Population-based cancer survivorship research: Experiences from Germany and the Netherlands

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ABSTRACT

Research into the well-being of cancer survivors in the post-treatment phase can face the potential challenge of identifying and recruiting survivors. Population-based cancer registries can address this challenge. Through linkage with national and state cancer registries, Germany and the Netherlands have a long history of conducting population-based survivorship studies. The CAESAR study from Germany and the PROFILES registry from the Netherlands are examples of large and comprehensive population-based survivorship studies assessing the well-being of (long-term) cancer survivors. This paper briefly describes the contributions studies such as CAESAR and PROFILES have made to cancer survivorship research at the patient, clinical, research, and societal level. Potential barriers associated with population-based survivorship research and directions are also discussed.

1. Introduction

A significant number of adult individuals are now living with cancer as a chronic illness. In 2012, more than 32 million individuals worldwide, including 9.7 million in Europe, were still alive 5 years after their cancer diagnosis [1]. This number is expected to increase substantially in the coming years due to the combined factors of an aging population, increased cancer incidence, and improved cancer detection and treatments [2,3]. The downside of the success of improved treatments is that while many cancer survivors are free of cancer, they may not necessarily live in good health. Cancer treatments can be debilitating and cancer survivors may have an increased risk for a range of adverse short- and long-term physical and psychosocial effects associated with cancer and its treatment [4]. Consequently, the well-being of this rapidly growing group living with a history of cancer is a topic of critical relevance as reflected in the commission of this special issue from the European Organisation for Research and Treatment of Cancer (EORTC).

2. Cancer survivorship

There is currently no consensus on the definition of a cancer survivor [5,6]. According to the US National Coalition for Cancer Survivorship (NCCS), an individual is considered a cancer survivor from the time of diagnosis through the balance of his or her life [7]. On the other hand, EORTC defines cancer survivor as an individual who has been diagnosed with cancer, has completed primary treatment (with exception of maintenance therapy), and has no evidence of active disease [8]. Cancer survivorship research therefore covers a wide spectrum encompassing physical, psychosocial, and economic issues of cancer impacting the well-being of survivors, beyond the acute diagnosis and treatment phases [9]. For instance, as survivors live longer, they are also more likely to experience late effects of their cancer and treatment, such as comorbidity or second primary cancers [4]. Furthermore, cancer survivorship research includes issues related to access and delivery of health care, and follow up care.

2.1. Patient-reported outcomes (PRO) data

Survivorship research generally incorporates both clinical and PRO data [10]. PRO data is defined as *any* report of a patient's health status *provided directly by the patient without amendment* or interpretation from a clinician or others [11]. PRO is an umbrella term that covers information on symptoms (e.g. fatigue), functioning (e.g. physical functioning, sexual functioning), health status, psychological distress/well-

being (e.g. depression, fear of recurrence, benefit finding), and overall health-related quality of life (HRQL) [12]. Based on the definition of PRO, it can also include information on health behaviors (e.g. physical activity), perceptions of quality of cancer care, health care utilization, and economic issues or challenges facing cancer survivors such as loss of income, return to work, difficulties obtaining financial services such as insurance, loans or mortgages [13,14].

2.2. Challenges of survivorship research

Although there is increased attention into the (long-term) needs and care of cancer survivors [15], research in the post-treatment survivorship phase still lags behind studies conducted during active treatment [16]. It can be a challenge to identify and recruit survivors in the post-treatment period to participate in cancer survivorship research [17].

3. Population-based cancer survivorship research

Population-based cancer registries can be a useful resource to overcome the challenge of identifying and recruiting cancer survivors, especially long-term survivors, for post-treatment research [18]. Cancer registries can be at national, state or regional level. Advantages of using cancer registries for survivorship studies include the wide geographic reach, large potential sample of survivors included into the registry regardless of treating facility, and the wealth of routinely collected demographic and clinical data (e.g. date of diagnosis, cancer stage) [19,20]. These advantages have been optimized for use in cancer survivorship studies [18]. Population-based survivorship studies are therefore expected to have better external validity and generalizability when compared with clinical studies.

3.1. Models of registry-based survivorship studies

Currently there are two models of registry-based studies [18]. In the first model, the cancer registry is used as a sampling frame from which potential study participants are identified. Once identified, these survivors are sent a PRO questionnaire. The collected PRO data are subsequently linked with the clinical data registered by the cancer registry. The second model collects PRO from sampled participants before linkage with a cancer registry.

This paper will briefly describe the range of survivorship research conducted through population-based cancer registries with focus on the experiences of Germany and the Netherlands. The coverage of studies will not be exhaustive but will focus on the authors' experiences in conducting research among adult long-term cancer survivors.

4. Population-based cancer survivorship research in Germany and the Netherlands

Germany and the Netherlands have a long history of conducting cancer survivorship research using population-based cancer registries [18]. The following briefly describes two of the largest and most comprehensive population-based survivorship studies assessing the well-being of (long-term) cancer survivors.

4.1. Germany

The CAESAR (Cancer survivorship: a multi-regional population-based) study was initiated between 2008 and 2009 to describe the needs and the physical, psychological, and economic well-being of 7000 long-term survivors of breast, colorectal or prostate cancer [21]. Cancer survivors diagnosed between January 1994 and June 2004 as registered in the participating cancer registries, and aged 20–75 years at diagnosis were eligible. Participants completed a comprehensive list of internationally validated questionnaires assessing domains as outlined in Fig. 1.

CAESAR consists of a "core" sample of cancer survivors (n = 4174) sampled and recruited from 5 population-based state cancer registries (Bremen, Hamburg, North Rhine-Westphalia, Rhineland-Palatinate and Saarland) in Germany between 2009 and 2011. It is further complemented by three existing population-based survivor cohorts from the German states of Saarland (VERDI and ESTHER-II) and Schleswig-Holstein (OVIS). The three pre-existing cohorts are briefly described below.

VERDI ('*Verlauf der diagnostischen Abklärung und der Lebensqualität bei Krebspatienten*' Course of diagnostics and quality of life in cancer patients) is a prospective population-based study of individuals living in Saarland who were diagnosed with breast, colorectal or prostate cancer between October 1996 and February 1998. Participants were recruited from all hospitals in Saarland and adjacent districts. The primary aim of the study was initially to evaluate diagnostic work-up in cancer patients [22,23] but was successfully converted to a survivorship study with PRO assessments at 1, 3, 5 and 10 years after diagnosis [24–28].

ESTHER-II ('*Epidemiologische Studie zu Chancen der Verhütung, Früherkennung und optimierten Therapie chronischer Erkrankungen in der älteren Bevölkerung*' Epidemiological investigations of the chances of preventing, recognizing early and optimally treating chronic diseases in an elderly population) is a large prospective clinical study that included residents of Saarland newly diagnosed with common forms of cancer, including breast, colorectal and prostate, between January 2001 and December 2003 [29]. Individuals diagnosed with the three indicated cancers who were not included in the ESTHER-II study were identified via Saarland cancer registry for inclusion into the CAESAR study to maximize representativeness and increase power.

Both the VERDI and ESTHER-II cohorts were followed-up in 2008 whereby respondents completed a list of internationally validated questionnaires that was similar to those completed by the CAESAR core sample.

OVIS ('*Onkologische Versorgung in Schleswig-Holstein*' Oncological Care in Schleswig-Holstein) included individuals diagnosed with melanoma, breast or prostate cancer between 2001 and 2003 as registered in the Schleswig-Holstein cancer registry. The study was initially designed to study differences in health care utilization and its impact on HRQL [30]. For the CAESAR study, only individuals diagnosed with breast or prostate cancer were re-contacted in 2009.

The cancer registries participating in the CAESAR study provided detailed demographic and clinical details. A follow-up to CAESAR study is currently in preparation and will include the collection of information on primary cancer treatment via the attending physician.

4.2. Netherlands

The PROFILES (Patient Reported Outcomes Following Initial treatment and Long-term Evaluation of Survivorship) registry was set up in 2009 for the purpose of collecting comprehensive longitudinal PRO from a dynamic cohort of cancer survivors [31]. The range of PRO collected is based on the conceptual model as outlined in Fig. 1. Potential participants for PROFILES studies are sampled from the Netherlands Cancer Registry (NCR). Participants have the option of completing either an online or a paper version of the PRO questionnaire [32]. Collected PRO data are linked with routinely registered clinical and vital status data accessed from the NCR. With a data set of PRO from over 20,000 survivors of various cancers, the PROFILES registry has been acknowledged as a unique infrastructure for the population-based study of cancer survivorship [33,34]. More information on the PROFILES registry is available on its website (www.profilesregistry.nl).

5. Contributions of population-based research to cancer survivorship

Population-based studies of (long-term) cancer survivorship have contributed significantly to the increasing awareness to the reduced or