 21879 and 28893) and by the Italian Ministry of Health (Ricerca Corrente) (no grant nember provided). The funding sources had no involvement in the study design, in the collection, analysis, and interpretation of data, in the writing of the report, and in the decision to submit the article for publication.

CONFLICT OF INTEREST STATEMENT

Emanuele Crocetti declares an epidemiological advice for Astrazeneca, not related to this study. The other authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Study is based on three different cohorts details are described in the Materials and Methods. Further information is available from the corresponding author upon request.

ETHICS STATEMENT

According to the Italian legislation,[51] population-based cancer registries collect pseudonymised personal data for surveillance purposes that do not need the collection of explicit individual consent, without any direct or indirect intervention on patients, therefore the approval of a research ethics committee was not required.

ORCID

Luigino Dal Maso https://orcid.org/0000-0001-6163-200X
Federica Toffolutti https://orcid.org/0000-0002-2907-0745
Angela De Paoli https://orcid.org/0000-0001-9864-6325
Fabiola Giudici https://orcid.org/0000-0002-4160-3479
Silvia Francisci https://orcid.org/0000-0002-1552-1744
Lauro Bucchi https://orcid.org/0000-0002-6771-8119
Manuel Zorzi https://orcid.org/0000-0001-6025-5214
Mario Fusco https://orcid.org/0000-0002-0311-3882
Adele Caldarella https://orcid.org/0000-0003-3439-2295
Silvia Rossi https://orcid.org/0000-0002-9815-2904
Roberta De Angelis https://orcid.org/0000-0001-7787-3043
Laura Botta https://orcid.org/0000-0002-2793-5338
Alessandra Ravaioli https://orcid.org/0000-0002-8778-6397
Antonino Musolino https://orcid.org/0000-0002-7979-6261

Lucia Mangone https://orcid.org/0000-0002-5089-5178
Enrica Migliore https://orcid.org/0000-0003-0121-6295
Margherita Ferrante https://orcid.org/0000-0001-7596-2464
Fabrizio Stracci https://orcid.org/0000-0002-7594-6680
Rossella Cavallo https://orcid.org/0009-0003-4830-621X
Walter Mazzucco https://orcid.org/0000-0001-5090-1366
Paola Ballotari https://orcid.org/0000-0003-4057-3535
Stefano Ferretti https://orcid.org/0000-0001-5241-2101
Giuseppe Sampietro https://orcid.org/0000-0001-8173-7810
Roberto Vito Rizzello https://orcid.org/0009-0006-6452-5529
Lorenza Boschetti https://orcid.org/0009-0000-1645-2587
Giuseppe Cascone https://orcid.org/0009-0001-8699-2586
Michael Mian https://orcid.org/0000-0003-2539-5996
Daniela Piras https://orcid.org/0009-0002-2606-7716
Rocco Galasso https://orcid.org/0000-0003-4831-6437
Pietro Seghini https://orcid.org/0000-0002-4311-0213
Emanuele Crocetti https://orcid.org/0000-0002-4649-2034
Diego Serraino https://orcid.org/0000-0003-0565-8920
Stefano Guzzinati https://orcid.org/0000-0002-4908-5506
Elena Demuru https://orcid.org/0000-0003-2979-4169
Sandra Mallone https://orcid.org/0000-0001-6686-6905
Andrea Tavilla https://orcid.org/0000-0003-1657-2196
Gemma Gatta https://orcid.org/0000-0003-4160-6458
Paolo Contiero https://orcid.org/0000-0001-6760-3605
Fabio Falcini https://orcid.org/0000-0002-0864-6266
Massimo Rugge https://orcid.org/0000-0002-0679-0563
Gianfranco Manneschi https://orcid.org/0000-0002-3785-526X
Martina Taborelli https://orcid.org/0000-0002-6731-7569
Stefano Rosso https://orcid.org/0000-0001-6816-2661
Fortunato Bianconi https://orcid.org/0000-0002-3132-0061
Maurizio Zarcone https://orcid.org/0000-0002-5311-1359
Maria Adalgisa Gentilini https://orcid.org/0000-0001-9113-1417

REFERENCES

1. Ferlay J, Ervik M, Lam F, et al. *Global Cancer Observatory: Cancer Today*. International Agency for Research on Cancer. 2024; Available: https://gco.iarc.who.int/today, Accessed September 11, 2023.
2. De Angelis R, Sant M, Coleman MP, et al. Cancer survival in Europe 1999-2007 by country and age: results of EUROCARE-5-a population-based study. *Lancet Oncol*. 2014;15:23-34. doi:10.1016/S1470-2045(13)70546-1
3. AIRTUM Working Group. Italian cancer figures, report 2016. Survival of cancer patients in Italy. *Epidemiol Prev*. 2017;41(2 Suppl 1):1-244. doi:10.19191/EP17.2S1.P001.017
4. Guzzinati S, Virdone S, De Angelis R, et al. Characteristics of people living in Italy after a cancer diagnosis in 2010 and projections to 2020. *BMC Cancer*. 2018;18:169. doi:10.1186/s12885-018-4053-y
5. Buzzoni C, Crocetti E, Guzzinati S, Dal Maso L, Francisci S, AIRTUM Working Group. Cancer incidence and mortality trends from 2003 to 2014 in Italy. *Tumori J*. 2019;105:121-137. doi:10.1177/0300891619839844
6. Nordenskjöld AE, Fohlin H, Arnesson LG, et al. Breast cancer survival trends in different stages and age groups—a population-based study 1989-2013. *Acta Oncol*. 2019;58:45-51. doi:10.1080/0284186X.2018.1532601
7. Minicozzi P, Walsh PM, Sánchez MJ, et al. Is low survival for cancer in Eastern Europe due principally to late stage at diagnosis? *Eur J Cancer*. 2018;93:127-137. doi:10.1016/j.ejca.2018.01.084
8. Araghi M, Arnold M, Rutherford MJ, et al. Colon and rectal cancer survival in seven high-income countries 2010–2014: variation by age and stage at diagnosis (the ICBP SURVMARK-2 project). *Gut*. 2021;70:114-126. doi:10.1136/gutjnl-2020-320625
9. Cardoso R, Guo F, Heisser T, et al. Overall and stage-specific survival of patients with screen-detected colorectal cancer in European countries: a population-based study in 9 countries. *Lancet Reg Health Eur*. 2022;21:100458. doi:10.1016/j.lanepe.2022.100458
10. Toffolutti F, Guzzinati S, De Paoli A, et al. Complete prevalence and indicators of cancer cure: enhanced methods and validation in Italian population-based cancer registries. *Front Oncol*. 2023;13:1168325. doi:10.3389/fonc.2023.1168325
11. SEER*Stat Software. Version 8.4.0 released April 2022. National Cancer Institute. Available: http://seer.cancer.gov/seerstat/ Accessed January 11, 2024.
12. Gatta G, Capocaccia R, Berrino F, Ruzza MR, Contiero P; EUROPREVAL Working Group. Colon cancer prevalence and estimation of differing care needs of colon cancer patients. *Ann Oncol*. 2004;15:1136-1142. doi:10.1093/annonc/mdh234
13. Dal Maso L, Guzzinati S, Buzzoni C, et al. Long-term survival, prevalence, and cure of cancer: a population-based estimation for 818902 Italian patients and 26 cancer types. *Ann Oncol*. 2014;25:2251-2260. doi:10.1093/annonc/mdu383
14. AIRTUM Working Group. Italian cancer figures, report 2014. Prevalence and cure of cancer in Italy. *Epidemiol Prev*. 2014;38(6 Suppl 1):1-144. doi:10.19191/EP14.6.S1.113
15. Shack LG, Shah A, Lambert PC, Rachet B. Cure by age and stage at diagnosis for colorectal cancer patients in north West England, 1997-2004: a population-based study. *Cancer Epidemiol*. 2012;36:548-553. doi:10.1016/j.canep.2012.06.011
16. van Erning FN, van Steenbergen LN, Lemmens VEPP, et al. Conditional survival for long-term colorectal cancer survivors in The Netherlands: who do best? *Eur J Cancer*. 2014;50:1731-1739. doi:10.1016/j.ejca.2014.04.009
17. Qaderi SM, Dickman PW, de Wilt JHW, Verhoeven RHA. Conditional survival and cure of patients with colon or rectal cancer: a population-based study. *J Natl Compr Canc Netw*. 2020;18:1230-1237. doi:10.6004/jnccn.2020.7568
18. Boussari O, Romain G, Remontet L, et al. A new approach to estimate time-to-cure from cancer registries data. *Cancer Epidemiol*. 2018;53:72-80. doi:10.1016/j.canep.2018.01.013
19. Romain G, Boussari O, Bossard N, et al. French network of cancer registries (FRANCIM). Time-to-cure and cure proportion in solid cancers in France. A population-based study. *Cancer Epidemiol*. 2019;60:93-101. doi:10.1016/j.canep.2019.02.006
20. Dal Maso L, Panato C, Guzzinati S, et al. Prognosis and cure of long-term cancer survivors: a population-based estimation. *Cancer Med*. 2019;8:4497-4507. doi:10.1002/cam4.2276
21. Xia C, Yu XQ, Chen W. Measuring population-level cure patterns for cancer patients in the United States. *Int J Cancer*. 2023;152:738-748. doi:10.1002/ijc.34291
22. Janssen-Heijnen MLG, Gondos A, Bray F, et al. Clinical relevance of conditional survival of cancer patients in Europe: age-specific analyses of 13 cancers. *J Clin Oncol*. 2010;28:2520-2528. doi:10.1200/JCO.2009.25.9697
23. Dal Maso L, Panato C, Tavilla A, et al. Cancer cure for 32 cancer types: results from the EUROCARE-5 study. *Int J Epidemiol*. 2020;49:1517-1525. doi:10.1093/ije/dyaa128
24. Kou K, Dasgupta P, Cramb SM, Yu XQ, Baade PD. Temporal trends in population-level cure of cancer: the Australian context. *Cancer Epidemiol Biomarkers Prev*. 2020;29:625-635. doi:10.1158/1055-9965.EPI-19-0693

25. Merrill RM. Conditional relative survival among female breast cancer patients in the United States. *Breast J*. 2018;24:435-437. doi:10.1111/tbj.12933
26. Jung SY, Jung KW, Ha J, et al. Different patterns of conditional survival of breast cancer patients by age and histologic types: evidence from the Korean Nationwide registry. *Cancer Epidemiol Biomarkers Prev*. 2019;28:1169-1176. doi:10.1158/1055-9965.EPI-18-1072
27. Janssen-Heijnen ML, van Steenbergen LN, Voogd AC, et al. Small but significant excess mortality compared with the general population for long-term survivors of breast cancer in The Netherlands. *Ann Oncol*. 2014;25:64-68. doi:10.1093/annonc/mdt424
28. Drouillard A, Bouvier AM, Rollot F, Faivre J, Jooste V, Lepage C. Conditional net survival: relevant prognostic information for colorectal cancer survivors. A French population-based study. *Dig Liver Dis*. 2015;47:597-601. doi:10.1016/j.dld.2015.03.013
29. Miller KD, Nogueira L, Mariotto AB, et al. Cancer treatment and survivorship statistics, 2019. *CA Cancer J Clin*. 2019;5:363-385. doi:10.3322/caac.21565
30. van der Meer DJ, Kramer I, van Maaren MC, et al. Comprehensive trends in incidence, treatment, survival and mortality of first primary invasive breast cancer stratified by age, stage and receptor subtype in The Netherlands between 1989 and 2017. *Int J Cancer*. 2021;148:2289-2303. doi:10.1002/ijc.33417
31. Puliti D, Bucchi L, Mancini S, et al. Advanced breast cancer rates in the epoch of service screening: the 400,000 women cohort study from Italy. *Eur J Cancer*. 2017;75:109-116. doi:10.1016/j.ejca.2016.12.030
32. Giudici F, Bortul M, Clagnan E, et al. Early effects of attendance to the Friuli Venezia Giulia (Northern Italy) mammography screening programme on the incidence of advanced-stage breast cancer: a cohort study. *Epidemiol Prev*. 2020;44:145-153. doi:10.19191/EP20.2-3.P145.037
33. Zorzi M, Mangone L, Anghinoni E, et al. Screening for colorectal cancer in Italy: 2011-2012 survey. *Epidemiol Prev*. 2015;39:108-114.
34. Zorzi M, Mangone L, Sassatelli R, et al. Incidence trends of colorectal cancer in the early 2000s in Italy. Figures from the IMPACT study on colorectal cancer screening. *Epidemiol Prev*. 2015;39(Suppl. 1):115-125.
35. Puliti D, Duffy SW, Miccinesi G, et al. Overdiagnosis in mammographic screening for breast cancer in Europe: a literature review. *J Med Screen*. 2012;1:42-56. doi:10.1258/jms.2012.012082
36. Welch HG, Prorok PC, Kramer BS. Breast-cancer tumor size and screening effectiveness. *N Engl J Med*. 2017;376:94-95. doi:10.1056/NEJMc1614282
37. Wieszczy P, Kaminski MF, Løberg M, Bugajski M, Bretthauer M, Kalager M. Estimation of overdiagnosis in colorectal cancer screening with sigmoidoscopy and faecal occult blood testing: comparison of simulation models. *BMJ Open*. 2021;11:e042158. doi:10.1136/bmjopen-2020-042158
38. Pancheri S, Pertile R, Armelao F, et al. A comprehensive assessment of the impact of a colorectal cancer screening program in a northern Italian area. *Dig Liver Dis*. 2022;54:400-406. doi:10.1016/j.dld.2021.03.016
39. Jakobsen LH, Andersson TM, Biccler JL, et al. On estimating the time to statistical cure. *BMC Med Res Methodol*. 2020;20:71. doi:10.1186/s12874-020-00946-8
40. Fusco M, Pezzi A, Benatti P, et al. Clinical features and colorectal cancer survival: an attempt to explain differences between two different Italian regions. *Eur J Cancer*. 2010;46:142-149. doi:10.1016/j.ejca.2009.07.005 PMID: 19695865.
41. Walters S, Maringe C, Butler J, Brierley JD, Rachet B, Coleman MP. Comparability of stage data in cancer registries in six countries: lessons from the international cancer benchmarking partnership. *Int J Cancer*. 2013;132:676-685. doi:10.1002/ijc.27651
42. Ito Y, Nakayama T, Miyashiro I, Ioka A, Tsukuma H. Conditional survival for longer-term survivors from 2000-2004 using population-based cancer registry data in Osaka. *Japan BMC Cancer*. 2013;13:304. doi:10.1186/1471-2407-13-304
43. Colonna M, Grosclaude P, Bouvier AM, Goungounga J, Jooste V. Health status of prevalent cancer cases as measured by mortality dynamics (cancer vs. noncancer): application to five major cancer sites. *Cancer*. 2022;128:3663-3673. doi:10.1002/cncr.34413
44. Botta L, Goungounga J, Capocaccia R, et al. A new cure model that corrects for increased risk of non-cancer death: analysis of reliability and robustness, and application to real-life data. *BMC Med Res Methodol*. 2023;23:70. doi:10.1186/s12874-023-01876-x
45. Yu XQ, De Angelis R, Andersson TML, Lambert PC, O'Connell DL, Dickman PW. Estimating the proportion cured of cancer: some practical advice for users. *Cancer Epidemiol*. 2013;37:836-842. doi:10.1016/j.canep.2013.08.014
46. Greenland S, Senn SJ, Rothman KJ, et al. Statistical tests, P values, confidence intervals, and power: a guide to misinterpretations. *Eur J Epidemiol*. 2016;31:337-350. doi:10.1007/s10654-016-0149-3
47. Francisci S, Capodaglio G, Gigli A, Mollica C, Guzzinati S. Cancer cost profiles: the Epicost estimation approach. *Front Public Health*. 2022;10:974505. doi:10.3389/fpubh.2022.974505 eCollection 2022.
48. Swinnen J, Keupers M, Soens J, Lavens M, Postema S, van Ongeval C. Breast imaging surveillance after curative treatment for primary non-metastasised breast cancer in non-high-risk women: a systematic review. *Insights Imaging*. 2018;9:961-970. doi:10.1007/s13244-018-0667-5
49. Scocca G, Meunier F. Towards an EU legislation on the right to be forgotten to access to financial services for cancer survivors. *Eur J Cancer*. 2022;162:133-137. doi:10.1016/j.ejca.2021.12.001
50. Dal Maso L, Santoro A, Iannelli E, et al. Cancer cure and consequences on survivorship care: position paper from the Italian Alliance against cancer (ACC) survivorship care working group. *Cancer Manag Res*. 2022;14:3105-3118. doi:10.2147/CMAR.S380390
51. Presidente del Consiglio dei Ministri. Decreto del Presidente del Consiglio dei Ministri, 3/3/2017,41 Identificazione dei sistemi di sorveglianza e dei registri di mortalità, di tumori e di altre patologie. 17A03142, GU Serie Generale n.109 del (12-05-2017). Available at: https://www.gazzettaufficiale.it/eli/id/2017/05/12/17A03142/sg last access: January 11, 2024.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Dal Maso L, Toffolutti F, De Paoli A, et al. Cure indicators and prevalence by stage at diagnosis for breast and colorectal cancer patients: A population-based study in Italy. *Int J Cancer*. 2024;155(2):270-281. doi:10.1002/ijc.34923