

## Cancer survivorship programs: time for concerted action

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Hematologists, specialists in cancer survivorship and patient advocates met in Bergamo, Italy (Nov 14-16, 2013) to highlight the physical, mental, psychosocial and financial challenges faced by cancer survivors and their families. Gaps in research and resources were all too apparent. This planned meeting perspective, not a formal consensus statement, reflects the key points mentioned by the participants during the discussions and the personal view of the authors. It proposes urgent action in key areas to ensure that people surviving cancer will suffer fewer long-term health problems than their predecessors and to contain costs.

### The scale of the problem

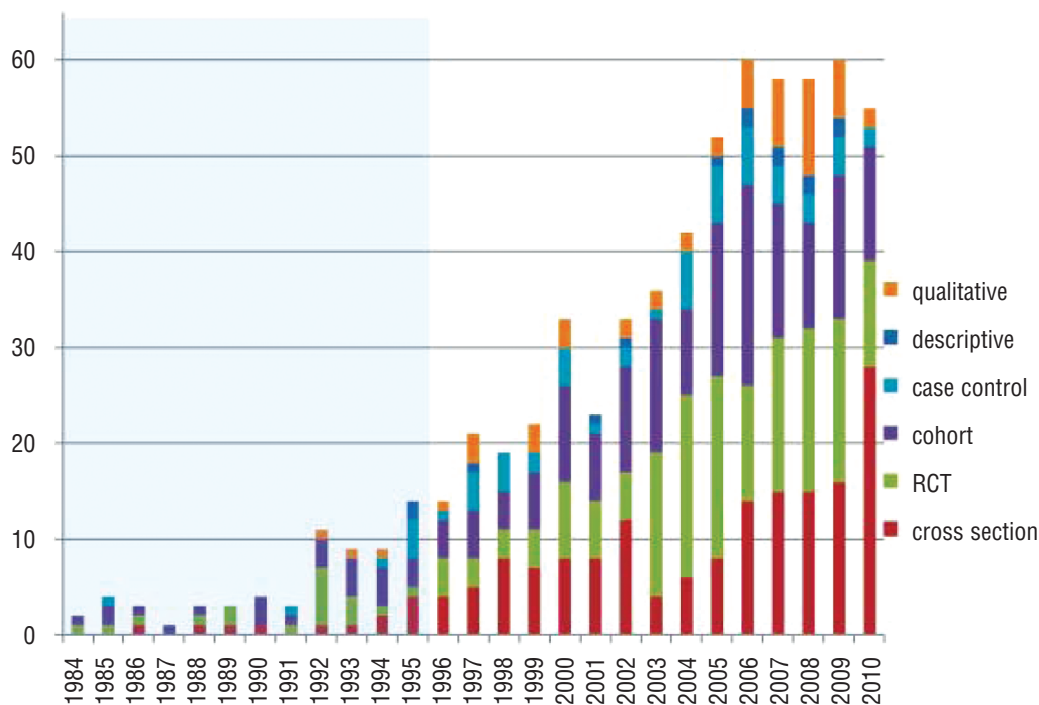
Advances in cancer screening and diagnosis, greater public awareness, and increasingly sophisticated and successful therapeutic strategies have achieved something remarkable. The diagnosis of cancer is no longer synonymous with a death sentence. The majority of cancer patients now survive their initial diagnosis. Recent data by the Surveillance, Epidemiology and End Results (SEER) program in the US show that two-thirds of all cancer patients survive for five years.<sup>1</sup> This rises to more than 80% survival in children aged 0-14 years.<sup>2</sup> The US has 13 million cancer survivors and

expects to have 18 million by 2022.<sup>3</sup> A similar trend is apparent in Europe and across the world, intensified by the shift in age demographics. In the UK, for example, 25% of all people aged over 65 years are expected to be diagnosed with cancer by 2040; many of them will survive and face novel problems.<sup>4</sup> These problems are in part recognized and expressed by the impressive increase in research activity into cancer survivorship worldwide (Figure 1).<sup>5</sup>

The physical, mental and psychosocial long-term consequences have been particularly well documented in survivors of childhood hematologic cancer. Evidence-based tools have been devised to prevent or treat long-term complications and have been validated. However, even where recommendations or guidelines have been established and patient advocacy groups are active adherence to those policies remains, at best, erratic. There is minimal coordination and many cancer types have no programs at all.

### Lessons from hematologic cancers

Cancer survivors can experience manifold health problems. Malignant and non-malignant late effects are well described. They may arise because of progression of the primary disease or as a consequence of the initial treatment. Surgery,



Note: shaded area indicates time period before the creation of the Office of Cancer Survivorship

Figure 1. Numbers of publications on cancer survivorship and type of research. Bars represent absolute numbers of publications by year and by type of research study on cancer survivorship (qualitative, quantitative, descriptive, case control study, cohort study, randomized controlled trial or cross-sectional study). Of note, the increase in publications since 1996, the year of the creation of the Office of Cancer Survivorship (<http://cancercontrol.cancer.gov/ocs/>).

**Table 1. Key interests of cancer survivorship focus groups and their inherent conflicts.**

Focus group	Main internal goal	Conflicts with other focus groups
Politician	Re-election	Short-term over long-term interests
Competent authorities	Safety Respecting laws	Legislation lags far behind innovations
Payers	Keep balance between funds and requests	Priorities ill defined Reduce short-term costs
Hospitals	Keep customers Ascertain benefit	Ascertain profit. Focus on financially attractive “customers”
Cancer center Referring center	Attract patients Interplay between local physicians and specialized center	Retain patients Retain 'control'
Local GP	Retain role as gatekeeper	Delegate responsibility for strategy but keep control of daily activities
Academic centers	Expand scientific merit Attract grants Use patients as teaching material	Few incentives for collaborations
Pharma / industry Donor registries	Sell products / devices Provide donors	No interest in comparative trials No interest in non-transplant strategies
Charities	Flourish Attract donations	Focus on local aspects Focus on short-term effects
Support groups Media	Attract members Sell news	Focus on news in media Focus on hot topics
Patients /families	Best outcome	Good health for “me” as an individual

*The table depicts in an abstract form the many key players involved in cancer survivorship activities, their main role and their potential conflicts of interest with other actors. It documents the absence of incentives for cross national or supranational collaboration, a major impediment for the creation of common cancer survivorship passport programs.*

chemotherapy, radiotherapy, combined modality therapy and/or hematopoietic stem cell transplantation (HSCT) exert profound effects on multiple organ systems. Treatment sequelae can appear early, late or very late, involving a combination of physical, psychosocial, societal and financial components. Most research has focused on survivors of childhood hematologic cancers and HSCT, providing an exemplar for devising how we could manage, support, monitor and care for all cancer survivors.

**Malignant late effects**

Patients with nearly all forms of cancer carry an increased risk of secondary malignancy. Disease progression has been the major cause of death for patients with non-Hodgkin lymphoma (NHL). Biological therapies used since 1997 have increased median survival to around 15 years but, even with this significant improvement, 20% of NHL patients diagnosed today will die of secondary malignancies. They are considered to be due mainly to the intensive chemotherapy regimens used in initial treatment.<sup>6</sup> In contrast, progression to overt acute leukemia in patients with chronic myeloproliferative neoplasms is more often inherent to the disease than the consequence of cytotoxic therapy with P32 or alkylators.<sup>7</sup>

**Non-malignant late effects**

Multinational observational studies have detailed the non-malignant physical side effects in patients with childhood malignancies or in recipients of HSCTs. High cumulative doses of anthracyclines reproducibly induce cardiac failure.<sup>8</sup> High-dose total body irradiation is directly linked with sterility or cataract induction. HSCT and other combined modality treatments have been associated with late

cardiotoxicity, reduced sexual and reproductive function, and premature aging. Cancer survivors suffer more frequently than their peers from reduced quality of life, post-traumatic stress disorder, fatigue, anxiety and depression; they are more frequently out of work, single or divorced.<sup>9</sup> The specific mechanisms associated with these non-malignant late effects remain poorly understood; very little information is available on how a cancer diagnosis, its treatment and long-term side effects affect the lives of the cancer patient and their family on a psychosocial level.

**The challenges of cancer survivorship care**

A structured follow-up program for cancer survivors can prevent late complications or detect early signs and permit early treatment.<sup>10</sup> In some specialized locations, recommendations are available; trained physicians and nurses organize follow-up clinics, patients’ organizations offer information, and healthcare providers cover the costs. This is far from the norm worldwide. The USA’s Institute of Medicine leads the way on how specialized centers could run annual follow-up visits to monitor survivors of childhood cancer treated by HSCT. They have set up recommendations for individualized survivorship care plans and have defined the ideal annual long-term follow-up visit. International guidelines for the long-term care of HSCT-treated cancer survivors were first published in 2006. Regular updates have been produced since by a working group representing the majority of the HSCT organizations worldwide.<sup>11</sup> This harmonization initiative provides a template that could be adapted for other types of cancers. However, with increased awareness, specific deficiencies and conflicts of interest have become appar-

ent. Stakeholders may have different goals, despite sharing common interests, and they might even compromise their own and others' good intentions (Table 1). Healthcare providers have no incentives for collaboration across borders, and there is a lack of funding. Even if recommendations and guidelines are generated, they are not self-sufficient. They are of no value if no funds are provided to sustain adherence in those contexts in which non-adherence by institutions is allowed to continue without intervention.

### Novel approaches to cancer survivorship programs

Professional organizations such as the Institute of Medicine, the European Hematology Association, the European LeukemiaNet, the American Society for Hematology, the American Society for Clinical Oncology, the Scottish Intercollegiate Guidelines Network,<sup>12</sup> and many others, are challenged to create harmonized guidelines for long-term follow up. Development of "Cancer Survivorship Passports",<sup>13</sup> that are standardized but adapted to the type of cancer and the individual patient's risks and needs are a major step forward. Still, renewed pressure is required to create networks, in which responsibilities between primary care, localized specialists and the cancer referral center are effectively defined and shared. These players should work together within the framework of a quality management system, with transparent and open communication. But incentives are needed to make this happen. Professional organizations need to make a convincing case to health care payers and competent authorities. Data collection and data analysis are not just a new form of research; they are an integral part of all cancer therapy.

Modern combined modality treatments can cost hundreds of thousands of euros. Applying such treatment without quality control measures comes close to malpractice. The costs associated with data collection and quality management are small compared to treatment costs and must be covered by the treatment payer. Adherence to a quality management system can improve survival and reduce costs.<sup>14,15</sup> Payers will understand this and will support such systems if professional organizations act decisively.

### Recommendations and conclusions

There is a crisis of responsibility towards cancer survivors. The time has come to raise awareness of these issues and to debate how Cancer Survivorship Programs in Europe and worldwide should expand to meet this huge area of unmet need. The "Cancer Survivorship Meeting Bergamo" has stipulated some specific recommendations.

Research and information on late sequelae should be coordinated at an international level with standardized data exchange. Professional organizations should harmonize recommendations. Evidence-based follow-up strategies should be embedded within a quality management system to ensure adherence. The lessons learned from childhood cancer or hematopoietic stem cell transplant survivors, their respective recommendations and guidelines, and the quality management systems "FACT" and "JACIE" could serve as a role model.<sup>14</sup>

Competent authorities should recognize that reimbursement plans for primary treatment have to include data collection and data analysis as integral parts of the therapy.<sup>16</sup> Lifelong monitoring of cancer survivors has to be recognized as an essential tool to generate data to show if and how new treatments aim at both increasing survival rates and decreasing risks for non-malignant late effects, and how they are impacting on health, quality of life and cost effectiveness. The numbers of elderly cancer survivors will continue to grow but research does not provide sufficient information to enable evidence-based guidelines to be formed. This can be achieved when data collection is integrated into the cost packages paid for cancer treatment.

Information technology tools have to be developed to establish standardized but individualized cancer survivor passports, adapted to specific cancer types, treatments and individual patients. They have to be integrated into networks that range from patients and their families to the primary care provider, local specialist, referring center and tertiary cancer referral center. Networks should be based on quality management systems with defined and transparent responsibilities for each partner involved, with incentives and external controls.

The respective professional organizations, competent authorities, patient's organizations and charities are challenged to act now.

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