Supportive Care in Cancer

Return to Work in European Cancer Survivors: A Systematic Review

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Abstract:	Purpose Return to work (RTW) of cancer survivors (CSs) fluctuates in different contexts. This systematic review searched for recent data on the RTW rate of CSs in Europe, investigating factors associated. Methods Bibliographic search covered the period from January 2010 to April 2017, with no language restrictions. European population-based studies assessing RTW rate after cancer diagnosis were included. We excluded studies focusing on a specific cancer diagnosis. Results Twelve observational studies, conducted in North-Western and Central Europe, were selected. The cohorts investigated included 280 to 46720 individuals diagnosed with cancer from 1987 to 2010. The median time frame between diagnosis and RTW verification was 2 years (0.2-23.4 years). RTW rate of CSs ranged from 39% to 77%. Among individuals employed at the time of diagnosis, RTW fluctuated from 60% to 92%, the latter registered in a sample with good prognosis. Factors associated with RTW cover the crucial areas of personal factors, work-related factors, cancer-related factors, and embrace support strategies that facilitate reintegration to work. Conclusions There is urgent need for data from Mediterranean and Central Europe, to understand whether RTW is problematic in CSs and whether socio-rehabilitative interventions are required to mitigate the potential negative impact of cancer on individuals and society.

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Return to Work in European Cancer Survivors: A Systematic Review

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Statement

This article does not contain any studies with human participants performed by any of the authors.

ABSTRACT

Purpose

Return to work (RTW) of cancer survivors (CSs) fluctuates in different contexts. This systematic review searched for recent data on the RTW rate of CSs in Europe, investigating factors associated.

Methods

Bibliographic search covered the period from January 2010 to April 2017, with no language restrictions. European population-based studies assessing RTW rate after cancer diagnosis were included. We excluded studies focusing on a specific cancer diagnosis.

Results

Twelve observational studies, conducted in North-Western and Central Europe, were selected. The cohorts investigated included 280 to 46720 individuals diagnosed with cancer from 1987 to 2010. The median time frame between diagnosis and RTW verification was 2 years (0.2-23.4 years). RTW rate of CSs ranged from 39% to 77%. Among individuals employed at the time of diagnosis, RTW fluctuated from 60% to 92%, the latter registered in a sample with good prognosis. Factors associated with RTW cover the crucial areas of personal factors, work-related factors, cancer-related factors, and embrace support strategies that facilitate reintegration to work.

Conclusions

There is urgent need for data from Mediterranean and Central Europe, to understand whether RTW is problematic in CSs and whether socio-rehabilitative interventions are required to mitigate the potential negative impact of cancer on individuals and society.

Keywords: Neoplasms, Return to Work, Europe, Survivors, Systematic Review Literature, Sick Leave

PURPOSE

In countries with high economic growth index, life expectancy and working age are increasing, phenomena that will result in growing numbers of people with chronic diseases, including cancer, in the workforce in the near future.

In fact, cancer incidence in the European Union (EU-28) is estimated to be over 500 new cases/year/100.000, excluding non-melanoma skin cancer [1], with an increasing trend projected until at least 2020 [2]. However, the long-term survival of cancer patients is steadily growing in all Western countries, thanks to early diagnostic methods and effective therapeutic strategies [3]. The average 5-year survival of malignant tumors has reached 54.2% [3] and nearly 50% of new diagnoses and more than 1/3 of cancer survivors (CSs) are people in their working age [4].

Cancer survivorship can be defined as the broad experience of living with, through, and beyond a cancer diagnosis [5]. A significant proportion of CSs experience impairments and symptoms which may diminish social functioning, for instance pain, fatigue, cognitive dysfunction, and mood disturbances [6, 7]. Thus, it has become imperative to understand the long-term implications of cancer survivorship on social outcomes, such as reintegration into the workplace after cancer treatment, as recommended by the European Cancer Patient's Bill of Rights (art. 3.4) [8].

Return to work (RTW) of individuals who survive cancer is a major goal, as it facilitates the patient’s ability to deal with the disease, recover personal identity and social role, and promote a healthier general condition [9-11]. Although the majority of employed CSs return to work, a meta-analysis by De Boer [12] indicated that individuals treated for cancer were 1.4 times more likely to be unemployed compared to healthy controls.

Certainly, unsuccessful RTW has a significant impact on direct and indirect social costs, which are paid for by healthcare systems or insurances, by patients and their families, by their employers and, lastly, by society. A quite recent inquiry estimated that, 5 years after diagnosis, the missed

overall income for the failed reintegration into work of CSs is equal to 3.2 billion euros [13]. Further costs, which are not always easily quantifiable, originate from the period of sick leave (SL), or the need to replace the worker when not reintegrated, or may be associated to a reintegration that encounters barriers. In Italy, it has been estimated that the socioeconomic impact linked to cancer-related productivity loss exceeds 8 billion euros [14].

Several review articles from both the United States and the European Union have reported an average rate of RTW of approximately 64%, with a wide range from 30% to 94%, registered in different contexts [15, 16]. However, the lack of methodological quality of the studies conducted in this field has been highlighted [15, 17]. Further, the generalizability of results is frequently limited, since reintegration to work may significantly differ depending on the context analyzed [18].

Given the increase in long-term survival of cancer patients, data regarding social reintegration and RTW should be constantly updated: information should be collected in quite homogeneous contexts and interpreted in light of the rapid changes in the socioeconomic and financial conditions of the area investigated. Consequently, the availability of up-to-date and contextualized data on the reintegration to work of CSs would make it possible to see whether there is a problem, and whether its size is such as to suggest implementing social and health policies to limit its potential impact on society.

Therefore, the principal aim of this study is to review the latest literature on the rate of RTW of CSs in Europe. Secondly, we want to identify those factors potentially associated with reintegration to work. Lastly, we present data regarding the duration of SL of CSs.

METHODS

Eligibility Criteria

Studies were included if they met the following criteria:

(1) included patients with cancer, (2) assessed employment status after cancer diagnosis (3) were European population-based studies.

To collect current information generalizable at the whole population of CSs in Europe, studies published before 2010 and studies focusing on a specific cancer diagnosis were excluded.

Search Strategy

We searched the following electronic databases: MEDLINE, CINAHL, EMBASE, PsycINFO and The Cochrane Library (all databases) from January 2010 to April 2017, with no language restrictions.

Search terms were (Work OR employment OR occupation OR labor OR labor market OR absenteeism OR sick leave OR sickness absence OR retirement OR pension OR disability pension OR work ability OR work disability OR wages OR job loss OR job performance OR career OR employer accommodation) AND neoplasm.

When available, subject heading terms such as Medical Subject Headings or Emtree terms were added in all searches. We adapted this search strategy to each database.

Additional records were searched through other sources to complement the database findings; manual search of reference lists of relevant literature reviews and indexes of peer-reviewed journals were used.

Study Selection

The literature search was conducted by an Information Specialist (C.B.) assisted by two healthcare professionals in the rehabilitation field (S.C. and S.P.). The abstracts of empirical studies which met the inclusion criteria were selected and evaluated independently by the latter two reviewers, who appraised full reports of potentially relevant articles for content and quality. Disagreements were resolved through consensus with a third investigator (S.F.).

Critical appraisal

The quality of included studies was scored by two independent reviewers (S.C. and S.P.) using section A of the Critical Appraisal Skills Programme (CASP) tool for Cohort Studies [19]. This tool

encompasses eight items associated to five major sources of potential bias in observational studies: adequate cohort recruitment, study attrition, accurate detection of exposure and of outcome, and identification of potential confounding factors. The two items on confounding were considered irrelevant to our study because in studies regarding prognosis, designed to predict a specific outcome based on a combination of several possible prognostic factors, confounding is not an issue. We therefore estimated the risk of potential bias on six items that could be marked as "yes", "no" or "can't tell". Agreement on the assessment was reached through consensus of the two reviewers, seeking help from a third (L.B.) when needed.

The CASP tool does not provide a minimum score for quality but the first two items assess pivotal requirements for observational studies: lack of satisfaction might suggest it is not worth proceeding with the report appraisal.

We established a priori that we would consider as high quality those research papers with CASP score ≥ 5 "yes" (≥ 83 % of the maximum attainable score), as moderate quality those which scored 3 or 4 "yes" (≥ 50% of the maximum attainable score), and as low quality those that scored less than 3 "yes." High-quality papers were judged as low risk of bias research, moderate quality papers were attributed a moderate risk of bias, and low-quality papers were considered at high risk of bias.

Data extraction

The following data were extracted: country of origin, study design, source for exposure verification (diagnosis), data collection period, time between diagnosis and RTW verification, main outcome measure and measurement strategy, demographic and clinical characteristics of the sample, response rate, RTW rates, and duration of SL. To accomplish the secondary aim of this study, the investigators listed a wide range of potential prognostic factors that might influence the RTW; those factors were identified on the basis of the reviewers' experience in the field of rehabilitation and by considering all the factors accounted for in the selected studies.

Where available, cancer sites and their representation in the sample were reported.

Qualitative analysis

The studies proved to be heterogeneous in terms of their characteristics, limiting the possibility of a quantitative analysis. Therefore, a qualitative analysis was performed to summarize the available evidence, accounting for the methodological quality of the report. For each study, the stated rate of RTW, the associated prognostic factors, and data regarding SL were collected. Also, the consistency of results among different studies was taken into account.

RESULTS

A total of 1309 citations were retrieved from electronic database search and manual search of reference lists. After the screening process, 99 full-text articles were assessed for eligibility and 87 were further excluded. Thus, this systematic review includes 12 research reports. (Figure 1)

Critical appraisal of the included studies

After scoring the 12 research reports, the overall agreement on the risk of potential bias measured on the six items of the CASP tool considered for quality appraisal proved to be moderate, with a Cohen's kappa of 0.479. Table 1 summarizes the critical appraisal of the included research reports. None of the studies was judged at high risk of bias and all of them satisfied at least one of the two pivotal requirements; thus, we included all the selected studies in the analyses of the results, based on the reported quality. One study did not clearly state the issue under investigation [20], whereas two studies did not adequately represent the primary sector (i.e., agriculture, forestry, fishery, and mining) [21, 22], which was under-represented in the data source investigated.

In most of cases, both the exposure and outcome were judged accurately defined and measured to minimize bias [23-30]. In two cases the measure of the exposure was judged at risk of bias because the investigators collected data on sickness absence, not taking into account individuals that continued working during cancer treatment [21, 22]. In one case, the outcome measure was

considered at risk of bias because nearly one half of general practitioners who were asked to engage patients in the research did not take part in the study [20]. The time between diagnosis and RTW verification was judged sufficient to assess employment status of CSs in all the included studies but, when data were collected by surveys, the rate of respondents ranged from the high risk of bias value of 27% [20] to the unquestionable 100% reached by Tison [30].

Description of studies included

Table 2 summarizes the characteristics of the 12 research reports included in this review, conducted in the United Kingdom, France, the Netherlands, Denmark, Norway, Finland, and Iceland. Central European countries were underrepresented and, with the only exception of the information collected in France, very scarce data were collected in Mediterranean Europe. Study designs were mostly cross-sectional surveys or registry studies collecting longitudinal data. The samples included individuals in their working age selected by cancer registries, occupational registries, health insurance schemes, or hospital departments. The cohorts investigated were diagnosed with cancer from 1987 to 2010 and data collection occurred from 1987 to 2012. In one study, these data were not reported and the attempts to contact the authors to fill the gap were unsuccessful [29]. The median time frame between diagnosis and RTW verification was 2 years (range 0.2-23.4 years).

Population studied

Table 3 summarizes the characteristics of the population under study. The size of the included samples varied from 280 to 46720 working age individuals treated for cancer. Breast cancer was the most represented cancer (n. 7355), followed by genital and prostate (n. 4868), gastrointestinal (n. 1973), upper aerodigestive tract/lung (n. 1512), blood cancer (n.1436), skin cancer (n.1197) urological not prostate (n.659), head and neck including thyroid (n.245), and unspecified sites (n.1250). One study did not report the number of individuals diagnosed with each cancer represented in the sample, and the attempts to receive detailed data from the authors were

unsuccessful [25]. The response rate to surveys ranged from 27% (questionnaire administered online or by telephone) to 100% (questionnaire administered by telephone or by mail).

Return to work in cancer survivors

Table 3 reports data regarding RTW rate, the factors associated to the outcome of interest and SL duration. Return to work of CSs in their working age was reported by four studies [20, 23, 25, 31] and ranged from 39% [25] to 77% [20].

Return to work in CSs employed at the time of diagnosis was reported by ten studies [21-24, 26-31]. Return to work in CSs employed at the time of diagnosis ranged from the 60% registered in the Netherlands [21] to the 92% registered in the United Kingdom [29]. However, the lower RTW rate was reported in reference to full RTW [21]. A higher and more realistic proportion of 69% would account for a certain number of individuals who gradually resume their job with a part-time schedule in the Netherlands [21].

Regarding the optimistic 92% RTW rate reported in the United Kingdom [29], the sample selected for this study included individuals who had completed treatments and excluded patients with metastatic cancer; the high rate of RTW might thus be explained by these selective inclusion criteria. As a matter of fact, the higher proportions of RTW detected with broader inclusion criteria were registered in Norway and slightly exceeded 80% [27, 31].

Regarding the two French studies, Marino [24] collected data of RTW in a specific subsample of individuals still employed, although not yet returned to work, already included in the broader cohort investigated by Paraponaris [23]. Thus, the 90% rate of RTW registered by Marino [24] should be interpreted within the framework depicted by Paraponaris [23], where 66.3% of CSs employed at the time of diagnosis did actually RTW.

Prognostic factors for return to work in cancer survivors

All the studies included in this review except one [21] analyzed factors that might facilitate or hinder RTW (Table 3). Factors analyzed were largely heterogeneous between studies. Protective factors

were positively associated to higher rates of RTW, or faster RTW, or higher number of hours worked by CSs per time unit. Risk factors were associated to lower rate of RTW, or slower RTW, or change in employment status.

The prognostic factors identified embrace the crucial areas of personal (sociodemographic) factors, work-related factors, and cancer-related factors, according to the International Classification of Functioning, Disability and Health [32]. Luker [20] found a positive association between the discussion of employment issues between patient and healthcare team and a higher number of hours worked per time unit: we consider this a rehabilitative intervention, facilitating the social reintegration of CSs. Factors associated to RTW, allocated to the corresponding category, are presented in Figure 2.

The associations of personal factors and cancer-related factors with RTW were verified in the majority of the selected studies, whereas the influence of work-related factors on reintegration at work was explored by five studies only [23, 24, 26, 27, 29]. Support provided by the healthcare team in coping with RTW issues was investigated in two studies, and was reported as prognostic factor for a successful participation in labor in both cases [20, 26].

Few studies also examined the associations between exposure and RTW in men and in women separately [20, 22, 24, 26, 31]. Male gender seems to act as a protective factor for RTW [20, 24]. In men, living with a partner and children was positively associated to RTW [31]. In women, weak support from work supervisors or from the healthcare professionals and being affected by blood cancer were negatively associated to RTW [22, 26, respectively].

Cooper [29] analyzed factors associated to RTW separately for each cancer diagnosis represented in their sample, but found no common elements. However, in breast CSs, working full-time and perceiving control over the effect of cancer at work acted as protective factors. Protective factors were also the perceived high level of physical functioning for head and neck CSs and the possibility to adopt a flexible work schedule for urological CSs.

Sickness absence of cancer survivors

The duration of SL was analyzed by six studies [20-24, 29]. The reporting of this data was highly heterogeneous. The average duration of SL was 6-12 months in two large samples analyzed, accounting for 5293 individuals [21, 24]. In some cases, SL lasted less than 6 months for a consistent proportion of the individuals under investigation [20, 24]. However, a proportion of 15 to 30% of CSs were still on SL 2 years after diagnosis [23, 24]. Long-lasting SL was associated with physically demanding work [23] and with blood, lung, and gastrointestinal cancers for 30% of individuals affected [22]. To a lesser extent, it was also associated with upper aerodigestive tracts and breast cancers, for nearly 20% of individuals affected [22, 23]. Of note, a longer duration of SL was associated with permanent employment, compared to fixed-term employment and self-employment ($p=0.042$) [24]. Finally, the time to full or partial RTW was significantly longer in the year 2008 than in 2002 ($p<0.01$) [21].

DISCUSSION

This systematic review provides current knowledge on CSs' RTW rate in North-Western and Central Europe. Of note, only one study was published in the Mediterranean Europe, and Central Europe is scarcely represented. This is particularly important given that participating in the workforce is determined by an interaction between job retention capacity beliefs, labor market conditions and welfare state. Indeed, within Europe, the impact of cultural, economic and financial factors on the economy vary in different areas, as well as dissimilarities in social security and healthcare systems exist. As a result, RTW rate may vary significantly from country to country throughout Europe [33].

Also, in the last decade the average growth rates of the EU-28 were 0.7% per annum, but negative growth rates were recorded for Greece, Italy, Croatia, and Portugal [34]. Therefore, this review pointed out the almost complete lack of updated data on RTW of CSs in countries highly affected by the crisis.

This review provided data regarding RTW in the general population of working age CSs and/or in CSs employed at the time of diagnosis. It also analyzed factors associated to work reintegration and duration of SL.

The estimated rates of RTW registered for North-Western and Central European CSs range from 39% [25] up to 77% [20]. In France, the only Mediterranean European country represented in this review, the rate of RTW was almost 56% [23], registered before the crisis of the EU Member States. Comparing these results with the employment rate of working age Europeans in 2014, it seems that employment rates of CSs are lower than those of the general population [35]. Notwithstanding, the same results suggest that many CSs are able and willing to work, because employment may be beneficial for general health in this population [9-11].

Unfortunately, when looking at the RTW rate of CSs employed at the time of diagnosis, a realistic estimate is between 69% [21] up to slightly more than 80% [27, 31]. Thus, this systematic review highlights a considerable chance of loss of employment for North-Western and Central European individuals treated for cancer. This finding is consistent with those underlined by de Boer [12] who, in 2009, conducted an extensive meta-analysis which, however, could not represent Central and especially Mediterranean Europe adequately.

In light of these findings, as cancer incidence is increasing and survival rates are improving, work reintegration is emerging as critical in the care of CSs in Europe, and interventions to address this issue should be recommended. However, the scientific community and policy makers must deal with the complete lack of knowledge of the phenomenon in a huge part of the continent. Without this information, implementing suitable and contextual interventions to address unemployment in CSs is unrealistic.

This review also points out factors that might facilitate or hinder RTW. According with the ICF classification, those predictors might be classified into three categories: personal, work-related, and cancer-related. Regarding personal factors, being female negatively affected resumption of work [20]. This finding was consistent with those of recent reviews focusing on predictors of RTW in CSs [36, 37]. Having children and/or living with a partner seem to act as protective factor for

both genders [24, 30, 31]. Conversely, being single, widowed, or divorced negatively influenced employment status [25]. A possible explanation for this phenomenon is that, in patients with cancer, the support of family members ameliorates emotional well-being, provides practical help in doing everyday chores, and assists with financial shortfalls [38].

It is well known that education and income levels are strongly linked to different social outcomes, including job [39]. Consistent with this postulation, this review shows that high income and high education level facilitated maintaining one's job [24, 27, 31], confirming previous findings [36]. Less educated people frequently have more physically demanding jobs, which are negatively associated to RTW [23, 26, 27]. However, also intellectual work, which requires solid cognitive abilities, may be affected by chemotherapy [27]. This was confirmed in a sample of gynecological CSs who were interviewed on their work experiences following diagnosis: while women who had had radiation were more likely to indicate limitations for physical tasks, women undergoing chemotherapy reported performance limitations in more analytical tasks, such as intensive concentration or analyzing data [40].

Additional work-related factors which are worth considering are the social environment and flexibility at work. The social work environment can be a barrier to participation when the person perceives discrimination or lack of support from the employer and colleagues [23, 24, 26, 27, 29], and this is particularly true for females [23, 26]. Thus, the support of the employer and/or the colleagues acted as facilitating factors for RTW [27]. Moreover, having flexibility about scheduling and how much work to do make it easier to reconcile work and treatment and to resume work after cancer [15, 29, 41].

A minority of the studies included in this review investigated work-related factors. This scarcity is particularly serious given that work-related factors have a pivotal role in RTW of CSs and can be modified. In fact, high proportion of patients experienced temporary changes in work schedule or work duties at the resumption of work [16] and individuals with high decision latitude resume work sooner [27], perhaps because those changes can easily be put into place.

The perspectives of CSs, employers, and health service providers on RTW and its accommodation process have recently been explored: employers claimed knowledge about cancer and RTW process to support survivors through the implementation of various types of accommodation, such as adopting graduated RTW plans with flexible scheduling, modifying work duties, providing retraining and support at the workplace, and modifying the physical work environment or providing adaptive aids [42, 43]. To address these needs, rehabilitation interventions aimed at reducing activity limitations and promoting social participation could be implemented, as suggested by a few studies included in this review [20, 26]. Personalized multidisciplinary rehabilitation interventions can also address limitations or symptoms specific to cancer site or therapy regimen, leading to higher RTW rates compared to usual care [44]. This is particularly important as, according to this review, chemotherapy causes side effects such as fatigue or cognitive problems [24] that, as already discussed, impact on work ability [6].

Multidisciplinary rehabilitation interventions could also positively affect the duration of SL [44], reducing the associated social costs. Data regarding SL can only be interpreted in light of the welfare policies of each European state, which is beyond the scope of this systematic review. However, according to our findings, cancer diseases entailed long-term absence from work by 15 to 30% of the diagnosed individuals [23, 24], with high impact of lung, blood, gastrointestinal and breast cancer [22], as partially confirmed by previous studies [45, 46].

A possible limitation of this study is that the search strategy adopted was temporally limited to the years 2010 – 2017. However, we chose to consider the most recent years because in this period Europe's economy underwent major changes due to the financial and economic crisis. To permit interpretation, data regarding employment rates should always be updated and collected in the context of interest; to our knowledge, this is the first systematic review that investigates RTW of European cancer patients in this historical period.

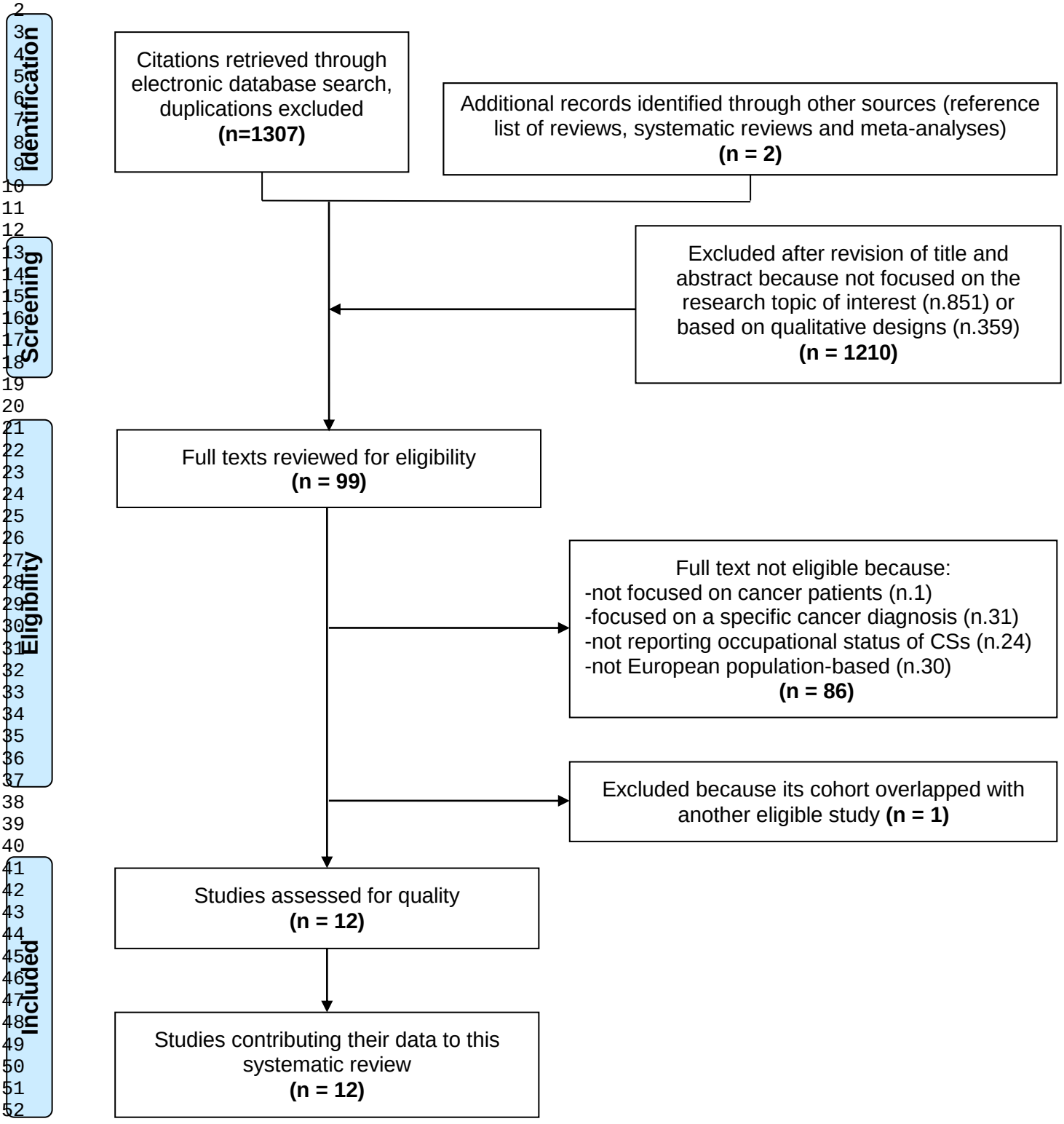
Despite this consideration, it is important to emphasize that this review does not provide exhaustive data from across Europe due to the lack of data available from Mediterranean and Central Europe since 2010. However, this limit is not attributable to any shortcomings in the search

strategy, since the same lack of data was also demonstrated by a previous, temporally exhaustive meta-analysis [12].

To conclude, this review adds current knowledge regarding CSs returning to work in North-Western Europe, highlighting the urgent need for data collected in the Mediterranean and Central region of Europe. It also provides an overview of the principal factors that might influence work resumption in this population and suggests conducting appropriate studies designed to thoroughly investigate how work-related factors might modify the RTW rate.

This information will help to implement multidisciplinary rehabilitation interventions tailored to the individual, feasible in the context of interest and effective in addressing unemployment in CSs.

Figure 1. Search Flow Diagram



Legend: CSs = Cancer survivors

Figure 2. Protective factors and risk factors associated with return to work (RTW)

Area	Protective factors	Risk factors
Personal	male gender medium-high income high education living with partner/children employed at diagnosis	female gender low income <30 and >50 years old
Work-related	support from supervisor support from colleagues decision latitude	discrimination at work low social support at work self-employment permanent job physically demanding work intellectually demanding work
Cancer-related	good prognosis	metastatic disease upper aerodigestive cancer lung cancer further diagnostic phase chemotherapy, active treatment adverse effects
Rehabilitative	discuss employment issue with HCPs	

Legend: HCPs = Health care professionals

Study	1)Did the study address a clearly focused issue?	2)Was the cohort recruited in an acceptable way?	Is it worth continuing?	3)Was the exposure accurately measured to minimize bias?	4)Was the outcome accurately measured to minimize bias?	7)Was the follow up of subjects complete enough?	8)Was the follow up of subjects long enough?	RISK of BIAS
[25] Fiva et al. (2010)	YES	YES	YES	YES	YES	YES	YES	LOW
[23] Paraponaris et al. (2010)	YES	YES	YES	YES	YES	CAN'T TELL	YES	LOW
[26] Lindbohm et al. (2011)	YES	YES	YES	YES	YES	YES	YES	LOW
[21] Roelen et al.(2011)	YES	NO	YES	NO	YES	YES	YES	MODERATE
[22] Roelen et al.(2011)	YES	NO	YES	NO	YES	YES	YES	MODERATE
[27] Torp et al.(2011)	YES	YES	YES	YES	YES	CAN'T TELL	YES	LOW
[28] Ross et al. (2012)	YES	YES	YES	YES	YES	CAN'T TELL	YES	LOW
[29] Cooper et al. (2013)	YES	YES	YES	YES	YES	YES	YES	LOW
[20] Luker et al. (2013)	NO	YES	YES	YES	NO	NO	YES	MODERATE
[24] Marino et al. (2013)	YES	YES	YES	YES	YES	YES	YES	LOW
[31] Torp et al. (2013)	YES	YES	YES	YES	CAN'T TELL	YES	YES	LOW

[30] Tison et al. (2016)	YES	YES	YES	YES	YES	YES	YES	LOW

Table 2. Characteristics of the included studies

Author (year)	Country	Study design	Source of exposure	Data collection period	Diagnosis occurrence	Follow-up (months)	Main outcome	Measurement of outcome
[25] Fiva et al. (2010)	Norway	Cross-sectional registry-study	Norwegian Cancer Registry	From 1987 to 2000	Not specified	60	Survival rate and employment status	Statistic Norway registers
[23] Paraponaris et al. (2010)	France	Cross-sectional survey	French Health Insurance Schemes, the French National Institute for Health and Medical Research and the French National Cancer Institute	Late 2004	Sep./Oct. 2002	24	Employment status	Questionnaire administered by telephone
[26] Lindbohm et al. (2011)	Finland, Norway, Iceland and Denmark	Cross-sectional survey	The files of one large hospital (Finland and Norway), or the cancer registry, (Denmark and Iceland).	2003 to 2005	1997 to 2002	12 to 96	Work changes†	Questionnaire administered by mail
[21] Roelen et al. (2011)	the Netherlands	Cross-sectional registry-study	ArboNed Occupational Health Service register	2002 to 2010	2002, 2005 and 2008	24	Sickness absence	ArboNed Occupational Health Service register
[22] Roelen et al. (2011)‡	the Netherlands	Cross-sectional registry-study	ArboNed Occupational Health Service register	2006 to 2008	2004, 2005 and 2006	24	Time to full-RTW	ArboNed Occupational Health Service register
[27] Torp et al. (2011)	Norway	Cross-sectional survey	Cancer Registry of Norway	Feb./Mar. 2008	2005 and 2006	15 to 39	Work changes	Questionnaire administered by mail

Author (year)	Country	Study design	Source of exposure	Data collection period	Diagnosis occurrence	Follow-up (months)	Main outcome	Measurement of outcome
[28] Ross et al. (2012)	Denmark	Cross-sectional survey	All hospital departments treating cancer patients in three Danish counties	2005 to 2006	0.2 to 23.4 years previously	Median 33, mean 48 (range 2 to 281)	Employment status	Questionnaire administered by mail
[29] Cooper et al. (2013)	United Kingdom	Longitudinal prospective	Hospitals in 3 UK Healthcare Trust	Not specified	Not specified	12	Factors influencing time to RTW	Questionnaire administered by mail
[20] Luker et al. (2013)	United Kingdom	Cross-sectional survey	Two cancer registries	Apr./Oct. 2011	2 to 3 years previously	24 to 36	Employment status	Questionnaire administered online or by telephone.
[24] Marino et al. (2013)§	France	Cross-sectional survey	Long Duration Disease File of the National Health Insurance Fund	Late 2004	Sep./Oct. 2002	24	Time to RTW	Questionnaire administered by telephone
[31] Torp et al. (2013)	Norway	Cross-sectional registry-study	Cancer Registry of Norway	1998 to 2004	1999	60	Employment status	Statistics Norway's Events database
[30] Tison et al. (2016)	France	Cross-sectional survey	French Cancer Survey and the French Labor Force Survey	2012	2010	24	Work changes	Questionnaire administered by telephone or mail

†Work changes= defined as mobility in the labor market among three transition states: employment, non-employment (unemployment or inactivity) and retirement, or making important changes in work situation, or change of employer; ‡ Roelen et al. (2011, c) study's cohort includes a subsample of 1522 individuals (sample 2) of the cohort investigated by Roelen et al. (2011, a); § Marino et al. (2013) study presents original data from a subsample of the cohort investigated by Paraponaris et al., 2010

Table 3. Results of the included studies

Author, year	n. †	average age (years)	m/f‡ (%)	Cancer sites in order of prevalence in the sample	Response rate (%)	RTW rate		Protective factors	Risk factors	SL* duration
						RTW § rate of CSs¶ (%)	RTW rate of CSs employed at diagnosis (%)			
[25] Fiva et al. (2010)	46720	48	41/59	Breast, lung, skin	100	39	Not measured	Being in the labor market prior to diagnosis	Metastatic disease at diagnosis	NR
[23] Paraponaris et al.(2010)	1725	47	33/67	Breast, upper aerodigestive tracts/lung, blood, colon/rectum, prostate, urogenital tumors	61	56	66	NR**	Low income Physically demanding work Upper aero-digestive cancer Lung cancer Discrimination in the workplace	≥ 2 years for 15% of CSs and for >20% of individuals with physically demanding work, upper aero-digestive tract or lung cancer
[26] Lindbohm et al. (2011)	2030	NR	NR	Breast, testicular, lymphoma, prostate	72	NR	75	NR	Physically demanding work Female gender only, weak support from the supervisor or from the healthcare team	NR
[21] Roelen et al. (2011)	4287	48	36/64	Breast, genitals, gastrointestinal, lung, skin, blood	100	NR	Full RTW: 80 in 2002, 74 in 2005, 60 in 2008 Partial RTW 85 in 2002, 80 in 2005, 69 in 2008	NR	NR	On average, 8.5 months in 2002 and 9.5 months in 2008
[22] Roelen et al. (2011)	5074	48	36/64	Breast, genitals, gastrointestinal, lung, skin, blood	100	NR	73 (full RTW)	NR	Older age associated to genital cancer Female gender only, blood cancer	≥ 2 years for nearly 30% of blood, lung and gastrointestinal CSs and for nearly 18% of breast CSs

[27] Torp et al. (2011)	1115	52	31/69	Breast, female genital organs, prostate, testicular, lymphoma, colon/rectum, lung, melanoma, bladder, central nervous system, thyroid, leukemia	54	NR	84	High education Medium income Support from supervisor Support form colleagues High decision latitude (at work)	Low social support at work Physically demanding work Intellectually demanding work Self-employment	NR
[28] Ross et al. (2012)	1490	63	36/64	Breast, gastrointestinal, lung, gynecological, prostate, urinary, head and neck, lymphoma, leukemia	68	NR	63	NR	Age ≥ 50 years Active treatment or further diagnostic phase Metastatic disease Lung cancer	NR
[29] Cooper et al. (2013)	280	55	44/56	Breast, urological, gynecological, head and neck	87	NR	92	In breast CSs only, working full-time, control over the effect of cancer at work In head and neck CSs only, high level of physical function In urological CSs only, flexible work schedule	In gynecological and head and neck CSs only, impact of cancer/treatment on life/work In urological CSs only, constipation	A median of 7.5 months for breast CSs, 4.5 months for head and neck and gynecology CSs; 5 weeks for urology CSs
[20] Luker et al. (2013)	382	50	24/76	Breast, colon/rectum, prostate, Hodgkin's disease, bladder	27	77	NR	Discussing employment issues with the HCPs***	Female gender	< 6 months for 50% of CSs 6-12 months for 34% of CSs
[24] Marino et al. (2013)	1006	49	32/68	Breast, upper aerodigestive tract/lung, blood, colon/rectum, prostate and other urogenital tumors	61	NR	90	Male gender High education Living with a partner Good prognosis	Permanent job Progressive disease Chemotherapy Side effects treatment related	Median duration 1 year ≤ 6 months for 36% of men and 25% of women > 2 years for 35% of men and 28% of women
[31] Torp et al. (2013)	3278	47	40/60	Breast, skin, prostate, testicular, colon, lymphoma, ovary, cervix, bladder, leukemia, endometrium, rectum, lung	100	73	80	High education Medium/high income Being employed or self-employed at diagnosis Male gender only, living with a partner and children	Age ≤30 or ≥ 50 Regional/distant cancer	NR
[30] Tison et al. (2016)	4110	60	42/58	Breast, prostate, thyroid, melanoma, colon/rectum, urogenital, upper aero-digestive tracts, non-	100	NR	71	Living with children	Older age Poorer prognosis	NR

										Hodgkin disease, lung	

Legend: †n. = number of patients included in the study; ‡m/f = male female ratio; §RTW = return to work; ¶CSs = cancer survivors; *SL = sick leave; **NR = Not reported or not measured;*** HCPs = Health care professionals

Conflict of Interest

The Chamber of Commerce and the GRADE Onlus of Reggio Emilia, together with the Local Health Authority-Institute of Research, supported one scholarship through which this study was conducted. However, as disclosed, nobody from the Chamber of Commerce nor from the GRADE Onlus participated to the study at any stage and they did not influenced any of the author during the implementation of this review. All of the authors have full control of all primary data and they agree to allow the journal to review their data if requested.

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