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**PERSPECTIVES** 

# Cancer Cure and Consequences on Survivorship Care: Position Paper from the Italian Alliance Against Cancer (ACC) Survivorship Care Working Group

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Abstract: A multidisciplinary panel of experts and cancer patients developed a position paper to highlight recent evidence on "cancer cure" (ie, the possibility of achieving the same life expectancy as the general population) and discuss the consequences of this concept on follow-up and rehabilitation strategies. The aim is to inform clinicians, patients, and health-care policy makers about strategies of survivorship care for cured cancer patients and consequences impacting patient lives, spurring public health authorities and research organizations to implement resources to the purpose. Two identifiable, measurable, and reproducible indicators of cancer cure are presented. Cure fraction (CF) is >60% for breast and prostate cancer patients, >50% for colorectal cancer patients, and >70% for patients with melanoma, Hodgkin lymphoma, and cancers of corpus uteri, testis (>90%), and thyroid. CF was >65% for patients diagnosed at ages 15-44 years and 30% for those aged 65-74 years. Time-to-cure was consistently <1 year for thyroid and testicular cancer patients and <10 years for patients with colorectal and cervical cancers, melanoma, and Hodgkin lymphoma. The working group agrees that the evidence allows risk stratification of cancer patients and implementation of personalized care models for timely diagnosis, as well as treatment of possible cancer relapses or related long-term complications, and preventive measures aimed at maintaining health status of cured patients. These aspects should be integrated to produce an appropriate follow-up program and survivorship care plan(s), avoiding stigma and supporting return to work, to a reproductive life, and full rehabilitation. The "right to be forgotten" law, adopted to date only in a few European countries, may contribute to these efforts for cured patients.

**Keywords:** cancer cure, survivorship, time-to-cure, personalized care models, right to be forgotten

#### Introduction

About 5% of the individuals in several European countries are living after a cancer diagnosis (eg, 3.6 million in Italy). The percentage is estimated to grow by approximately 3% per year<sup>1–3</sup> and a large proportion of these people (eg, 24% of the cancer patients in Italy¹ and 29% in the USA)³ are alive 15 or more years after diagnosis. Patients living after a cancer diagnosis include those under treatment, those who are disease-free but remain at excess risk of recurrence, those who have treatment-related chronic conditions,⁴ and those who have the same life expectancy as the general population (ie, are cured). For the latter group of patients, several studies in the last decade have provided evidence of cure 7–14 and highlighted its clinical implications. Patients living many years after cancer diagnosis and the end of treatment need to be recognized as cured and require specific interventions.

The aim of this position paper is to summarize the growing evidence related to the concept of "cancer cure" and to reach a consensus on the possible use of the definition. This is a prerequisite to support a new paradigm of survivorship care capable of addressing the consequences of the evidence for clinicians and patients alike, as well as to promote initiatives for a complete rehabilitation at both national and European level. Within the framework of the Italian Alliance Against Cancer (ACC)<sup>17</sup> – an Oncology Network founded in 2002 by the Italian Ministry of Health, including 28 research hospitals (IRCCS), cancer patient associations, and the Italian Institute of Health (ISS)-, a multidisciplinary panel of experts (cancer epidemiologists, oncologists, haematologists, psychologists) and stakeholders (cancer patients) reviewed the current knowledge on the topic. The main issues were selected during the first three meetings of the complete Working Group and five subsequent monthly meetings were conducted by panellists to summarize the results described in this paper.

In the first paragraph, we provide a description of how major indicators of cancer cure are defined and estimated. In the second paragraph, a brief narrative review describes the results for indicators of cancer cure, reported in several countries, for the most common neoplasms. In the following paragraph, we discuss the possible consequences of recently published epidemiological results on the current paradigm of survivorship, taking into account the different points of view. In particular, we provide a brief discussion of consequences on medical surveillance (clinical view), survivorship care plan (public health view), and patients (socioeconomic and legal aspects).

# Measurable Indicators of Cancer Cure: How are They Defined and Estimated?

Categorizations of cancer patients were generally based on survival time length, even though some cancer types/sites (eg, testicular or papillary thyroid carcinomas) are rarely fatal and are curable in nearly all patients. The vast majority of individuals diagnosed with the most common cancer types (eg, breast, colorectal, and prostate carcinomas) become long-term survivors and are alive 5 years after diagnosis or more.<sup>8,18</sup> Other individuals are living after a diagnosis of a cancer type (eg, chronic lymphocytic leukaemia and follicular lymphoma) that can be controlled, but not cured, with ongoing or periodic treatments and standardized follow-up.<sup>15,18–20</sup> However, it is well recognized that all major types of cancer therapy, in particular if administered during childhood, can determine unwanted long-term side effects on tissues and organ systems that may impair a person's health and quality of life.<sup>18</sup> Side effects are mostly related to the cancer site, type, length, and cumulative dose of treatment(s) (surgery, radiotherapy, chemotherapy, or hematopoietic stem cell transplantation).<sup>21</sup>

Several authors have broadened the meaning of "cure" to a "measurable" epidemiological/statistical concept, defined as a null excess death risk due to cancer compared to the general population.<sup>5,6</sup> The epidemiological indicators of "cancer cure" are based on the observation that among patients with almost all cancer types/sites, the risk of death is higher in the first 2 years after diagnosis, while it progressively decreases thereafter. For many cancer patients (eg, colorectal, stomach), the excess risk of death due to cancer becomes negligible after a few years, and they reach a life expectancy similar to that of the general population of comparable age and sex. For other patients (eg, those diagnosed with breast, bladder, or prostate cancer) the excess risk of cancer death decreases over time but persists for many years, although it is worth stressing that the majority of the patients will not die as a result of cancer.<sup>8</sup>

The two most commonly estimated indicators of cancer cure are cure fraction and time-to-cure. Cure fraction (CF, also called cure proportion)<sup>10,13</sup> represents the proportion of cancer patients diagnosed in a given time period experiencing the same mortality rates as their peers in the general population. Cure fraction is estimated through specific statistical models (eg, parametric mixture or flexible models) fitting patients' survival observations.<sup>5,6</sup> Examples of cure fraction calculation are shown in <u>Supplementary Figure 1A</u>. These statistical models can also be used to forecast survival for longer follow-up periods than those observed.

A key assumption of the cure models is that a proportion of patients will not die of the disease. This assumption can be validated when the observation period is long enough to allow zero excess risk of death, while it remains an assumption that still provides a very good fit of the data in other cases. When non-negligible excess mortality estimates still exist 15 years or more after diagnosis, CF should be interpreted as the proportion of patients who will not die as a result of cancer. This holds true regardless of whether the excess mortality is still non-negligible many years after diagnosis and the relative survival does not reach a plateau. In addition, it should be kept in mind that several cancer patients may hardly reach the same expected death rate of the general population, because of the competitive risks associated with lifestyle factors. The CF definition is conceptually the same as the one proposed for cure after childhood cancer: "cure refers only to the original disease regardless of any potential for, or presence of, disabilities or side effects of treatment". It is also reassuring that the results from different cure models largely overlap, in particular for the most common cancer types/sites, when estimated on sufficiently large study populations and with a sufficiently long follow-up period (≥20 years).

Another clinically relevant indicator of long-term survival and cancer cure is called time-to-cure (TTC), calculated as the number of years needed for cancer patients to reach a similar life expectancy to their peers. The probability of a patient surviving an additional 5 or 10 years (conditional relative survival, CRS) after having already survived a given number of years is used to estimate TTC. Supplementary Figure 1B shows two examples of TTC calculation. Death rates of cancer patients overlap those in the general population when their 5-year CRS approaches 100%, and the excess risk of death is considered negligible when the 5-year CRS (red lines) exceeds 95%. <sup>7,24</sup> Several authors used observed CRS (Supplementary Figure 1B, blue lines)<sup>24</sup> or different statistical methods to estimate TTC or conceptually similar low-risk thresholds for patients living after a cancer diagnosis. <sup>12,13</sup> It should be noted that the estimation of TTC is sensitive to the choice of the CRS threshold (ie, 90% or 95% to fix a low risk of recurrence/death or the margin of clinical relevance) and methodological approach used, 7,12,13,24,25 in particular for cancer types with non-negligible long-term excess mortality rate (eg, prostate or breast cancer). Future epidemiological studies should provide estimates of long-term prognosis and cancer cure by stage and cancer subtypes, as well as, a definition of TTC shared between clinicians and epidemiologists, specifically by cancer type and host (eg, age). Despite potential limits of application in some circumstances. 26,27 the presented cancer cure indicators are unambiguously defined and they are measurable and reproducible, eg, the estimation of the same indicators can be performed in different countries and periods in areas with coverage by population-based cancer registries.

## Available Estimates of Cure Fraction and Time-to-Cure from Population-Based Studies

Table 1 presents the CF of the most common neoplasms as reported in several high-income countries. On average, CF was >60% for breast and prostate cancer patients in all examined population-based studies, indicating that two-thirds of patients with the two most common cancer types in women and men, respectively, will die for causes other than cancer. The CF was consistently above 50% even for patients with colorectal cancer (50–60%), cervical cancer (60–75%), and over 75% for patients with melanoma (75–90%), Hodgkin lymphoma (80%), and cancer of corpus uteri, testis (>90%), and thyroid. The proportion was between 30% and 50% for patients with cancer of the oral cavity, connective tissue, ovary, kidney, bladder, and non-Hodgkin lymphomas (Table 1). When stratified by age at diagnosis, two-thirds of cancer patients diagnosed at ages 15–44 years and one-third of patients aged 65–74 years were expected to be cured. Considering all cancer patients diagnosed in the early 2000s, the CF was approximately 40% in men and 50% in women. 8,11

Table I Cure Fraction<sup>a</sup> (%) by Cancer Type, Country, and Sex, Estimated in Population-Based Studies

	Europe <sup>8</sup>		ltaly <sup>11</sup>		France <sup>b</sup> , 13		Belgium <sup>98</sup>		Norway <sup>10</sup>		Australia <sup>14</sup>	
	М	w	М	w	М	w	М	w	М	w	М	w
All types	39	51	39	52								
Oral cavity and pharynx	27	41	19	28	_	-			42	31	51	55
Oesophagus	10	13	7	12	-				10	17	14	18
Stomach	19	23	23	28	19	25	22	30	21	22	23	25
Colon/Rectum	49	52	52	56	47	53	51	57	53	57	56	58
Liver	5	7	3	4		-			10	9	П	12
Gallbladder	14	13	11	10					18	15	16	17
Pancreas	4	5	4	6	6	4	6	6	8	4	6	7
Larynx	36	23	17	17	-	-						_
Lung	8	10	8	13	-	_			10	14	10	13
Skin melanoma	76	86	75	83	85	90	75	84			83	90
Connective tissue	53	52	49	53	48	35						
Breast		66		67		79						73
Cervix uteri		64		63		77		65				51
Corpus uteri		76		70		63		74				75
Ovary		36		35		22				35		29
Prostate	63		75		80						76	
Testis	94		94		96							
Kidney	47	41	44	51	49	54			49	43	55	57
Bladder	48	48	59	69	37	40			69	63		
Brain	12	15	11	12	15	-			-	60	9	9
Thyroid	70	87	83	95	81	99						-
Hodgkin lymphoma	67	75	70	77								-
Non-Hodgkin lymphoma	24	30	36	37					42	-	48	52
Multiple myeloma	10	П	П	15							20	21
Leukaemias	18	22							51	51	39	40

**Notes:** <sup>a</sup>Estimated for adults as the proportion of cancer patients expected to reach the same death rates as the general population of the same sex and age. <sup>b</sup>Age group 65–74.

Few studies have assessed the CF by cancer stage, which is among the most important prognostic factors. A study conducted in the United States indicated that CF was 73% after local breast cancer (approximately half of all cases), 37% after regional disease, and 3% when a distant metastasis was present at diagnosis. In Sweden, a CF of approximately 100% was reported for patients with stage IA malignant melanoma (46% of all melanomas) and a non-negligible CF (ie, >20%) was observed even for stage III. These results are consistent with an Italian population—based study the stage III.

Table 2 Time-to-Cure<sup>a</sup> (Years) by Cancer Type, Country, and Sex, Estimated in Population-Based Studies

	Europe <sup>b</sup> , <sup>8</sup>		Italy <sup>b</sup> , 11		France <sup>13</sup>		Europe <sup>24</sup>	USA <sup>99</sup>	Australia <sup>26</sup>
	М	w	М	w	М	w	M+W	M+W	M+W
Oral cavity and pharynx Oesophagus	17 7	18 6	>20	>20	_				
Stomach	7	8	16	13	10	10			10
Colon/Rectum	8	8	10	9	П	9	8		5–10
Liver	20	14			-	10			
Gallbladder	8	7							
Pancreas	6	6			8	10			>10
Larynx	>20	>20			-				>10
Lung	9	9			_				
Skin melanoma	6	2	6	6	5	5	7 (M), 2(W)	2	3
Connective tissue	9	12	14	12	7	12			
Breast		15		17		П			>10
Cervix uteri		4		6		7	4		5
Corpus uteri		7		Ш		П	10	5	
Ovary		10		12		П			
Prostate	17		17		12			0	>10
Testis	<		<		0		0	0	
Kidney	17	>20	>20	>20	13	12			
Bladder	19	16	16	Ш	13	12			>10
Thyroid	<	<i< td=""><td>&lt; </td><td>&lt; </td><td>0</td><td>0</td><td>0</td><td>0</td><td>0</td></i<>	<	<	0	0	0	0	0
Hodgkin lymphoma	3	2	7	4				3	
Non-Hodgkin lymphoma	>20	>20	>20	>20					
Multiple myeloma	>20	>20	>20	>20					
Leukaemias	>20	>20	>20	>20				5°	

**Notes**: <sup>a</sup>Defined as time to reach conditional 5-year relative survival >95%. <sup>b</sup>More frequent 10-year age group (65–74, 15–44 for melanoma, cervix, testis, thyroid, and Hodgkin lymphoma). <sup>c</sup>Acute lymphoid leukemias, all ages.

showing that melanoma patients with thin lesions ( $\leq 1$ mm, 60% of all cases) had the same life expectancy as the general population and, consequently, can be considered cured.

TTC was consistently less than 1 year for thyroid or testicular cancer patients, often diagnosed below the age of 45 years (Table 2). TTC was <10 years for patients with several cancer types/sites (ie, colon/rectum, skin melanoma, Hodgkin lymphoma, cervix uteri), approximately 10 years for patients with cancer of the stomach, gallbladder, corpus uteri, and ovary. Instead, a small but not negligible excess risk of death was present even 10 years after the diagnosis of breast or prostate cancer. In particular, a TTC of approximately 10 years was found in women aged 45–64 years with breast cancer, but it was 15 years or more for those aged below or above 45–64 years. Several authors have also reported a TTC (or high risk period 12) shorter than 2 years for patients with localized breast, <sup>12,32,33</sup> prostate, or colorectal

cancers.<sup>34</sup> A relevant long-term excess risk of death (TTC>15 years) remained for patients aged 65–74 years with laryngeal, liver (in men), prostate, bladder, and kidney cancer, and for all hematologic neoplasms except Hodgkin lymphoma in both sexes.

Among children with cancer, overall 5-year survival is above 80%<sup>35-37</sup> and even longer (ie, 15-year) survival was only slightly lower (<4% in children and <5% in adolescents) than 5-year survival.<sup>36</sup> Although a higher risk of death (for the specific neoplasm as well as for other diseases) has been reported among childhood cancer survivors as compared to their peers in the general population,<sup>38-40</sup> the vast majority of cured children requires personalized organ-specific follow-up aimed at anticipating and controlling possible long-term side effects of treatment (eg, second neoplasms, cardiac, pulmonary, or endocrine complications) and supporting social rehabilitation.<sup>41</sup>

# Possible Consequence of Evidence of Cancer Cure on Cancer Survivorship Care

### A New Paradigm Based on Cancer Cure to Be Integrated in the Cancer Care Pathway

Cancer is not a single disease, but it is made up of many different biological entities. Each of them is different, behaves differently, warrants different treatment and has different outcomes. These differences also apply to cancers that initially develop in the same primary site. Research, genetics and treatments have all evolved and have allowed the creation of a personalized risk-adapted medicine and a modification of the clinical cancer experience.<sup>42</sup>

The natural history of cancer diseases records an acute phase, followed by a chronic one and, even more frequently, by a complete, lasting remission. Each phase is characterized by different interventions and needs and makes cancer survivorship a formal period of care, with a developing set of care interventions specific to different groups, and cannot be managed alike in terms of clinical follow-up and care. The risk stratification of the disease phase is strategically relevant for the purpose of designing and implementing personalized models of care. <sup>15,43–45</sup> This categorization might help to answer the need of fostering adequate surveillance and global care for some patients and avoid subjecting others to psychological burdens of overmedicalization and potential social stigmatization. <sup>42,46</sup>

In the last decade, the use of the word "cured" has been extensively debated, as a consequence of the increasing survival rates for several cancers in Europe, 46–48 with a quarter of Italian cancer patients who can be considered as already cured, 49 supporting the need to promote survivorship care as an essential component of oncology. 50

As observed above, cure is a reasonable assumption when survival curves tend to stabilize. Thus, the word "cured" should refer, in fact, to persistent clinical remission of a tumour (ie, very low risk of further tumour recurrence or death), regardless of the presence or absence of late or long-term sequelae of treatments.<sup>51</sup> The correct application of the word "cured" should consider the time elapsed since cancer diagnosis, which should be such that the patients' risk of death, due to cancer, does not exceed that of their peers in the general population. In other words, cancer patients can only be described as "cured" when their life expectancy is undistinguishable from that of a general population of the same sex and age. When appropriate, the word "cured" can be used in the clinical setting while communicating with patients and their families, but should always be accompanied by counseling about prevention, screening, genetic counseling (when indicated), and promotion of lifestyle habits aimed at maintaining good general health. <sup>46,52</sup>

# Medical Follow-Up: Management of Late Effects

The development and implementation of a pragmatic, patient-centred care delivery approach across the continuum of care is crucial to favour the best long-term health to every patient, and also to promote the equity of cancer care. Surveillance after the acute phase is important because it should allow for timely diagnosis of cancer relapses, and/or treatment of related long-term complications; facilitate the screening and early diagnosis of any second malignancies; and finally promote preventive measures such as diet modification, smoking cessation, physical activity, and other lifestyle changes aimed at maintaining health. Control of disease evolution is a classic approach to pathology-oriented care in clinical practice. The frequency and intensity of monitoring for cancer relapse decrease every year from diagnosis onwards, with a drastic decrease occurring 3–5 years after treatment. Conversely, individuals living years beyond a cancer diagnosis face an increased risk of many health issues, also including short- and long-term adverse effects of

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treatments and psychosocial challenges. In addition to cancer itself, these health risks are caused by treatments as well as genetic backgrounds, lifestyle, and environmental factors. Moreover, the increasing age of cured cancer patients is accompanied by the potential development of other diseases, and any related damaging effects of cancer treatment may increase the need to start rehabilitation programs.

Consequently, the two main issues encountered in cured patients are multi-comorbidity and long-term treatment side effects. The latter can either occur during or early after treatment and be long-lasting, or occur long after the end of treatment. Late side effects can be classified into a) side effects affecting specific systems (organ alterations, endocrine abnormalities, premature ageing, and others); b) functional changes (incontinence, lymphoedema, ostomies, osteoporosis, arthritis, fertility issues, and others); and c) second malignancies. 58,59

The need for prevention of subsequent tumors stems from the observation that cancer patients are more likely to develop a subsequent malignant neoplasm than the general population.<sup>60–62</sup> In particular, people living after a childhood tumour have a cumulative 8% risk of developing a second tumor later in life.<sup>63</sup> This event can be attributed to the mutagenic risk of radiotherapy and chemotherapy, which is further aggravated in patients with a genetic predisposition to cancer. As a consequence, quality care for these patients should consider individual genetic susceptibility, in addition to the classic domains of type and cumulative doses of treatments<sup>64–66</sup> and ageing.

Other commonly cited cancers include myeloblastic leukaemia, breast, bone, thyroid, and bladder cancer. A second tumor can also occur in the same organ as, for instance, breast and colorectal cancer, so continuous mammography and colonoscopy surveillance are required. Therefore, any gradual downsizing of follow-up should be done taking care not to hinder the efficacy of surveillance for non-cancer diseases. When this occurs, this may reflect either an inability to plan for surveillance related to the risk of treatment-related adverse sequelae or the presence of barriers caused by an inadequate system. 8

Due to the increase in the life expectancy of patients, today's focus is increasingly directed to quality of life after cancer.<sup>69</sup> That is why we can no longer postpone development of care models that meet patient needs using a risk-stratified approach considering the original cancer and its treatment, as well as comorbidity and late psychosocial and economic effects.<sup>70</sup> This model must involve the general practitioner (GP) along with the oncologist for a common care action, where the GP could be the coordinator for patients at low risk of disease progression but with comorbidity, while patients with high risk of relapse could be referred to the oncologist or specialized clinics.

Currently, an adequate follow-up care program for cured cancer patients should be the result of a global assessment, beginning with the individual patient's characteristics (pre-existing comorbidity, familial history, genetic susceptibility, and lifestyle, which over time is an important contributor to the burden of late effects, together with socio-economic status), specific disease (cancer histology, primary site, biological and molecular features, and stage), cancer treatment (years from the completion of therapy, surgery, type and doses of chemotherapy, radiotherapy, and bone marrow transplantation), and the current and foreseeable rehabilitation needs.

Of course, the psychological, sexual, nutritional, and cognitive well-being of the cured person is an integral part of the multidisciplinary assessment of rehabilitation needs for survivors. The appearance of symptoms such as emotional distress or cognitive alterations in the areas of memory, learning, calculation, reasoning should lead to a specialist evaluation and to rehabilitation approaches (ie, improvement of sleep, chronic pain, fatigue).<sup>71</sup>

These aspects should be deeply analysed and integrated to produce an appropriate follow-up timeline that develops and changes over the years after diagnosis. An adequate follow-up program aims to detect late side effects early on, impacting on the health status of the potentially cured patient.

## Survivorship Care Plan

During the transition phase to primary care settings, appropriate awareness of late effects on the part of patients and/or health providers is crucial to avoid misdiagnosis, which may lead to delayed and/or inappropriate treatment, and to severe and irreversible consequences of cancer and its treatment. A complete assessment of patients and their environment is essential to direct appropriate investigation.<sup>72</sup> Genetic information should also be relied on to personalize the follow-up care program for the growing population of cancer survivors.

A care plan represents a relevant opportunity because it provides patients and their caregivers and general practitioners with a detailed summary of the treatment received, of potential late or long-term side effects, and recommendations about the type and timing of any test useful for early diagnosis of subclinical effects that could become clinically relevant in the future and represent new comorbidities, as well as proposals for the application of a correct lifestyle. 72,73

A survivorship care plan is a detailed plan for a patient's follow-up care, after the end of treatment. 74,75 For cancer patients, an organ- and gender-specific plan is based on the type of cancer and treatment the patient received. A survivorship care plan shall include personalized schedules for physical examinations, medical tests for health problems that may occur months or years after treatment ends, and cognitive, psychological, nutritional and sexual, rehabilitation. It must also include information to help meet the patient's social, legal, and financial needs. It may include referrals to specialists and recommendations for a healthy lifestyle, including physical activity and quitting smoking. This is especially relevant to those categories of people cured of cancer who present risk factors for several illnesses that could compromise their fitness status and quality of life. 76

A survivorship care plan should be delivered soon after the period of acute treatment to all patients, following a multidimensional care, follow-up, and rehabilitation needs assessment. Thus, it should be tailored and updated regularly, according to the patient's conditions. It can be an important tool not just for professionals, to establish continuity of care and rehabilitation, but also for the patients' empowerment in managing strategies to improve their health and quality of life. Good examples are the Treatment Summary and Survivorship Care Plan by the American Society of Clinical Oncology, 78 the ESMO Patient Guide Survivorship, 79 the "Life after Cancer" guidelines, 80 and the paediatric European Survivorship Passport. 21 These experiences may be considered as prototypes of the Cancer Survivor Smart Card announced for the coming years by the European Commission in its Europe Beating Cancer Plan.

#### Survivorship Care Models for Cured Patients

Evidence on how to provide the best cancer survivor care is inconclusive. 81,82 Among the different proposals to organize survivorship care, 77,83 two major models are usually considered. The first integrates cancer-specific activities in the primary care setting, where general practitioners and specialty doctors collaborate in the context of community-based healthcare services. 52,82 This model considers that cancer survivorship must be integrated with the cure of other chronic diseases and with preventive services and seems to be more applicable to the last phase of survivorship. 44 The information provided should empower the patient and/or caregiver to obtain prevention and supportive care from the general practitioner and local services, as well as ensuring a better integration of cancer rehabilitation and survivorship care. In addition, the model should also be suited to address the socio-economic needs of cancer survivors.<sup>84</sup> The second model is based on multidisciplinary care (MDT), where medical oncologists and other specialty doctors within a cancer centre are the pillars of care, and GPs participate as members of the MDTs. This model may be more relevant for early survivorship periods and childhood cancer patients. In this context, among the different relevant institutions for cancer care and research, the EU has recently given special attention to comprehensive cancer centres that are defined as organisational entities with a clear central governance spanning cancer care, research, and education.<sup>85</sup> Despite the globally increasing number of cancer survivors and the research efforts devoted to cancer survivorship research, 84 little evidence exists regarding the potential advantages and effects on health outcomes of different survivorship care models. 82 Examples of models of care for childhood cancer survivorship have been recently reported by the PanCare group. 73 For these reasons, research to ensure the best way to define how to appropriately address all the aspects of the cancer continuum is urgently needed.

## Socio-Economic Aspects: Return to Work

A fundamental aspect of quality of life for cured cancer patients is social rehabilitation: return to school or work and to a productive life. The occupational situation of people diagnosed with cancer has been shown to considerably deteriorate 2 years after diagnosis. 86 The most vulnerable people are the youngest and the oldest; married people; people with low educational levels; those with insecure, temporary working contracts; and those working in small and medium-size businesses. Return-to-work support should be integrated early into the cancer care pathway, exploring the feasibility of adequate or progressive return to work and discussing with employers reasonable adjustments of the working

conditions.<sup>87</sup> Work-environment-directed interventions aim at adapting workplace environment, equipment, tasks, and working time patterns to the needs of the cancer survivor. Both health care providers and employers have a role to play. Supportive return-to-work interventions can be directed to employers. Employers can also play an important role in supporting survivors' return-to-work process by exploring the possibilities of changes in job functions and by encouraging cancer survivors to acquire new skills, by facilitating flexible working hours and options (remote working, part-time work). Economic benefits should help employers who agree to adapt the workplace to the needs of cancer survivors and help self-employed workers to adapt their workplace and business to address health needs. Trade unions should close agreements with employers' representatives about the benefits of retaining human resources by applying reasonable adaptations of the working conditions.

### Legal Aspect: The Right to Be Forgotten

Occupational rehabilitation cannot be effective as long as cancer survivors still experience discrimination and exclusion from access to insurance services and loans or credit services connected to life insurance. Indeed, a previous cancer diagnosis is still considered equivalent to a poorer life expectancy, and the stigma remains, regardless of the actual condition of cured or chronic disease. Cured cancer patients are often denied eligibility in adoption procedures, as well as in obtaining a driving licence. Against such discriminations, it is necessary to implement even in Italy a "right to be forgotten" law, similar to the laws recently adopted in France, Belgium, the Netherlands, Luxembourg, and Portugal. 88–90 These regulations avoid inequity in accessing insurance and credit services, by protecting the cancer survivors' right to not disclose their having had cancer, after a given recurrence-free interval has elapsed (namely 10, 5, or fewer years after the end of treatment, depending on cancer type and host). These time intervals are conservative but in substantial agreement with those presented in the second paragraph (Table 2), and they underscore the first consequences of epidemiological evidence of cancer cure.

Lastly, the European Parliament resolution of 16 February 2022 on "Strengthening Europe in the fight against cancer – towards a comprehensive and coordinated strategy" calls on Member States to foster cancer survivors' retention at work, ability to return to work, and improve their reintegration into social activities and the labour market, as well as advocating measures for their rehabilitation. In addition, it calls on all Member States to guarantee the right to be forgotten to all European patients 10 years after the end of their treatment, and up to 5 years after the end of treatment for patients whose diagnosis was made before the age of 18 years.

# Final Remarks/Proposals

Many epidemiological studies in the last decade have provided estimates of cancer cure largely consistent in different high-income countries, through calculation of several measurable and reproducible epidemiological indicators. On this basis, the acceptance and dissemination of the term "cured" have increased in oncology literature and clinical practice
46,51 and there is a consensus among members of our working group on the use of the presented indicators of cancer cure.

The use of the word "cured" in relation to cancer could facilitate a) a return to one's relational and professional life after cancer diagnosis and treatment by reducing the risk of employer and insurance discrimination, as well as more subtle forms of social discrimination; b) providing long-term care in different settings to reduce patients' exposure to psychological trauma, for instance, when surveillance takes place in the same settings where acute care was received. 46,92

On the other hand, use of the term "cured" may also be misleading, obscuring the fact that periodic disease-oriented diagnostic follow-up will be required for many years or even decades, whereas its use offers the perception that this testing can be omitted because the condition of being "cured" makes the risk of dying from cancer negligible, compared to the corresponding non-cancer population.

Finally, categorization may reduce the stigma of the disease that persists in many cultures and countries, by setting clear standards for the necessary survivorship care of each patient in a perspective similar to that of other major chronic diseases, such as cardiovascular diseases, where the stigma is almost nonexistent. Based on previous considerations, it is time to tailor follow-up and rehabilitation for cured cancer patients according to the individual risk of both recurrence or death and late effects of treatment.

The definition of cancer care presented here, as all simplifications, cannot address all individual, personal, or social aspects of long-term survivorship care. General agreement was reached by our working group on the definition of cancer survivor and cured patient, but there was overwhelming consensus on the importance of classifying or characterizing cancer survivor populations. A categorization of persons now broadly defined as cancer survivors can provide support to risk-based survivorship care, new clinical and organizational approaches, and improved follow-up and surveillance recommendations and guidelines. In addition, communication with patients and families and patient adherence to clinical recommendations could be improved, as well as effectiveness of survivorship care in different delivery settings.

In the current scenario of cancer survival, virtual care programs might address chronic, complex survivorship needs, integrating roles and responsibilities of both providers and patients, and improving the health system's capacity. <sup>94</sup> The establishment of a digital platform, fully integrated with electronic medical records and accessible by health providers and patients, represents an ambitious challenge to ultimately improve life after cancer.

Finally, the awareness that some cancer patients are cured has relevant clinical, psychological, economic, and social implications; first of all, it provides an opportunity to improve quality of life by changing the way former patients view themselves. Moreover, the achievement of a complete rehabilitation and return to work will have an important impact for the sustainability of the welfare systems. The purpose of this position paper was to highlight the rationale for pursuing the goals indicated by the European Parliament (and funded by the Recovery and Resilience Facility), to stimulate national Parliaments to approve a law on the right to be forgotten, as well as to point national agencies and research and care institutes in the direction of more efficient management of long-term survivorship and care for cured people. 95–97

### **Data Sharing Statement**

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

### Acknowledgments

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# **Funding**

This work was supported by the Italian Ministry of Health (Ricerca Corrente Reti IRCCS, RCR-2021-23671213, National program in personalized oncology for the IRCCS of the Alliance Against Cancer network, WP 14) and by the Italian Association for Cancer Research (AIRC) (Grant no. 21879). 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.

#### **Disclosure**

Prof. Armando Santoro's Conflict of Interest Disclosure: Advisory Board: BMS (BRISTOL-MYERS-SQUIBB)/SERVIER/GILEAD/PFIZER/EISAI/BAYER/MSD (MERCK SHARP & DOHME). Consultancy: ARQULE/SANOFI/INCYTE. Speaker's Bureau: TAKEDA/BMS/ROCHE/ABB-VIE/AMGEN/CELGENE/SERVIER/GILEAD/ASTRAZENECA/PFIZER/ARQULE/LILLY/SANDOZ/EISAI/NOVARTIS/BAYER/MSD. Paolo Tralongo is the Coordinator of Survivorship Guidelines for AIOM (Italian Association of Medical Oncology). The other authors declare no competing interests in this work.

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