Work ability and fatigue in cancer survivors on long-term sick leave

Peter van Muijen

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Contents

1

General introduction

Considering the burden of cancer in the working age population, this thesis specifically addresses Cancer-Related Fatigue (CRF) and work ability in cancer survivors. Both topics are related to long-term sick leave and work participation in cancer survivors and need to be addressed in order to support them to find a way back to work (1-4). The following case illustrates the challenges a cancer survivor may face during a vocational rehabilitation trajectory, that eventually leads to a work disability assessment. Simultaneously, this case pictures the potential questions an insurance physician (IP) may need to answer, in assessing the work disability claim.

Mrs. F., a 39-year old divorced shop assistant working in a supermarket, is on sick leave since she was diagnosed with breast cancer almost two years ago. She had surgery and was treated with chemotherapy. She also used Herceptin and as a result suffered from left ventricular dysfunction, which improved afterwards. Previous medical history reports recurrent episodes of head-ache and an obsessive compulsive disorder treated adequately in the past. Although she recently visited her general practitioner (GP) asking for sleeping pills, the check-ups she had at the hospital were reassuring until now. She has applied for a disability benefit and visits the local office of the Social Security Agency (SSA). She tells the IP that over the last year, several times she tried to start working again. Initially, as she felt insecure about return to work (RTW), she asked her oncologist what to do. The oncologist reassured her, said that everything was fine so far, and that she should take her time and RTW when she felt ready for it. But then, it did not work out, even though at first her employer was very supportive in allowing her to retreat to the canteen of the supermarket if she felt the need to take a rest. She agreed to start with some cleaning work, assist in the supply chain just by checking stock and store for supplies, and took care of the coffee machine that customers may use freely. Even so, just after one hour of work, she would become increasingly tired. As RTW in the shop was no success, soon the Occupational Health Physician (OP) advised to switch to administrative tasks to which the employer agreed with some reluctance, as this meant shifting staff and tasks. Soon after she started in her new tasks, her co-worker, who was supposed to help her out in the office, went on maternity leave. As Mrs. F. was not trained to be an office worker, she felt that she was not up

to keeping the administration running smoothly. She also struggled with numbers and figures due to poor concentration. She once almost ordered the same products twice at the distribution center. This made her insecure and therefore she checked her work every now and then, as she was afraid to make mistakes that could be costly in the end. Now, she manages to work a few hours in the morning in administration, only to find herself lying on the couch at home in the afternoon. As a result, house-keeping and looking after her two children have become difficult. Moreover, her youngest son is not doing well at school now, about which she started to worry. She claims that she can only work a few hours per day at most and definitely not every day. That is, she has things to take care of at home as well and at the moment does not know how to cope and keep things organized.

FACTS AND FIGURES ON CANCER AND WORK

Over the last decades, the number of new cancer cases has grown worldwide (5). While in 2012 there were an estimated 14.1 million new cancer cases (6), by 2030, the global burden is expected to grow to 21.7 million new cases and 13 million cancer deaths per year (7). Nowadays, about 32.6 million people are globally living with cancer within 5 years of diagnosis, of whom 9.1 million in Europe (8). Specifically in the Netherlands, the incidence of cancer was 104,988 in 2015. This number will increase up to 123,000 in 2020, which for a part relates to the effect of an aging society (9). Currently, cancer is no longer equivalent to an incurable disease with fatal prognosis, because of advances made in cancer screening and treatment (10). As a result, cancer survival rates have improved markedly over the last decades in Western countries, e.g., 5-year survival rates in the Netherlands grew from 47% in 1993 to 62% in 2012 (11).

Not only the ageing society, but also the increased entry of women at the workplace and the introduction of a government policy that discourages early retirement, contributed to the growing percentage of workers aged 60 years or over in the Netherlands. That is, in 1996 only 16% of persons above 60 years had a job, while today more than 50% of this group is at work (12). Moreover, in the

Netherlands, as in other Western countries such as Denmark and Spain, changes regarding the retirement pension age are ongoing, in that this age has been raised from 65 to 67 years (13). While about 40% of those diagnosed with cancer in the Netherlands in 2014 was of working age, it is expected that these developments will also affect the number of cancer diagnoses in active workers.

CANCER-RELATED FATIGUE AND WORK ABILITY

The impact of cancer and its treatment, e.g., chemotherapy, may be a burden long after this treatment has been completed. That is, CRF, nausea, pain, physical limitations, cognitive limitations, sleep disorders and depression are frequently reported sequelae (14;15). Poor health can reduce work ability and act as a barrier towards work participation (16).

CRF, the most prevalent side-effect, is known for its prolonged course, and today around 10 million people suffer from CRF worldwide (15). It is defined as 'significant fatigue, diminished energy, or increased need to rest, disproportionate to any recent change in activity level, to be present every day or nearly every day during the same 2-week period in the past month, as well as the presence of additional symptoms' (17). It can be described as 'a persistent, subjective sense of tiredness related to cancer and cancer treatment that interferes with usual functioning' (1). The pathophysiology of CRF is poorly understood and aetiological factors seem to co-exist (18). That is, the most commonly identified causes include direct effects of cancer and tumor burden, treatment side effects, psychosocial factors, exacerbating comorbid symptoms and comorbid medical conditions (19). Being diagnosed with cancer and/or experiencing side-effects of treatment may limit the work ability of cancer survivors (20).

Work ability is defined as the overall fit of the worker with his/her job demands. It is a concept by which a worker judges his/her abilities to participate in work, which can be measured using the Work Ability Index (WAI) questionnaire (21). It can be used to assess health hazards at both the individual and group level by targeting factors related to both the worker and his/her working environment. Work

ability also concerns the interaction between these two against the background of the workers' private/social network. Factors related to the worker, e.g., health, occupational competence, attitude and motivation, may interact with environmental factors such as job demands, the organization of the working community and its management. Ultimately, even society at large relates to the concept of work ability, e.g., by social security legislation regarding sickness benefits and work disability grants. Also, moral codes, e.g., how society and individuals value the meaning of work and work participation, are linked with work ability. Next to being a measure to monitor healthy workers in the workplace, work ability has also shown to be of value to assess the results of vocational rehabilitation among cancer survivors (20). This indicates the relevance of work ability in cancer survivors on long-term sick leave.

CANCER SURVIVORSHIP AND WORK PARTICIPATION

Workers with a chronic illness, among whom cancer survivors, view having work or being able to RTW as the third most important aspect that contributes to the quality of life, after the ability to go out, and to engage in social activities (22). Specifically in cancer survivors, work participation may act as a food-hold to regain control, lead the way back to former life and help to resume social contacts. It may help to improve self-confidence and overcome side-effects of the disease and treatment, and reduces potential financial loss associated with sick leave or work disability (23-27). Next to the cancer survivors' benefits, work participation of cancer survivors is of interest to society at large in that it reduces loss of production and costs of sick leave compensation or work disability benefits.

For workers in general, work participation relates to keeping a balance between (personal) resources and job demands. Specifically in cancer survivors, adequate support by the partner/spouse, employer and coworkers, but also experiencing good health, having a high self-efficacy and being motivated, can help to meet job demands, such as high working hours and challenges related to physical, psychological, cognitive, social and/or emotional functioning at work (28).

Case: 'She agreed to start with some cleaning work, but as RTW in the shop was no success she switched to administrative tasks. The employer agreed with some reluctance...'

Work participation of cancer survivors has been studied for over four decades now and its relevance is widely acknowledged (29-33). As the first papers on cancer survivorship and work participation appeared, the focus mainly was on work participation at short term, i.e., within a year of diagnosis, at which stage (active) treatment has usually ended. Later in time, the long-term effects of diagnosis and treatment on work participation gained attention as well. That is, it has been recognized that cancer survivors may face ongoing health problems long after successful completion of treatment (34-37). Therefore, nowadays more prospective studies, targeting at long-term effects of cancer and treatment, are conducted as cancer survivors may experience side-effects of treatment with a temporary or even permanent character (31). These may limit their functional abilities and, as a consequence, act as a barrier towards work participation (29;38;39). That is, previous studies have reported a poor outcome on work participation specifically in cancer survivors compared to healthy matched controls (40;41). It is assumed that this may reflect a form of discrimination of cancer survivors in the workplace and relates to the stigma of cancer within the occupational setting, the fear of recurrence, insecurity felt by stakeholders, such as the worker, employer, and physicians alike. Consequently, this may lead to irrational beliefs and attitudes that may interact and eventually obstruct work participation (42).

Case: 'The oncologist said that she should take her time and RTW when she felt ready for it…'

However, positive changes have occurred since the first studies were published that addressed work participation of cancer survivors. Nowadays, an average of 89% of cancer survivors is able to return to work within two years post diagnosis (31).

DEFINING WORK PARTICIPATION OUTCOMES

Next to differences in the definition of both short-term and long-term periods of sick leave, studies vary in the way work participation outcomes are described. In the literature, several outcome measures are used, e.g., (time to) RTW, days of sick leave, sickness benefit, employment status, time to job loss, annual wage loss, disability pension, and work disability (31). For a part, the outcome measures used are likely to be linked with the social security legislation that applies to the population studied, which, as we know, differs between countries. This can make the results of studies between countries difficult to compare. In this respect, the concept of work ability may serve as an alternative that allows a worker to estimate his/her abilities to participate in work, irrespective of actual working status or sick leave.

WORK DISABILITY ASSESSMENT IN THE NETHERLANDS

While measuring work ability using the WAI seems straightforward, assessing work disability claims, as performed by the Dutch SSA, is more complex.

Case: 'She manages to work a few hours in the morning in administration, only to find herself lying on the couch in the afternoon…'

In the Netherlands, workers may apply for a work disability benefit after sick leave lasting 24 months. During this initial 24-month sick leave period, the sick-listed worker and the employer are obliged to participate in a RTW trajectory in which both parties carry responsibility. This is described in the Dutch Gatekeeper Act, a law designed to reduce the inflow towards work disability compensation schemes. Usually during the 24-month sick leave, a sick-listed worker with an employment contract sees an OP on a regular basis; the OP is contracted by the employer and gives advice on the steps to be taken in the RTW trajectory. In case of unemployment, sick-listed workers are advised by the SSA.

In case a worker needs to apply for a work disability benefit, an IP working for the SSA, assesses the worker's functional abilities. The process of assessment of

functional abilities is complex and depends on a variety of medical and non-medical factors. That is, the concept of work disability relates to medical, organizational, jurisdictional and social factors that each can play a role and/or may interact. The IP may use several sources of information in assessing functional abilities, but the interview with the sick-listed worker usually acts as the most important one in this process. Next to this, the IP may use guidelines and/or information provided by third parties, e.g., a GP, the OP or a clinician, as to decide on functional abilities. Although the information, as gathered by the IP, predominantly targets at cancer survivors, we must realize that in the decision making process that underlies an assessment, also characteristics of the IP play a role, such as IP's experiences related to assessing CRF and cancer survivors' functional abilities, and/or IP's adherence to guidelines.

Finally, as a result of the assessment, the IP gives a description of functional abilities using the Functional Abilities List (FAL), which has 106 items covering six domains, i.e., personal functioning, social functioning, adjustment to physical environmental demands, dynamic movements, static postures, and working hours. In the assessment, an IP should consider that legislation requires that work disability, which is defined by wage loss, may only be assumed if claimed functional limitations and disease can be linked in a causal relationship.

Case: 'She has things to take care of at home as well and at the moment does not know how to cope…'

Nonetheless, it must be noted that, according to Dutch law, work disability can be assumed even in absence of a clear diagnosis. That is, as long as the IP reports consistency between impairments, functional limitations and handicaps, work disability compensation can be granted (43).

Next, if applicable and based on the FAL, a labour expert assesses the loss of former wages earned, which can be either (1) less than 35%, (2) in between 35 to 80%, or (3) over 80% of former wages earned. Workers are granted a work disability benefit if loss of income exceeds 35% of former wages. If a worker has no labour capacities, the IP has to evaluate the sustainability of this disability. That is, the evaluation of the prognosis of abilities has consequences as to what benefit act the claimant is entitled (WGA: Benefit Act for the non-durable fully disabled

and for those with functional abilities having a wage loss of more than 35%; IVA: Benefit Act for the fully and durable disabled). The assessment of the prognosis of abilities, by the IP, therefore has more implications than it used to have in the former Disability Insurance Act (WAO). However, it relates to the expected prognosis of functional abilities only and not to the course and prognosis of the underlying disease.

PITFALLS IN DISABILITY ASSESSMENT

There are several potential problems the IP may encounter in assessing cancer survivors' functional abilities. As cancer survivors approach the end of the 24-month sick leave period, the long-term side-effects of the disease and treatment experienced may be difficult to assess. Especially in case subjective feelings, such as distress, depressive symptoms or CRF, prevail. Next, a prognosis towards the course of functional abilities may seem unclear. However, the outcome of the assessment regarding the sustainability of functional abilities is very relevant to both the cancer survivor and society. It relates to timely identifying cancer survivors being either able or unable to RTW, and the need to provide support, either financially by provision of a work disability grant, or by initiating a vocational rehabilitation program.

The introductory case of Mrs. F. illustrates the complexity of work disability assessments in cancer survivors. That is, it demonstrates that in assessing a work disability claim, during the interview, a cancer survivor may give a vast amount of information that an IP needs to address and explicate. In this respect, we may question which elements, as presented in the cancer survivors' history, an IP sees as important and relevant.

RESEARCH QUESTIONS

In the case presented, the information given can be arranged into a number of topics that seem related to health status, personal circumstances, work demands, job support and accommodation, legislation and client's perception. An IP usually sorts and weighs this information and eventually a decision making process evolves leading to a FAL describing both cancer survivors' functional abilities and their durability. Regarding the assessment of work disability at 24-month sick leave of cancer survivors, the following questions may arise:

Question 1: Which factors are known to predict RTW in cancer survivors on long-term sick leave?

Question 2: Which factors are associated with work disability in cancer survivors at 24-month sick leave?

Question 3: Which factors predict CRF and work ability in cancer survivors at long-term follow-up, after the assessment of work disability?

Question 4: Which factors do IPs consider in assessing CRF and abilities in cancer survivors at 24-month sick leave?

Finding the answers to these questions may be to the benefit of cancer survivors who are on long-term sick leave, and at risk for work disability. Also, it may support IPs in assessing work disability claims of cancer survivors.

MAIN OBJECTIVE AND OUTLINE OF THESIS

Considering the expected increase of cancer survivors at working age and the positive effect of work participation in cancer survivors in general, the main objective of this thesis is to identify predictive factors for CRF and work ability in cancer survivors on long-term sick leave.

– In Chapter 2, a systematic review is described on predictors of RTW and employment in cancer survivors. The objective of this study was to provide an overview of the prognostic factors for RTW and employment of cancer survivors.

- In Chapter 3, a longitudinal study on prognostic factors of work disability in employed cancer survivors is presented. The purpose of this study was to identify prognostic factors of work disability at 24-month sick leave in sick-listed employed cancer survivors at short-term, i.e., 10-month sick leave.
- The results of a cross-sectional study on factors associated with work disability in employed cancer survivors at 24-month sick leave are presented in Chapter 4. The objective of this study was to disclose factors associated with work disability in cancer survivors at 24-month sick leave.
- The main study of this thesis is described in Chapter 5, in which the results of a prospective cohort study on predictive factors for both CRF and work ability in cancer survivors beyond 24-month sick leave are presented. The aim of this study was to identify prognostic factors related to both CRF and work ability in cancer survivors on long-term sick leave.
- In Chapter 6, a cross-sectional study on coping and health complaints, functional limitations, work ability and work status of long-term sick-listed cancer survivors is described. The purpose was to investigate the possible mediating role of active and passive coping between health complaints and functional limitations, work ability and work status, in cancer survivors on long-term sick leave.
- The results of a qualitative focus group study that describes IPs' perspectives related to the work disability assessment of cancer survivors are presented in Chapter 7. In this study, aspects IPs consider in assessing work disability of cancer survivors, their experiences related to the assessment of CRF, the use of cancer specific guidelines and needs related to the use of a prediction rule that targets to support work disability assessments, are described.

In the final Chapter 8, the main findings of the separate studies listed above are discussed, interpreted and connected into a framework leading to recommendations for future research.

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2

Predictors of return to work and employment in cancer survivors: a systematic review

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ABSTRACT

The objective of this study was to provide an overview of the prognostic factors for return to work and employment of cancer survivors. Cohort studies were selected if the population consisted of cancer patients between 18 and 65 years of age, with return to work, employment or equivalent concepts as main outcome measure, studying at least one prognostic factor. The methodological quality of the included studies and level of evidence for each prognostic factor were assessed. Twenty-eight cohort studies met the inclusion criteria. Heavy work and chemotherapy were negatively associated with return to work. Less invasive surgery was positively associated with return to work. Breast cancer survivors had the greatest chance of return to work. Old age, low education and low income were negatively associated with employment. Moderate evidence was found for extensive disease being negatively associated with both return to work and employment, and for female gender being negatively associated with return to work. The review shows that in cancer survivors, a limited number of prognostic factors of return to work and employment can be identified. Physicians primarily engaged in the process of vocational rehabilitation of cancer survivors should be aware of the potential role these factors exert.

INTRODUCTION

The growing number of cancer patients of working age has increased the need for research into their work perspectives (1). Earlier diagnosis, developments in treatment and follow-up have led to an increase of the survival. However, surviving cancer does not mean surviving without complaints, which may be long-term or even permanent, and may have implications for the ability to work. In view of these recent developments, cancer should be perceived less as a terminal illness, but as a chronic disease (2).

Cancer patients' return to work is important both for society and the individual. For society, there may be an economic loss due to work disability. For the individual, being able to work is important for identity. It enables the patient to regain a sense of normality and control (3;4). It is a symbol of recovery, raises the self-esteem and can help to overcome the negative effects of treatment (5-7). Having work or being able to return to work contributes to the quality of life, (8) which patients view as the third most important aspect of quality of life, after the ability to go out or to engage in social activities (9). However, for some patients the experience of having cancer leads to a reassessment of life goals, meaning that the patient may decide not to return to work, but to participate in another way in society.

With the increase of survivors of cancer, there is a growing number of studies examining prognostic factors for work disability, return to work, or equivalent concepts (10;11). Although a major part of cancer survivors return to work, results of a recent meta-analysis, including cross-sectional studies, of cancer survivors and unemployment indicated that cancer survivors were 1.4 times more likely to be unemployed than healthy control participants (12). Still, previous reviews showed a lack of methodological quality (6;7). Since return to work or obtaining employment of cancer survivors is complex and depends on a variety of medical and non-medical factors, prognostic research will help to identify those able to return and those at risk for unemployment. It will help to form groups for whom it is useful to implement an intervention. Such research will also clarify when return to work is no longer a possibility. To our knowledge, no systematic review of such prognostic studies has been performed so far in this context. The aim of the study

is to identify and value strength of prognostic factors of return to work and employment in cancer survivors. The results of the study may contribute to the design of studies aimed to enhance cancer survivors' vocational rehabilitation.

METHODS

Search strategy

Online searches of Medline, Embase, PsycINFO, (pre-)Cinahl, and CENTRAL were conducted until June 2011, using Boolean operators to group synonymous terms for three filters: cancer, work participation outcomes, and prognostic studies. Eligible for inclusion were prospective cohort studies, examining at least one prognostic factor for work participation or equivalent concepts, in cancer patients between 18 and 65 years of age. A maximum four-month period of recall related to the baseline measurement was allowed. References cited in published original and review papers were examined until no further studies were found.

Two groups of two authors (NW/DB and IS/PvM) reviewed the selection of studies independently, on predetermined inclusion criteria, and excluded the studies that did not meet these criteria. In total, 16 studies were included by NW/DB and 12 by IS/PvM (N=28). Initial exclusion was based on title, abstract, and keywords. If it was not clear whether the study had to be excluded, then the full text of the article was examined and reviewers discussed the assessments until consensus was reached. If not, a fifth author was consulted (AS).

Quality assessment

The quality of the included studies was scored by two independent reviewers (IS/PvM), using the Quality In Prognosis Studies (QUIPS) tool, a quality assessment list (13). The checklist contains 20 items related to six major sources of potential biases in prognostic studies in systematic reviews: bias due to study participation, study attrition, prognostic factors measurement, outcome measurement, study confounding, or statistical analysis and presentation. To assess the quality of the included articles, the risk of potential bias on each item was independently scored

by the two reviewers. After scoring the 28 articles the overall agreement on the risk of potential bias related to the six categories of the QUIPS list proved to be low with a Cohen's Kappa of 0.15. Considering the QUIPS list is a non-validated instrument, it probably gives room for personal interpretation of presented definitions. Therefore, the protocol was changed such that agreement on quality assessment had to be reached by consensus of the two reviewers. If consensus was not achieved, the opinion of two other authors (NW/DB) was used for the assessment.

The items on confounding were considered irrelevant as in studies regarding prognosis, the study design used to predict a specific outcome based on a combination of several possible prognostic factors, confounding is not an issue (14-16). For each of the five remaining QUIPS categories high quality ("+") was scored if there was low risk of bias, moderate quality ("+/-") with moderate risk, and low quality ("-") if there was high risk of bias. To strengthen the discriminative capacity of the assessment, a scoring algorithm (15) was used. The five categories of the QUIPS list were given a maximum of 15 points each. For all items we assigned five points in case of low risk of bias, and two and a half, and zero in case of moderate and high risk of bias, respectively. In the category patient selection bias, containing five items, we assigned three points in case of low risk of bias, one and a half, and zero in case of moderate and high risk of bias, respectively. A priori, we chose to consider ≥ 60 points (≥ 80% of the maximum attainable score) as high quality, between 45 and 60 points (≥ 60% of the maximum attainable score) as moderate/high quality, and < 45 points as low quality studies.

Data extraction

The following data were extracted: country of origin, study population, number of patients, diagnosis, study design, outcome measures, moments of measurements, drop-out percentage, duration of follow-up, and prognostic factors for work participation. The prognostic factors were classified into three categories: factors related to the person, the disease, and the environment, according to the International Classification of Functioning, Disability and Health (ICF) of the World Health Organization (17).

Qualitative analysis

The studies proved to be heterogeneous in respect of study characteristics, limiting the possibility of a quantitative analysis. Therefore a qualitative analysis (18) was performed to summarize the available evidence for the predictive value of the prognostic factors. In this analysis, the number of studies evaluating a specific prognostic factor, the methodological quality of these studies and the consistency of results were taken into account. Findings were consistent if ≥ 75% of the studies reporting on a factor showed the same direction of the association. Five levels of evidence, based on statistically significant data only, were defined (19,20); (1) strong evidence (consistent associations found in at least two high-quality cohorts); (2) moderate evidence (consistent associations found in one high-quality cohort and at least one low-quality cohort); (3) weak evidence (association found in one high-quality cohort or consistent associations found in at least three low-quality cohorts); (4) inconclusive evidence (association found in less than three low-quality cohorts); inconsistent evidence (findings irrespective of study quality). Using 60% of the maximum attainable score as used in the quality assessment as a threshold, studies were redefined into high (> 60% score) or low (≤ 60 % score) quality cohorts, respectively.

RESULTS

Included studies

In total, 3,554 potentially relevant articles were identified. Articles were excluded on assessment of title, keywords, abstract, and language (N=3,202). A total of 352 full text articles were retrieved and examined. Full text articles (N=324) were excluded, because they did not match the inclusion criteria.

Finally, by process of elimination 28 articles were included. No additional articles were identified by reference screening.

Seventeen studies were conducted in Europe, (21-37) 8 in North America (38-45) and three in Asia (46-48). In 11 studies, the study design was a retrospective cohort, which involved prospectively recorded data (21;24;25;27;30-33;35;47;48).

In two studies, the design was both a retrospective and prospective cohort (23;39). Furthermore, 15 prospective cohort studies were included (22;26;28;29;34;36-38;40-46). In total, 17 studies reported on a cohort in a clinical setting, (22;23;26;28;29;34;36-46) 7 on a population-based cohort, (24;25;27;33;35;47;48) and four on a cohort of an occupational health service (21;30-32).

Table 2.1 shows an overview of the main study characteristics. The outcome measurements as described in the articles, were grouped into two categories. First, outcomes related to absence or return to work (RTW) (e.g., days of absence, sick leave, sickness absence, weeks of absence, RTW, time to RTW, and rate of RTW), were grouped in category *RTW*. Second, outcomes related to employment status, e.g. unemployment, time to job loss, time to re-employment, employment, and "not working", were grouped in category *employment*.

Methodological quality

The overall quality score (Table 2.2) ranged from 22.5 to 75 points with a median score of 54. Based on our cut-off of ≥ 60 points and ≥ 45 points, we found 12 articles of high quality, 8 articles of moderate quality, and 8 articles of low quality.

Prognostic factors

A variety of different prognostic factors was identified and grouped into socio-demographics (Table 2.3), job characteristics (Table 2.4), and disease-related topics (Table 2.5). The tables present factors for which significant date were found.

Table 2.1 Characteristics of the included studies

Author, yr (ref)	Country		Study population*		Site	FU (wk)	Measurement†	Outcome(s)‡
		N	Age in yrs (mean)	m/f (%)				
Balak, 2008 (21)	Netherlands	72	18-65 (49.2)	0/100	Breast	104	Database	RTW
Bergman, 1987 (22)	Sweden	44	≤64 (53)	75/25	Lung	105	Quest	RTW
Borget, 2007 (23)	France	194	18-80 (46.7)	26/74	Thyroid	52	Quest	Days of absence, sick leave
Bouknight, 2006 (38)	USA	443	30-64 (50.8)	0/100	Breast	78	Quest (T)	RTW
Bradley, 2006 (39)	USA	445	30-64 (52.3)	46/54	Breast, prostate	35	Quest (T)	Days of absence
Buckwalter, 2007 (40)	USA	239	≥21 (52.7)	76/24	Head and neck	52	Quest	RTW
Carlsen, 2008 (24)	Denmark	236993	30-60	30/70	Multiple	1040	Database	Unemployment
Choi, 2007 (46)	Korea	305	≥18 (54.6)	100/0	Stomach, liver, colorectal	104	Quest	Time to job loss, time to re-employment
Eaker, 2011 (25)	Sweden	4761	20-59	0/100	Breast	260	Database	Sickness absence, sickness benefit, disability pension
Emmanouilidis, 2009 (26)	Germany	25	17-70 (50)	76/24	Thyroid	9	Quest	Days of absence
Fiva, 2010 (27)	Norway	46720	21-59	ns	Multiple ns	260	Database	Employment
Johnsson, 2007 (28)	Sweden	270	29-54 (45)	0/100	Breast	104	Quest	Not working

Table 2.1 Characteristics of the included studies (continued)

Author, yr (ref)	Country	Study population*			Site	FU (wk)	Measurement†	Outcome(s)‡
		N	Age in yrs (mean)	m/f (%)				
Johnsson, 2009 (29)	Sweden	132	18-64	0/100	Breast	44	Quest	RTW
Kirchhoff, 2010 (41)	USA	197	≥22	ns	Multiple	260	SF-36	RTW
Kornblith, 2009 (42)	USA	802	ns	0/100	Endometrium	26	Quest, FACT-G, SF-36, BPI, BI	Time to RTW
Lauzier, 2008 (43)	Canada	459	23-71	0/100	Breast	52	Quest (T)	Annual wage lost, weeks of absence, comp. wage loss
Oberst, 2010 (44)	USA	714	30-64 (55.4)	0/100	Breast, prostate	78	Quest (T)	Employment
Park, 2008 (47)	Korea	5296	25-55	74/26	Multiple	312	Database	Time to job loss, time to re-employment
Park, 2009 (48)	Korea	4991	25-55	74/26	Multiple	260	Database	Time to job loss, time to re-employment
Roelen, 2011 (31)	Netherlands	5074	18-60 (47.7)	36/64	Multiple	104	Database	Time to RTW (full-time)
Roelen, 2011 (30)	Netherlands	5234	ns	ns	Multiple	104	Database	Time to RTW (full-time; part-time)
Roelen, 2011 (32)	Netherlands	3357	ns	0/100	Breast	52	Database	Time to RTW (full-time; part-time), RTW (full-time)
Sjövall, 2012 (33)	Sweden	2738	15-64	49/51	Multiple	52	Database	Days of absence

Table 2.1 Characteristics of the included studies (continued)

Author, yr (ref)	Country	Study population*			Site	FU (wk)	Measurement†	Outcome(s)‡
		N	Age in yrs (mean)	m/f (%)				
Spelten, 2003 (34)	Netherlands	235	19-58 (42.9)	40/60	Multiple	78	MFI, CES-D PSQI, RSCL, CFQ, VBBA	Time to RTW, rate of RTW
Sultan, 2006 (45)	USA	537	38-79 (58)	100/0	Prostate	13	Quest (T)	Time to RTW
Taskila, 2004 (35)	Finland	25084	15-60	ns	Multiple	156	Database	Employment
van den Brink, 2005 (36)	Netherlands	384	ns (52)	49/51	Rectal	104	Quest, QoL, VAS, RSCL	RTW
Verbeek, 2003 (37)	Netherlands	100	≤55 (42)	ns	Multiple	78	Quest (T), MFI, CES-D, PSQI, RSCL, CFQ, VBBA	Time to RTW

*Study population: ns; not specified; †Measurement: Database: records of government institutions (e.g., Cancer registry, National health insurance claims data, National statistics department, National hospital discharge register or Occupational health service); Quest: questionnaire (ns) containing items on, e.g., socio-demographics, health-related issues, employment characteristics; (T)=by telephone; SF-36=Medical Outcomes Study-Short Form; FACT-G=Functional Assessment of Cancer Therapy Scale-General; BPI=Brief Pain Inventory; BI=Body Image; MFI=Multidimensional Fatigue Inventory; CES-D=Center for Epidemiological Studies-Depression scale; PSQI=Pittsburg Sleep Quality Index. RSCL=Rotterdam Symptom Checklist; CFQ=Cognitive Failures Questionnaire; VBBA=Dutch Questionnaire on Experience and Judgement of Work; QoL=Quality Of Life questionnaire; VAS scale=QoL Visual Analog Scale; ‡Outcome(s): RTW=Return To Work; comp. wage loss: compensation wage loss.

Table 2.2 Results of quality assessment

Author, yr (ref)	Study participation	Study attrition	Measurement of prognostic factors	Measurement of outcomes	Statistical analysis & presentation	Quality score (points)	Quality*
Fiva, 2010 (27)	15	15	15	15	15	75	+
Carlsen, 2008 (24)	15	12.5	15	15	15	72.5	+
Park, 2008 (47)	15	15	15	12.5	15	72.5	+
Sjövall, 2012 (33)	15	10	15	15	15	70	+
Roelen, 2011 (32)	15	15	15	7.5	15	67.5	+
van den Brink, 2005 (36)	12	10	15	12.5	15	64.5	+
Eaker, 2011 (25)	15	5	12.5	15	15	62.5	+
Park, 2009 (48)	13.5	7.5	15	15	10	61	+
Verbeek, 2003 (37)	10.5	5	15	15	15	60.5	+
Roelen, 2011 (31)	10.5	10	15	10	15	60.5	+
Bradley, 2006 (39)	15	5	12.5	12.5	15	60	+
Lauzier, 2008 (43)	15	10	15	10	10	60	+
Spelten, 2003 (34)	12	7.5	15	10	12.5	57	+/-
Kornblith, 2009 (42)	12	12.5	10	15	5	54.5	+/-
Bergman, 1987 (22)	13.5	15	12.5	10	2.5	53.5	+/-
Johnsson, 2009 (29)	10.5	5	10	10	15	50.5	+/-
Oberst, 2010 (44)	13.5	10	2.5	7.5	15	48.5	+/-
Roelen, 2011 (30)	15	7.5	7.5	10	7.5	47.5	+/-
Taskila, 2004 (35)	12	15	7.5	10	2.5	47	+/-

Table 2.2 Results of quality assessment (continued)

Author, yr (ref)	Study participation	Study attrition	Measurement of prognostic factors	Measurement of outcomes	Statistical analysis & presentation	Quality score (points)	Quality*
Emmanouilidis, 2009 (26)	3	15	15	10	2.5	45.5	+/-
Buckwalter, 2007 (40)	9	12.5	10	12.5	0	44	-
Choi, 2007 (46)	6	0	12.5	12.5	12.5	43.5	-
Bouknight, 2006 (38)	10.5	7.5	7.5	5	12.5	43	-
Kirchhoff, 2010 (41)	7.5	5	7.5	10	12.5	42.5	-
Borget, 2007 (23)	12	15	15	0	0	42	-
Balak, 2008 (21)	13.5	0	7.5	15	0	36	-
Johnsson, 2007 (28)	9	10	5	10	5	34	-
Sultan, 2006 (45)	15	0	5	2.5	0	22.5	-

*Quality: + = high, +/- = moderate, - = low

Table 2.3 Socio-demographics

Study	Prognostic variables	Effect	Follow-up ≤1 yr**	Follow-up >1 yr**	Outcome††
Sultan (45)	Age*	β (SE)	-0.28 (0.11; p=0.014)		Time to RTW (part-time)
Sultan (45)	Age*	β (SE)	-0.63 (0.14; p=0.000)		Time to RTW (full-time)
Van den Brink (36)	Age (<55)	β	9.80 (p=0.001)	26.40 (p=0.001)	RTW
Bouknight (38)	Age (high vs low)†	OR (CI)	*0.96 (0.93-1.00)*	0.95 (0.91-0.99)	RTW
Spelten (34)	Age (10-year category)	HR (CI)	0.76 (0.62-0.93)		Time to RTW
Roelen (31)	Age (35-44; 45-54; ≥55) vs < 35 years†‡	HR (CI)		0.80 (0.60-0.90); 0.60 (0.50-0.80); 0.40 (0.30-0.60)	Time to RTW (full-time)
Park (47)	Age (30-39; 40-49; 50-55) vs 25-29 years	HR (CI)		0.68 (0.56-0.84); 0.73 (0.60-0.89); 1.23 (1.01-1.50)	Time to job loss
Park (47)	Age (30-39; 40-49; 50-55) vs 25-29 years	HR (CI)		*0.83 (0.53-1.31); 0.81 (0.53-1.25)*;0.54 (0.34-0.56)	Time to re-employment
Roelen (32)	Age (<40; 40-50; >50) in 2002 vs 2008	%	55 vs 40; 46 vs 41; 59 vs 46		RTW (full-time)
Roelen (32)	Age (<40; 40-50; >50) in 2004 vs 2002§	HR (CI)	*1.01 (0.72-1.42)*; 1.30 (1.03-1.65); *1.00 (0.78-1.30)*		Time to RTW (part-time)
Roelen (32)	Age (<40; 40-50; >50) in 2008 vs 2002§	HR (CI)	*0.93 (0.65-1.35)*; 1.31 (1.03-1.67); *0.91 (0.71-1.18)*		Time to RTW (part-time)

Table 2.3 Socio-demographics (continued)

Study	Prognostic variables	Effect	Follow-up ≤1 yr**	Follow-up >1 yr**	Outcome††
Carlsen (24)	Age (30-39; 40-49; 50-60)† patients vs controls	RR (CI)		*1.05 (1.00-1.10)*; 1.12 (1.10-1.20); 1.18 (1.10-1.30)	Unemployment
Fiva (27)	Gender†	β (SE)		0.02 (0.01)	Employment
Park (47)	Gender (female vs male)	HR (CI)		1.59 (1.40-1.80)	Time to job loss
Park (47)	Gender (female vs male)	HR (CI)		0.56 (0.41-0.75)	Time to re-employment
Borget (23)	Gender (female vs male)	OR (CI)	4.32 (1.40-13.35)		Sick leave
Roelen (31)	Gender (female vs male)	HR (CI)	0.60 (0.50-0.90)		Time to RTW (full-time)
Kirchhoff (41)	Gender (female vs male)	HR (CI)		0.54 (0.29-0.99)	RTW
Van den Brink (36)	Education (high school)	β	-22.00 (p<0.001)	-27.00 (p<0.001)	RTW
Van den Brink (36)	Education (<high school)	β	-32.80 (p<0.001)	-38.90 (p<0.001)	RTW
Fiva (27)	Education (yrs; 11-12; 13; 14; 14-17; ≥18)	β (SE)		0.05 (0.01); 0.09 (0.01); 0.09 (0.01); 0.13 (0.01); 0.16 (0.01)	Employment
Choi (46)	Education (<high school; high school) vs ≥college	HR (CI)		*1.63 (0.94-2.83)*; 1.86 (1.11-3.11)	Time to job loss

Table 2.3 Socio-demographics (continued)

Study	Prognostic variables	Effect	Follow-up ≤1 yr**	Follow-up >1 yr**	Outcome††
Eaker (25)	Education (high; middle; unknown) vs low level at 5yrs post treatment¶	OR (CI)		0.76 (0.61-0.93); *0.86 (0.71-1.03); 0.44 (0.09-2.23)*	Sickness absence
Carlsen (24)	Education (high school; further educ.; other/unknown) vs vocational†	RR		*1.05 (1.00-1.10)*; 0.70 (0.70-0.80); *0.86 (0.70-1.10)*	Unemployment
Carlsen (24)	Education (high school; further educ.; other/unknown) vs vocational*	RR		*0.88 (0.80-1.00)*;0.61 (0.50-0.70); *0.99 (0.70-1.50)*	Unemployment
Taskila (35)	Education (primary; vocational; polytechnic; university) pat. vs contr.	RR (CI)		0.81 (0.78-0.84); 0.88 (0.85-0.91); 0.94 (0.90-0.98); *0.96 (0.93-1.00)*	Employment
Park (47)	Income (low vs high)	HR (CI)		2.76 (2.40-3.18)	Time to job loss
Park (47)	Income (low vs high)	HR (CI)		0.61 (0.40-0.95)	Time to re-employment
Carlsen (24)	Income (<€22.000; €22-30.000; €30-38.000; unknown) vs >€38.000†	RR		*1.08 (1.00-1.20)*; 1.48 (1.40-1.60); 1.30 (1.20-1.40); 1.44 (1.30-1.70)	Unemployment
Carlsen (24)	Income (<€22.000; €22-30.000; €30-38.000; unknown) vs >€38.000*	RR		2.38 (2.00-2.90); 1.97 (1.70-2.30); 1.46 (1.30-1.70); 1.66 (1.30-2.10)	Unemployment

Table 2.3 Socio-demographics (continued)

Study	Prognostic variables	Effect	Follow-up ≤1 yr**	Follow-up >1 yr**	Outcome††
Roelen (30)	Residential region (central, south, east, north) vs west	β (CI)		-0.16 (-0.32-0.00); *-0.11 (-0.26-0.04); 0.16 (-0.32-0.01); -0.05 (-0.24-0.15)*	Time to RTW (full-time)
Carlsen (24)	Degree of urbanicity (very high; high; moderate; low) vs very low†	RR (CI)		*0.91 (0.80-1.00)*; 0.77 (0.70-0.80); *1.04 (1.00-1.10); 1.00 (0.90-1.00)*	Unemployment
Carlsen (24)	Degree of urbanicity (very high; high; moderate; low) vs very low*	RR (CI)		*0.87 (0.70-1.00)*; 0.71 (0.60-0.80); *0.93 (0.80-1.10); 1.11 (1.00-1.30)*	Unemployment

Prognostic variables: *male; †female; ‡genital cancer (not significant for all ages: blood malignancies, gastro-intestinal-, lung- and skin cancer); §otherwise not significant from 2003 through 2008 for all ages; ¶stage I-IIb, adjustment for sickness absence 1 year before diagnosis, education, tumour size, having lymph nodes, stage and treatment; education; post treatm.=post treatment; further educ.=further education; pat. vs contr.=patients vs controls; **Follow-up: not significant data in italic. ††Outcome: RTW=return to work.

Table 2.4 Job characteristics

Study	Prognostic variables	Effect	Follow-up ≤1 yr§	Follow-up >1 yr§	Outcome¶
Johnsson (29)	Job-strain (high vs low)	OR (CI)	0.10 (0.00-0.80)		RTW
Bouknight (38)	Heavy lifting (yes vs no)	OR (CI)	0.42 (0.18-0.99)	*1.20 (0.48-3.20)*	RTW
Bergman (22)	Job demand (light; heavy)	Proportion		0.63; 0.19	RTW
Spelten (34)	Physical workload (in quartiles)	HR (CI)	0.81 (0.68-0.96)		Time to RTW
Bouknight (38)	Employer discriminiation (yes vs no)	OR (CI)	0.27 (0.10-0.71)	*0.49 (0.18-1.40)*	RTW
Bouknight (38)	Employer accommodation (yes vs no)	OR (CI)	2.20 (1.03-4.80)	2.30 (1.06-5.10)	RTW
Fiva (27)	Work-hours (h/week; 14-19; 20-29; ≥30)	β (SE)		0.23 (0.02); 0.28 (0.02); 0.31 (0.02)	Employment
Lauzier (43)	Self employment (yes; no)	mean (CI)	28 (24-31); 33 (32-34); p=0.005		Weeks of absence
Roelen (30)	Occupational class (high; medium) vs low	β (CI)		-0.31 (-0.57 to -0.04); *-0.14 (-0.32-0.03)*	Time to RTW (part-time)
Sultan (45)	Type of occupation (blue vs white collar)	β (SE)	10.82 (2.63; p=0.000)		Time to RTW (full-time)
Park (47)	Type of occupation (company worker vs public servant)	HR (CI)		1.49 (1.38-1.60)	Time to job loss

Table 2.4 Job characteristics (continued)

Study	Prognostic variables	Effect	Follow-up ≤1 yr§	Follow-up >1 yr§	Outcome¶
Choi (46)	Type of occupation (manual; semi manual) vs sedentary labor	HR (CI)		2.40 (1.50-3.84); *1.16 (0.72-1.86)*	Time to job loss
Carlsen (24)	Type of occupation (self empl; assis. partner; manual; other) vs non manual*	RR		*0.97 (0.80-1.20)*; 0.77 (0.70-0.90); 1.42 (1.30-1.50); 2.00 (1.80-2.30)	Unemployment
Carlsen (24)	Type of occupation (self empl; assis. partner; manual; other) vs non manual†	RR		0.49 (0.40-0.60); ns; 1.77 (1.60-2.00); 2.07 (1.60-2.70)	Unemployment
Taskila (35)	Being employed (patients vs controls)‡	RR (CI)		0.88 (0.86-0.90)	Employment
Roelen (30)	Job tenure (yrs; 6-10; 11-20; >20) vs 0-5	β (CI)		0.18 (0.04-0.33); *0.12 (-0.04-0.28); 0.03 (-0.14-0.20)*	Time to RTW (full-time)
Bradley (39)	Leave of absence (yes vs no)*	β (SE)	83.05 (10.46)		Days of absence
Bradley (39)	Leave of absence (yes vs no)†	β (SE)	25.66 (9.70)		Days of absence
Roelen (30)	Company size (no. employees; 75-500; 500-5000; >5000) vs <75	β (CI)		*-0.10 (-0.28-0.08); -0.13 (-0.31-0.05)*; -0.56 (-0.82 to -0.29)	Time to RTW (part-time)

Table 2.4 Job characteristics (continued)

Study	Prognostic variables	Effect	Follow-up ≤1 yr§	Follow-up >1 yr§	Outcome¶
Roelen (30)	Company size (no. employees; 75-500; 500-5000; >5000) vs <75	β (CI)		*-0.11 (-0.26-0.04); -0.10 (-0.25-0.05)*; -0.54 (-0.76 to -0.33)	Time to RTW (full-time)
Verbeek (37)	Sub-optimal performance by occupational physician (yes vs no)	HR (CI)	0.50 (0.30-0.80)		Time to RTW
Verbeek (37)	Sub-optimal continuity of care by occupational physician (yes vs no)	HR (CI)	0.50 (0.30-0.90)		Time to RTW

Prognostic variables: *female; †male; self empl.=self-employed; assis.partner=assisting partner; ‡type of occupations with significant data: technical, science, artistic work, administration, sales, agriculture, manufacturing, services, transport and communication, not significant are mining and defense forces; no.=number; §Follow-up: not significant data in italic; ns=not specified; ¶Outcome: RTW=return to work.

Table 2.5 Disease

Study	Prognostic variables	Effect	Follow-up ≤ 1 yr**	Follow-up >1 yr**	Outcome§§
	Treatment				
Kornblith (42)	Laparotomy; laparoscopy	median	45; 42; p=0.040		Time to RTW
Van den Brink (36)	Surgery and radiotherapy	β	-11.40 (p=0.019)	-4.90 (p=0.019)	RTW
Bradley (39)	Surgery and radiotherapy*	β (SE)	-15.63 (7.12; p<0.050)		Days of absence
Johnsson (29)	Axillary dissection (yes vs no)	OR (CI)	0.10 (0.00-0.60)		RTW
Eaker (25)	Breast-conserving vs mastectomy†	OR (CI)		0.71 (0.59-0.86) **	Sickness absence
Eaker (25)	Breast-conserving vs mastectomy†	OR (CI)		0.77 (0.63-0.95)††	Sickness absence
Spelten (34)	(Surgery and chemo; surg. and radio; all other comb) vs surgery	HR (CI)	0.24 (0.12-0.48); 0.57 (0.35-0.91); 0.49 (0.26-0.95)		Time to RTW
Lauzier (43)	Chemo (yes; no)	mean (CI)	40 (38-41); 21 (19-23); p<0.001		Weeks of absence
Johnsson (29)	Chemo (yes vs no)	OR (CI)	0.10 (0.00-0.70)		RTW
Eaker (25)	Chemo (yes vs no)†	OR (CI)		1.55 (1.29-1.86) **	Sickness absence
Johnsson (28)	Chemo (yes vs no)	OR (CI)		2.60 (1.20-5.50)	Not working
Buckwalter (40)	(Single treatment; multimodal treatment) ‡	%	(30; 70) / (57; 43)		RTW

Table 2.5 Disease (continued)

Study	Prognostic variables	Effect	Follow-up ≤ 1 yr**	Follow-up >1 yr**	Outcome§§
Balak (21)	(Chemo; multimodal) vs no adjuvant treatment	HR (CI)		0.31 (0.12-0.81); 0.24 (0.10-0.54)	RTW (full-time)
Balak (21)	(Chemo; multimodal) vs no adjuvant treatment	HR (CI)		0.27 (0.10-0.72); 0.19 (0.08-0.45)	RTW (part-time)
Eaker (25)	Hormone (yes vs no)†	OR (CI)		1.25 (1.08-1.46)**; *1.08 (0.90-1.29)* ††	Sickness absence
Bradley (39)	Hormone and radiotherapy; no treatment (male)	β (SE)	-21.23 (3.69); -27.39 (4.53)		Days of absence
Emmanouilidis (26)	Recombinant human Thyroid Stimulating Hormone (yes; no)	mean (SD)	5.90 (7.10); 28.80 (20.80); p=0.035		Days of absence
Borget (23)	Recombinant human Thyroid Stimulating Hormone (yes; no)	mean (SD)	3.10 (11.50); 11.20 (19.90); p<0.001		Days of absence
Borget (23)	Recombinant human Thyroid Stimulating Hormone (no vs yes)	OR (CI)	3.58 (1.30-9.90)		Sick leave
	TNM staging				
Choi (46)	(stage II; III; IV) vs stage I	HR (CI)		*1.62 (0.91-2.88); 1.62 (0.95-2.77)*; 2.49 (1.42-4.38)	Time to job loss

Table 2.5 Disease (continued)

Study	Prognostic variables	Effect	Follow-up ≤ 1 yr**	Follow-up >1 yr**	Outcome§§
Choi (46)	(stage II; III; IV) vs stage I	HR (CI)		*0.63 (0.24-1.66); 0.49 (0.19-1.28)*; 0.13 (0.04-0.47)	Time to re-employment
Fiva (27)	Regional; distant; unknown	β (SE)		-0.13 (0.01); -0.30 (0.01); -0.06 (0.01)	Employment
Bouknight (38)	(Local; Regional-distant) vs in situ	OR (CI)	*0.54 (0.23-1.30)*; 0.23 (0.08-0.65)	*0.77 (0.33-1.80); 0.66 (0.25-1.80)*	RTW
Bergman (22)	Advanced vs less advanced disease	proportion		0.15; 0.47; p=0.027	RTW
Buckwalter (40)	Advanced vs less advanced disease‡	%	(82; 18) / (47; 53)		RTW
	Tumor site				
Taskila (35)	(Lung; breast) §	RR (CI)		0.45 (0.34-0.59); 0.95 (0.92-0.98)	Employment
Eaker (25)	Breast (patients vs controls)	RR (CI)		1.36 (1.30-1.43)††; 1.31 (1.24-1.38)††	Sickness absence
Choi (46)	(Liver; colorectal) vs stomach	HR (CI)		0.26 (0.10-0.69); *0.73 (0.29-1.88)*	Time to re-employment
Park (47)	(Liver; thyroid; lung; colorectal) vs stomach	HR (CI)		0.66 (0.45-0.97); 1.50 (1.03-2.20); *0.79 (0.55-1.16); 0.96 (0.70-1.32)*	Time to re-employment
Sjövall (33)	(Colon; rectal; lung; breast; prostate)¶	ratio (CI)	2.47 (2.10-2.84); 3.29 (2.84-3.75); 4.31 (3.84-4.77); 2.18 (1.83-2.53); 1.58 (1.28-1.88)		Days of absence

Table 2.5 Disease (continued)

Study	Prognostic variables	Effect	Follow-up ≤ 1 yr**	Follow-up >1 yr**	Outcome§§
Spelten (34)	(Haematology; breast; female genital; other types; gastrointestinal) vs male genital	HR (CI)	0.24 (0.10-0.61); 0.45 (0.24-0.86); 0.55 (0.33-0.92); 0.35 (0.14-0.84); *0.82 (0.43-1.57)*		Time to RTW
Park (47)	(Thyroid; lung; brain and cns; leukemia; non Hogdkin; colorectal; liver) vs stomach	HR (CI)		0.72 (0.60-0.87); 1.31 (1.12-1.53); 1.32 (1.04-1.66); 1.58 (1.23-2.03); *0.95 (0.71-1.26); 1.04 (0.91-1.20); 1.11 (0.97-1.27)*	Time to job loss
Roelen (30)	(Lung; gastrointestinal; blood; breast; other; male genital; female genital) vs skin	β (CI)		1.88 (1.51-2.25); 1.35 (1.03-1.66); 1.56 (1.17-1.94); 1.06 (0.76-1.37); 1.19 (0.85-1.53); 0.63 (0.27-0.98); *0.26 (-0.06-0.58)*	Time to RTW (part-time)
Roelen (30)	(Lung; gastrointestinal; blood; breast; other; male genital; female genital) vs skin	β (CI)		1.61 (1.31-1.92); 1.31 (1.05-1.56); 1.50 (1.19-1.81); 1.08 (0.84-1.33); 1.08 (0.81-1.36); 0.71 (0.43-1.00); *0.22 (-0.04-0.48)*	Time to RTW (full-time)

Prognostic variables: *female; stage I-IIb, adjustment for sickness absence 1 year before diagnosis, education, tumour size, having lymph nodes, stage and treatment; ‡ patients who discontinued employment because of cancer / patients whose employment was not affected by cancer; §patients vs referents; also significant: nervous system, leukemia, stomach, NonHogdkin, cervix, rectum, bladder, ovary, corpus uteri, colon and not significant prostate, testis, kidney, (non) melanoma, Hodgkin, thyroid; ¶mean sick days in patients divided by the corresponding mean value in matched referents; **Follow-up: not significant data in italic; ††at 3 yrs follow-up; ‡‡at 5 yrs follow-up; §§Outcome: RTW=return to work.

Socio-demographics

Age

Age was reported in 16 articles, (21;23;24;28-32;34;36;38;39;41;45-47) of which half showed significant data (24;31;32;34;36;38;45;47). Sultan et al. (45) found an earlier return to work as age increased, whereas van den Brink et al. (36), Bouknight et al. (38) and Spelten et al. (34) found a later return to work in higher aged patients. Roelen et al. (31) also found higher age to be associated with a later return to work, but only in part of the population studied. Park et al. (47), in a mixed cohort (both genders and various sites) found higher age to be related to a reduced chance of employment as did Carlson et al. (24). Five out of 8 articles reporting significant data were classified as high quality articles (24;31;32;36;47), one was classified as moderate quality (34), two as low quality (38;45). One out of 8 articles, showing no significant data, was classified as high quality (39), two were classified as moderate quality and five as low quality.

Gender

Gender was described in six articles, (23;27;30;31;41;47) of which one showed no significant data (30). Of the remaining five papers three showed a negative influence of female gender on return to work (23;31;41), and two on employment (27;47). Three out of five articles reporting significant data were classified as high quality (27;31;47), and two as low quality (23;41). The article showing no significant data was of moderate quality (30).

Education

In 11 articles (24;25;27;28;35;36;38;39;41;43;46) education was studied, of which four reported no significant data (28;38;39;41). Lower education was associated with less or later return to work (36), a negative influence on return to work up to five years after diagnosis (25), and a decreased chance of employment for both men and women (24;35;46). Five out of 7 articles reporting significant data were classified as high quality (24;25;27;36;43), one as moderate quality (35), and one as low quality (46), respectively. Of the four articles showing no significant data one was classified as high quality (39), and three as low quality (28;38;41).

Income

In four articles income was studied (24;39;46;47), of which one (high quality) article reported lower income related to less or later return to work (39), but data were not significant. Three articles examining income showed a negative association between income and employment (24;46;47). Two of these articles reporting significant data were high quality (24;47). One article reporting no significant data was of low quality (46).

Marital status

Marital status was examined in 8 studies (24;27;28;38;39;41;45;46). Three of these 8 studies reported significant data (24;27;45). One reported quicker return to work for married men (45). Being single, widowed or divorced had a negative effect on employment (27), but these findings were contradicted by the study of Carlsen et al. (24), who found an opposite effect. Two out of three articles reporting significant data were classified as high quality (24;27) and one as low quality (45). Of the five articles reporting no significant data one was of high quality (39) and four of low quality (28;38;41;46).

Race and urbanicity

In one out of two studies (38;39) examining race, an effect on return to work was found with African-American breast cancer survivors having a decreased chance of return to work than Caucasian breast cancer survivors. This was a low quality article (38). The study reporting no significant data was a high quality article. One (high quality) article reported a high degree of urbanicity to be associated with a greater chance of employment (24).

Job characteristics

Job demands

Five studies (22;29;34;38;39) examined physical exertion as a job demand, of which four (22;29;34;38) reported significant data. Johnsson et al. (29) and Bouknight et al., (38) both studying breast cancer patients, found that job-strain and

heavy lifting were negatively associated with return to work. Heavy job demands was found to hamper return to work in lung cancer patients (22). Also, Spelten et al. (34) found that high physical workload was negatively associated with return to work. Three (22;29;34) out of four articles reporting significant data were of moderate quality and one, (38) was of low quality. The article reporting no significant data was of high quality (39).

Job content

Working hours were studied by Lauzier et al. (43) and Fiva et al. (27), both high quality articles, only the latter finding a significantly positive relationship between working hours and employment. Self-employment (43) was associated with earlier return to work. Self-employed men and women assisting their partner, were found to have a greater chance of employment (24). Occupational class and type of occupation were presented in six articles, (24;30;38;45-47) of which one did not report significant data (38). Roelen et al. (30), found that a high occupational class was related to a quicker return to work. However, this was only found for part-time work, and regarding full-time work or a specific type of occupation no significant data were found. Sultan et al. (45) found a shorter time to return to work (full-time) in white collar workers. Also, manual workers, compared to non-manual workers, had a decreased chance of employment (24;46), as it was for company workers versus public servants (47). Two of the five articles reporting significant data were of high quality (24;47), one of moderate quality (30), and two of low quality (45;46). The article reporting no significant data was of low quality (38).

Job tenure

Three articles described job tenure or employment status, two reporting significant data (30;43). Lauzier (43), found no association between job tenure and return to work. Roelen et al. (30) however, found that cancer survivors who were employed six to 10 years returned to full-time work later than those employed less than five years. Taskila et al. (35) reported cancer survivors compared with healthy matched referents to be at greater risk of unemployment. One article was of high quality (43) and two of moderate quality (30;35).

Employee benefits

Five articles reported on employee benefits (30;37-39;43). The possibility to take a leave of absence had a negative effect on return to work (39). Employer accommodation defined as all possible interventions made by employer to facilitate the vocational rehabilitation of the employee, was positively associated with return to work (38) as was a greater company size (30). Inadequate occupational health care was related to decreased return to work (37). The article reporting on perceived social support and return to work showed no significant data (43). Three out of five articles reporting significant data were of high quality (37;39;43), one of moderate quality (30), and one of low quality (38).

Disease

Treatment

Treatment modalities, such as surgery, chemotherapy, radiotherapy or hormone therapy, either solitary or combined, were presented in 13 articles (21;23;25;26;28;29;34;36;38-40;42;43), of which one reported no significant data (38). Patients who had surgery only showed to resume work earlier compared to patients having had multimodal treatment (34;36). However, an opposite effect was also found (39). Less invasive surgery was associated with earlier return to work compared to more extensive surgery (29;42), and was reported to be positively related with return to work even at three and five years of follow-up (25). In four articles chemotherapy was reported to prolong the time to return to work (21;28;29;43). However no significant results were reported regarding radiotherapy only and return to work (21;25;29;38). Prolonged endocrine treatment after a diagnosis of breast cancer was reported to be negatively associated with return to work (25), whereas the specific use of recombinant human Thyroid Stimulating Hormone showed earlier return to work (23;26). Four out of 12 articles reporting significant data were of high quality (25;36;39;43), four of moderate quality (26;29;34;42), and four of low quality (21;23;28;40). The article reporting no significant data was of low quality (38).

Morbidity

The effect of extensive or limited disease was presented in 8 articles (22;25;27;38-40;43;46), of which four reported significant data (22;27;40;46), indicating that more extensive disease was related to a prolonged time to return to work and a smaller chance of employment. One out of four articles reporting significant data was of high quality (27), one of moderate quality (22), and two of low quality (40;46). Three out of four articles reporting no significant data were of high quality (25;39;43), and one of low quality (38). Tumour site was examined in 7 articles (25;30;33-35;46;47) and all of these reported significant data, e.g. presenting different chances on return to work for specific sites. Three of these were of high quality (25;33;47), three of moderate quality (30;34;35), and one of low quality (46).

Levels of evidence

In Table 2.6, an overview of the prognostic factors and the strength of association for return to work and employment is presented. Prognostic factors of return to work with strong evidence were physical exertion, less invasive surgery, chemotherapy, and cancer site. Less physical exertion and less invasive surgery were both positively associated with return to work, chemotherapy negatively. Employees diagnosed with breast cancer compared to those with colorectal cancer or lung cancer were more likely to return to work. Moderate evidence was found for gender and extensive disease. Women, as well as cancer survivors with more extensive disease, were less likely to return to work. Prognostic factors of employment for which strong evidence was found were age, education, and income. Older age was associated with increased risk of unemployment. Prolonged education and higher income were associated with decreased risk of unemployment. Moderate evidence was found for the association of more extensive disease and increased risk of unemployment.

Table 2.6 Level of evidence

	Return to work					Employment				
	QS†>60%		QS†≤60%		LoE‡	QS†>60%		QS†≤60%		LoE‡
	Total no. articles	No. articles significant data	Total no. articles	No. articles significant data		Total no. articles	No. articles significant data	Total no. articles	No. articles significant data	
Socio-demographics										
Age	7	4	5	2	weak	2	2	2	0	strong
Gender	2	1	2	2	moderate	2	2			inconsistent
Education	4	3	2	0	weak	3	3	2	1	strong
Income	1	0			insufficient	2	2	1	0	strong
Marital status	1	0	3	1	inconclusive	2	2	2	0	inconsistent
Race	1	0	1	1	inconsistent					
Urbanicity						1	1			weak
Job-characteristics										
Physical exertion	4	3	1	1	strong					
Working hours	1	0			insufficient	1	1			weak
Self-employment	1	1			weak	1	1			weak
Occupational class	1	1	2	1	weak	2	2	1	1	weak
Job tenure	2	1			weak	1	1			weak
Sick leave	1	0	1	0	inconclusive					

Table 2.6 Level of evidence (continued)

	Return to work					Employment				
	QS†>60%		QS†≤60%		LoE‡	QS†>60%		QS†≤60%		LoE‡
	Total no. articles	No. articles significant data	Total no. articles	No. articles significant data		Total no. articles	No. articles significant data	Total no. articles	No. articles significant data	
Employer accommodation			1	1	inconclusive					
Employer discrimination			1	1	inconclusive					
Inadequate ohc*	1	1			weak					
Social support	1	0			insufficient					
Disease										
Surgery only	3	3			weak					
Less invasive surgery	3	3			strong					
Chemotherapy	2	2	2	1	strong			1	1	inconclusive
Radiotherapy	2	0	2	0	inconclusive			1	0	insufficient
Extensive disease	4	1	2	2	moderate	1	1	1	1	moderate
Site	4	4			strong	2	2	1	1	weak

*ohc=occupational healthcare; †QS=quality score; ‡LoE=level of evidence.

DISCUSSION

This study aimed to identify prognostic factors of return to work and employment in cancer survivors based on prospective cohort studies. We found strong evidence that physical exertion, less invasive surgery, chemotherapy, and cancer site were prognostic factors for return to work, and that age, education, and income were prognostic factors for employment.

Main findings, interpretation and comparison with other studies

In recent years, a growing number of studies on cancer survivorship and return to work have been published. As design, methodology, and populations studied vary, pinpointing potential prognostic factors of return to work of cancer survivors requires caution. In this respect, a need for uniformity has been stated earlier (7). A limited number of reviews on the subject has been published describing results of previous studies in either a quantitative and/or qualitative way (6;49-56).

The present study shows that job demands, such as heavy work, create a barrier for cancer survivors to return to work. This result concurs with the findings of other reviews (52;54;56) that reported manual work acting as a barrier to return to work and fits the model (7) describing functional status and health perceptions interacting on work outcomes.

In this study, inconclusive evidence on employer accommodation and discrimination, and weak evidence for the role of the occupational health care worker on return to work were found. The need to improve efforts of oncology specialists, primary care providers and occupational health professionals, in the return to work process has been stated earlier (49) and findings of this study underline this. Strong evidence was found for the association between socio-demographic factors (age and education) and employment status of cancer survivors, but weak evidence on return to work. This finding is consistent with the results presented in a review by Spelten et al. (6), who reported socio-demographic characteristics not to be related with return to work, finding mixed associations for increasing age. In the present study, however, weak evidence for increasing age and return to work was found with older employees having a smaller chance. These different findings

can be explained by the small number of prospective cohort studies included in the aforementioned review, that also reported on studies with a cross-sectional design. Also, a more recent review (54) reported that elderly, lower educated and blue collar workers were less likely to be employed.

In the present study, moderate evidence was found on gender with women having a smaller chance to return to work compared to men, which concurs with findings reported by Mehnert (52). However, the evidence for gender on employment was inconsistent as associations showed opposite directions.

Higher income, also found to act as a strong prognostic factor of employment status, is possibly associated with a higher level of education leading to better paid work. This in turn could be associated with less physical job demands as present in white collar workers versus blue collar workers, and therefore facilitate return to work of higher educated persons, for which weak evidence was found. As reported earlier (49), lower levels of educational achievement are often associated with physically demanding jobs paying poorer salaries.

Disease related factors, e.g. negative effects of treatment modalities, were found to be strongly associated with return to work, which concurs with earlier reviews (52;53). If invasive surgery leads to a greater loss of functional capacity and hampers vocational rehabilitation, alternative treatment options with less impact are to be considered if medically justified and available. Cancer site was strongly associated with return to work, which was also found in earlier reviews (49;54). It was found that survivors diagnosed with breast cancer had the greatest chance of return to work followed by colorectal, and lung cancer survivors. The same order was found on the chance of employment, but the evidence found was weak. The association between cancer survivorship and unemployment has been reported by de Boer et al. (12), who in a meta-analysis found that cancer survivors, compared to healthy controls, were more likely to be unemployed. Although suggested by Amir and Brocky (49) that different social welfare systems may relate to work decisions of cancer survivors, after adjustment for diagnosis, age, and background unemployment rate, no difference between the unemployment risk of cancer survivors in the US and Europe was found. Moderate evidence for extensive disease was found on both return to work and employment. It is likely that more extensive

disease is associated with more limitations in functional capacities due to a greater negative influence of symptoms, possible greater burden of combined treatment modalities and related side effects, and eventually a more unfavourable prognosis. These issues are all leading to a trajectory in which return to work and employment are more difficult to reach.

Strengths of this review

Earlier articles have described factors that influence return to work or employment of cancer survivors, examining and presenting the results of both cross-sectional and cohort studies in a qualitative or quantitative way (6;49-56). In this review, only cohort studies with a prospective design, presenting quantitative data, minimizing recall bias by allowing a maximum period of retrieval at baseline of 4 months, were included. Only studies with data that examined a working-age population were included, and articles on late effects of childhood cancer or that analysed data on home-makers and students were excluded. In order to assess the value of potential prognostic factors, a proved method of quality assessment of articles was performed as well as a best evidence synthesis. Therefore, the methods applied in this study are believed to generate sufficient strength on prognostic factors identified and add valuable information to the existing body of knowledge.

Limitations of this review

The search strategy was restricted to articles published in English and in journals available in the used databases. This might have led to language or publication bias by missing relevant studies. Due to design, in two studies (23;39) the maximum recall period of baseline data, set at a 4 months maximum, was met only for a part of the population studied. However, this was accounted for in the analysis of both studies and proved to be irrelevant to the outcome of interest. As data were not pooled in a quantitative meta-analysis our conclusions rest on a qualitative assessment of available evidence. Some prognostic factors, for which strong evidence was found, rest on a small number of studies of a specific cancer site. Therefore, we should be cautious to generalize these results. Although we used a previously described way of methodological quality assessment (15), the QUIPS list is a non-validated instru-

ment leaving room for subjective evaluation. However, the QUIPS list is designed for prognosis studies addressing all common sources of bias, which as an instrument we thought to be relevant related to the subject of our study. The allocated quality marks that were used to discriminate study quality as well as chosen cut-off points however, remain arbitrary. The same applies to the grouping of outcome definitions used in the included studies in either a main category return to work or employment. In order to discriminate outcomes and allocate these in either a category *RTW* or *employment*, we assumed the concepts of absence and return to work to share a common though inverse relationship, with cancer survivors able or unable to retain a position and start up work again yes or no despite the diagnosis. This in contrast to the outcomes grouped in the category *employment* thatwe assumed to share the common aspect of having paid work yes or no.

Resetting the quality related threshold value from 60% to 50% of maximum attainable score, transforms previously judged low quality articles into high quality articles. By doing so, previously found moderate evidence, e.g., for gender as well as extensive disease on return to work, and for extensive disease on employment, would change into strong evidence. However, lowering the threshold value would not change previously found weak evidence into moderate evidence as the number of assessed articles is too small to be susceptible for such a change. Likewise, resetting the quality related threshold value upwards from 60% to 70% of maximum attainable score, would change strong evidence found for less invasive surgery and chemotherapy on return to work into moderate evidence, but would have no effect on previous moderate evidence found. This shows that a shift of threshold value would, to a certain degree, either influence moderate evidence found in upward direction or strong evidence found in a downward direction.

Recommendations

Higher age and lower education, both negatively associated with employment of cancer survivors, indicate that the work perspective of elderly and lower educated cancer survivors can be influenced positively. Therefore, government policy combined with willingness of employers, should address this specific group of employees by means of legislation accommodating return to work and providing

education, acting as an intervention tool in vocational rehabilitation. Also, gradually starting up work again after a period of sick leave combined with a trajectory of learning new skills, can support patients to overcome the negative side effects of treatment, restore confidence and give room to adapt to altered circumstances. The fact that physical exertion is negatively associated with return to work of cancer survivors, can act as a signal to both employers and occupational health care professionals, and address the need to adjust the physical load of job demands. Next to this a supportive attitude and adequate communication between the employee and other stakeholders is advised, and seems equally important. Finally, physicians concerned with the care of cancer survivors should be aware of the fact that certain treatment modalities can act as a barrier in return to work and should take this into consideration in advising their patients if confronted with questions on the topic. However, at the same time they should realize that patients can benefit from encouragement in taking up former responsibilities, irrespective of the social welfare system or legislation present.

Considering the number of selected studies retrieved by the literature search, the heterogeneous nature and the quality of these studies, the results underline the need to increase the number of high quality cohort studies implementing more uniformity in prospective studies in order to identify potential strong factors or yet undisclosed factors that influence return to work and/or employment of cancer survivors. Using a limited number of validated questionnaires could lead to more uniformity in studies and add more strength to present existing evidence.

Final conclusions

This study shows that a limited number of prognostic factors on cancer survivors' return to work and/or employment can be identified. There is a need for more high quality prospective studies in order to enhance interventions supporting the vocational rehabilitation of cancer survivors. Efforts to reach more uniformity in design and methods are called for.

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3

Prognostic factors of work disability in sick-listed cancer survivors

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ABSTRACT

Sick-listed cancer survivors may face lasting side-effects, even after a successful completion of treatment. As a consequence, they are at risk of work disability, which may lead to job loss. Knowledge of prognostic factors of work disability may support cancer survivors in their trajectory of vocational rehabilitation. The purpose of this study was to identify prognostic factors of work disability in sick-listed cancer survivors. From the first day of sick-leave (T0),a cohort of 131 cancer survivors was followed for 24 months. Included participants were aged between 20 and 63 years. Data were collected, using questionnaires, at 10 months (T1) after reporting sick. The level of work disability, i.e., entitlement for disability compensation, was assessed by an insurance physician and a labour expert at 24 months (T2). Univariate and multiple logistic regression analyses were performed. In the univariate analysis, 14 variables were found to be associated with the level of work disability at 24 months. These factors were related to socio-demographics, health characteristics, work-related characteristics, and return to work (RTW) expectations.Multiple logistic regression showed that at 10-month sick-leave, perception of health care providers on cancer survivors' work ability and experienced influence on RTW, both reported by workers, were significantly associated with the level of work disability at 24 months. It seems in the interest of cancer survivors to take an active role in planning their RTW trajectory and to discuss RTW with their health care providers. The potential role healthcare providers may play in counselling cancer survivors on RTW must not be underestimated. Cancer survivors may benefit in having control on their RTW trajectory.

INTRODUCTION

Cancer survivors are at risk of negative long-term effects on both employment status and work ability due to treatment modalities and/or diagnosis. For example, lasting side-effects, such as fatigue, cognitive and/or physical impairments, can have a negative impact in meeting job demands (1). Therefore, there is a need to improve efforts on providing cancer survivors with supportive services related to rehabilitation and adaptation to disabilities (2). For cancer survivors, return to work (RTW) can have a positive effect on perceived health and well-being. Also, it can provide social connections, support self-esteem, help to overcome negative side-effects of treatment (3;4), and RTW usually has positive financial consequences. That is, compensation of wage-loss due to sick-leave or work disability benefits cover only a part of loss of income and/or for a restricted period of time. Therefore, RTW is in the interest of the worker. Next to this, it is in the interest of society at large as RTW reduces the costs of sick-leave and loss of productivity.

In 2006, the estimated age-standardised incidence rates per 100,000 persons with cancer in Europe was estimated at 439.7 for men and 303.0 for women (5). As survival rates have increased over the last decades, e.g., due to improved treatment modalities, the number of cancer survivors has grown accordingly. In addition, a recent report of the Dutch Cancer Society, based on nationwide collected data over the period 1989-2007, showed an increase of the incidence and prevalence of cancer in the Netherlands (6). In this period, the incidence increased from 55,746 in 1989 to 87,300 in 2007. In 2011, the Dutch Cancer Registration reported a further increase of the incidence up to 100,577. Meanwhile, during 1989-2007, the standardised survival rate increased from 47% to 59%. As a consequence, the number of cancer survivors in the Dutch working age population has risen. This calls for efforts in order to provide workers with adequate RTW trajectories and reduce avoidable labour force exit of cancer survivors. A previous study showed that an average 64% of Dutch cancer survivors are able to RTW with full earnings within 18 months of sick-leave (7). This complies with the average of 63.5% of cancer survivors able to RTW, found in a systematic review of 64 peer-reviewed studies worldwide, conducted between 2000 and 2009 (8). Although the majority

of cancer survivors is able to resume work within a two-year period, the number of Dutch workers, sick-listed because of cancer, that have to apply for a work disability benefit, is still extensive (9).

In the Netherlands, in a trajectory of RTW, a sick-listed worker holding a labour contract is usually supported by an occupational physician. Social security legislation allows the worker and employer a maximum period of sick-leave of two years, with full RTW as the most favourable outcome. In the process of vocational rehabilitation and RTW of cancer survivors, besides health status, other aspects play an important role. Specifically, in a recent study, age, gender, level of education and physical exertion showed to be significantly associated with RTW (10). In the event of completing a two-year period of sick-leave, a worker can apply for a work disability benefit, which is assessed by the Dutch Social Security Agency (SSA). The assessment of functional abilities is done by an insurance physician. If applicable, based on the physicians' report, a labour expert calculates the loss of former wages earned. Both professionals are employed by the SSA. Workers are granted a benefit if loss of income exceeds 35% of former wages earned (11).

Though ill health in general increases the likelihood of labour force exit into unemployment and disability pension (12), a previous study showed that factors, such as the disease, workers' perception of work disability, legislation and the opinion of the environment, were all associated with the outcome of the work disability assessments (13). In 2009, over 3100 workers diagnosed with cancer applied for a work disability benefit (9). On assessment by the Dutch Social Security Agency (SSA) about 35% of these workers were judged fit to work either with or without adaptations. The remaining 65% were granted a full work disability benefit having a loss of income of over 80% of former wages earned. These figures underline the earlier reported need to improve counselling of cancer survivors, willing to RTW (14;15). This is important as the outcome of work disability assessment and failure of a previous vocational rehabilitation trajectory seem related. That is, in the process of vocational rehabilitation, addressing problems encountered at early stage may influence the work disability assessment outcome. A previous study showed the number of cancer survivors able to RTW, to increase from 24% at six months to 50% at 12 months of sick-leave (7). At 18-month sick-leave the rate of RTW was

64%. These numbers seem to indicate the importance of timely supporting cancer survivors able to RTW.

Usually, within the first year of sick-leave, the majority of cancer survivors complete active treatment. The patient may then be able to regain control and take up former roles, should side-effects of treatment diminish and general health improve. Studying possible prognostic factors of RTW when active treatment has finished seems indicated. If prognostic factors of work disability can be identified at early stage, workers may benefit in choosing effective measures to facilitate vocational rehabilitation and RTW. Therefore, this study aims to identify prognostic factors associated with work disability in sick-listed cancer survivors.

METHODS

Design

Our study involved a longitudinal cohort of sick-listed workers (with an employment contract), registered at the SSA. The data collected for this study was part of a national cohort study (16). Starting the first day of sick-leave (T0), our cohort was followed for 24 months. Two measurements were taken, the first measurement at 10 months after reporting sick (T1) and the outcome measurement at 24 months after reporting sick (T2). The questionnaires were sent to members of the study population at their home address. Questionnaires were received at an external research facility outside the SSA. Upon receipt, questionnaires were anonymised and archived securely. Respondents participated on a voluntarily base.

Study population

Participants of the national cohort study were selected through the head office of the SSA. Potentially eligible participants of this study had to be on a 10-month period of sick-leave in October 2007. During the period of inclusion, which started in December 2006 and ended in February 2007, 12,127 sick-listed workers, who were aged between 16 and 64 years and were holding a labour contract, were identified as potentially eligible participants. They received a questionnaire at

baseline and, by replying, entered the study. From this cohort, we selected a subset of participants to create our cohort (n=131), which consisted of workers who, on assessment of a work disability benefit at the SSA at 24 months of sick-leave, were registered with a diagnosis of cancer.

Parameters

The independent and dependent variables listed below were collected through questionnaires as used in earlier studies (13;17-25). The potential independent prognostic variables at T1 were socio-demographics, health characteristics, work-related characteristics, and RTW expectations (Table 3.1). Socio-demographics, health characteristics and work-related characteristics were incorporated as these

Table 3.1 Independent variables of work disability

Prognostic variables at 10 months (T1)
Socio-demographics
Age
Gender
Marital status
Education
Health characteristics
Perceived health
History of perceived health
Work-related characteristics
Job demands
Job tenure
Company size
Work status
Reported support on RTW
Experienced influence on RTW
Employer accommodation
RTW expectations*
Perception of work ability (health care providers)
Perception of work ability (worker)

*as reported by respondents

are known factors relating to work ability outcomes in general, making it possible to evaluate and compare the results of this study with the existing literature. An additional reason to incorporate work-related characteristics was that they seem more amendable to possible interventions. RTW expectations, examining beliefs and attitudes, were selected to cover the behavioural aspects of labour participation.

INDEPENDENT VARIABLES

Socio-demographics

The following socio-demographic characteristics were determined: (a) age (in years), (b) gender (male; female), (c) marital status (married or living with partner; single, widowed or divorced), and (d) educational level (primary school; lower vocational education; lower secondary school; intermediate vocational education; upper secondary school; upper vocational education; university).

Health characteristics

The following health characteristics were determined: (a) perceived health (based on a self-reported single item: “In general, how is your state of health now?”; answer categories were: poor; moderate; good), and (b) history of perceived health (based on a self-reported single item: “Over the last 9 months, has your health improved, been the same or deteriorated?”; answer categories were: has improved; stayed the same; has deteriorated).

Work-related characteristics

The following work-related characteristics were assessed: (a) job demands (questions with answer categories “yes” or “no”: working in the evening/ at night/ in the week-end, heavy physical demands, heavy psychological demands, working under pressure of time), (b) job tenure (<12 months; ≥12 months), (c) company size (no. of employees: ≤10; 11-25; 26-50; 51-100; 101-250; >250), (d) work status (working yes or no), (e) support on RTW (by occupational health service; employer;

lack of support in general), (f) influence on RTW over the previous period as experienced by worker (substantial; some; none), and (g) employer accommodation (by adjustment of: tasks; working hours; none made).

RTW expectations

Regarding health, the participant was asked whether he/she expected a full RTW in the future (single item variable; perception of work ability as reported by worker: "Do you think your health will permit a full RTW (again) in the future?"; answer categories were: yes, at the same job; yes, in another field of work; I don't expect it; I don't know). Also, regarding RTW, the participant was asked about the involved health care providers' opinions on the subject, related to his/her possibilities (single item variable; perception of work ability by health care providers: "How does your occupational physician, general practitioner and/or specialist judge your possibilities to start your work again?"; answer categories were: they think I am capable of starting work again; they doubt it; they think I am unable; they have different opinions on this; I don't know).

DEPENDENT VARIABLE

The primary outcome variable was the level of work disability after 24 months of sick-leave. This was operationalized by dichotomizing the results of the work disability assessments, the entitlement for disability compensation, as performed by the SSA. In the Netherlands, the level of work disability is assigned to one out of four categories, depending on wage loss or sustainable absence of functional abilities. If functional abilities are assessed present, wage loss can be either (1) less than 35%, (2) in between 35 to 80%, or (3) over 80% of former wages earned. The compensation granted can be none, partial, or complete, respectively. If a person has no labour capacities (sustainable absence of functional abilities) the claimant is granted (4) a compensation by the Benefit Act for the fully and sustained work disabled. The participants with a wage loss of less than 80% were grouped together, as well as those with a wage loss equal to or more than 80% and those

with a permanent and sustainable work disability. Herewith, workers assessed still able to earn an income were distinguished from those unable to earn an income, i.e., incomplete versus complete work disability.

STATISTICAL ANALYSIS

The following variables were binominal: gender (male, female) as well as shift work, physical workload, mental work load, time pressure, work status, support by occupational health service, support by employer, lack of support in general, reduction of tasks, reduction of hours and lack of employer accommodation, all having a yes versus no answering category. Also binominal was job tenure (<12 months; ≥12 months). The following variables were dichotomized: age (<50 vs. ≥50 years) using the median as a cut-off point, marital status (married/partner vs. single/ widowed/ divorced), and company size (no. of employees: ≤50; 51-250). The categorical variables perceived health, history of perceived health, experienced influence on RTW, perception of work ability by health care providers and perception of work ability by worker, were not recoded.

The relationship between independent prognostic variables at 10-month sick-leave (T1) and the binominal level of disability at 24 months (wage loss <80%; ≥80%) was analysed with logistic regression analysis. Prior to this, univariate analyses (Chi-square test or Fishers' exact test, if conditions of Chi-square test were not met) between the independent prognostic variables and the level of work disability at 24-month sick-leave were performed. For the univariate analyses, a cut-off for p-values of 0.20 was chosen. The independent variables of univariate analysis were tested for multicollinearity and accepted in the logistic model if correlation coefficients were ≥-0.6 and ≤0.6 (26). The multivariate logistic analysis incorporated four groups of variables, socio-demographics, health characteristics, work-related characteristics and RTW expectations, in this order and in consecutive steps. For the first four steps, a cut-off for p-values of 0.20 was chosen. For the fifth and final step, a cut-off for p-values of 0.10 was chosen. The first step incorporated socio-demographic variables, irrespective of the level of significance of univariate

analysis. In the second (health characteristics), third (work-related characteristics) and fourth (RTW expectations) step significant results of the predecessor step were added. In the fifth step, only significant variables of the predecessor step were analysed.

The multivariate logistic analysis incorporated four groups of variables, socio-demographics, health characteristics, work-related characteristics and RTW expectations, in this order and in consecutive steps. The order in which the variable groups were added was based on the assumption of variables being less to more amendable or conditional to the consecutive group. The association for each identified prognostic variable and the dependent variable was calculated using odds ratios (OR). The Hosmer-Lemeshow test was used to assess the goodness of fit. All analyses were performed using SPSS15.0.1 (27).

RESULTS

Characteristics of the study population

At 10 months sick-leave (T1), 12,127 questionnaires were sent. A total of 4,019 was returned of which 3,978 could be linked with the SSA data. Of these, 131 respondents were diagnosed with cancer. In Table 3.2, the characteristics of the cohort of cancer survivors (n=131) at T1 are presented. Related to the category socio-demographics, we found that respondents' mean age was 49.2 years (SD 7.2 years), and 33% were men. The majority (75%) of respondents was in a relationship, and the highest level of education was lower secondary school. Related to the category health characteristics, we found that perceived health was reported as poor by 24% of the respondents. In the same category, specifically history of perceived health, 40% of respondents reported deterioration of health. In the category work-related characteristics, specifically job demands, 35% of respondents reported physical work load. With regard to reported support on RTW, we found that 52% of respondents received support by an occupational health service, and 47% of respondents reported support by their employer. In the category RTW expectations, specifically perception of work ability by health care providers, 34% of

Table 3.2 Characteristics of the cohort of cancer survivors

Variables			n* (%)
Socio-demographics			
Age (in years)	≤50		66 (52)
	>50		62 (48)
Gender	Male		42 (33)
	Female		86 (67)
Marital status	Married/ partner		99 (77)
	Single		16 (13)
	Widowed		4 (3)
	Divorced		9 (7)
Education	Primary school		33 (26)
	Lower vocational education		65 (51)
	Lower secondary school		30 (23)
Health characteristics			
Perceived health	Poor		32 (24)
	Moderate		77 (59)
	Good		22 (17)
History of perceived health	Improved		53 (40)
	Same		26 (20)
	Deteriorated		52 (40)
Work-related characteristics			
Job demands	Shift work	Yes	64 (50)
		No	65 (50)
	Physical work load	Yes	45 (35)
		No	84 (65)
	Mental work load	Yes	46 (36)
		No	82 (64)
	Time pressure	Yes	60 (47)
		No	67 (53)
	Job tenure	<12 months	6 (5)
		≥12 months	106 (95)

Table 3.2 Characteristics of the cohort of cancer survivors (continued)

Variables			n* (%)
Company size	No. employees ≤ 10		85 (66)
	No. employees 11-50		0 (0)
	No. employees 51-100		25 (19)
	No. employees 101-250		19 (15)
Work status	Working		52 (41)
	Not working		74 (59)
Reported support on RTW	Support by OHS†	Yes	67 (52)
		No	62 (48)
	Support by employer	Yes	61 (47)
		No	68 (53)
	Lack of support in general	Yes	23 (18)
		No	106 (82)
Experienced influence on RTW		Substantial	61 (51)
		Some	31 (26)
		None	27 (23)
Employer accommodation	Reduction of tasks	Yes	12 (9)
		No	117 (91)
	Reduction of hours	Yes	13 (10)
		No	116 (90)
	Lack of employer accommodation	Yes	38 (30)
		No	91 (70)
RTW expectations			
Perception of work ability (health care providers)	They think I am fit		41 (34)
	They doubt it		14 (12)
	They don't think I can		26 (21)
	They have different opinions		5 (4)
	I don't know		36 (29)
Perception of work ability (worker)	Not fit		37 (29)
	Fit for own job		45 (35)
	Fit for other job		14 (11)
	I don't know		32 (25)

* due to missing data n varies (range: 112-131); †OHS: Occupational Health Service

respondents reported their health care provider to have positive expectations on their work ability. In total, 41% of the respondents reported to be working.

Regarding the dependent variable, we found that of the 131 cancer survivors, 33 had less than 35%, 25 between 35% and 80%, and 28 over 80% loss of former wages earned, as assessed by the SSA at 24-month sick-leave. In 45 participants, no labour capacities (full and sustained work disability) were present. They were granted a compensation by the Benefit Act for the fully and sustained work disabled.

Factors associated with work disability

Results of the univariate analyses, in which the relationship between the independent variables at 10 months (T1) and the level of work disability at 24-month sick-leave were tested, are presented in Table 3.3. In these analyses, we used a cut-off for p-values of 0.20. We found statistically significant associations at a level of $p<0.20$ for age, education, perceived health, time pressure, work status, support by occupational health service, support by employer, lack of support in general, experienced influence on RTW, reduction of tasks, reduction of hours, lack of employer accommodation, perception of work ability by health care providers and perception of work ability by worker. Specifically, age over fifty, low education, poor perceived health, lack of support in general, lack of employer accommodation, low work ability as perceived by health care providers, and low work ability as perceived by worker were all negatively associated with the level of work disability. A positive work status, receiving support by occupational health service, receiving support by employer, positive experienced influence on RTW, having reduction of tasks and having reduction of hours were all positively associated with the level of work disability. Also, high time pressure was positively associated with the level of work disability.

The associations found in the final step of the multiple logistic regression analysis are presented in Table 3.4. The Hosmer-Lemeshow test revealed that the prediction model had a moderate fit ($p = 0.65$ for the prediction model). Due to missing data, 128 cases were entered in the first step of multiple logistic regression model. Of the 14 significant univariate variables ($p<0.20$), two remained in the final

Table 3.3 Univariate associations between independent variables and work disability

Prognostic variables		Odds Ratio (95%CI)	p-value*
Socio-demographics			
Age		0.59 (0.29-1.20)	0.141
Gender		0.82 (0.39-1.73)	0.602
Marital Status†			0.770
	Divorced	2.80 (0.55-14.16)	
	Widowed	2.40 (0.24-23.88)	
	Single	0.62 (0.22-1.80)	
Education‡			0.190
	Lower vocational education	0.45 (0.19-1.09)	
	Lower secundary school	0.50 (0.18-1.40)	
Health characteristics			
Perceived health§			0.003
	Moderate	2.44 (0.90-6.65)	
	Poor	7.65 (2.24-26.12)	
History of perceived health‖			0.324
	Same	1.21 (0.47-3.10)	
	Deteriorated	1.80 (0.83-3.94)	
Work-related characteristics			
Shift work		1.16 (0.58-2.34)	0.665
Physical work load		0.73 (0.35-1.53)	0.407
Mental work load		1.41 (0.68-2.92)	0.351
Time pressure		0.53 (0.26-1.08)	0.078
Job tenure		2.71 (0.47-15.45)	0.401¶
Company size**			0.350
	No. employees ≤ 10	1.70 (0.62-4.65)	
	No. employees 51-100	2.44 (0.72-8.31)	
Work status		3.55 (1.69-7.47)	0.001
Support by OHS††		0.53 (0.26-1.08)	0.081
Support by employer		0.49 (0.24-1.00)	0.050
Lack of support in general		2.53 (0.93-6.92)	0.064

Table 3.3 Univariate associations between independent variables and work disability (continued)

Prognostic variables		Odds Ratio (95%CI)	p-value*
Experienced influence on RTW‡‡			0.026
	Some	1.99 (0.83-4.82)	
	None	3.60 (1.33-9.76)	
Reduction of tasks		0.35 (0.09-1.22)	0.088
Reduction of hours		0.30 (0.09-1.04)	0.048
Lack of employer accommodation		2.86 (1.25-6.57)	0.011
RTW expectations			
Perception of work ability (health care providers) §§			0.000
	They doubt it	4.91 (1.35-17.89)	
	They don't think I can	11.46 (3.47-37.85)	
	They have different opinions	1.82 (0.27-12.38)	
	I don't know	7.09 (2.60-19.36)	
Perception of work ability (worker) ‖ ‖			0.004
	Fit for own job	0.20 (0.08-0.53)	
	Fit for other job	0.49 (0.14-1.78)	
	I don't know	0.71 (0.25-1.98)	

*Result of Chi Square test. †Reference category: married/living with partner; Reference category: primary school; §Reference category: good; ‖Reference category: improved; ¶Result of Fisher exact test; **Reference category: no. employees 101-250; ††OHS: Occupational Health Service; ‡‡Reference category: substantial; §§Reference category: they think I am fit; ‖ ‖Reference category: not fit

step of the multiple logistic analysis. These were experienced influence on RTW and perception of work ability by health care providers. No experienced influence on RTW and negative perception of work ability by health care providers were both negatively associated with the level of work disability ($p<0.10$). If the cancer survivor experienced no influence on RTW, the risk of work disability increased (OR 5.27 CI 1.58-17.56). If health care providers expressed doubts on the subject, i.e.,

Table 3.4 Multivariate associations between independent variables and work disability

Step (N)	Prognostic variables		Odds Ratio (95% CI)	p	H-L*
1 (128)	Socio-demographics		n.s. †		0.99
2 (131)	Perceived health‡			0.006	0.69
		moderate	2.59 (0.94-7.14)	0.065	
		poor	7.92 (2.20-28.51)	0.002	
3 (112)	Experienced influence on RTW§			0.192	0.24
		some	2.56 (0.90-7.33)	0.079	
		none	1.86 (0.54-6.42)	0.324	
4 (114)	Experienced influence on RTW§			0.028	0.63
		some	1.50 (0.54-4.19)	0.439	
		none	5.43 (1.57-18.78)	0.008	
	Perception of work ability health care providers‖			0.022	
		They doubt it	4.47 (1.03-19.44)	0.046	
		They don't think I can	13.10 (2.56-66.93)	0.002	
		They have different opinions	1.69 (0.23-12.62)	0.608	
		I don't know	6.22 (1.67-23.16)	0.006	
5 (114)¶	Experienced influence on RTW§			0.026	0.65
		some	1.42 (0.52-3.88)	0.491	
		none	5.27 (1.58-17.56)	0.007	
	Perception of work ability health care providers‖			0.002	
		They doubt it	4.23 (1.05-17.10)	0.043	
		They don't think I can	10.18 (2.88-35.96)	0.000	
		They have different opinions	1.65 (0.22-12.48)	0.628	
		I don't know	5.53 (1.88-16.23)	0.002	

*Result Hosmer-Lemeshow test; † n.s. = no significant results; ‡Reference category: good; §Reference category: substantial; ‖ Reference category: They think I am fit. ¶ The model of step five is based on the significant variables of step four exclusively.

they thought the cancer survivor was unable to resume the former job or if the cancer survivor did not know their opinion on the subject, risk of work disability increased also (OR 4.23 (CI 1.05-17.10), (OR 10.18 (CI 2.88-35.96) and OR 5.53 (CI 1.88-16.23), respectively).

DISCUSSION

Main findings

The aim of this study was to identify prognostic factors of work disability in sick-listed cancer survivors. Dependent variables were analysed in a hierarchical way. At 10-month sick-leave, experienced influence on RTW and perception of health care providers on work ability, as reported by respondents, were both associated with the outcome of the work disability assessment at 24 months.

Comparison with other studies

Over the last decade, an increasing number of longitudinal studies investigating the work participation of cancer survivors, have been published (3;8;20;22;24;28-41). Commonly used outcomes in these studies are work ability, RTW, time to RTW, time to job loss, time to re-employment or employment. In the current study, wage loss related to a certain level of work disability, acted as primary outcome. This is an important outcome measure as it expresses the assessment of both an insurance physician and labour expert. It encloses health related aspects, functional abilities, presence of skills and level of education of the worker.

The results of this study, i.e., the association found between experienced influence on RTW and work disability, emphasizes the need for cancer survivors to actively engage in their trajectory of vocational rehabilitation. Taking responsibility and less dependency on the performance of other stakeholders involved may reduce the risk of work disability. This finding partially concurs with a previous study in which suboptimal performance by occupational health physicians was negatively associated with the outcome of a RTW trajectory (15). Also, the results of our study concur partially with findings of an early study showing that factors,

such as workers' perception of abilities and the opinion of the environment, were all associated with work disability (13). Although Dutch social security legislation has been adapted since and has become more stringent in granting work disability claims, our study showed that under the condition of a serious disease being present, work disability was still associated with work ability as perceived by health care providers. In our cohort, 75% of cancer survivors were compensated for loss of income due to work disability. Comparison with other studies shows that cancer survivors facing wage loss is common and related to a reduction of working hours and/or loss of work-related abilities (22;42-44). However, none of these studies report on the association between perception of health care providers and work disability of cancer survivors. There are numerous studies on assessment of sick-leave by health care providers and prognostic factors of RTW. However, the majority of these studies focus on musculoskeletal or mental health problems in a primary health care setting, and have a limited period of follow-up (45-50). Therefore, our findings add new information to prognostic factors associated with work disability in cancer survivors.

In our cohort, the multivariate analysis of variables such as education and social support, showed no association with the outcome of the work disability assessment and related compensation of wage loss. This is in contrast with the results of a cohort study of 459 breast cancer survivors, exploring wage loss over the first 12 months following a early diagnosis of breast cancer (22). In this study, a higher percentage of wages lost was significantly associated with a lower level of education, lower social support, and shorter job tenure. The heterogeneous character of our cohort, the specific legislation and sample size could possibly act as an explanation for the differences found. More research on these topics is to be considered.

In previous studies the percentage of workers that report work limitations varies in between 20 to 59 %, which is likely to be related to design, characteristics of the population studied, and differences in outcome measurement (22;42-44;51-54). Factors found to be associated with work disability were e.g., work-related characteristics, socio-demographics, disease and stage, and co-morbidity, with shorter job tenure, lower income, lower education and greater burden of disease leading up to more disabilities. Though, in the univariate analysis of our study,

some of these variables, such as age, education, work status, reduction of tasks and working hours, and perceived health, also were associated with work disability. In our multivariate analysis, however, this association was lost. The unexpected univariate significant association found between time pressure and reduced risk of work disability could relate to the uneven distribution of men and women or sample size of the cohort. In the multivariate analysis, this association was lost. Eventually in the final step of multivariate analysis experienced influence on RTW and the perception of health care providers on workers' work ability, as reported by respondents, showed to be significantly associated with the outcome of the work disability assessment.

Strengths and limitations

Strength of this study is that the population studied originated from a nationwide randomly sampled cohort of sick-listed workers. Herewith, the study covered the entire Dutch working population having a fixed contract. The prospective design made it possible to identify potential prognostic factors. As prospective studies on this subject are limited, results add valuable information. Also, the primary outcome of the study is based on the assessment by an independent insurance physician and labour expert following uniform guidelines based on national legislation being practised at all SSA offices nationwide.

A limitation of this study is that tumour type and stage of disease, which we generally know to be associated with RTW outcomes, were not specified. Also, the presence and role of comorbidity could not be accounted for. Next to this, the number of men and women was unequal. The number of respondents assessed at 24 months of sick-leave was half the number expected. This could imply potential selection bias with workers possibly in a more favourable health condition able to RTW, not applying for a disability benefit. Moreover, the dataset did not allow a non-response analysis questioning the representativeness of the studied cohort. Also, the highest level of education in the cohort was lower secondary school. In this respect the cohort does not seem to represent the average Dutch working population. Also, due to missing data the number of complete cases available in the final step of the multivariate analysis dropped to 89%. The total of 131 respon-

dents may have limited the statistical power of the study. Regarding our finding, i.e., perception of work ability by health care providers, we must bear in mind that data were self-reported by cancer survivors, not necessarily representing the opinion of health care providers involved. Finally, the study results are under influence of Dutch social security legislation hampering generalisation to cancer survivors in other countries.

Practical implications

Having influence on a RTW trajectory seems positively related in reducing the risk of work disability. This emphasizes the relative importance of cancer survivors actively taking the lead in this process. As such, they may consider themselves as the principal stakeholder seeking advice from other parties involved. Also, they may seek help related to queries on the possibilities to start up activities at the regular workplace with adaptations, or seek practical advice on alternative interventions, such as education or vocational training. In the Netherlands, developments in enhancing RTW of cancer survivors, i.e., the initiation of specialized outpatient clinics targeting at, and offering advice and support in RTW queries, are promising.

Considering the effect of health care providers' RTW expectations at 10-month sick-leave, this emphasizes the need for an evidence based advice in counselling sick-listed cancer survivors. That is, health care providers should be aware of potential consequences of statements and advice given. Next to this, the need for clear communication on RTW expectations between health care providers and the sick-listed cancer survivor seems to be apparent. Therefore, all physicians engaged in caring for sick-listed cancer survivors should feel free to discuss aspects of RTW with their patient.

Final conclusions

We conclude that having no influence on RTW as well as negative expectations of health care providers on cancer survivors' work ability might be associated with a increased risk of work disability. Health care providers should be aware of their potential role in counselling cancer survivors in a RTW trajectory in which employee and employer share responsibilities making a joint effort. More research

on these topics, enhancing RTW of cancer survivors and communication between cancer survivors and their health care providers, is called for.

Conflicts of interest and Source of Funding

PvM is employed by the Dutch Social Security Agency. The study was funded by the Research Center for Insurance Medicine. For the remaining authors no conflicts of interest were declared.

Ethical standards

The authors declare the project to be exempt from review by a medical research ethics committee in accordance with the local regulatory guidelines and standards for human subjects protection in the Netherlands (Medical Research Involving Human Subjects Act (WMO), 2005).

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4

Factors associated with work disability in employed cancer survivors at 24-month sick leave

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ABSTRACT

Identification of factors associated with work disability in cancer survivors on long-term sick leave may support these survivors in choosing effective measures to facilitate vocational rehabilitation and return to work. Therefore, this study aims to disclose factors associated with work disability in cancer survivors at 24 months of sick leave. A cross sectional study was conducted. The study population consisted of employed sick-listed cancer survivors, aged between 18 and 64 years. They received a questionnaire at 24-month sick leave, the maximum period of sick leave allowed by Dutch social security legislation. Data were linked with the outcome of work disability assessment, as performed by the Dutch social security agency. A hierarchical multivariate logistic regression analysis was performed to identify factors associated with work disability. Data of 351 valid cases were analysed. The multivariate analysis showed that, for cancer survivors at 24-month sick leave, Dutch nationality, higher education, receiving hormone therapy, metastatic disease, physical limitations and low self-reported work ability were associated with an increased risk for work disability. This study identified factors associated with work disability of employed cancer survivors at 24 months of sick leave. The results of the current study may serve as a starting point to investigate the course of work disability beyond the maximum period of 24 months of sick leave. In order to enhance work participation of cancer survivors beyond this term, prospective data on work disability in the Netherlands are required.

BACKGROUND

In the last decade, work participation of cancer survivors has received growing attention worldwide (1). Previous studies have shown that cancer survivors are at risk for job loss, unemployment and work disability (2-9). Cancer survivors who are unable to resume a former job not only face the risk of a financial loss (10). That is, job loss can have a negative effect on recovery as well (11). Return to work (RTW) may help cancer survivors to regain control, lead the way back to the former normal life, strengthen their self-confidence and support them to overcome negative side-effects of treatment (12;13). Also, enhancement of work participation of cancer survivors is to the advantage of society at large, in reducing the costs of sick leave and work disability benefits, as well as productivity loss (14). Therefore, the prevention of work disability in cancer survivors needs ongoing attention.

The impact of cancer and the potential side-effects of the treatment can lead to functional limitations, physical and/or psychological disabilities. This may create a barrier to work participation (15-17). For instance, functional limitations leading to job changes or even exit from work were reported by 11% of breast cancer survivors in a study by Peuckmann et al. (18). Further, in a cohort of male and female cancer survivors (mixed diagnoses), 27% of men and 32% of women reported work disabilities (7). Also, in a cohort of cancer survivors (mixed diagnoses) with follow-up lasting between one to five years, 20% of respondents reported cancer-related disabilities and only half of those reporting disabilities were able to work (19). Functional limitations and reduced work productivity can last up to several years after diagnosis, as reported by Yabroff. In this study, significant differences between cancer survivors and matched controls were found (20).

A number of factors negatively associated with work participation of cancer survivors have been identified. These factors are related to socio-demographics (e.g., old age, low education, low income), the disease (e.g., tumor site, chemotherapy, advanced tumor stage) and work-related characteristics (e.g., physical work demands) (1;15). Still, the need to disclose unidentified factors associated with work participation of cancer survivors remains. That is, factors associated with work disability of cancer survivors present at a 24-month sick leave term, are

poorly investigated. Most studies focus on RTW, are either based on hospital data or data of an occupational health service and relate to a period of absence from work of three up to 18 months (21;22). During this period, relatively shortly after diagnosis, potential long-term sequelae of cancer and cancer treatment, possibly associated with work disability, may not be apparent.

Recently, a number of factors associated with work disability assessment outcomes were identified. That is, in a prospective study it was reported that at 10-month sick leave, perception of health care providers on cancer survivors' work ability and experienced influence on RTW, both reported by workers, were significantly associated with the level of work disability at 24 months (23). As factors at 10-month sick leave exert an influence on work disability at 24 months, this questions what factors are associated with sustained work disability as assessed at 24-month sick leave and beyond. Identification of barriers of work participation, i.e., factors associated with work disability at specific points in time, can make it possible to offer the adequate support, using resources in an optimal way. Therefore, this study aims to identify factors associated with the level of work disability at 24-month sick leave in cancer survivors. Herewith, the level of work disability is defined as wage loss related to functional limitations, which is present practice in the Dutch social security system.

METHODS

Design

A cross-sectional design was used for the current study, for which two data sources were used: 1) questionnaire data, and 2) register data of work disability assessments. The period of inclusion started in July 2011 and ended in February 2012. Data were collected when study participants approached the maximum term of 24-month sick leave and applied for a work disability benefit at the Dutch Social Security Agency (SSA). In the Netherlands, the SSA is responsible for the assessment of work disability of workers on long-term sick leave. The assessment of functional abilities at 24-month sick leave (the maximum period allowed by law)

is done by an insurance physician. If applicable, based on the physician's report, a labour expert calculates the loss of former wages earned. In 2009, 65% of Dutch cancer survivors who applied for a work disability benefit was granted a full work disability benefit (24). This implies a wage loss of ≥ 80% of former wages earned.

Questionnaires were sent to the participants at their home address. Upon receipt, data of the questionnaires were linked to SSA data. The study was approved by the Medical Ethics Committee of the VU University Medical Center.

Study population

The study population consisted of sick-listed employed workers (hereafter designated as workers) who were registered at the SSA. They were aged between 18 and 64 years. All workers had a reported diagnosis of cancer, and were approaching a sick leave term of 24 months. Diagnosis had to be confirmed within the first six months of sick leave. Workers were excluded if they received active chemotherapy and/or radiotherapy treatment, if they had a previous diagnosis of cancer but applied for a work disability benefit due to another somatic or psychiatric disorder, if they were self-employed, if they were applying for a revision of a previous work disability assessment, or if they were employed in a so-called sheltered workplace.

Study procedure

Potentially eligible participants of our study were selected at the head office of the SSA. During the period of inclusion, the list of new work disability benefit applications was checked by one author (KBG or PvM) every week. Based on this list of social security numbers and corresponding documents, we selected the sick-listed workers with a diagnosis of cancer, as reported in the attached medical records. After starting the selection, in case of doubt, cases were included based on consensus. Potentially eligible participants received a questionnaire, an informed consent form, and information stating the aim and background of the study. A postage-paid return envelope (to the Research Center for Insurance Medicine at the EMGO + Institute at the VU University Medical Center) and an introductory letter, by the chief medical officer of the SSA, were added. This letter stated the independency of the researchers and stressed that participation would be of no

influence on the outcome of the work disability assessment. Participants had to complete the informed consent form by hand and affix a signature. On receipt of the signed informed consent form and the questionnaire, we linked the latter with personal data (i.e., family name, address, birth date), as collected at the SSA head office, and entered these data in a secured database. The chief medical officer of the SSA gave permission to access the SSA's registry data. A reminder was sent after two weeks. Also, a reminder was sent in case of a missing signature on the informed consent form. Questionnaires of respondents lacking a completed form were destroyed. All respondents received a gift voucher.

Workers who reported to receive chemotherapy and/or radiotherapy and workers of whom the main reason for application was not cancer-related, were excluded. They were sent a letter explaining the reason of exclusion. The questionnaires were checked for completeness and, if necessary, respondents were contacted to supply missing data.

Variables

The independent and dependent variables were collected through questionnaires as used in earlier studies on cancer survivorship and return to work (1;11;25-27).

INDEPENDENT VARIABLES

Socio-demographics

The following socio-demographic characteristics were determined: (a) age (in years), (b) gender (male; female), (c) marital status (single; married / living with partner; divorced / widowed), (d) number of children, (e) principal wage earner (yes; no), (f) educational level (no education / primary school / lower vocational education; secondary school; vocational education / upper secondary school; upper vocational education / university), (g) nationality (Dutch; non-Dutch).

Health determinants

The following health characteristics were assessed: (a) tumor type, (b) extensive disease (negative lymph nodes; positive lymph nodes; metastasis), (c) treatment modalities (surgery; radiotherapy; chemotherapy; hormone therapy; bone marrow transplant; immunotherapy), (d) being free of disease (yes; no; don't know), (e) comorbidity (number of additional diseases). Physical symptom burden was measured using (f) the physical dimension score of the Sickness Impact Profile (SIP), covering three scales, i.e., Body Care and Movement, Ambulation, and Mobility (28). Also, (g) fatigue, (h) depressive mood, and (i) global health were measured using the Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F) (29), the Center for Epidemiologic Studies Depression Scale (CES-D) (30), and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC-QLQ-C30) (31), respectively.

Work-related determinants

The following characteristics of the previous job held were determined: (a) type of job (white collar; civil servant; blue collar; health care worker), (b) job tenure (in years), (c) working hours (hours/week), (d) shift work (yes; no), (e) managerial tasks (yes; no), (f) number of supervised co-workers, (g) work demands (psychological; physical; both), (h) company size (number of employees), and (i) work ability expectations (same; increase; decrease; don't know). Related to the present (j) work status (working; not working), (k) the actual number of working hours were determined. Finally, with the first three items of the Work Ability Index (WAI) (1) current work ability compared to life time best, (m) current work ability related to physical work demands and (n) current work ability related to psychological work demands, were measured (32).

DEPENDENT VARIABLE

The primary outcome variable was the level of work disability after 24 months of sick leave. This was operationalised by dichotomising the results of the work

disability assessments, the entitlement for work disability compensation, as performed by the SSA. In the Netherlands, the level of work disability is assigned to one out of four categories, depending on wage loss or sustainable absence of functional abilities. If functional abilities are assessed present, wage loss can be either (1) less than 35%, (2) in between 35 to 80%, or (3) over 80% of former wages earned. The compensation granted can be none, partial, or complete, respectively. If a person has no labour capacities (sustainable absence of functional abilities) the claimant is granted (4) a compensation by the Benefit Act for the fully and sustained work disabled. The participants with a wage loss of less than 80% were grouped together, as well as those with a wage loss equal to or more than 80% and those with a permanent and sustainable work disability. Herewith, workers assessed as still being able to earn an income were distinguished from those unable to earn an income, i.e., incomplete versus complete work disability.

STATISTICAL ANALYSIS

The following variables were binominal: gender, nationality, work status, principal wage earner, shift work, managerial tasks, and treatment modalities. A number of variables was dichotomized: age, job tenure, working hours per week in previous job, the number of supervised co-workers, working hours per week in present job, scores of the SIP, FACIT-F, EORTC-QLQ-C30, and WAI, using the median as a cut-off point. For the CES-D, the variable was dichotomized at a score of 16, the predetermined cut-off point most often used for likely cases of clinical depression (30). Categorical variables were marital status, number of children, education, type of job, work demands, company size, comorbidity, tumor type, extensive disease, and being free of disease.

The association between independent variables and the binominal level of work disability at 24 months (wage loss <80%; ≥80%) were analysed with univariate and multivariate methods. For univariate analysis, a Chi-square test was performed using a cut-off for p-values of 0.20. The remaining significant independent variables of univariate analysis were then tested for multicollinearity and accepted in a

logistic regression model if correlation coefficients were ≥ -0.6 and ≤0.6 (33). Next, for each category of variables, i.e., socio-demographics, work-related characteristics and health characteristics, multiple logistic regression analysis was performed, using a backward stepwise method. For each category of variables, this resulted in a logistic regression model presenting variables associated with work disability at 24 months of sick leave. Next, using the results of these three backward stepwise models a final model was built. In this final model, variables of the three categories i.e. socio-demographics, health determinants and work-related determinants were added in consecutive order. This resulted in a final model, presenting variables associated with work disability at 24 months of sick leave, controlling in a hierarchical way for socio-demographics, health determinants and work-related determinants. The association for each independent variable and the level of work disability at 24 months was calculated using odds ratios (OR). In the logistic regression analyses, a cut-off for p-values of 0.1 (Wald statistics) for independent variables was chosen. The Hosmer-Lemeshow test was used to assess the goodness of fit. All analyses were performed using SPSS 20 (34).

RESULTS

Characteristics of the study population

During the period of inclusion, 13,023 employed workers applied for a work disability benefit. Of these 1,307 had a diagnosis of cancer of whom 995 met the inclusion criteria. These 995 workers were sent a questionnaire, of whom 528 responded. Based on exclusion criteria (i.e., data retrieved from received questionnaires) and based on supplementary SSA data, 136 of the respondents were excluded. Finally, 392 cancer survivors were included. In 41 of the 392 cancer survivors, the level of work disability could not be retrieved, leaving 351 valid cases. The mean age of these respondents was 51.1 years (SD 7.4 years) and 36% were men. The majority (79%) was in a relationship and 27% was educated at high vocational or university level. Related to the category health determinants, more specifically tumor type, breast cancer was reported in 40%, haematological cancer in 14%,

and cancer of the digestive system in 13% of the cases. Other tumor types were reported in 33% of cancer survivors. Related to extensiveness of disease, 52% of respondents reported having negative lymph nodes and 42% reported being free of disease. In the category work-related determinants, 40% of respondents worked in a blue collar job and 29% in a white collar job. A total of 60% of the respondents reported their company to have > 100 employees, and 40% reported to be actually working in paid labour. Positive work ability expectations were reported by 35% respondents, and 17% expected work ability to stay the same.

Level of work disability

Regarding the dependent variable, we found that of the 351 cancer survivors, 92 had less than 35%, 101 between 35 and 80%, and 97 over 80% loss of former wages earned, as assessed by the SSA at 24-month sick leave. In 61 of the cancer survivors, no labour capacities (full and sustained work disability) were present.

Cancer survivors and determinants of work disability

Results of the univariate analyses, in which the relationship between the independent variables and the level of work disability at 24-month sick leave were tested, are presented in Table 4.1 and 4.2. In the multivariate analyses, all variables that showed a p-value of <0.2 in the univariate analyses (n = 21) were used to build a final multivariate model. The backward stepwise analyses showed associations at a level of $p < 0.1$ for nationality, education, extensive disease, hormone therapy, being free of disease, the physical dimension score (SIP), global health (EORTC-QLQ-C30 score), work demands, and current work ability compared to life time best score (WAI). These nine variables were entered in the hierarchical model in consecutive order as listed above. The last (ninth) step of the hierarchical multivariate analyses is presented in Table 4.3. The Hosmer-Lemeshow test revealed that this model had a good fit ($p = 0.948$). In this final model, we found associations at a level of $p < 0.1$ for nationality, education, hormone therapy, extensive disease, the physical dimension score (SIP), and current work ability compared to life time best score (WAI). Specifically, cancer survivors of non-Dutch nationality were less at risk for work disability than their Dutch counterparts (OR 0.15; CI 0.02-0.95); an

Table 4.1 Characteristics of employed cancer survivors*

Variables	Categories	n (%)	Disability (<80%; ≥80%)	p-value
			n (%); n (%)	
Socio-demographics				
Gender	Male	125 (36)	68 (54); 57 (46)	0.870
	Female	226 (64)	125 (55); 101 (45)	
Age in years	< 52	163 (46)	98 (60); 65 (40)	0.072
	≥ 52	188 (54)	95 (50); 93 (50)	
Marital status	Single	35 (10)	22 (63); 13 (37)	0.413
	Married/living with partner	278 (79)	153 (55); 125 (45)	
	Divorced/widowed	38 (11)	18 (47); 20 (53)	
No. of children	None	90 (26)	55 (61); 35 (39)	0.576
	1	46 (13)	24 (52); 22 (48)	
	2	139 (40)	75 (54); 64 (46)	
	> 2	76 (21)	39 (51); 37 (49)	
Principal wage earner	Yes	193 (55)	109 (56); 84 (44)	0.465
	No	156 (45)	82 (53); 74 (47)	
Nationality	Dutch	340 (97)	184 (54); 156 (46)	0.069
	Non-Dutch	11 (3)	9 (82); 2 (18)	
Education	None/ primary/ lower vocational	91 (26)	49 (54); 42 (46)	0.102
	Secondary school	60 (17)	25 (42); 35 (58)	
	Vocat. education/ upper sec. school	105 (30)	63 (60); 42 (40)	
	Upper vocat. education/ university	94 (27)	56 (60); 38 (40)	
Health determinants				
Tumor type	Mamma	143 (40)	93 (65); 50 (35)	0.024
	Urinary tract	20 (6)	11 (55); 9 (45)	
	Urogenital (m)	11 (3)	5 (46); 6 (54)	
	Urogenital (f)	17 (5)	10 (59); 7 (41)	
	Respiratory tract	24 (7)	6 (25); 18 (75)	
	Digestive system	45 (13)	21 (47); 24 (53)	
	Head and neck	18 (5)	12 (67); 6 (33)	
	Haematological	50 (14)	25 (50); 25 (50)	

Table 4.1 Characteristics of employed cancer survivors* (continued)

Variables	Categories		n (%)	Disability (<80%; ≥80%)	p-value
				n (%); n (%)	
	Central nerve system		10 (3)	4 (40); 6 (60)	
	Other		13 (4)	6 (42); 7 (58)	
Extensive disease	Negative lymph nodes		180 (52)	103 (57); 77 (43)	0.001
	Positive lymph nodes		116 (34)	72 (62); 44 (38)	
	Metastasis		50 (14)	16 (32); 34 (68)	
Treatment modalities	Surgery	yes	242 (69)	141 (58); 101 (42)	0.066
		no	109 (31)	52 (48); 57 (52)	
	Radiotherapy	yes	210 (60)	114 (54); 96 (46)	0.748
		no	141 (40)	79 (56); 62 (44)	
	Chemotherapy	yes	253 (72)	134 (53); 119 (47)	0.221
		no	98 (28)	59 (60); 39 (40)	
	Hormone therapy	yes	107 (30)	69 (65); 38 (35)	0.018
		no	244 (70)	124 (51); 120 (49)	
	Bone marrow transplant	yes	19 (6)	6 (32); 13 (68)	0.035
		no	332 (94)	187 (56); 145 (44)	
	Immunotherapy	yes	31 (9)	18 (58); 13 (42)	0.718
		no	320 (91)	175 (55); 145 (45)	
Being free of disease	Yes		147 (42)	99 (67); 48 (33)	0.000
	No		106 (31)	42 (40); 64 (60)	
	Don't know		94 (27)	48 (51); 46 (49)	
Comorbidity	No. of additional diseases 0		195 (56)	112 (58); 83 (52)	0.324
	No. of additional diseases 1		51 (14)	31 (61); 20 (39)	
	No. of additional diseases 2		52 (15)	25 (48); 27 (52)	
	No. of additional diseases ≥ 3		53 (15)	25 (47); 28 (53)	
Work-related determinants					
Type of job	White collar		102 (29)	59 (58); 43 (52)	0.459
	Civil servant		33 (9)	15 (45); 18 (55)	
	Blue collar		139 (40)	73 (53); 66 (47)	
	Health care worker		77 (22)	46 (60); 31 (40)	
Job tenure in years	≤ 10		173 (49)	97 (56); 76 (44)	0.687
	> 10		178 (51)	96 (54); 82 (46)	

Table 4.1 Characteristics of employed cancer survivors* (continued)

Variables	Categories	n (%)	Disability (<80%; ≥80%)	p-value
			n (%); n (%)	
Working hours a week	≤ 32	177 (50)	90 (51); 87 (49)	0.116
	> 32	174 (50)	103 (59); 71 (41)	
Shift work	Yes	115 (33)	67 (58); 48 (42)	0.371
	No	235 (67)	125 (53); 110 (47)	
Managerial tasks	Yes	70 (20)	41 (59); 29 (41)	0.488
	No	278 (80)	150 (54); 128 (46)	
No. of supervised co-workers	≤ 7	35 (50)	18 (51); 17 (49)	0.225
	> 7	35 (50)	23 (66); 12 (34)	
Work demands	Psychological and physical	168 (48)	93 (55); 75 (45)	0.084
	Psychological	106 (30)	65 (61); 41 (39)	
	Physical	76 (22)	34 (45); 42 (55)	
Company size	No. of employees 1-9	37 (10)	21 (57); 16 (43)	0.379
	No. of employees 10-99	104 (30)	51 (49); 53 (51)	
	No. of employees ≥ 100	208 (60)	119 (57); 89 (43)	
Work ability expectations	Same	40 (17)	36 (90); 4 (10)	0.000
	Increase	79 (35)	64 (81); 15 (19)	
	Decrease	31 (13)	15 (48); 16 (52)	
	Don't know	81 (35)	58 (72); 23 (28)	
Work status	Working	141 (40)	122 (87); 19 (13)	0.000
	Not working	210 (60)	71 (34); 139 (66)	
Actual working hours per week	≤ 20	79 (56)	64 (81); 15 (19)	0.030
	> 20	62 (44)	58 (94); 4 (6)	

*Due to missing data n varies (range: 70–351); p-value: result of Chi-square test, univariate associations between independent variables and work disability.

Table 4.2 Questionnaire scores of employed cancer survivors

Variables	Cut-off value*	n (%)	Disability (<80%; ≥ 80%)	p-value†
			n (%); n (%)	
Physical dimension score (SIP; 0–100)	≤ 3.77‡	179 (51)	129 (72); 50 (28)	0.000
	> 3.77	172 (49)	64 (37); 108 (63)	
Fatigue (FACIT-F; 0–52)	≤ 27§	173 (49)	73 (42); 100 (58)	0.000
	> 27	178 (51)	120 (67); 58 (33)	
Depressive mood (CES-D; 0–60)	≤ 16‖	188 (54)	114 (61); 74 (39)	0.017
	> 16	163 (46)	79 (49); 84 (51)	
Global health (EORTC-QLQ-C30; 0–100)	≤ 58.33¶	160 (46)	61 (38); 99 (62)	0.000
	> 58.33	191 (54)	132 (69); 59 (31)	
Current work ability (WAI; 0–10)	≤ 4**	143 (48)	52 (36); 91 (64)	0.000
	> 4	158 (52)	131 (83); 27 (17)	
Physical demands (WAI; 0–5)	≤ 3††	142 (62)	97 (68); 45 (32)	0.003
	> 3	86 (38)	74 (86); 12 (14)	
Psychological demands (WAI; 0–5)	≤ 3‡‡	121 (52)	83 (69); 38 (31)	0.021
	> 3	110 (48)	90 (82); 20 (18)	

* Cut-off value = median (except for CES-D; the predetermined cut-off point is used here); † Result of Chi-square test; Range as reported by participants: ‡ 0-79.83; § 0-52; ‖ 0-57; ¶ 0-100; ** 0-10; †† 1-5; ‡‡ 1-5.

education at the level of secondary school (OR 4.80; CI 1.72-13.42) and vocational education/upper secondary school (OR 2.78; CI 1.16-6.69) were both associated with an increased risk for work disability when compared to the lowest educational category. Further, receiving hormone therapy (OR 2.20; CI 1.08-4.47), having metastatic disease (OR 4.51; CI 1.65-12.34) and reporting a high level of physical complaints (SIP) (OR 2.62; CI 1.34-5.14) were all associated with an increased risk for work disability. A high score on current work ability compared to life time best (WAI) (OR 0.09; CI 0.04-0.19) was associated with a decreased risk for work disability.

Table 4.3 Multivariate associations between independent variables and work disability in employed cancer survivors

Variables	Categories	Odds Ratio (95%CI)	p-value
Socio-demographics*			
Nationality	Dutch; non-Dutch	0.147 (0.02-0.95)	0.044
Education			0.015
	None/ primary/ lower vocational education	ref.	
	Secondary school	4.80 (1.72-13.42)	0.003
	Vocational education/ upper sec. school	2.78 (1.16-6.69)	0.022
	Upper vocational education/ university	1.68 (0.65-4.38)	0.286
Health determinants*			
Being free of disease			0.358
	Yes	ref.	
	No	1.44 (0.64-3.23)	0.380
	Don't know	1.69 (0.80-3.57)	0.166
Hormone therapy	No; yes	2.20 (1.08-4.47)	0.029
Extensive disease			0.013
	Negative lymph nodes	ref.	
	Positive lymph nodes	1.23 (0.60-2.52)	0.582
	Metastasis	4.51 (1.65-12.34)	0.003
Physical dimension score (SIP; 0–100)	≤ 3.77; > 3.77†	2.62 (1.34-5.14)	0.005
Global health (EORTC-QLQ-C30; 0–100)	≤ 58.33; > 58.33‡	0.83 (0.40-1.70)	0.607
Work-related determinants*			
Work demands			0.109
	Psychological and physical	ref.	
	Psychological	1.04 (0.50-2.19)	0.913
	Physical	2.51 (1.05-6.01)	0.039
Current work ability (WAI; 0–10)	≤ 4; > 4§	0.09 (0.04-0.19)	0.000

*For binairy variables the reference value is listed first; Range as reported by participants: † 0–79.83; ‡ 0–100; § 0–10

DISCUSSION

Main findings

The aim of this study was to identify determinants associated with work disability defined as wage loss related to functional limitations, at 24-month sick leave in cancer survivors. For cancer survivors at 24 months of sick leave, Dutch nationality, higher education, hormone therapy, metastatic disease, a high physical dimension score (SIP) and low current work ability, compared to life time best score (WAI), were associated with an increased risk for work disability.

Interpretation of the findings and comparison with other studies

In this study, we found that higher education (at the level of secondary school and vocational education/upper secondary school) was associated with an increased risk for work disability. This result differs from previous studies, possibly due to the specific legislation applied in the Netherlands, in which work disability not only relates to limitations and loss of functional abilities, but to wage loss as well. As a consequence, if less paid jobs are associated with a low educational level, then it is likely that on assessment of work disability, a low educated cancer survivor suffers only little wage loss. That is, a low educated cancer survivor still able to work and earn a major part of the previous income is less likely to be granted a disability benefit. The mechanism involved could also relate to the presence of disease induced disabilities and limitations, making it harder to meet the cognitive job demands of the better educated white collar workers. As a consequence, higher educated white collar workers face wage loss, as only less complex and consequently less paid jobs meet their remaining abilities. The suggested mechanism mentioned above agrees with the findings of previous studies, which have reported long-term negative effects of diagnosis and treatment on the ability to memorize, concentrate, direct attention and solve problems (35-37). The results of previous studies indicate that in cancer survivors a low educational level is negatively associated with work participation. This in turn calls for a policy in order to support these workers in their vocational rehabilitation.

We also found that workers of non-Dutch nationality had a decreased risk for work disability. This finding must be interpreted with caution and may be due to coincidence, considering the small number of these workers in our study (n = 11).

Also, we found that receiving hormone therapy was associated with an increased risk for work disability. In breast cancer survivors, this could be due to the occurrence of treatment induced menopausal symptoms, resulting from hormone therapy, that may have a negative impact on cognitive tasks and/or social and emotional aspects of work ability (38). Our findings indicate that side effects of hormone therapy should not be underestimated and suggest that risk for work disability at 24-month sick leave may be reduced if at the start of hormone therapy attention is given to possible side effects of treatment. That is, job and workplace accommodations and offering alternative tasks may support those suffering from side effects of hormone therapy and may facilitate work participation.

Cancer survivors with metastatic disease had an increased risk for work disability. This finding concurs with previous studies that describe the negative relationship between the extensiveness/burden of disease and work ability (39-42). Metastatic disease and a related poor health condition, due to symptoms such as fatigue, combined with negative side-effects of ongoing treatment may limit functional abilities. Symptoms associated with metastatic disease may add up to such an extent that even activities of daily living are difficult to meet and work participation is not possible (43).

Related to the SIP, we found that as the number of limitations in the physical domain of the SIP increases, the risk for work disability increases as well. Our finding concurs with the results of a previous study on cancer survivors (mixed diagnoses) and work disability, which indicated that survivors were leaving the labour force or were functioning less fully at work than before becoming ill (44). In this study, the strongest predictors of work disability were physical dysfunction, measured by the SIP, and disease stage.

Finally, in our sample of cancer survivors, a high score on work ability (WAI current) was associated with a reduced risk for work disability. This finding agrees with the results of a previous study in which work ability assessed at six months sick leave (using the WAI) strongly predicted RTW at 18 months (25). Therefore,

considering our findings, it is possible that during sustained sick leave, measurement of self-assessed work ability at fixed intervals may also be helpful to identify cancer survivors at risk for work disability after a period of 24-month sick leave.

Strengths and limitations

A strength of our study is that the sample was drawn from the entire Dutch working population. Another strength is that the primary outcome of the study was not self-reported but based on the assessment by an independent insurance physician and a labour expert, following uniform guidelines, based on national legislation being practised at all SSA offices nationwide. This warrants a uniform procedure by which work disability is judged. However, in assessing functional abilities of workers, insurance physicians use a standardized List of Functional Abilities (LFA), which is a non-validated instrument (45). Also, a previous study on work disability assessments found small to moderate systematic variations in the outcome of work disability assessments related to inter-doctor variations, which can be considered a limitation of the present study (46). Another limitation of the study is its cross-sectional design, which makes it impossible to disclose causal relationships. Also, the study results relate to Dutch social security legislation, in which functional limitations and wage loss define the level of work disability. This impedes the generalisation to workers in other countries.

Practical implications

Work participation of cancer survivors may be enhanced if factors hindering this process are identified and open to change or otherwise given attention in a supportive way. This study identified six factors associated with work disability of employed cancer survivors at 24-month sick leave. The association of nationality with work disability needs further clarification, considering the small number of respondents in our study of non-Dutch nationality. For future studies, a policy to sample a sufficient number of workers of non-Dutch nationality is advised. The level of former education may also help to identify sick listed workers at risk for work disability and, though educational level may not be changed easily, vocational training and courses that focus on acquiring new skills may support sick listed cancer

survivors and enhance their work participation. Caregivers involved in vocational rehabilitation must be aware of possible long-term impact of hormone therapy on work disability, encourage cancer survivors to reveal and discuss possible side effects of hormone therapy and advise measures to cope with these, preferably at the start of therapy. The presence of metastatic disease is a factor unlikely to change, but to caregivers involved, this aspect may serve as a warning sign and draw attention to individuals at risk for work disability. Likewise, monitoring of physical limitations during prolonged sick leave may help to identify those at risk for work disability. In cancer survivors apt to rehabilitation, these limitations could possibly diminish with the use of tailored interventions that may reduce the risk for work disability. The data suggest that, considering the results of a previous study on repeated work ability scores (25), monitoring self-assessed work ability scores during sustained sick leave, may support the identification of cancer survivors at risk for work disability at 24-month sick leave. For a part, our results may also apply to cancer survivors abroad. Therefore, in the European context, further research on long term effects of hormone therapy, the survey of physical limitations and use of self-assessed work ability in identifying cancer survivors at risk for work disability, is suggested.

Conclusions

The results of the current study may serve as a starting point to investigate the course of work disability beyond the 24-month sick leave term. In order to enhance work participation of cancer survivors beyond this term, prospective data on work disability are required and called for.

Competing interests

PvM is employed by the Dutch Social Security Agency. For the remaining authors, no conflicts of interest were declared.

Authors' contributions

All authors were involved in designing the study. KBG and PvM collected and analysed the data. All authors reviewed the data and were involved in final analysis

and conclusions. PvM and SD wrote the first draft of the manuscript to which all authors subsequently contributed. All authors read and approved the final manuscript.

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5

Predictors for fatigue and work ability in cancer survivors on long-term sick leave

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Submitted

ABSTRACT

Over time, the number of cancer survivors of working age has grown. Workers diagnosed with cancer are at risk for job loss and/or work disability, e.g., due to fatigue or poor work ability. The aim of this study is to identify predictors related to fatigue and work ability in cancer survivors on long-term sick leave. Addressing these predictors may support work disability assessments. Participants, included in this longitudinal cohort study, were between 18 and 64 years of age, diagnosed with cancer and applied for a work disability benefit. Questionnaire data and register data of the Dutch Social Security Agency were used. Univariate and multivariate linear regression analyses were applied to identify predictors. Fatigue was predicted by being divorced or widowed (B=-2.82), having received chemotherapy (B=2.20), sickness impact (B=-0.34), having depressive symptoms (B=-0.29), fatigue at baseline (B=0.31), and working in health care (B=-2.31). Work ability was predicted by being principal wage earner (B=-0.64), having received chemotherapy (B=0.80), being free of disease (B=-0.48), sickness impact (B=-0.05), global health (B=0.02), work ability at baseline (B=0.43), and wage loss (B=-0.61). Socio-demographics, health- and work-related factors are associated with fatigue and work ability in cancer survivors on long-term sick leave. These factors may be used in assessing work disability of cancer survivors. If addressed, they may enhance uniformity in work disability assessments.

BACKGROUND

In Europe, the incidence of cancer in the adult population has increased and exceeded 3.45 million in 2012 (1). The number of cancer survivors of working age has grown as well, as survival rates have increased due to implemented screening programs and better treatment modalities. However, workers diagnosed with cancer face difficulties in return to work (RTW) and are at risk for job loss and/or work disability (2).

In 2013, in the Netherlands, over 4,200 workers diagnosed with cancer had to apply for a work disability grant, of whom 65% received a complete disability benefit, meaning a wage loss of ≥80% of former wages earned. Cancer survivors who need to apply for a work disability benefit not only face job loss and unemployment, their chances for re-employment are also reduced (3). Simultaneously, they have to compete with healthy co-workers and are at risk for employer discrimination, i.e., their medical history is sometimes seen as a potential risk for recurrent or prolonged sick leave (4). Work disability in the Netherlands is assessed by insurance physicians (IPs) working for the Social Security Agency (SSA). They decide on functional abilities present and assess sustainability of limitations. IPs have to make a judgment on information provided by the patient and/or third parties, e.g., a clinical specialist or an occupational physician. IPs usually judge both medical and non-medical factors, but may find it hard to assess symptoms, like pain or fatigue (5).

In cancer survivors, Cancer Related Fatigue (CRF) is a common complaint and different from fatigue as experienced after strenuous activities, normally alleviated by sleep or taking rest. The prevalence of CRF varies, seems related to the stage and nature of the disease, and to treatment modalities (7). It is often experienced as a distressing symptom with extensive impact on all aspects of daily functioning, including parenting, social life, and work (6). Since work may offer cancer survivors a sense of control, allows social contacts, helps to overcome negative side-effects, improves self-confidence and has financial benefits, work ability needs to be addressed as well, next to fatigue.

Therefore, the aim of this study is to identify predictive factors related to fatigue and to work ability in cancer survivors at 24-month sick leave. It may help the IPs to identify those at risk for a complete and permanent work disability, and to identify those likely to recover and to RTW at later stage.

METHODS

Design

This is a longitudinal study of sick-listed workers diagnosed with cancer, registered at the Dutch Social Security Agency (SSA). Employed sick-listed workers were eligible for the study if they approached the maximum term of 24-month sick leave and applied for a disability benefit. The period of inclusion lasted from July 2011 until February 2012. Data were gathered at 24-month sick leave (baseline; T0) and at follow-up, 12 months later (T1). We used questionnaire data, which were linked to data of the SSA. The Medical Ethics Committee of the VU University Medical Center approved the study.

Study population

Participants were between 18 and 64 years of age, had a first diagnosis of cancer and approached a 24-month sick leave term. Participants were excluded if they received active chemotherapy and/or radiotherapy at baseline and if they applied for a revision of a previous assessment. Also, self-employed or workers employed in a sheltered workplace were excluded.

Study procedure

Potentially eligible participants of our study were selected at the SSA. Based on social security numbers and corresponding documents, we selected the sick-listed employed workers with a diagnosis of cancer and at baseline eligible participants received a questionnaire. On receipt, both at baseline and follow-up, questionnaires were checked for completeness and non-respondents were sent a reminder after two weeks (8).

Variables

The independent and dependent variables were gathered by questionnaires as used in previous studies on cancer survivorship, fatigue and work ability (9-13), and from SSA register data.

Dependent variables

The primary outcome variables in this study were the level of fatigue at one-year follow-up, measured by using the Functional Assessment of Chronic Illness-Fatigue scale (FACIT-F) (14), and current work ability compared to life time best work ability, at one-year follow-up, measured with the first question of the Work Ability Index (WAI) (15).

INDEPENDENT VARIABLES

Socio-demographics

The following socio-demographic characteristics were gathered: age, gender, marital status, number of children, principal wage earner, educational level, and nationality.

Health determinants

The following health characteristics were assessed: tumor type, extensive disease, being free of disease, and comorbidity. Physical symptom burden was measured using the physical dimension score of the Sickness Impact Profile (SIP) (16). Fatigue, depressive mood, coping, and global health were measured using the FACIT-F, the Center for Epidemiologic Studies Depression Scale (CES-D) (17), the Utrecht Coping Scale (UCL) (18), and the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30 (EORTC-QLQ-C30) (19), respectively.

Work-related determinants

The following characteristics of the previous job held were determined: job type, job tenure, working hours, shift work, work demands, company size, and managerial tasks. Also, present work status and current work ability were assessed.

SSA data

The following data were retrieved from the SSA: the level of work disability, expressed by wage loss in percentage of former wage, and the followed vocational rehabilitation trajectory during sick leave.

STATISTICAL ANALYSIS

Both univariate and multivariate methods were used to identify predictors of fatigue and work ability. A simple bivariate linear regression was used to test which variables were associated with the dependent variables at one-year follow-up. For these tests, a cut-off for p-values of 0.20 was used. Next, the remaining significant independent variables of the univariate analyses were tested for multi-collinearity and accepted in a multivariate linear model if correlation coefficients were ≥ -0.7 and ≤ 0.7 (20). For each category of variables, i.e., socio-demographics, health determinants, work-related determinants and SSA data, separate multivariate models were built, using a backward stepwise method. For all multivariate analyses, a cut-off for p-values of 0.10 was used.

Further, using the results of the separate multivariate models for each dependent variable, a final model was built in which variables were added in consecutive order, thereby controlling in a hierarchical way for socio-demographics, health determinants, work-related determinants and SSA data. All analyses were performed using SPSS 20 (21).

RESULTS

Characteristics of the study population

During the inclusion period, 13,023 employed workers applied for a work disability benefit, of whom 1,307 had cancer. At follow-up, 336 valid cases remained in the study (see Figure 5.1). The mean age was 51.2 years (SD 7.4 years) and 32% was men. The variables that tested significantly in univariate analyses are presented in Table 5.1.

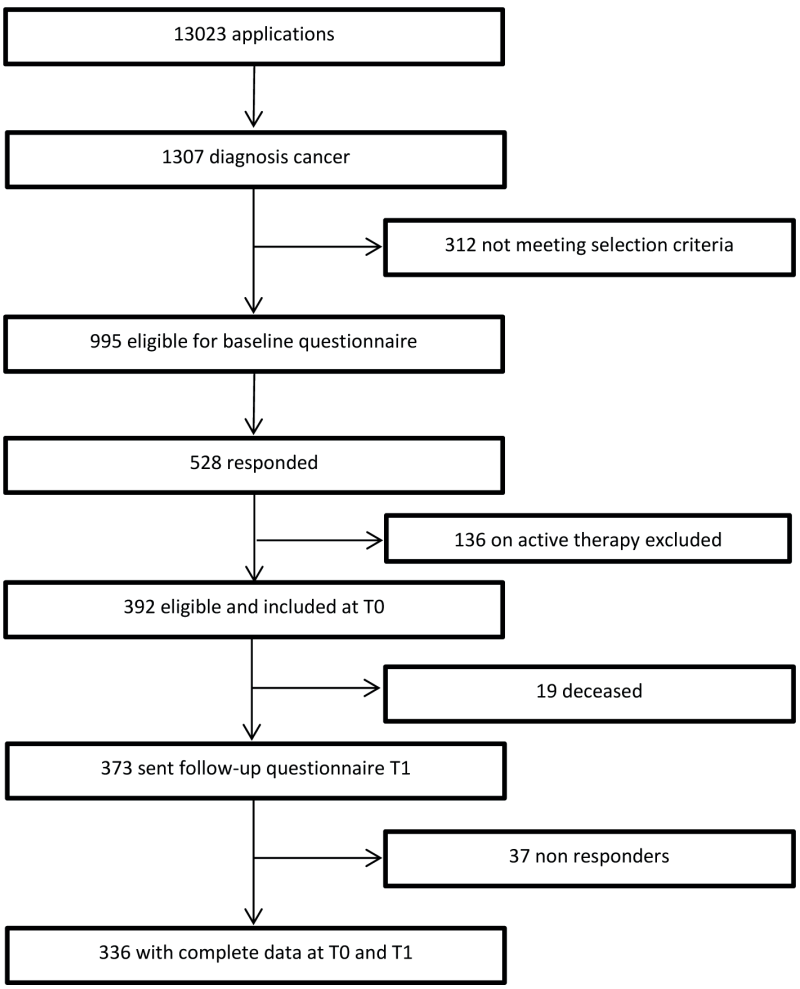

Figure 5.1

Table 5.1 Characteristics of employed cancer survivors at baseline and univariate associations with fatigue and work ability at follow-up

Variables *	Categories		Fatigue		Work ability	
Socio-demographics		**Mean (SD)**	**B †**	**p-value**	**B †**	**p-value**
Age (years)		51.2 (7.38)	0.11	0.18	-0.05	0.02
		N (%)	**B †**	**p-value**	**B †**	**p-value**
Gender	Male (ref)	106 (32)				
	Female	230 (68)			0.80	0.01
Marital status	Married/living with partner (ref)	267 (80)				
	Single	35 (10)	2.65	0.19	0.35	0.48
	Divorced/widowed	34 (10)	-6.27	0.00	-0.86	0.09
Number of children	None (ref)	87 (26)				
	1	44 (13)	-2.89	0.16		
	2	135 (40)	0.81	0.60		
	>2	70 (21)	-1.83	0.30		
Principal wage earner	Yes	175 (52)	-1.68	0.17	-0.80	0.00
	No (ref)	159 (48)				
Education	None/primary school/lower vocational education (ref)	84 (25)				
	Secondary school	51 (15)			0.80	0.09
	Vocational education/upper secondary school	103 (31)			1.35	0.01
	Upper vocational education/university	97 (29)			1.05	0.00
Health determinants						
Tumor type ‡	Mamma (ref)	154 (46)				
	Urinary tract	21(6)	-2.80	0.28	-2.00	0.00
	Urogenital (m)	9 (3)	-0.67	0.86	-1.96	0.04
	Urogenital (f)	13 (4)	-1.57	0.62	-0.57	0.46
	Respiratory tract	17 (5)	-4.22	0.14	-1.77	0.01
	Digestive system	39 (12)	1.51	0.45	-0.34	0.48
	Head and Neck	13 (4)	2.81	0.38	-0.18	0.81
	Heamatological	48 (14)	0.08	0.96	-0.40	0.37

Table 5.1 Characteristics of employed cancer survivors at baseline and univariate associations with fatigue and work ability at follow-up (continued)

Variables *	Categories			Fatigue		Work ability	
			N (%)	**B †**	**p-value**	**B †**	**p-value**
	Central nerve system		9 (3)	-2.12	0.58	-1.11	0.22
	Other		13 (4)	-9.24	0.00	-2.11	0.00
Extensive disease	Negative lymph nodes (ref)		176 (53)				
	Positive lymph nodes		113 (34)			0.56	0.09
	Metastasis		42 (13)			-0.28	0.55
Treatment modalities	Surgery	Yes	242 (72)			0.49	0.14
		No (ref)	94 (28)				
	Chemo-therapy	Yes	245 (73)	3.60	0.01	0.98	0.00
		No (ref)	91 (27)				
	Hormone therapy	Yes	107 (32)			0.93	0.00
		No (ref)	229 (68)				
Being free of disease	Yes (ref)		153 (46)				
	No		92 (28)	-5.08	0.00	-1.57	0.00
	Don't know		88 (26)	-3.17	0.00	-1.33	0.00
Comorbidity	Yes		150 (45)	-4.38	0.00	-0.53	0.08
	No (ref)		186 (55)				
			Mean (SD)	**B †**	**p-value**	**B †**	**p-value**
Physical dimension score (SIP; 0-100)			6.33 (7.84)	-0.70	0.00	-0.16	0.00
Depressive mood (CES-D;0-60)			16.11 (10.96)	-0.62	0.00	-0.10	0.00
Coping (UCLActive tackling;7-28)			17.72 (3.84)	0.48	0.00	0.07	0.08
Coping (UCLAvoidance;8-32)			15.94 (3.24)	-0.45	0.02	-0.08	0.07
Coping (UCLSeeking social support;6-24)			13.22 (3.49)	0.25	0.16	0.06	0.19
Coping (UCLPassive reacting;7-28)			11.95 (3.74)	-1.42	0.00	-0.22	0.00

Table 5.1 Characteristics of employed cancer survivors at baseline and univariate associations with fatigue and work ability at follow-up (continued)

Variables *	Categories		Fatigue		Work ability	
		Mean (SD)	**B †**	**p-value**	**B †**	**p-value**
Coping (UCLExpression of emotion;3-12)		5.36 (1.68)	-1.42	0.00	-0.13	0.16
Global health (EORTC-QLQ-C30:0-100)		57.60 (20.62)	0.28	0.00	0.07	0.00
Fatigue (FACIT-F;0-52) ‡		27.68 (11.01)	0.66	0.00	0.12	0.00
Work-related determinants		**N (%)**	**B †**	**p-value**	**B †**	**p-value**
Type of job	White collar (ref)	96 (29)				
	Civil servant	33 (10)	-2.99	0.18	-1.44	0.01
	Blue collar	127 (37)	-1.65	0.28	-0.88	0.02
	Health care worker	80 (24)	-4.18	0.01	-0.69	0.10
Shift work	Yes	231 (69)	-2.19	0.10		
	No (ref)	104 (31)				
Work demands	Psychological and physical (ref)	152 (45)				
	Psychological	106 (32)	2.52	0.05	0.64	0.04
	Physical	77 (23)	-1.17	0.57	-0.89	0.08
Managerial tasks	Yes	66 (20)	2.16	0.16		
	No (ref)	267 (80)				
Work status	Working (ref)	141(42)				
	Not working	195 (58)	-4.36	0.00	-1.83	0.00
		Mean (SD)	**B †**	**p-value**	**B †**	**p-value**
Work ability (WAI;0-10)		4.84 (2.72)	1.94	0.00	0.68	0.00
SSA data§		**N**	**B †**	**p-value**	**B †**	**p-value**
Wage loss	<80% (ref)	202 (60)				
	≥ 80%	134 (40)	-4.15	0.00	-2.37	0.00
Vocational rehabilitation	In own company (ref)	259 (77)				
	Outside own company	28 (8)	-0.33	0.88	-0.73	0.16
	None	49 (15)	-8.12	0.00	-2.34	0.00

Variables that tested significant at fatigue or work ability at a cut of p-value of 0.20 are depicted; † Unstandardized coefficients; ‡ Synonym of FACT-F; § Social Security Agency.

For both dependent variables, a number of variables were not significant at cut-off p-value of 0.20 and left out of further analysis (data not shown). Also, as a limited number of tumour types tested significantly in univariate analysis for both outcome variables, the variable tumour type was left out of multivariate analysis. Table 5.2 depicts the results of the multivariate analysis of the models related to the grouping of independent variables, i.e., socio-demographics, health determinants, work-related determinants, and SSA data.

Table 5.2 Multivariate associations of grouped variables at baseline associated with fatigue and work ability at follow-up

Models and variables	Categories		Fatigue		Work ability	
			B (beta)*	**p-value**	**B (beta)***	**p-value**
Model of Socio-demographics			N = 332; R^2 = 5		N = 331; R^2 = 6	
Marital status	Married/living with partner (ref)					
	Single		3.33 (0.09)	0.10		
	Divorced/widowed		-6.11 (-0.17)	0.00		
Number of children	None (ref)					
	1					
	2		2.23 (0.10)	0.08		
	>2					
Principal wage earner	Yes				-0.77 (-0.14)	0.01
	No (ref)					
Education	None/primary/lower vocational (ref)					
	Secondary school				0.78 (0.10)	0.10
	Vocational education/upper secondary school				1.34 (0.23)	0.00
	Upper vocational education/university				1.01 (0.17)	0.01
Model of Health determinants			N = 326; R^2 = 51		N = 324; R^2 = 37	
Treatment modalities	Chemotherapy	Yes	2.05 (0.08)	0.04	0.57 (0.09)	0.04
		No (ref)				
	Hormone therapy	Yes			0.64 (0.11)	0.02
		No (ref)				
Being free of disease	Yes (ref)					
	No					
	Don't know				-0.74 (-0.12)	0.00

Table 5.2 Multivariate associations of grouped variables at baseline associated with fatigue and work ability at follow-up (continued)

Models and variables	Categories	Fatigue		Work ability	
		B (beta)*	**p-value**	**B (beta)***	**p-value**
Physical dimension score (SIP; 0-100)		-0.34 (-0.24)	0.00	-0.09 (-0.25)	0.00
Depressive mood (CES-D; (0-60)		-0.31 (-0.30)	0.00		
Global health (EORTC-QLQ-C30; 0-100)				0.03 (0.23)	0.00
Fatigue (FACIT-F; 0-52)†		0.31 (0.30)	0.00	0.05 (0.19)	0.00
Model of Work-related determinants		N = 324; R^2 = 20		N = 327; R^2 = 39	
Type of job	White collar (ref)				
	Civil servant				
	Blue collar				
	Health care worker	-3.42 (-0.13)	0.01		
Work ability (WAI; 0-10)		1.96 (0.44)	0.00	0.68 (0.62)	0.00
Model of SSA data‡		N= 334; R^2 = 7		N= 332; R^2 = 20	
Wage loss	<80% (ref)				
	≥80%	-2.14 (-0.09)	0.10	-2.05 (-0.37)	0.00
Vocational rehabilitation	In own company (ref)				
	Outside own company	-0.32 (-0.01)	0.88	-0.72 (-0.07)	0.14
	None	-6.92 (-0.22)	0.00	-1.15 (-0.15)	0.01

* B: Unstandardized coefficients; beta: standardized coefficients; † Synonym of FACT-F ; ‡ Social Security Agency.

Predictors for fatigue and work ability in cancer survivors

The level of fatigue was predicted by being divorced or widowed (B=-2.82), having received chemotherapy (B=2.20), sickness impact (B=-0.34), having depressive symptoms (B=-0.29), fatigue at baseline (B=0.31), and health care job (B=-2.31). Work ability was predicted by being principal wage earner (B=-0.64), having received chemotherapy (B=0.80), being free of disease (B=-0.48), sickness impact

Table 5.3 Hierarchical multivariate model of variables at baseline associated with fatigue and work ability at follow-up

Variables	Categories		Fatigue		WAI	
			B (beta)*	**p-value**	**B (beta)***	**p-value**
			N = 325; R^2 = 53		N= 322; R^2 = 50	
Marital status	Married/living with partner (ref)					
	Single					
	Divorced/widowed		-2.82 (-0.08)	0.05		
Principal wage earner	Yes				-0.64 (-0.12)	0.00
	No (ref)					
Treatment modalities	Chemotherapy	Yes	2.20 (0.08)	0.03	0.80 (0.13)	0.00
		No (ref)				
Being free of disease	Yes (ref)					
	No					
	Don't know				-0.48 (-0.08)	0.06
Physical dimension score (SIP; 0-100)			-0.34 (-0.24)	0.00	-0.05 (-0.16)	0.00
Depressive mood (CES-D; 0-60)			-0.29 (-0.28)	0.00		
Fatigue (FACIT-F; 0-52)†			0.31 (0.31)	0.00		
Global health (EORTC-QLQ-C30; 0-100)					0.02 (0.15)	0.00
Work ability (WAI; 0-10)					0.43 (0.40)	0.00
Type of job	White collar (ref)					
	Civil servant					
	Blue collar					
	Health care worker		-2.31 (-0.08)	0.03		
Wage loss	<80% (ref)					
	≥80%				-0.61 (-0.11)	0.02

* B: Unstandardized coefficients; beta: standardized coefficients; † Synonym of FACT-F.

(B=-0.05), global health (B=0.02), work ability at baseline (B=0.43), and wage loss (B=-0.61) (see Table 5.3).

DISCUSSION

Main findings

The aim of this study was to identify predictors of fatigue and work ability in cancer survivors on long-term sick leave. The main findings are that chemotherapy treatment is associated with a decrease of fatigue and an increase of work ability, whereas having more physical complaints, i.e., a higher sickness impact, is associated with an increase of fatigue and a decrease of work ability.

Interpretation of the findings

In this study, two outcomes were examined, i.e., fatigue and work ability, as these topics are very relevant in assessing work disability claims of cancer survivors.

Partner support, i.e., being married or living with a partner, was associated with a decrease in fatigue. As a previous study by Li et al. (2013) described spousal caring to have a positive effect on psychological distress in cancer survivors, it is possible that fatigue is reduced by partner care as well (22).

The long-term course of fatigue and its surprising association with chemotherapy, i.e., survivors who were treated with chemotherapy reported lower levels of fatigue, seems unclear. That is, in a recent population-based study in long-term cancer survivors, receiving chemotherapy was found to be associated with higher fatigue levels (23). However, in a previous longitudinal study in breast cancer survivors, no relationship between adjuvant therapy and fatigue was found (24). Close to 75% of our respondents received chemotherapy, these respondents reported lower levels of fatigue at baseline compared to respondents without chemotherapy. We assume this reflects a selection among previously sick-listed cancer survivors not having received chemotherapy. Namely, in these cancer survivors (without chemotherapy), the majority of those with low levels of fatigue have already returned to work, and therefore are not in need to apply for a work disability benefit at24 months of sick leave. Consequently, among those who did not receive chemotherapy, only those with a more unfavourable prognosis related to RTW (i.e., with high fatigue levels) might be represented in the cohort. They have a higher risk of long-term sick leave, and consequently do need to apply for

a work disability benefit. Among the survivors who did receive chemotherapy this selection might be less obvious. That is, chemotherapy treatment usually has a prolonged course that might hinder early RTW.

Cancer survivors often face long lasting limitations in physical and psychological functioning due to fatigue and/or distress, that are connected with the disease and/or treatment modalities (25;26). Likewise, our study showed that cancer survivors, reporting more physical limitations at baseline, had higher levels of fatigue at follow-up. Furthermore, the presence of more depressive symptoms at baseline was associated with increased fatigue at follow-up. This indicates that cancer survivors may benefit from accurate assessment of depressive symptoms and timely treatment of a depressive disorder. Our results, that concur with results of previous studies (27-31), indicate that in cancer survivors on long-term sick leave depressive symptoms remain an important predictor associated with fatigue beyond two years of sick leave.

Predictors associated with fatigue, i.e., physical, psychological, social, cognitive and behavioural factors, have been reported in several studies (32-34). In our study, the strongest predictor related to fatigue at follow-up was the level of fatigue at baseline. This means that by timely measuring fatigue, patients at risk for long-term fatigue can be identified.

Results also showed that a job in health care, compared to white collar work, was associated with increased fatigue. It is possible that this relates to job demands, i.e., physical or psychological demands, that are less amendable to adaptation in health care jobs. Also, in health care, irregular working hours and shift work could act as a barrier to RTW. It is likely that office workers compared to health care workers have more possibilities in adjusting their worksite (35).

Related to work ability, findings showed that principal wage earners were at risk for a decrease in work ability, i.e., compared to non-principal wage earners their outcome on work ability was less positive. A possible explanation is that principal wage earners experience more distress and find it harder to adapt to previous job demands and (full time) working hours.

Chemotherapy treatment was also associated with an increase of work ability. Probably this relates to the fact that in respondents having completed

chemotherapy, work ability may initially be perceived as low, due to side-effects. However, as time passes by and negative side-effects of treatment lessen, work ability increases. Next to this, as with fatigue, in cancer survivors not subjected to chemotherapy, our finding could be associated with a selection process before inclusion in the study. That is, previously sick-listed cancer survivors, not having received chemotherapy and with better work ability, have already returned to work, while cancer survivors not having received chemotherapy with lower work ability remain on sick leave until the 24-month term is reached.

Just as found for fatigue, cancer survivors who experienced a higher level of physical limitations at baseline, were also at risk for a decrease in work ability. This might be related to physical limitations interfering with functional abilities that cancer survivors use as resource and rely on in meeting job demands. This finding agrees with the results of a previous study in which physical limitations and work-related problems were directly related to lower levels of work ability (36).

Furthermore, a better global health status was associated with an increase of work ability, which also has been reported by other studies (37;38). Finally, cancer survivors with a wage loss >80% at baseline were found to face a lower level of work ability at follow-up, compared to those with a wage loss ≤80%. This finding shows that extensive loss of functional abilities, as expressed by wage loss, might have a poor long-term outcome related to work ability.

Strenghts and limitations

A strength of our study is that it covers the entire Dutch population of employed workers registered at the SSA. Also, the cohort has a heterogeneous character related to tumour types, age and education. As far as we know, this is the first study targeting predictors in cancer survivors on long-term sick leave that apply for a work disability benefit, using a longitudinal design. In the analyses, variables were grouped and a stepwise hierarchical analysis was performed, thereby the strongest predictors were identified.

A limitation of the study is that the data were largely self-reported. However, next to objective SSA data, several validated questionnaires were used. Another limitation is the fact that the sample had an uneven distribution related to gender

and diagnosis; almost two third of the respondents was female and half of the total population reported a diagnosis of breast cancer. Also, the distribution of wage loss differed from historical data. Probably, in our cohort, predominantly cancer survivors with better functional abilities who are able to participate in work were considered. Finally, a selection bias towards cancer survivors with a health condition that impedes RTW is likely to play a role. We may assume that employed cancer survivors who experience a good health condition after finishing treatment, for a large part succeed in RTW within 24 months of sick leave. They do not have to apply for a work disability benefit and therefore are not represented in our cohort.

Practical implications

In the assessment of work disability claims, the identification of predictors may be supportive to the stakeholders involved. It may enhance an uniform way of assessment, which is to the benefit of cancer survivors applying for a work disability benefit. It could help to identify patients that may expect further improvement of abilities and further reduction of symptoms, such as fatigue, which is a very common complaint in cancer survivors.

Conclusion

In this study, socio-demographics, health- and work-related factors proved to be associated with fatigue and work ability in cancer survivors on long-term sick leave, applying for a disability benefit. If predictors are identified at early stage and consequently addressed, uniformity in assessing work disability claims of cancer survivors on long-term sick leave may be enhanced.

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6

The mediating role of coping between self-reported health complaints and functional limitations, self-assessed work ability and work status of long-term sick-listed cancer survivors

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Submitted

ABSTRACT

Our purpose was to investigate the possible mediating role of active and passive coping between self-reported health complaints and functional limitations, as assessed by an insurance physician (IP), self-assessed work ability, and work status in cancer survivors on long-term sick leave. Validated questionnaires were used for self-reported health complaints, work ability and work status. The functional limitations of the respondents were transformed into scales for mental and physical limitations, and limitations in working hours. Using Lisrel, we constructed a model with coping in a mediating role. Active coping mediated between fewer self-reported physical limitations, more depressive symptoms, better cognitive functioning and more fatigue on the one hand, and more physical limitations and limitations in working hours on the other hand. Passive coping played no mediating role and was associated with more self-reported depressive symptoms only. More functional limitations were associated with lower self-assessed work ability of cancer survivors, and with not being at work, whereas higher self-assessed work ability was associated with being at work. Regarding the role of active and passive coping strategies in cancer survivors on long-term sick leave, more longitudinal research is needed to confirm causality.

BACKGROUND

In the previous years, the incidence and prevalence of cancer have increased. As a result of new developments in early detection and treatment modalities, the survival rate has increased as well (1-4). Because of this, nowadays, cancer can be more considered a chronic condition and less as a terminal illness (2). However, recovery from cancer and surviving cancer may come with complaints, as a result of diagnosis and treatment, that are long-term or even permanent (5). Long-term complaints of cancer survivors, such as fatigue, depressive symptoms, and physical complaints, may influence daily functioning, including (potential) work participation of all workers, either self-employed, employed, or temporarily unemployed (6). Also, specifically in cancer survivors with jobs characterised by a cognitive or emotional workload, fatigue can have a negative impact on mental capacity. As a result, they can experience problems on tasks that demand long-term concentration and attention (7). Further, physical complaints can play a negative role when physical workload is substantial. Moreover, a combination of cognitive and physical job demands can make return to work (RTW) even more difficult.

RTW of cancer survivors is important for the individual and society. From the societal perspective, it is important to reduce avoidable work incapacity, which may lead to economic loss. For the individual, loss of work often means financial loss (8). Also, participation in work is important for the identity, as it provides a social connection and relates to health perception. Furthermore, RTW after cancer treatment enables a person to regain a sense of normality and control (9;10). It is a symbol of recovery, raises the self-esteem and can help to overcome the negative effects of treatment (9;11). Being able to work is viewed by persons suffering from an illness as the third most important aspect of quality of life, after the ability to get out and to engage in social activities (12;13).

In the Netherlands, as sick-listed workers approach a two-year sick leave term, their functional limitations are assessed by an insurance physician (IP), working for the Dutch Social Security Agency (SSA) (14). In 2013, over 4200 workers diagnosed with cancer applied for a work disability benefit. Of these, almost 1600 were granted a complete and permanent work disability benefit. Another 1100 were

granted a complete work disability benefit on a temporary basis. It is expected that in future the number of claims of cancer survivors will increase, since both the retirement age and the mean age of workers will increase (15;16). Therefore, research on vocational rehabilitation of cancer survivors calls for ongoing attention.

Previous studies have reported an association between self-assessed work ability and RTW (17;18). Consequently, the way cancer survivors handle their disease, treatment and side effects, possible loss of control and changing roles could be related to coping behavior and strategies. An influential theory in understanding adjustment to stressors, such as cancer, is Lazarus and Folkman's Stress and Coping model (19;20). In this model, coping is defined in terms of strategies to handle demands that go beyond perceived resources. The model states that the reaction to a potential stressor is mediated by the individual's cognitive appraisals and consequently direct the coping response. According to Stanton et al. (21), in cancer survivors, coping strategies are applied in two ways, i.e., for problem solving and managing cancer-related distress. These strategies are usually classified as active or passive (22). Active coping strategies refer to cognitive or behavioral efforts to alleviate stressful circumstances, and passive coping strategies refer to being focused on the emotional response to a problem. Alternatively, coping strategies have been defined as either approach coping (strategies directed towards a threat) or avoidant coping (strategies that deflect from a threat) (23).

Several studies in cancer survivors report positive associations of active coping and negative associations of passive coping with health indicators (24;25). In outpatients with metastatic colorectal cancer, Unger et al. (24) found that internal health beliefs, considered as a form of active coping, were positively associated with health-related quality of life. Opposite to this, passive coping strategies, together with depression and neuroticism, were negatively associated with health-related quality of life. In a meta-analysis, Roesch et al. (23) found that regarding prostate cancer, men who followed an active approach, were better off psychologically and physically than men who were less active, and used more avoidant coping strategies. In a cross-sectional study on coping in breast cancer survivors, Bishop & Warr (25) found that active coping was associated with less disability, while passive coping was associated with greater disability. If the same association applies to coping

strategies and RTW or vocational rehabilitation, RTW of cancer survivors may be enhanced by addressing their coping strategies.

Therefore, the aim of our study was to investigate whether coping plays a mediating role (26;27) in the associations between self-reported health complaints and (a) functional limitations, as assessed by an IP, (b) self-reported work ability and (c) work status. We expected that self-reported health complaints were associated with an active and/or passive coping strategy. Also, we expected that an active and/or passive coping strategy was associated with (a) functional limitations, as assessed by an IP, (b) with self-assessed work ability and (c) with being at work.

METHODS

Study design and procedure

The present study was part of a longitudinal cohort study with a baseline measurement (T0), i.e., at the end of the two years sick leave term, and one year follow-up (T1). The Medical Ethical Commission (MEC) of the VU University Medical Center (VUmc) in Amsterdam (the Netherlands) gave permission for the study under the condition that cancer survivors on active treatment with chemotherapy and/or radiotherapy were excluded. For the present cross-sectional study, we used the baseline measurement of the cohort, for which self-reported questionnaire data were gathered and informed consent was given. Also, data were retrieved from the SSA, including a list of functional limitations, as assessed by an IP.

All cancer survivors (one-third of them was still working) who applied for a work disability benefit at the SSA from July 2011 until January 2012 were screened. They were potentially eligible for participation if they submitted a first application and had a diagnosis of cancer (multiple tumour sites). All potentially eligible participants were sent a questionnaire on receipt of their work disability application. The returned questionnaires were assessed on exclusion criteria, as formulated by the researchers and approved by the MEC.

Measures

According to a previously described method of factor analyses and internal consistency analyses (28-30), the functional limitations of cancer survivors (Functional Ability List; FAL), as assessed and documented by the IPs, were converted into three additive scales: (1) mental limitations (FALM), (2) physical limitations (FALP), and (3) limitations in working hours (FALH). Because the three scales were highly skewed, their values were transformed into ordinal variables with three classes (0 = no limitations, 1 = limitations, 2 = severe limitations).

With the questionnaire, background characteristics, hereafter named exogenous variables, such as socio-demographics, work- and disease-related characteristics were obtained (see table 6.1). The questionnaire also held items related to self-reported health complaints, coping, self-reported work capacity, and work status (hereafter named endogenous variables, see table 6.1). The following self-reported health complaints using validated Dutch versions of questionnaires, were measured:

Table 6.1 Exogenous and endogenous variables

Exogenous variables*	Mean	Med	SD
Age in years	52.4	53.2	7.58
Education (scale 1-5) †	2.99	3.00	0.86
Job hours (scale 1-4) ‡	2.87	3.00	0.93
Job tenure in years	25.7	26.0	10.75
Kind of job exposure (scale 0-3) §	1.75	2.00	0.85
	%		
Nonnative Dutch; yes‖	10.2%		
Temporary contract; yes‖	20.1%		
Shift work; yes‖	30.8%		
Commercial services; yes‖	16.5%		
Comorbidity; yes‖	7.1%		
Breast cancer; yes‖	47.0%		
Radiotherapy; yes‖	61.0%		
Chemotherapy; yes‖	72.3%		
Hormonal therapy; yes‖	34.3%		

Table 6.1 Exogenous and endogenous variables (continued)

Endogenous variables ¶	Mean	Med	SD	Min	Max	Alpha
SIPB (rec) (scale 0-2) **: SIP of body care and movement	0.84	1.00	0.83	0.0	2.0	0.73
SIPA (rec) (scale 0-2) **: SIP of ambulation	0.75	0.50	0.83	0.0	2.0	0.68
QLG: global health	57.09	58.33	20.22	0.0	100.0	0.89
QLP: quality of life of physical functioning	71.84	73.33	16.90	20.0	100.0	0.71
QLR: quality of life of role functioning	49.77	50.00	27.56	0.0	100.0	0.86
QLE: quality of life of emotional functioning	61.83	66.67	28.14	0.0	100.0	0.90
QLC: quality of life of cognitive functioning	59.55	66.67	29.64	0.0	100.0	0.74
QLS: quality of life of social functioning	59.98	66.67	28.85	0.0	100.0	0.79
FACIT-F: fatigue	27.60	27.00	10.97	3.0	52.0	0.87
CES-D: depressive symptoms	17.05	15.00	11.37	0.0	57.0	0.77
WAIC: work ability	4.13	4.00	2.35	0.0	10.0	NA
UCLA: dimension active coping	0.0	-0.03	1.0	-2.86	3.06	NA
UCLP: dimension passive coping	0.0	0.02	1.0	-2.82	2.67	NA
FALM (rec) (scale 0-2) **: mental limitations	0.98	1.00	0.86	0.0	2.0	0.59
FALP (rec) (scale 0-2) **: physical limitations	0.99	1.00	0.81	0.0	2.0	0.65
FALH (rec) (scale 0-2) **: limitations in hours of work	0.88	1.00	0.70	0.0	2.0	0.92
	%					
WORK: having paid work: (yes)	32.0%					

* n=364, med=median, sd=standard deviation; † Education: 1= primary school, 2=lower vocational education, 3=vocational education/upper secondary school, 4=upper vocational education, 5= university; ‡ Job hours (in hours): 1=0 (not working), 2=7-24, 3=25-36, 4=>36; § Kind of job exposure: 0=not applicable, 1=largely psychic, 2=psychic and physical, 3=largely physical; ‖yes is favorable direction; ¶ After imputation, before normalization; n=364; rec=recoded, med=median, sd=standard deviation, min= minimum value, max=maximum value, alpha=Cronbach's alpha, NA=not applicable; UCLA & UCLP: factor scores of the coping measurement model, a high score is more coping; Favorable direction of other variables: for SIPB, SIPA, CES-D, FALM, FALP, FALH: low score; for QLG, QLP, QLR, QLE, QLC, QLS, FACIT-F, WAIC, age, education, job hours, job tenure: high score; for job exposure: more physical.** 0= no limitations, 1=limitations, 2=severe limitations. Model fit parameters of coping measurement model (constructed with the 7 UCL scales): Degrees of Freedom = 6; Normal Theory Weighted Least Squares Chi-Square = 3.932 (p = 0.686); Root Mean Square Error of Approximation (RMSEA) = 0.0; Normed Fit Index (NFI) = 0.993; Standardized Root Mean Square Residual (SRMR) = 0.0184.

- Fatigue (using the Functional Assessment of Chronic Illness Therapy-Fatigue Scale; FACIT-F). The FACIT-F is a 13-item questionnaire (all items scored on a five-point Likert scale) with a range of 0 to 52; a higher score on this scale means less fatigue (31-34).
- Depressive symptoms (using the Center for Epidemiologic Studies Depression Scale; CES-D). The CES-D consists of 20 items with a four-point Likert response scale. The scores range from 0 to 60; a score ≥ 16 is an indicator of probable depression. Higher scores mean a higher burden (35-37).
- Quality of life (using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-C30; EORTC-QLQ-C30), with the global health scale (QLG) and five functional scales, namely physical (QLP), role (QLR), cognitive (QLC), emotional (QLE) and social functioning (QLS), all with a range in score from 0 to 100. For Global health (QLG) a high score represents a high quality of life and for the functional scales a high score represents a high / healthy level of functioning (38-40).
- Physical limitations due to sickness (using the Sickness Impact Profile; SIP), with the subscale body care and movement (SIPB) and the subscale ambulation (SIPA), both with a range in score from 0 to 100 in which a high score indicates more health problems (41-43). These variables were transformed into ordinal variables with three classes (0= no limitations, 1= limitations, 2= severe limitations).
- Self-reported work ability (using the Work Ability Index WAI) (44;45), with the general question that asks participants to estimate their current work ability (WAIC) compared to their lifetime best work ability. It has a range from 0 to 10 with a high score indicating a better work ability.
- Coping (using the Utrecht Coping List; UCL) (46-49), covering seven coping strategies i.e., 'active tackling', 'palliative reacting', 'avoidance', 'seeking social support', 'passive reacting', 'expression of emotion', and 'reassuring thoughts'. For each scale all items are scored with a four-point Likert response scale, with a higher score meaning a greater tendency to behave in conformity with the strategy tested.

Work status of participants (WORK) was assessed using the question 'Are you currently fully or partially (again) at work'; the answer 'Yes, I have paid work' was considered confirmatory positive.

Analysis

The representativeness of the included participants related to gender and age was compared to all potentially eligible participants, and found to be satisfactory. In order to analyse the most relevant exogenous variables, possible confounding variables were identified using regression analysis. Variables that were left in the last step of the regression analysis were selected if $p < 0.10$. Next, the seven coping strategies of the UCL were reduced into two dimensions, postulating two latent variables in the coping measurement model: a more active coping dimension and a more passive coping dimension (UCLA and UCLP). Further, with the `International Classification or Functioning, Disability and Health' model as global starting point (Figure 6.1), we constructed a basic structural model in which the direct effects of self-reported health complaints on functional limitations, as assessed by an IP, were as follows:

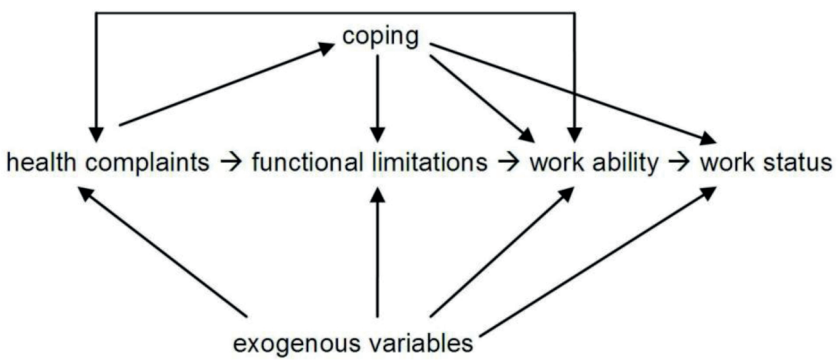

Figure 6.1 The research model in this study

– Self-reported limitations related to physical functioning, and quality of life related to physical functioning have direct effects on physical limitations, as assessed by an IP.

– Quality of life concerning role, emotional, cognitive and social functioning, self-reported fatigue, depressive symptoms, and lower self-assessed work ability have direct effects on mental limitations, as assessed by an IP.
– Self-reported quality of life concerning global health, self-reported fatigue and depressive symptoms have direct effects on limitations in working hours, as assessed by an IP.

In the basic (structural) model, we assumed functional limitations, as assessed by an IP, to have direct effects on self-assessed work ability, which in turn has a direct effect on having paid work (again). The associations between the endogenous variables, i.e., health complaints and work ability, were modelled as associations of disturbance terms (i.e., unexplained variances). Direct effects of the coping variables (UCLA and UCLP) on the other relevant endogenous variables (FALM, FALP, FALH, WAIC, and WORK) were implemented if the related bivariate correlation was > 0.10. Also, in the basic model only exogenous variables with a significant direct effect on endogenous variables were selected. From the basic model, we selected the significant estimated direct effects and associations between the disturbance terms. Then, a final (structural) model was fitted. All models were constructed using Lisrel (50).

RESULTS

Study population

Between July 2011 and January 2012, 26,464 disability benefit applications were received, of which 1,615 reported a diagnosis of cancer. Of these, cancer survivors with a sick leave period less than two years (n=343) were excluded. Next, eligible participants (n = 1272) were sent a questionnaire of whom 662 responded (52%). Of these, 98 respondents were excluded as they were still under treatment with chemotherapy and/or radiotherapy. Also, 80 respondents were excluded based on additional data of the SSA and 120 respondents were excluded, as a completed FAL was missing. In total, 364 respondents were included in this cross-sectional study.

For these 364 respondents, the FAL contained functional limitations, as assessed and noted by the IP.

Exogenous variables

The exogenous variables of the 364 respondents that tested significantly in the regression analyses (cut-off for p-value <0.10) are shown in table 6.1. The variables that were not significant (gender, having children, being bread winner, marital status, having managerial tasks, company size, metastatic disease, ongoing treatment, number of treatment modalities) were left out of further analyses.

The majority (68%) of the included respondents were women, were in a relationship (78%), and 74% had children. The mean age was 52 years, and 10% was non-native Dutch. About 30% of respondents had irregular working hours, 17% had managerial tasks, and mean job tenure was 26 years. Comorbidity was reported by 7% of respondents and 44% reported metastatic disease. Of the respondents, 47% had breast cancer; the other 53% had other sorts of cancer, such as cancer of the urogenital (13%) or digestive system (11%). The majority of respondents reported a treatment history of chemotherapy (72%) and/or radiotherapy (61%).

Endogenous variables

In table 6.1, descriptive statistics and Cronbach's alpha of the endogenous variables are presented. The reliability of the scale for mental limitations (FALM) and physical limitations (FALP) were relatively low, but acceptable. Regarding actual work status, 32% of respondents were at work, either partially or fully.

Coping measurement model

The seven UCL coping scales all had a moderate to good reliability, with Cronbach's alphas ranging from 0.68 ('avoidance' and 'reassuring thoughts') to 0.85 ('seeking social support'). The coping measurement model had a good fit and showed that the active coping dimension (UCLA) loaded on the scales for 'active tackling', 'palliative reacting', 'seeking social support' and 'reassuring thoughts' with standardized factor loadings of 0.39, 0.88, 0.41 and 0.50, respectively. The passive coping dimension (UCLP) loaded on the scales for 'palliative reacting',

'avoidance', 'passive reacting' and 'expression of emotion', with standardized factor loadings of 0.40, 0.51, 0.66 and 0.64, respectively.

Final structural model

Since the basic (structural) model had an important number of direct effects that were not statistically significant (data not shown), the model was adjusted into a final (structural) model. In table 6.2, direct effects of exogenous variables on endogenous variables are presented. The size of the (standardised) coefficients of most of these effects was less than 0.16, with four exceptions for stronger associations: a temporary contract with having no work (β = 0.25), older age with a higher score for emotional functioning (β = 0.19), higher education with more active coping (β = 0.18), and breast cancer with more active coping (β = 0.25).

In table 6.3, direct effects and associations between endogenous variables in the final model are presented:

- More physical limitations (FALP) were associated with more physical health complaints (SIPA, SIPB, QLP), and with not having paid work (WORK). There was no association between physical limitations (FALP), and a lower self-assessed current work ability (WAIC).
- More mental limitations (FALM) were associated with poorer cognitive functioning (QLC), more self-reported fatigue (FACIT-F), and lower self-assessed current work ability (WAIC). They were not associated with a lower quality of live concerning role, emotional, and social functioning (QLR, QLE, QLS), nor with more depressive symptoms (CES-D). More limitations in working hours (FALH) were associated with more self-reported fatigue (FACIT-F), and with lower self-assessed current work ability (WAIC). More limitations in working hours were not associated with a lower self-reported global health (QLG), nor with more depressive symptoms (CES-D). Instead, there was a weak association with fewer depressive symptoms (CES-D).
- Lower self-assessed current work ability (WAIC) was associated with not having paid work (WORK).

Only two 'Modification Indices' in the final (structural) model were significant, suggesting: a) a direct effect from mental limitations (FALM) to limitations in

Table 6.2 Direct effects from exogenous to endogenous variables in conformity with the final model

From	Temporary contract	Age	Education	Non-native Dutch	Job hours	Shift work	Kind of job exposure	Sector commercial services	Job tenure	Co-morbidity	Radio therapy	Chemo therapy	Hormonal treatment	Breast cancer
To														
SIPB			-0.11	0.11						0.10				
SIPA			-0.13	0.09										-0.09
QLG				-0.13					0.10					0.10
QLP			0.14	-0.15										
QLR							-0.09					0.08		
QLE	-0.12	0.19	0.07	-0.12		-0.10		-0.07	-0.08		0.07		-0.07	
QLC		0.09		*-0.08*	-0.12					*-0.07*		-0.09		-0.11
QLS				-0.13	-0.09								0.11	
FACIT-F				-0.11					0.09			0.07		
CES-D	0.08	-0.11		0.16										0.10
UCLA			0.18											0.25
UCLP		-0.13	0.12								*-0.08*		*-0.07*	
FALM	0.13		0.12							-0.11				
FALP		0.09			-0.12									
FALH	-0.10											0.11		-0.15
WAIC	-0.12													
WORK	0.25				*-0.09*		*0.09*		-0.09			0.12		-0.13

All coefficients have been standardised ($p \leq 0.05$), except coefficients in *Italic* ($0.05 < p \leq 0.10$). SIPB: sickness impact of body care and movement. SIPA: sickness impact of ambulation (for SIPB & SIPA: a low score is less sickness impact). QLG: global health. QLP: quality of life of physical functioning. QLR: quality of life of role functioning. QLE: quality of life of emotional functioning. QLC: quality of life of cognitive functioning. QLS: quality of life of social functioning (for all Quality of Life scales: a high score is better quality of life). FACIT-F: fatigue (a high score is less fatigue). CES-D: depressive symptoms (a low score is less symptoms). UCLA: dimension of active coping. UCLP: dimension of passive coping (for UCLA & UCLP: a high score is more coping). FALM: mental limitations. FALP: physical limitations. FALH: limitations in hours of work (for all FAL scales: a low score is less limitations). WAIC: work ability (a high score is more work ability). WORK: having paid work now (a low score is having paid work).

Table 6.3 Direct effects and associations between endogenous variables in conformity with the final model

From	SIPB	SIPA	QLG	QLP	QLR	QLE	QLC	QLS	FACIT-F	CES-D	UCLA	UCLP	FALM	FALP	FALH	WAIC
To																
UCLA		-0.13				*-0.14*	0.18		-0.24	-0.25		fixed				
UCLP	*0.09*			0.16						0.62						
FALM							-0.22		-0.18					**0.12**	**0.23**	
FALP	0.15	0.23		-0.13	*-0.10*						0.13				**0.16**	
FALH									-0.42	*-0.13*	0.11					
WAIC	**-0.36**	**-0.33**	**0.49**	**0.50**	**0.49**	**0.27**	**0.27**	**0.36**	**0.52**	**-0.38**			-0.10		-0.12	
WORK														0.09		-0.36

All coefficients have been standardised ($p \leq 0.05$), except coefficients in *Italic* ($0.05 < p \leq 0.10$). The **bold** coefficients are associations of the disturbance terms (the unexplained variances). The associations of the disturbance terms between the endogenous variables of the self-reported heath status (SIPB, SIPA, QLG, QLP, QLR, QLE, QLC, QLS, FACIT-F, CES-D) are not given in the table. SIPB: sickness impact of body care and movement. SIPA: sickness impact of ambulation (for SIPB & SIP A: a low score is less sickness impact). QLG: global health. QLP: quality of life of physical functioning. QLR: quality of life of role functioning. QLE: quality of life of emotional functioning. QLC: quality of life of cognitive functioning. QLS: quality of life of social functioning (for all Quality of Life scales: a high score is better quality of life). FACIT-F: fatigue (a high score is less fatigue). CES-D: depressive symptoms (a low score is less symptoms). UCLA: dimension active coping (a high score is more coping). UCLP: dimension passive coping (a high score is more coping). FALM: mental limitations. FALP: physical limitations. FALH: limitations in hours of work (for all FAL scales: a low score is less limitations). WAIC: work ability (a high score is more work ability). WORK: having paid work now (a low score is having paid work).
Model fit parameters of the final model: Degrees of Freedom = 217; Normal Theory Weighted Least Squares Chi-Square = 179.469 (p = 0.970) Root Mean Square Error of Approximation (RMSEA) = 0.0; Normed Fit Index (NFI) = 0.976; Standardized Root Mean Square Residual (SRMR) = 0.0337.

working hours (FALH) and b) an association between the disturbance terms of self-reported fatigue (FACIT-F) and limitations in working hours (FALH). As associations between the involved endogenous variables were already in the final model, no further adjustment of the model was needed. The explained variances in the final model were 15% for active coping (UCLA), 40% for passive coping (UCLP), 17% for mental limitations (FALM), 27% for physical limitations (FALP), 15% for limitations in working hours (FALH), 11% for self-assessed current work ability (WAIC), and 28% for work status (WORK).

The mediating role of coping

The direct effects ($p \leq 0.05$) in the final (structural) model are depicted in figure 6.2 and show the various pathways from self-reported health complaints through coping and/or through functional limitations, as assessed by an IP, to self-assessed work ability and work status.

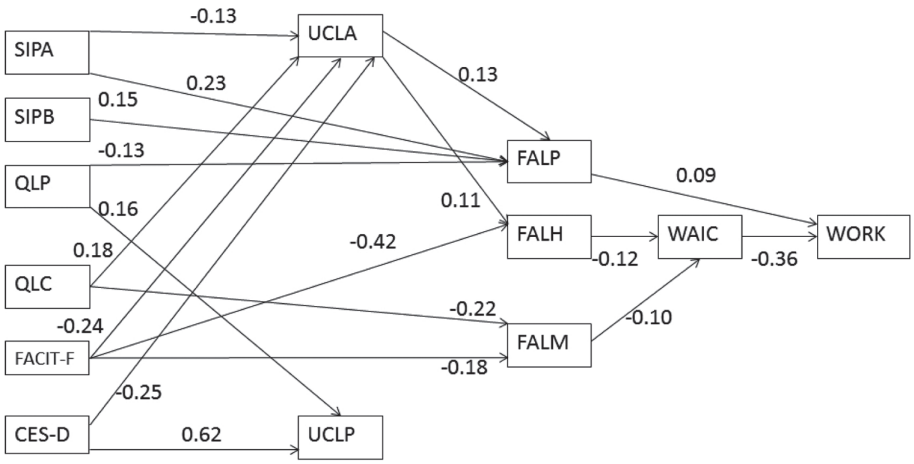

Figure 6.2 Direct effects of the final model
All direct effects have been standardised; only direct effects with $p \leq 0.05$ are shown. SIPA: sickness impact of ambulation; SIPB: sickness impact of body care and movement (for SIPA & SIPB: a low score is less sickness impact); QLP: quality of life of physical functioning; QLC: quality of life of cognitive functioning (for QLP & QLC: a high score is better quality of life); FACIT-F: fatigue (a high score is less fatigue); CES-D: depressive symptoms (a low score is less symptoms); UCLA: dimension of active coping; UCLP: dimension of passive coping (for UCLA & UCLP: a high score is more coping); FALM: mental limitations; FALP: physical limitations; FALH: limitations in hours of work (for all FAL scales: a low score is less limitations); WAIC: work ability (a high score is more work ability); WORK: having paid work now (a low score is having paid work).

Concerning the mediating role of coping, various self-reported health complaints (i.e., SIPA, QLC, FACIT-F and CES-D) had indirect, significant ($p \leq 0.05$) or marginally significant ($0.05 < p \leq 0.10$) associations through active coping (UCLA) with physical limitations (FALP) and limitations in working hours (FALH). However, these indirect associations were small ($\beta < |0.032|$).

DISCUSSION

Most important findings

In this study, the mediating role of coping in the associations between self-reported health complaints and (a) functional limitations, (b) self-reported work ability and (c) work status was examined. We found a small mediating role of active coping (UCLA) between self-reported health complaints and functional limitations (FALM, FALP, FALH), as assessed by an IP. A mediating role of passive coping (UCLP) was not found. Passive coping was only associated with more self-reported depressive symptoms (CES-D) and a higher quality of life of physical functioning (QLP).

Mental limitations (FALM) were associated with poorer cognitive functioning, more self-reported fatigue, and lower self-assessed work ability. We found associations between physical limitations (FALP) and self-reported physical complaints, but not with lower self-assessed work ability. Limitations in working hours (FALH), were associated with more fatigue, and lower self-assessed work ability, but not with global health (QLG), nor with more depressive symptoms. Lower self-assessed work ability was also associated with not having paid work.

Interpretation of the findings

Findings indicate that in cancer survivors, active coping may play a mediating role between more self-reported health complaints, and both more self-reported fatigue and functional limitations. Contrary to our hypothesis, we found no mediating role for passive coping. An explanation could be that, in our study, the active coping dimension and the passive coping dimension measured two different constructs, as they proved to be completely orthogonal to each other. Not surprisingly,

passive coping was associated with more self-reported depressive symptoms and active coping with fewer self-reported depressive symptoms. However, active coping was also associated with more self-reported fatigue; we will discuss this point further on.

Because passive coping loaded heavily on the 'passive reacting' strategy, one may expect a positive association between passive coping and mental limitations (FALM). A possible reason for not finding such a relationship could be that cancer survivors with a passive coping strategy are less inclined to express themselves during the assessment interview with the IP, as they possibly more often tend to avoid a dispute.

In our study, active coping was associated with more physical limitations and limitations in working hours, as assessed by an IP. Possibly, the cancer survivors with an active coping strategy have better cognitive functioning and fewer problems with the impact of physical sickness. As such, a recent meta-analysis reported positive outcomes on psychological well-being and physical health in cancer survivors that used adaptive coping strategies, and avoided disengagement forms of coping (51).

In our study, we also found that more self-reported health complaints and lower self-assessed work ability were associated with physical limitations, mental limitations and limitations in working hours. Mental limitations were not associated with self-reported social, role, and emotional functioning, which in general seem to be important aspects in the context of work participation. Apparently, in assessing the mental capacity, IPs did not consider these aspects, despite the fact that the FAL carries items for social and emotional functioning. It is possible that complaints related to these aspects were not fully recognised by the IP.

The role of coping in cancer survivors

Contrary to the results of previous studies (23-25;52;53), we found that active coping was associated with more functional limitations and, indirectly, with a lower self-assessed work ability and with not having paid work. Nevertheless, we found associations of active coping with fewer self-reported limitations for ambulation, better cognitive functioning (QLC), and fewer depressive symptoms. In our study,

the direction of these associations concur with results of other studies. However, in our study, active coping was associated with more self-reported fatigue. It may be possible that cancer survivors at two-year sick leave, suffering from fatigue, adopt a more active coping style as a strategy to overcome fatigue. Also, it may be possible that people who engage in active coping overcharge themselves and as a result become more fatigued. Moreover, the concept of coping, as assessed in two orthogonal dimensions and studied using a cross-sectional design, rules out the possibility of exploring a more dynamic situation. That is, cancer survivors may use several strategies alternatively, depending on specific circumstances, at different moments in time. More research on this topic is needed to examine which interpretation is valid.

The role of self-assessed work ability

In this study, we found that a higher self-assessed work ability was associated with fewer physical functional limitations (FALP) and less reduction in working hours (FALH). This result concurs with a recent study of disability applicants with all kind of diseases (54) showing that they were capable of predicting the outcome of their work disability benefit application. That is, the combination of a reported low perceived work ability and the expectation of being granted a disability benefit predicted the actual outcome of the disability assessment.

In a prospective study of employed cancer survivors (with various cancers) treated with curative intent, De Boer et al. (17) found that self-assessed work ability, reported during treatment, predicted RTW. This was independent of age and clinical factors. In concordance with this study, we found that higher self-assessed work ability was associated with being at work (again). This is a relevant finding considering the mean age of the population studied (52 years), and the fact that, at time of the data collection, workers in the Netherlands were expected to participate in work until retirement age at 65 years.

Strengths and weaknesses

Strength of our study is that we used validated questionnaires. Also, multivariate analysis was used to examine the associations between self-reported health

complaints, coping, functional limitations, self-assessed work ability and work status, taking into account potential confounders. Furthermore, we believe results of the study have added value as for instance our results concur with results of the aforementioned study by De Boer et al. (17), reporting on longitudinal data of Dutch cancer survivors treated with curative intent. Moreover, as far as we know, this is the first study that examines the mediating role of coping with functional abilities and self-reported health complaints in cancer survivors, who apply for a disability benefit at two-year sick leave. It may serve as a starting point for further research targeting at cancer survivors at risk for work disability.

An important weakness of our study is its cross-sectional design, i.e., causal relations cannot be proved, in spite of the use of a structural model with 'cause' and 'effect' variables. A third of the questionnaires of respondents was received after the IP completed their FAL. It is possible that the answers of these cancer survivors were influenced by the assessment. Also, it is possible that the cancer survivors who attended the work disability assessment after completing the questionnaire somehow prepared themselves for this assessment. Either way, in theory, our study could have had an impact on the assessment of functional limitations by an IP. Fact is that, in the Netherlands, to support the IP and enhance uniformity in the assessments, in recent years evidence-based guidelines have been introduced. However, despite present guidelines, it is still possible that the assessing IP may be biased in choosing the topics that he/she believes to be important. Consequently, the role of the IP in the assessment seems relevant and may also introduce bias. Also, current legislation related to work disability benefits may introduce a certain bias, in that workers and/or employers may sometimes feel forced to make unfavorable choices in a RTW trajectory, as to prevent a possible financial sanction the SSA may impose. Furthermore, one may doubt whether self-assessed work ability can be measured independently from work status in a cross-sectional design. That is, cancer survivors in paid work may assess their work ability related to actual working conditions.

In addition, a mixed cancer group is used in this study. Cancer is a heterogeneous disease and depending on tumour site and stage the prognosis, treatment, and side-effects of treatment may differ. This may influence the coping strategies

that individual cancer survivors use and, e.g., in those with a very unfavorable prognosis, lead to a predominantly passive coping strategy. Therefore, there may be different (psychological and physical) disease-related outcomes associated with specific coping strategies. Furthermore, we studied the possible role of coping using the results of a measurement model with a broad 'active' and 'passive' dimension. Maybe it would have been more appropriate to study each of the seven coping strategies that the UCL encompasses separately (55;56). Moreover, our results may be influenced by the fact we studied coping without taking coping resources (e.g., optimism and social support) into account.

Relevance for insurance physicians

Considering the results of this study, there is insufficient evidence to advice IPs to support an active coping strategy in cancer survivors on long-term sick leave. More longitudinal research is needed to confirm the role of active and passive coping strategies in these cancer survivors.

To the best of our knowledge, for the first time, an association has been determined between the FAL and self-reported health complaints of cancer survivors, applying for a disability benefit. Results indicate that, in the assessment of functional abilities, IPs may give more attention to cancer survivors' social, role, and emotional functioning. This may eventually support the judgement on limitations, enhance vocational rehabilitation, and RTW of cancer survivors. Consequently, social, role, and emotional functioning in cancer survivors could be addressed during IPs' meetings, being an obligatory part of permanent education related to keeping registration as a physician in the field of insurance medicine. In future research on work disability assessments, the use and added value of a standard topic list, which addresses these items in work disability assessment interviews, should be considered. That is, results indicate that, e.g., items such as parenting and taking part in family life (social functioning), usual daily activities and leisure time activities (role functioning), distress and worries (emotional functioning) should be part of such a list, and always be questioned in assessment of work disability claims of cancer survivors. Other items that may be considered for such a topic list relate to,

e.g., support (by partner, employer and/ or in general), experiences in vocational rehabilitation, and perceived meaning of work (57).

Conclusion

In cancer survivors active coping played only a small mediating role between both physical limitations and limitations in working hours (as assessed by an IP) and depressive symptoms, cognitive functioning, and both self-reported fatigue and physical limitations related to ambulation.

Also, both more self-reported health complaints and lower work ability were associated with more functional limitations (as assessed by an IP). However, self-reported social, role, and emotional functioning were not associated with mental limitations, as assessed by an IP. This is remarkable as these factors seem to be important in the context of work participation. Also, more functional limitations (as assessed by an IP) were associated with not being at work, whereas higher self-assessed work ability was associated with being at work (again).

Authors' contributions

AJMS, PvM and SFAD designed the study. AJMS performed the statistical analysis and wrote a first version of the manuscript. PvM and SFAD revised the manuscript and AJvdB commented on the manuscript. PvM and SFAD designed the questionnaire. PvM, SFAD and AJvdB coordinated the data collection. All authors read and approved the final manuscript.

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Declaration of interest

The authors report no conflicts of interest. Funding sources: AJMS and PvM are funded by the Dutch Social Security Agency. The study sponsor had no (decisive) role in the study design, in the collection, analysis, or interpretation of the data, in the writing of the case reports, or in the decision to submit the paper for publication.

Ethical standards

The authors declare the project to comply with the local regulatory guidelines and standards for human subjects protection in the Netherlands (Medical Research Involving Human Subjects Act (WMO), 2005).

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7

Work disability assessment of cancer survivors: insurance physicians' perspectives

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ABSTRACT

Assessing work disability in cancer survivors is a complex decision making process. In the Netherlands, insurance physicians (IPs) employed by the Dutch Social Security Agency (SSA) play a key role in assessing work disability of cancer survivors on long-term sick leave. Aim of this study was to investigate aspects IPs consider in assessing work disability in cancer survivors, their experiences related to the use of guidelines and their needs related to the use of a prediction rule that aims to support work disability assessments. A qualitative study involving three consecutive focus group interviews, using a predetermined topic list was performed. The interviews were recorded, transcribed and independently analysed using standard procedures of thematic analysis. The 29 participating IPs reported feeling responsible primarily for making correct assessments of cancer survivors' work disability, in which they predominantly investigate medical factors. Secondarily, non-medical factors related to the person, their work and/or their social environment were considered. Adherence to guidelines aiming to support IPs making such assessments was variable. We found that in assessing work disability among cancer survivors on long-term sick leave, IPs considered medical and non-medical factors. The relevance of non-medical factors became more prominent in cases where medical issues were less obvious. There seems to be a need to enhance adherence to guidelines in order to support the work disability assessment of cancer survivors. The development of an implementation strategy for a prediction rule to support the work disability assessment of cancer survivors should be considered.

INTRODUCTION

In 2012 3.45 million new cancer cases were reported in Europe (1), of which half involved people of working age (15 to 64 years) (2). Recent advances in cancer management have resulted in improved survival in Europe (1;3) leading to an increased number of employees with a history of cancer, as the majority of those diagnosed at working age are able to return to work (RTW) within 18 months of sick leave (4;5). However, functional ability limitations may act as a barrier to RTW. As treatment of cancer may result in long lasting side-effects, there is a growing risk of work disability in cancer survivors (5).

In the Netherlands, cancer survivors may apply for a work disability benefit after sick leave lasting two years. Insurance physicians (IPs) play an important role in assessing these claims. If applicable, the IP describes cancer survivors' functional abilities using the Functional Abilities List (FAL), a standardised form made up of six sections containing a total of 106 items. Workers are granted a benefit if loss of income exceeds 35% of former wages (6).

The concept of work disability is not only based on medical factors, since organizational, jurisdictional and social factors play a role as well (7,8). These factors result in a complex decision making process of both a medical and non-medical nature (9). In order to determine cancer survivors' work disability, an IP may use several sources of information, e.g., an interview followed by physical examination, medical information as supplied by third parties and documented vocational rehabilitation efforts (10). Previous studies have reported that IPs particularly rely upon the patient interview as a major data source (11;12). Therefore, the work disability assessment is partly based on patient reported information. As the assessing IP may be biased in choosing the topics that he/she believes to be important, the role of the IP in deciding the outcome of the assessment merits scrutiny (13).

In order to support IPs and enhance the uniformity of assessments, a number of evidence-based guidelines have been introduced in recent years in the Netherlands (14). In relation to cancer, guidelines concerning breast and colon cancers have been implemented. Such guidelines may support IPs in assessing symptoms such as cancer-related fatigue (CRF). However, whether such guidelines help IPs assess

functional abilities and symptoms in cancer survivors and the extent to which they are valued by IPs has not been reported. Therefore, this study aimed to investigate IPs' experiences in assessing work disability in cancer survivors. Specifically, the objectives were to identify factors that IPs consider relevant in assessing functional abilities, and the role of CRF in particular, and to assess IPs' adherence to available guidelines. Additionally, their need for a new prediction rule (i.e., a tool with the best combination of medical signs, symptoms and other findings to predict the probability of a specific outcome) aimed at supporting work disability assessment of cancer survivors was examined. The rationale of the study was that addressing potential gaps in IPs' performance will eventually lead to an improved quality of assessments, to the benefit of cancer survivors applying for disability benefit.

METHODS

This qualitative study was based on focus group interviews. Each focus group consisted of IPs with a diverse background of job tenure and experience in social insurance medicine. They were recruited at two local Dutch Social Security Agency (SSA) offices, located in the South-west of the Netherlands, and were engaged in work disability assessments on a daily basis. According to Dutch law, no ethical approval was necessary for this study, as the participants were not subject to any intervention.

The interviews were conducted during the regular monthly meetings of the IPs in January and February 2014. These meetings are an obligatory part of permanent education required by the Royal Dutch Medical Association for continuing registration as a physician in the field of insurance medicine. In the group interviews, five topics were discussed: (1) general experience of IPs in the assessment of cancer survivors' work disability, including questions about the experience of IPs in judging cancer survivors' work disability and factors associated with RTW beyond a two-year sick leave period that IPs consider to be important; (2) the experience of IPs in assessing CRF in cancer survivors and factors they considered relevant in determining the nature and course of CRF; (3) IPs' opinions on the practical value

of the FAL when used in the assessment of CRF in cancer survivors; (4) IPs' use of guidelines in assessing cancer survivors' work disability; and (5) the IPs' opinion, needs and demands related to the design and practical value of a prediction rule to support the work disability assessment of cancer survivors beyond two-years' sick leave.

After the audiotapes were transcribed, PvM and DAKvdA conducted separate and independent analysis using ATLAS.ti 5.2 software. We performed standard procedures of thematic analysis, which consisted of six phases (15). PvM started with phase one to four and made a preliminary codebook. Next DAKvdA independently started with phase one to four using the preliminary codebook as a reference guide adding new codes. In phase one, we studied the data by reading and re-reading the transcripts, noting first impressions and ideas for codes. In phase two, we started generating initial codes that we assigned to the data. In phase three, we sorted the list of initial codes and merged them to create codes of a less detailed order, which were gathered in potential themes. In phase four, we reviewed the themes, checking whether the data from the merged codes still corresponded to the potential theme that was assigned to it. Next the assigned themes were considered in relation to the entire data set. In phase five, PvM and DAKvdA discussed the results of their analysis, the themes they created and the data that corresponded to them. The themes were refined until consensus was reached. In phase six, PvM reported the results.

RESULTS

Sixteen male and 13 female IPs, aged between 28 and 64, participated in the meetings. Four were in training and job tenure ranged from two to thirty-nine years.

Three themes relating to the general experience of IPs in assessing cancer survivors' work disability were identified: the cancer survivors' perspective, the IPs' perspective and medical factors (Table 7.1).

Table 7.1 List of questioned topics, identified themes and connected quotes as retrieved from the focus group meetings

Topic	Themes	Quotes
General experience insurance physicians (IPs)	Cancer survivors' perspective	*"Work has become less important. They have a different view on life, judge other things more important now."*
	IPs' perspective	*"Let me put it this way, you want to do the right thing."*
	Disease related aspects	*"Sometimes you see workers with metastatic disease who want to work, but truly, are unable to, but just won't see. This, I find difficult."*
Cancer-Related Fatigue (CRF)	General perception of IPs related to the assessment of CRF	*"We all see women who successfully ended breast cancer treatment, but still report fatigue. Well, what are you going to do?"*
	Topics IPs question in assessing CRF	*"If they had a treatment with great impact, I am more likely to agree."* *"So, you take into account the stage, treatment, medication."*
	Assessment of CRF	*"If you have the impression that someone has a strong motivation, but still says he can't increase RTW efforts, you are more likely to accept this."*
Functional Abilities List (FAL)	General usability of the FAL	*"Using the FAL, you can describe everything."* *"Sometimes complaints are hard to translate, I mean, fatigue may also have an effect on cognitive functioning."*
	Aspects related to a reduction of working hours	*"I think disease is the most important factor to take into account. You got to have an objective base to proceed to a realistic reduction in working hours."*
Guideline adherence	Positive opinions	*"I think it's a good base. Both guidelines (i.e., breast cancer and colorectal cancer) hold lots of information, neatly listed, which I find convenient."* *"I think that's a major advantage, just follow the steps, read the text, check your issues and make up your mind."*
	Negative opinions	*"I think they are out-dated, so I hardly use them."* *"It's not always applicable, and if you choose not to adhere to the guideline, you'll have extra work in that you have to report and explain your arguments."* *"The moment translation towards work ability shows up, it stops."*

Table 7.1 List of questioned topics, identified themes and connected quotes as retrieved from the focus group meetings (continued)

Topic	Themes	Quotes
Prediction rule	General requirements of a prediction rule	*"It should be easy to use and have added value, it must be reliable."* *"It should be a validated list."*
	Potential impact towards daily practice	*"A prediction rule could prove its usefulness to us, but to clinicians as well."* *"It could also be useful to an occupational health physician, as in the end, it may lead to an intervention and facilitate a RTW trajectory."*

With regard to the cancer survivors' perspective, IPs reported the ability to participate in work and society to be a major point of interest for cancer survivors. However, a possible opinion shift among cancer survivors regarding the meaning of work, due to the nature of their experience of the diagnostic process, disease and treatment, was also recognized. IPs reported being faced with a dilemma when cancer survivors present subjective feelings of misery, which are not supported by clinical data.

With regard to the IPs' perspective, IPs reported feeling responsible for assessing cancer survivors' work disability correctly. They also considered survivors' needs and barriers related to RTW trajectories, and reported on difficulties met in assessing sustained work disability, e.g., in survivors with recurrent sick leave during a RTW process. Regarding medical factors, IPs reported that cancer survivors form a heterogeneous group. Tumour type, prognosis, treatment modalities and side-effects were topics always considered in the assessment and IPs reported that the presence of extensive or metastatic disease usually lead to sustained work disability. The first topic also included questions related to factors associated with RTW after two-years' sick leave. In analysing these data, factors related to the person, disease, work and environment were identified (Table 7.2). Factors related to the person could be allocated to the socio-demographic, physical or psychological domains.

Three themes related to CRF were identified: the general perception of IPs regarding the assessment of CRF, the factors they usually consider in assessing CRF and the way they assess CRF. All participants shared the general experience that

Table 7.2 Factors insurance physicians consider when assessing return to work in cancer survivors beyond two-years' sick leave categorized into person, disease, work and environment *

Person			Disease	Work	Environment
Socio-demographics	*Physical domain*	*Psychological domain*			
Age	Physical condition	Expectations	Tumour site	Employment status	Partner support
Marital status	Limitations	Cognition	Prognosis	Job satisfaction	Co-worker support
Income	Daily activities	Motivation	Side effects	Job load / work load	Employer support
Socio-economic class	Social activities	Perception	Extensive disease	Job loss	Health care provider support
	Well-being	Coping	Comorbidity	Shift work	Support in general
		Fear of recurrence	Depression	Vocational rehabilitation	Economy
		Psychosocial stress	Treatment modalities	Job stress	Labour market
		Meaning of work	Prolonged treatment	Company size	
		Knowledge	Hormone treatment	Heavy work	
			Fatigue		

*Factors can be either positively or negatively associated with return to work depending on their direction.

CRF is difficult to assess, especially in cancer survivors who successfully complete treatment, but still report CRF. IPs reported being puzzled by survivors with comparable diagnoses, treatment and stage, who presented a wide range of experienced levels of fatigue. The factors usually considered in assessing CRF were related to the disease, the person and/or their environment (Table 7.3). IPs reported giving specific attention to the impact of CRF on daily functioning, both at home and at work. IPs also took additional information provided by third parties, e.g., a GP, into account in their assessment of CRF. The third theme was related to the CRF assessment process. Initially, IPs gathered and weighed medical factors, such as diagnosis and disease stage, that could explain the presence of CRF. Next, they assessed the effect of these factors on survivors' functioning. In cases where relevant medical factors were less evident IPs looked for factors they judged to be circumstantial, such as those related to social functioning (e.g., leisure time activities) or role functioning (e.g., parenting). In assessing the weight of circumstantial factors IPs paid specific attention to motivation and recovery behaviour. For example, if a person appeared to be highly motivated to RTW (e.g., by improving their physical condition by exercising), but still reported fatigue to be a barrier, IPs tended to see CRF as a plausible barrier impeding RTW.

Table 7.3 Factors insurance physicians consider when assessing Cancer-Related Fatigue in cancer survivors beyond two-years' sick leave, categorized into person, disease, and environment *

Person	Disease	Environment
Daily activities	Diagnosis	Social activities
Need for recovery	Prognosis	Social support
Need for rest/sleep	Metastasis	RTW trajectory
Rest/sleep behaviour	Treatment modalities	Information by third parties
Recovery behaviour	Comorbidity	
Pre-morbid functioning	Medication	
Meaning of work	Coping	
Motivation	Sickness behaviour	
	Rehabilitation	
	Evolution of fatigue	

*Factors can be either positively or negatively associated with Cancer-Related Fatigue depending on their direction.

Two themes linked to the general experience of IPs in using the FAL were identified: the general usability of the FAL and factors related to a reduction of working hours, one of the items of the FAL. Additionally, the FAL has items related to psychosocial, cognitive and physical functioning.

IPs reported the FAL to be adequate in providing the potential to describe the abilities they judged present and to be suitable for aspects of physical functioning. However, they considered it to be less well designed in respect of aspects of cognitive functioning and not well suited to monitor a RTW trajectory. They also sometimes felt that the final result of the work disability assessment, considering the result of the labour experts' report, did not match their personal opinion. With regard to the second theme, if IPs advised a worker to reduce the number of working hours, this commonly eventually led to a certain level of work disability. Medical factors were reported to be the most important factors considered in recommending a reduction of working hours. Personal or work-related factors were judged less significant. However, if someone was working part-time in a RTW programme and still asked for a reduction in working hours, arguments related to the actual job demands and daily functioning were given full attention, with aspects of quality of life being considered as well. IPs considered that next to demands related to daily work, cancer survivors should be able to engage in other social activities as well, either at home or outside.

With regard to guideline adherence, participants reported positive and negative opinions. IPs who were less positive considered the use of guidelines to be time-consuming, and that they were out-dated, non-specific and too common. They reported that their use did not support their professional judgement in translating gathered data (i.e., information provided by GP, consultant, occupational health service and cancer survivor) into functional abilities. However, participants who held a more positive opinion thought guidelines were helpful as a source of information. They also reported the guidelines provided a starting point by which certain issues could be addressed, supporting their decision related to the assessment.

Related to the prediction rule, two themes were identified: the general requirements of a prediction rule, and its potential impact on daily practice.

As to general requirements, IPs considered a simple and easy to use design a necessity. A prediction rule should take little time to use, should have added value for the work disability assessment and should be both valid and reliable. Regarding the use of a prediction rule in daily practice, IPs discussed its influence on communication with cancer survivors, professional judgment and autonomy and other stakeholders (e.g., GP or legal advisor). For example, they questioned the use of a prediction rule in an appeal procedure, especially if the outcome of an applied prediction rule contradicted the final result of the disability assessment.

DISCUSSION

IPs in this study reported feeling responsible for the correct assessment of cancer survivors' work disability, in which they predominantly investigated medical factors. However, non-medical factors played a role as well. While guidelines have been distributed to support them in this process, adherence to such guidelines was reportedly varied.

A strength of this study is that we used a semi-structured interview with a predetermined topic list, the output of which was used as input for the next interview. All relevant topics presented and discussed in consecutive groups were captured and data saturation was reached. The participants formed a heterogeneous group in terms of gender, age and experience, leading to a broad spectrum of opinions being exchanged. A limitation is that the study relates to Dutch social security legislation, so that the applicability of results to work disability assessments in other countries may be limited. However, we believe that in assessing work disability IPs use a biopsychosocial model that integrates individual physical and/or psychological functioning with an environmental and social background, so that next to biomedical factors (disease, symptoms and treatment), the model also takes patients' social functioning (in family, and working-life) and the societal system designed to deal with the effects of disease (e.g., the healthcare system and physicians' roles) into account. Although the concept of work disability may differ in different countries (8), the biopsychosocial model has characteristics that can be

applied universally, irrespective of specific legislation and context. Consequently, the factors identified in our study may be of interest to those engaged in work disability assessments in other countries as well.

Our findings are not surprising as, under Dutch legislation, work disability may only be assumed if claimed functional limitations and disease can be linked in a causal relationship. Our findings agree with the results of a previous study describing factors that IPs take into account in assessing short- and long-term work disability (17). In this study, IPs reported medical factors and factors related to participation (e.g., in family life, such as childcare, and in work, such as job demands) to be most often considered in the work disability assessment, whereas less attention was given to personal and environmental factors.

Next to medical factors, our study also identified factors related to the person, work and environment that IPs consider in assessing work disability, such as physical condition, job demands and co-worker support. In this respect, our findings match closely the results of a recent study (10) describing factors IPs generally report to be relevant in promoting or hindering RTW in employees on long-term sick leave.

It seems that long-term ill-defined complaints, such as distress or CRF in cancer survivors, present IPs with a dilemma. Consequently, after two years of sick leave, IPs find it hard to judge these complaints as related to disease. As a consequence, IPs look for circumstantial evidence, such as information provided by a vocational rehabilitation report, that may confirm consistency in impairments, functional limitations and handicaps that the IP has to assess (16).

The results of our study concur with previous studies that have identified factors related to the disease, person, work and environment as relevant when assessing RTW ability (4;10;17;18). This may explain IPs' poor adherence to guidelines with regard to the work disability assessment of cancer survivors, since they ask about topics they consider relevant and routinely use in practice. Another study showed that poor guideline adherence could also result from IPs feeling obliged to follow predetermined steps that they perceive as intrusive to their professional autonomy (19). Also, as our participants stated, adherence to a guideline will not automatically give the answers to pertinent issues discussed during the work disability as-

sessment. This finding concurs with the results of a previous study showing serious deficiencies in following implemented guidelines (20). However, non-adherence to guidelines may have a negative effect on uniformity in exploring topics that an IP has to consider in assessing work disability. It may therefore lead to inequality in work disability assessment outcomes that should be avoided or reduced to a minimum. Therefore, this calls for measures to improve guideline adherence.

Finally, in line with their critical appraisal of guidelines, IPs were sceptical about the practical value and use of a prediction rule. As adherence to a guideline is dependent on several factors, e.g., its format and the attitude and self-efficacy of the physician, one might expect the same factors to influence adherence to a prediction rule (19;21;22).

To conclude, our results suggest that in assessing work disability in cancer survivors on long-term sick leave, IPs predominantly consider medical factors. To a lesser extent, non-medical factors related to the person, work and/or social environment are considered as well. The relevance of these non-medical factors becomes more prominent in cases where medical factors are less obvious.

KEY POINTS

- In assessing work disability of cancer survivors on long-term sick leave, both medical and non-medical factors have to be considered.
- There seems to be a need to enhance guideline adherence. Implementation of new guidelines or prediction rules requires a tailored strategy.
- Regular peer-to-peer meetings discussing barriers and facilitators in applying guidelines and/or prediction rules could be part of such a strategy and favour their implementation.

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CONFLICT OF INTERESTS

PvM is employed by the Dutch Social Security Agency. For the remaining authors, no conflicts of interest were declared.

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8

General discussion and conclusions

In Chapter 1, we introduced the case of Mrs. F., a 39-year old breast cancer survivor working as a shop assistant. The case illustrates the queries the IP may need to address in assessing a work disability claim at the 24-month sick leave term. As we previously left the IP's office while Mrs. F. presented her medical history, the discussion now starts with a follow-up on her case description.

As the IP has studied all relevant documents, received to assess the vocational rehabilitation efforts (which proceeds the assessment of the work disability claim) prior to meeting Mrs. F., it is clear to the IP that she was treated with curative intent. During the interview, the IP gives Mrs. F. room to tell about her complaints and current circumstances, and makes sure that all relevant items that the guideline breast cancer lists, are addressed. Next, based on the medical history and physical examination, the IP discusses that a full RTW in the previous job held, at the moment, seems difficult. On the other hand, there seem no arguments to advice a complete and sustainable work disability, meaning that functional abilities have to be described in which part-time work seems a logical starting point. Since Mrs. F. elaborates on being fatigued most of the time, the IP explains to Mrs. F. that, based on all relevant factors, it is expected that these complaints eventually will subside and that her work ability will increase. Mrs. F. is a bit hesitant and discusses her worries and problems in daily functioning, for which reason the IP suggests that she completes a set of questions, that relate to future prospects on fatigue and work ability. They agree that she completes these questions at her convenience at home and that she will return them by mail. On receipt, the IP calculates the predicted values on fatigue and work ability, based on the answers given, and next, Mrs. F. is contacted to discuss the results. Being reassured by the IP on hearing the outcome of her future prospects, she is now more confident in meeting the labour expert and making further plans related to RTW. Mrs. F. agrees to the proposed re-assessment, that the IP thinks is indicated at a one-year term.

In the past, cancer survivors reported that IPs paid little attention to CRF and/or cognitive limitations and that IPs were unaware of the impact of CRF and cognitive limitations on daily functioning. This study was conducted as one of the SSA's initiatives to give more attention to cancer survivorship. The main aim of this study was to identify predictive factors for CRF and work ability in cancer survivors on long-

term sick leave. Two objectives acted as a starting point to target this goal, i.e., the need to (1) enhance work participation of cancer survivors, and (2) support IPs in assessing work disability claims of cancer survivors. The present chapter starts with an overview of findings and answers to the research questions, briefly presenting the results of the separate studies. This is followed by a discussion in which the answers to the research questions act as point of departure and are linked to the two objectives mentioned above. Subsequently, some methodological considerations are put forward, after which the key messages and recommendations related to future research as well as practice and policy are listed.

A SUMMARY OF THE MAIN FINDINGS AND ANSWERS TO THE RESEARCH QUESTIONS

Question 1: Which factors are known to predict RTW in cancer survivors on long-term sick leave?

In Chapter 2, the results of a systematic review on predictors of RTW and employment in cancer survivors of working age are described. Heavy work and chemotherapy were negatively associated with RTW. Less invasive surgery was positively associated with RTW. Old age, low education and low income were negatively associated with employment. Breast cancer survivors had the greatest chance to RTW. Moderate evidence was found for extensive disease being negatively associated with both RTW and employment, and for female gender being negatively associated with RTW.

Question 2: Which factors are associated with work disability in cancer survivors at 24-month sick leave?

In Chapter 3, this question is addressed by a secondary data analysis, i.e., a prospective study on prognostic factors of work disability in sick-listed cancer survivors. A cohort of 131 sick-listed employed cancer survivors was followed for two years and data were collected at 10- and 24-month sick leave. Analysis showed that at 10-month sick leave, negative perception of health care providers on cancer

survivors' work ability and little experienced influence on RTW, both as reported by respondents, were associated with increased risk for work disability at 24 months.

Next, in Chapter 4, the results of a cross-sectional study in cancer survivors (n=351) applying for a work disability grant at 24-month sick leave are described. Results showed that at 24-month sick leave an increased risk for work disability was associated with Dutch nationality, higher education, hormone therapy, metastatic disease, high level of sickness impact, and low work ability.

Question 3: Which factors predict CRF and work ability in cancer survivors at long-term follow-up, after the assessment of work disability?

In Chapter 5, the results of the main study, a prospective cohort study on predictors for CRF and work ability in cancer survivors at long-term follow-up, i.e., after assessment of work disability, are presented. Analysis showed that higher level of fatigue in cancer survivors was predicted by being divorced or widowed, a higher level of sickness impact, having depressive symptoms, and working in health care. A lower level of fatigue was predicted by having received chemotherapy and lower fatigue at baseline. A higher score on work ability was predicted by having received chemotherapy, better global health and better work ability at baseline. Being principal wage earner, uncertainty related to being free of disease, a higher level of sickness impact, and higher level of wage loss predicted a lower score on work ability.

Question 4: Which factors do IPs consider in assessing CRF and abilities in cancer survivors at 24-month sick leave?

In Chapter 7, the results of a focus group study on factors IPs consider in assessing CRF and work disability of cancer survivors are presented. This qualitative study relates to the experiences of IPs in assessing CRF and functional abilities of cancer survivors, their use of guidelines and their needs related to the use of a prediction rule that targets to support work disability assessments. The IPs reported to feel responsible for correct assessment of cancer survivors' work disability, in which they predominantly investigated medical factors. Next, non-medical factors related to the person, work and/or social environment were considered. Adherence to existing guidelines, i.e., the guidelines on colorectal cancer and breast cancer, that aim to support IPs in the assessment, proved to be diverse. In discussing the need

and design of a prediction rule, its influence on communication with other stakeholders, e.g., the cancer survivor or his/her OP, was addressed as an important issue. Related to daily use IPs thought a prediction rule should be valid, reliable and easy to use.

Besides the studies mentioned above, that aim to answer the research questions, the mediating role of coping between health complaints and work status in cancer survivors was studied as well. The results of this cross-sectional study are described in Chapter 6. Only for active coping such a mediating role was found.

DISCUSSION OF THE RESULTS

In this thesis, CRF and work ability in cancer survivors form a central theme, connecting the separate studies. Taking the work disability assessment at 24-month sick leave as a starting point, the studies described in the previous chapters specifically relate to the cancer survivor and the IP, who are both engaged in the work disability assessment, as applicant and assessor.

In order to meet the first objective of this thesis, i.e., to enhance work participation of cancer survivors, there is a need to know which factors relate to RTW and employment in cancer survivors. These factors may provide a framework that, during sick leave, can be considered in a vocational rehabilitation trajectory that, if unsuccessful in case full RTW is not reached, usually proceeds the work disability assessment. The topics RTW and employment were addressed in Chapter 2. The association of chemotherapy in hindering RTW, as found in literature, seems to oppose the result found in our main study (Chapter 5). However, as discussed in Chapter 5, a selection bias could play a role here in that among applicants who did not receive chemotherapy, only those with a more unfavourable prognosis related to RTW (i.e., with high fatigue levels) might be represented in the cohort. That is, in cancer survivors not treated with chemotherapy, the majority of those with low levels of fatigue have already returned to work, and therefore are not in need to apply for a work disability benefit. Among the survivors who did receive chemotherapy this selection might be less obvious. That is, chemotherapy treatment

usually has a prolonged course that might hinder early RTW. Furthermore, we should consider that in our systematic review, the studies targeting the association between chemotherapy and RTW addressed breast cancer survivors only, whereas our study relates to a cohort with mixed diagnoses. Also, in these studies, RTW was measured at different time points, i.e., at 10 months and 24 months, while our main study relates to a cohort with work ability being predicted one year after the work disability assessment, i.e., 36 months after the first day of sick leave.

In a previous longitudinal Dutch study of breast cancer survivors, persistent fatigue was associated with the duration of former treatment, but not associated with type of surgery, type of adjuvant therapy and time since finishing treatment (1). In that study, high anxiety, high impairment in role functioning and low sense of control over fatigue symptoms at baseline were predictors of persistent fatigue. To conclude, different designs and study populations may form an explanation for the aforementioned results that, related to the associations found between chemotherapy and both CRF and work ability, seem contradictory and are possibly partly caused by selection bias.

In case RTW in cancer survivors during sick leave fails, at the end of the sick leave term, the need to apply for a work disability grant is inevitable. In this respect, to provide the IP with an evidence-based and supportive framework, we need to know which factors relate to work disability at 24-month sick leave. This topic, that relates to our second objective, i.e., supporting the IP in assessing the work disability claim, was addressed in Chapter 3 and 4. Related to the results presented in Chapter 3, it is interesting to see that nowadays, as also reported three decades ago, health care professionals' negative views on RTW expectations were associated with a higher risk for work disability. However, it should be noted that attribution of cancer survivors' own expectations towards the reported health care professionals' views may also play a role here. The results described in Chapter 4 show that poor health condition and/or a self-reported low work ability are contributing to the risk for work disability. This indicates that somehow (core) factors, that in the past were identified as associated with work disability (2), nowadays are still relevant. These have not lost their importance, even though over the years health care improved and legislation changed.

Considering the results presented in Chapter 3, surely in the Netherlands, clinical medicine is sometimes blamed for having too little interest in working life of patients (3), which might partly relate to the way responsibilities in care and cure are being operationalized. That is, different stakeholders (GP, clinician, OP and IP) each have their own perspective and treatment goals, which defines their relationship with the sick-listed worker. As treatment goals do not always converge, vocational rehabilitation of a cancer survivor on sick leave is sometimes obstructed (4). However, next to paying more attention to working life aspects of cancer survivors in clinical care, it seems there is room for improvement in caring for them in occupational medicine and insurance medicine as well. More specifically in providing continuity in care and communication (5;6). That is, in assessing work disability claims of cancer survivors, we need to address the role of the IP in this process as well. This aspect is considered in discussing the results presented in Chapter 7.

Finally, at 24-month sick leave, on assessment of the work disability claim, it may be helpful to know the future prospects of cancer survivors related to fatigue and work ability beyond 24-month sick leave, considering the potential long-term effects of treatment and/or the disease. This topic is addressed in Chapter 5, and two models, which predict CRF and work ability one year after the work disability assessment, are presented. These models may provide a foothold to plan and/or initiate a vocational rehabilitation trajectory in cancer survivors, and as such aim at the second objective of this thesis. Related to CRF, several factors were associated with a higher level of fatigue. The results concur with results of previous studies and indicate that perhaps complaints can be reduced, by considering medication and/or offering support and counseling, combined with tailored physical exercise (7;8). As it is, these aspects should be discussed during the work disability assessment if applicable, as they are potentially open to a positive change and to a cancer survivor's benefit.

Next to studying factors associated with RTW, employment, work disability and work ability (see Chapter 2, 3, 4, and 5, respectively) it seems desirable to explore the association between behavioral aspects and RTW in cancer survivors as well, considering that "functioning and disability are results of the interaction

between the health conditions of the person and their environment" (9). In assessing a cancer survivor's work disability, the IP also has to judge behavioral aspects. Therefore, in Chapter 6, the focus is on cancer survivor's characteristics in that coping behavior is examined, and its relation with RTW. In this study, which used the ICF model as global starting point, we found a small mediating role of active coping, but a mediating role of passive coping was not found. However, passive coping was associated with more self-reported depressive symptoms. This finding is relevant as depressive symptoms are frequently reported by cancer survivors (10-12). However, in the assessment of work disability, specifically mood and anxiety disorders are not always recognized by IPs (13). This underlines the need to promote guideline adherence in IPs, specifically as guidelines on depression and anxiety disorders in insurance medicine are available and have been implemented previously. Moreover, a recent study (14) found indications that, related to describing functional abilities, adherence to the guideline depression resulted in a higher inter-rater reliability. In this respect, guideline adherence seems to promote uniformity, although it should be noted that the result of this study was not statistically significant.

As already mentioned, the IPs' characteristics were studied in Chapter 7, considering that, related to work disability claims of cancer survivors, it is not only important to know which factors need to be assessed (Chapter 2, 3, 4, 5 and 6), but also if these factors are assessed, and how. In order to access this "black box", i.e., questioning the IPs' motives, attitudes and beliefs, the way by which IPs usually assess CRF and work disability in cancer survivors was addressed in a qualitative way. We found that in the work disability assessment of cancer survivors, IPs investigate several factors related to the person, disease, work and environment (displayed in Chapter 7, Table 7.2). These factors largely concur with the factors found in both literature (Chapter 2) and quantitative studies of this thesis (Chapter 3, 4, 5, and 6). It therefore seems that the IPs share common knowledge, and are aware of the factors that need to be questioned. However, this does not necessarily mean that these factors are always discussed with cancer survivors during the work disability assessment. Current results also suggest that adherence to existing guidelines is relevant, as these present the domains of role functioning, e.g., social functioning,

work functioning (and their related factors), that need to be addressed by IPs. As such, guidelines offer an evidence-based body of knowledge along which work disability can be assessed.

GENERIC AND DISEASE-SPECIFIC FACTORS ASSOCIATED WITH WORK DISABILITY

In Chapter 7, we specifically targeted at the role of IPs in assessing cancer survivor's work disability. In the past, similar studies that aimed to disclose factors IPs consider in assessing work disability of sick-listed workers were published, although not specifically addressing cancer survivors (15;16). One of these studies showed that, according to the ICF model, IPs addressed a wide range of items of which "environmental factors" (assistance, workplace factors) and "personal factors" (coping, motivation) were under reported compared to factors related to "function and structures" (mood, attention) and/or "participation" (family life, social life) (15). Also, related to the prognosis of work ability, this study showed that particularly disease-related factors (course, severity) were considered. Furthermore, in assessing musculoskeletal disorders, the "function and structure" domain of the ICF was mentioned as the most important, whereas in psychiatric disorders "participation" was most frequently addressed (15). Does this mean that IPs have several strategies in assessing work disability, depending on diagnosis? And if so, does this imply that in assessing work disability, in each strategy the importance of specific (prognostic) factors varies? As our focus group study did not quantify the factors that IPs most frequently use in assessing cancer survivors' work disability, these questions cannot be answered. However, related to using certain strategies, our study indicated that IPs do use a certain strategy in that predominantly disease-related factors are questioned in assessing functional abilities, and, next, non-medical factors are addressed in order to support their decision. Still, the same may apply to other sick-listed workers with chronic diseases, such as congestive heart disease or COPD, as well. That is, next to CRF in cancer survivors, IPs have to assess functional abilities related to fatigue in other conditions as well

and may encounter similar problems in finding the arguments to support their decision. In other words, are there specific factors that the IP needs to consider in assessing work disability in cancer survivors, or can the IP use a generic core set of factors, applicable to all sick-listed workers (on long-term sick leave)?

A systematic review, based on five cohort studies and not specifying diagnosis, identified 16 factors, e.g., poor general health, low income, own prediction of non-RTW, associated with long-term sick leave (17). However, only weak evidence was found for older age and previous sick leave being associated with long-term sick leave. Moreover, insufficient evidence was found for work-related factors being associated with long-term sick leave. As we also found weak and inconclusive evidence for both age and previous sick leave associated with RTW, respectively (Chapter 2), we could say that these findings concur, irrespective of diagnosis. However, as described in our review on prognostic factors for RTW and employment in cancer survivors, we found strong evidence for the association between both job- and disease-related characteristics with RTW. This indicates that perhaps specific disease-related prognostic factors and generic factors co-exist, the latter shared by all workers on long-term sick leave, e.g., negative self-perceived RTW expectations, older age, and low education. To illustrate, in a large Dutch cohort of unemployed and temporary agency workers with psychological problems, positive RTW expectations proved to be a prognostic factor for work participation at the long term (18).

Also, in a previous Delphi study, in which IPs were questioned on the most relevant factors usually discussed in work disability assessments, without specified diagnosis, six factors liable to hinder RTW and three factors promoting RTW were identified. All but one of these factors, i.e., secondary gain of illness, were also addressed in our focus group study as factors considered in work disability assessment of cancer survivors. Again, this seems to indicate that in assessing work disability claims, IPs use a core set of factors irrespective of diagnosis. Next, the IP may add disease-related factors to the questions used in the interview, in order to assess the work disability claim.

As it is, assessing functional abilities and work disability in cancer survivors at 24-month sick leave can be a challenging task, in which many aspects have to be

addressed. This includes possible future prospects related to abilities, and if applicable RTW. In order to facilitate the IP in addressing these aspects, a prediction rule was developed based on the data gathered in the main study (Chapter 5) that may help the IP to decide on planning a re-assessment.

THE DEVELOPMENT (AND USE) OF A PREDICTION RULE IN INSURANCE MEDICINE

A short history on prediction rules

The third research question concerns prognostic factors of CRF and work ability in cancer survivors on long-term follow-up. This question was addressed in Chapter 5, and based on the results a prediction rule was developed for both outcomes (see appendix). Contrary to insurance medicine, the development, introduction and use of prediction rules in (clinical) medicine has a history of over 50 years now. In order to develop a register of clinical prediction rules relevant to primary care, in a review, Keogh et al. (2014) found 434 prediction rules, reported between 1965 and 2009 (19). These rules were predominantly studied in primary care or in the setting of emergency departments, and mostly connected with cardiovascular or respiratory disease, and musculoskeletal conditions. Also, the number of studies on prediction rules applicable in hospital care, throughout all clinical disciplines, has increased exponentially over these years.

As such, it seems that, nowadays in medicine, prediction rules, e.g., to assess the risk of pulmonary embolism or an acute coronary syndrome, form a indissoluble part of the (diagnostic) tools a GP or clinician may use (20). In contrast, development of prediction rules applicable in occupational medicine or insurance medicine, seems to lag behind. That is, in occupational medicine over the last decades only a limited number of studies on prediction rules, specifically related to job loss, sick leave and RTW, were published. These studies particularly addressed musculoskeletal conditions, i.e., low back and/or shoulder problems (21-25), occupational allergic diseases (26), common mental disorders (27;28), or self-rated health (29;30). In insurance medicine, studies on prediction rules are almost non-

existent, although recently a prediction rule on the risk of a work disability benefit in construction workers on sick leave, using the WAI score as a predictor, was developed (31).

Why use prediction rules?

To explain the increasing attention for prediction rules in medicine over the past decades, we should consider their added value. That is, in medicine, normally a physician sets a diagnosis based on patient's history, physical examination, and other tests. Using experience and knowledge, a physician goes through a decision making process in which gathered findings are connected and interpreted to set an accurate diagnosis and prognosis. Actually, this procedure seems to fit any physician, either working in primary care, hospital care, occupational or insurance medicine. A prediction rule quantifies the assets that the various aspects of the patient regarding medical history, physical examination, and other tests make towards the diagnosis, prognosis, and/or expected effects of treatment. Basically a prediction rule, based on research, aims to increase the accuracy of physicians' diagnostic and prognostic assessment (32;33). Likewise, the quality of the IP's assessment may be enhanced by using a prediction rule.

The need to develop prediction rules in insurance medicine

Considering the numerous studies on prediction rules that relate to general practice and clinical medicine, it is tempting to try and see if they can be used in occupational medicine or insurance medicine as well. Unfortunately, in occupational medicine and insurance medicine, the outcomes of interest usually are quite different from those applied in hospital or primary care. This stresses the need to develop prediction rules specifically targeting outcomes of interest related to occupational medicine and/or insurance medicine. That is, the OP or IP may use the outcome of such a prediction rule as an argument in an advice, e.g., on RTW or sustainability of functional abilities. As such, a prediction rule that targets work ability beyond 24-month sick leave, for a part may also relate to the work disability assessment at 24-month sick leave. In this respect, we should consider the last of the four tasks the IP has on assessing a work disability claim, i.e., the IP has to (1)

assess the social medical case history, (2) evaluate the followed treatment and therapy, (3) assess functional abilities, and (4) assess sustainability of functional abilities. It seems clear that, in a narrow sense, considering the nature of the work disability assessment at 24-month sick leave, a prediction rule on work ability modelled like we did, does not address the work disability claim at 24-month sick leave as such. Based on the used methodology, it is clear that a prediction rule that targets work ability beyond 24-month sick leave, does not relate to the work disability claim directly. Next to this methodological aspect, our prediction rule neither addresses the first three of the aforementioned tasks. However, in a broader sense, our model not only serves as a tool to predict future work ability, but also, indirectly, may relate to the work disability assessment at 24-month sick leave as such. That is, in case of uncertainty related to sustainability of functional abilities, in combination with a full loss of former wages earned (80-100%), the outcome of the prediction rule may support the decision to either grant or deny a complete and durable work disability benefit (IVA) at 24-month sick leave.

Prediction rules and evidence-based medicine

In the past, the Dutch health council reported that there was a need to strengthen the scientific base of insurance medicine (34;35). For a part, the council's recommendation has been met, e.g., by the development and implementation of guidelines, by the several research projects that are ongoing, and by the numerous scientific publications (36). As a next step, the development of prediction rules in insurance medicine seems logical. It can be considered as a part of evidence-based medicine that needs to be promoted to meet the standards of good (clinical) practice, which relates to all physicians, irrespective of their function and discipline.

Benefits of prediction rules in insurance medicine

Based on the results of the cohort study (Chapter 5), the development and use of a prediction rule targeting work ability in cancer survivors beyond long-term sick leave may be to the benefit of the cancer survivor, the IP and society as a whole. That is, from the cancer survivor's perspective, with the use of a prediction rule, uniformity in assessments can be enhanced, and this may add to the quality of

assessments in general. Moreover, the use of a prediction rule targeting work ability beyond long-term sick leave may help to identify those at risk for sustainable work disability. Consequently, in case of poor prognosis related to work ability, immediate access to and granting of a full and sustainable work disability benefit can be considered. This may reduce financial worries or worries related to possible future re-assessments, and as a result, support the cancer survivor's quality of life. Simultaneously, in cancer survivors, the prediction of future improvement of work ability may open the opportunity to offer a vocational rehabilitation trajectory. Next to the cancer survivor's benefit, the introduction of a prediction rule in insurance medicine may be to the advantage of the IP. It may support the IP in deciding on sustainability of functional abilities and therefore the need to plan a future re-assessment. The introduction of a prediction rule in insurance medicine may also be to the benefit of society at large, in that lawfulness is applied in assessing work disability benefit claims. Moreover, it may help to reduce the number of unnecessary re-assessments, which leaves room for other professional activities, either by the IP or the labour expert. Therefore, it could eventually help to cut societal costs as a result of optimizing services.

Vocational rehabilitation and cancer survivorship

The prediction rule targeting work ability in cancer survivors may not only support the decision on sustainability of functional abilities, it may also help to decide to start a vocational rehabilitation trajectory, even beyond 24-month sick leave. The importance to enhance vocational rehabilitation in cancer survivors has already been reported in several studies (37-39) and was also addressed in Chapter 2 and 3 of this thesis. The results presented in Chapter 3 showed that experienced influence on a RTW trajectory was positively associated with work disability at 24-month sick leave. Even though this study described prognostic factors measured at 10-month sick leave, experienced influence on a RTW trajectory at later stage, i.e., at 24-month sick leave, may possibly also be positively associated with RTW outcomes beyond 24 months. Supporting this assumption are the findings described in Chapter 6, regarding the mediating role of coping measured at 24-month sick leave, that point in the direction of a positive association between

active coping and RTW. That is, taking control and responsibility, meaning having influence in an RTW trajectory by active coping, seems positively associated with RTW, even at 24-month sick leave.

To conclude, as stated previously and found in literature, having control is important for cancer survivors, and RTW even beyond 24-month sick leave may enhance this. Also, optimizing the start of a vocational rehabilitation trajectory may reduce costs, e.g., in case re-employment is enhanced, considering the 1.4 times increased risk (RR 1.4; 95% CI 1.2-1.6) for unemployment in cancer survivors (all diagnoses) (40). In addition, a prolonged and negative effect on work participation in cancer survivors was reported in a recent study in Dutch breast cancer survivors (41). In this study, an increased risk for disability benefits up to 10 years after diagnosis was found (HR 2.0; 95% CI 1.6-2.5), with higher risks for younger patients. This result again stresses the need to support cancer survivors in RTW. However, we should bear in mind that, until now in the Netherlands, no evidence on cost-effectiveness related to vocational rehabilitation in cancer survivors at long-term sick leave exists. That is, in a Dutch hospital based multi-center RCT that aimed to enhance RTW in female cancer survivors, treated with curative intent and mean sick leave of 193 days, no differences related to quality of life, work ability, work functioning or costs, between the intervention group and usual care group, were found (42). Still, it is expected that in cancer survivors vocational rehabilitation and supportive psychosocial interventions, may be cost effective (43).

Disadvantages of a prediction rule

Introduction of a prediction rule targeting work ability in cancer survivors comes with disadvantages as well. As IPs stated in the focus group study (Chapter 7), a prediction rule should be reliable, valid and easy to use. Therefore, acceptance and adherence to a prediction rule, considering the experiences related to the previously implemented guidelines, seems to warrant a pilot or implementation strategy. Next, we should also consider that related to the outcome, apart from true positives, a prediction rule will also identify false positives and false negatives, the latter actually being missed true positives. Regarding the false positive cases this may imply unjustified re-assessments, or offering a vocational rehabilitation

trajectory in which selected participants are unable to meet demands, and may reach over their limits, which can negatively influence health and well-being. Opposite to this, for false negatives it would mean withholding cancer survivors potential possibilities to participate in work or delay RTW. For this reason, internal and external validation of a prediction rule, using a second dataset, is customary. Subsequently, once implemented a prediction rule should be checked for its practical relevance and impact as well (44).

To conclude, the use of a prediction rule targeting work ability in cancer survivors by no way means leaving out the IP's critical appraisal of facts and findings during assessment, it can be supportive and should be used as such.

METHODOLOGICAL CONSIDERATIONS

In each of the previous chapters, methodological strengths and limitations were addressed. Some additional methodological and practical considerations are discussed next. The first objective of this thesis was operationalized by performing a systematic review targeting prognostic factors, associated with RTW and employment (or similar outcomes), that stakeholders should consider in supporting cancer survivors who are willing to RTW. However, we should remind that this thesis specifically aims at circumstances as present in the Netherlands. In this respect, we may question if a literature search, even though a quality assessment on the level of evidence was done, based on studies performed in several countries all over the globe, each having a health care system and social security legislation of its own, is capable to answer topics raised. That is, Dutch social security legislation and probably labour market conditions are quite different compared to those abroad, especially in countries outside Europe. Therefore, generalization of results and their meaning towards daily practice of insurance medicine in the Netherlands should be considered cautiously. On the other hand, the results of the review may be of value in case a factor proves to be relevant in several countries, irrespective of the societal differences related to labour market conditions and/or legislation.

In addressing the second objective of this thesis we should consider that, related to our main study (Chapter 5), we were unable to perform a non-response analysis and only used data of employed workers, as the inclusion of unemployed workers (i.e., those without a fixed contract) was less successful. Especially the latter was disappointing, as we know that unemployed workers have a vulnerable position on the labour market (45;46). Also, related to the prediction models, we should consider that in our cohort, compared to historical data, the fraction of respondents with a sustainable complete and temporary complete work disability was low, i.e., 16% and 25% respectively. As it is, in the Netherlands from 2006 up to 2013, the fraction of cancer survivors granted a sustainable and complete work disability benefit at 24-month sick leave, increased from 31% up to 38%. For those granted a temporary complete benefit there was a decrease from 35% down to 27%. However, overall through these years, the fraction of those with a wage loss less than 80% remained stable at about 35%. Therefore, the data imply that particularly respondents with more favourable outcomes responded and participated in the cohort study. This, along with the uneven gender distribution of one male for every two female respondents, impedes generalizability. Regarding Chapter 7, that describes the focus group study, targeting IPs' perspectives related to the work disability assessment of cancer survivors, 29 IPs from only two SSA offices were recruited, which may seem a limitation towards representativeness. However, as the results of this study, in which data saturation was reached, concur with results of a previous study, in which 102 IPs (recruited nationwide) were questioned on the most relevant factors usually discussed in work disability assessments (16), this aspect seems unimportant.

KEY MESSAGES

– Prognostic factors of RTW, employment, CRF and work ability in cancer survivors can be identified (Chapter 2 and 5). In this respect, job demands, health condition, RTW expectations and support from other stakeholders seem factors closely connected with work participation of cancer survivors. Knowledge of

these factors is a necessary condition to correctly judge sustainability of functional abilities in the assessment of work disability claims of cancer survivors.
- In cancer survivors, a prediction rule based on identified factors may support IPs in the decision of who should be reassessed for future work ability (Chapter 5 and 7).
- During the first year of sick leave, timely and adequate vocational rehabilitation of cancer survivors can positively influence the outcome of the work disability assessment (Chapter 3). This calls for swift identification of facilitators and barriers of RTW that subsequently should be addressed to enhance vocational rehabilitation if possible.
- The role of the IP in assessing work disability claims, e.g., in questioning all potential factors that relate to work participation, is important (Chapter 7). The IP should be aware of his/her role, attitude and preferences, and consequently, the use of guidelines and/or prediction rules may help to enhance uniformity and add to the quality of the assessments as indicated by previous research.
- The cancer survivors' coping style seems associated with the outcome of work disability assessments and work participation of cancer survivors (Chapter 3 and 6).

RECOMMENDATIONS

Recommendations for future research

- Considering the results described in Chapter 3, further research on the association of early stage RTW interventions with work disability at 24-month sick leave in cancer survivors is called for. In this respect, specifically in cancer survivors, the role of RTW expectations and coping behavior seem interesting topics that future research may address.
- Given the long-term effects of the disease and/or treatment in cancer survivors that may last up to several years, further research on long-term effects beyond the term that we examined, i.e., three years after first day of sick leave, is needed.

- New prospective studies should be designed to identify those who are working at 24-month sick leave, and those who are not, and examine their characteristics and experiences in RTW over time.
- Results of such research could then perhaps be used to initiate intervention studies that may help to identify the best practice to support RTW in cancer survivors at, or beyond, 24-month sick leave.
- As such, this in turn may also lead to further research in that we may examine RTW outcomes and costs in those receiving the usual care, as provided by the SSA, compared to those offered a tailored vocational rehabilitation.
- New prospective studies may also give the opportunity to develop new prediction rules, and supply data to validate existing ones.
- In research that targets work participation of cancer survivors, researchers should make an effort to converge the design of studies, and should consider using uniform outcome measures, e.g., WAI score in studies on work participation and/or work ability. This may help to compare the results of separate studies and add more strength to the level of evidence found.
- To enhance uniformity in assessing work disability claims, future research should also address the IPs' compliance with already identified factors, known to be associated with work disability.
- Future research should particularly address unemployed sick-listed workers, i.e., cancer survivors without a fixed contract, as these seem more vulnerable related to prolonged unemployment and/or work disability, compared to employed cancer survivors on sick leave.

Recommendations for practice and policy

- IPs should be aware of the meaning of the prognostic factors that were identified and address these in assessing work disability benefit applications of cancer survivors. Future expectations, meaning of work, perceived work ability and perceived support should always be assessed.
- Our results may be used in updating existing guidelines, e.g., on breast cancer and colorectal cancer, presenting a overview of relevant factors that IPs may use.

- The development and validation of prediction rules in insurance medicine needs more attention.
- The use of a prediction rule as a triage tool to plan future reassessments in insurance medicine should be advocated.
- Prior to their implementation, newly developed prediction rules should be piloted. This may help to assess the practical validity of a prediction rule, the need for further adaptation, and reduce the risk for non-compliance once implemented.
- IPs should be encouraged to participate in small scale pilot projects and be facilitated by their management to do so.
- In using a prediction rule, e.g., for work ability in cancer survivors, the consequence would be to develop a policy related to offering a vocational training for those in need for further (tailored) support.
- More attention for (quality of) working life of patients in clinical medicine is needed considering the results described in Chapter 2 and 7, in which both cancer survivors and IPs report on the role of a health care provider and its association with RTW.

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A

Appendix

In this model, the predicted value (Y_{pred}) relates to work ability one year (T1) after the work disability assessment at 24-month sick leave (T0). Hereby, work ability is defined as the answer to the first (single item) question of the Work Ability Index. The answer to this question is measured on a scale of 0 to 10. It relates to the score of the current work ability compared to life time best.

$Y_{pred} = 2.43 + (X_1 * -0.64) + (X_2 * 0.8) + (X_3 * -0.48) + (X_4 * -0.05) + (X_5 * 0.02) + (X_6 * 0.43) + (X_7 * -0.61)$

Table 1 Characteristics of the variables

Variables	Label	Value / (scale)
X_1	Principal wage earner	Yes = 1
		No = 0
X_2	Chemotherapy	Yes = 1
		No = 0
X_3	Being free of disease	Yes = 0
		Don't know = 1
		No = not predictive
X_4	Physical dimension score (SIP)	Continuous (0-100)
X_5	Global health score (EORTC-QLQ-C30)	Continuous (0-100)
X_6	Work ability score at baseline (WAI)	Continuous (0-10)
X_7	Wage loss at 24-month sick leave	<80% = 0
		≥80% = 1

The sensitivity and specificity of the model were tested with a cut-off value of an increase in the work ability score of 2 points between the baseline (T0) and follow-up (T1) measurement. The model identified 76% of cases as true positive and 77 % of cases as true negative. Sensitivity was 37% and specificity 95%.

Table 2 Characteristics of the model; measured and predicted change in work ability score

	Measured change < 2 (n)†	Measured change ≥ 2 (n)	N
Predicted change < 2 (n)*	211	63	274
Predicted change ≥ 2 (n)	12	37	49
N	223	100	323

* Predicted change = (Y_{pred}) - work ability T0. † Measured change = work ability T1 - work ability T0

S

Summary

Over the last decades, the incidence of cancer has grown. Fortunately, due to advances made in medicine, e.g., screening programs and improvement of treatment modalities, the number of cancer survivors has increased as well. Simultaneously, the number of cancer survivors of working age has grown. In the Netherlands, the majority of cancer survivors of working age succeeds in return to work (RTW) prior to the maximum term of 24 months sick leave, but still, each year, over 4,200 sick-listed workers with a diagnosis of cancer have to apply for a work disability benefit. These work disability claims are processed by the Social Security Agency, for which insurance physicians (IPs) assess functional abilities and their sustainability. At times this can be difficult in cancer survivors, as IPs may find it hard to assess symptoms, such as distress, pain or fatigue. Data provided by the Netherlands Cancer Registry, related to the incidence and prevalence of cancer, indicate that the number of cancer survivors of working age will continue to grow over the coming years. Consequently, the number of cancer survivors that need to apply for a work disability benefit is expected to increase as well.

As cancer survivors are at risk for job loss, unemployment, and work disability, this thesis addresses work participation of these survivors at 24-month sick leave and beyond. In cancer survivors, work participation, next to providing an income, may help to regain self-confidence, overcome side-effects and lead the way back to former life. Therefore, there is a need to enhance work participation of cancer survivors on long-term sick leave (first objective). Simultaneously, there is a need to support IPs in assessing work disability claims of cancer survivors (second objective). These objectives were addressed by the identification of predictive factors for cancer-related fatigue (CRF) and work ability in cancer survivors on long-term sick leave. Specifically, CRF and work ability were studied, as both topics relate to work participation in cancer survivors. That is, CRF is a very common symptom in cancer survivors that can negatively influence all aspects of functioning, including working life, and may last a long time. Likewise, work ability in cancer survivors can be reduced due to side-effects of treatment, that may also last for several years or even be permanent. Knowledge of predictors of CRF and work ability in cancer survivors on long-term sick leave may help to identify those at risk for work disability, and support cancer survivors in vocational rehabilitation and RTW. Next,

it may support IPs in assessing work disability claims of cancer survivors, enhance uniformity in these assessments and add to the quality of care.

In order to meet the two objectives, the following research questions were posed:

Question 1: Which factors are known to predict RTW in cancer survivors on long-term sick leave?

Question 2: Which factors are associated with work disability in cancer survivors at 24-month sick leave?

Question 3: Which factors predict CRF and work ability in cancer survivors at long-term follow-up, after the assessment of work disability?

Question 4: Which factors do IPs consider in assessing CRF and abilities in cancer survivors at 24-month sick leave?

The first research question is addressed in Chapter 2, in which a systematic review on predictors of RTW and employment in cancer survivors is presented. The objective of this study was to provide an overview of the prognostic factors for RTW and employment of cancer survivors. Longitudinal prospective cohort studies were selected if the population consisted of cancer patients between 18 and 65 years of age, with RTW, employment or equivalent concepts as main outcome measure, studying at least one prognostic factor. The methodological quality of the included studies and level of evidence for each prognostic factor were assessed. Twenty-eight cohort studies met the inclusion criteria. Heavy work and chemotherapy were negatively associated with RTW, whereas less invasive surgery was positively associated with RTW. Also, breast cancer survivors had the greatest chance to RTW. Old age, low education and low income were negatively associated with employment.

The second research question is addressed in chapter 3 and 4. In Chapter 3, the results of a quantitative secondary data analysis describing prognostic factors of work disability at 24-month sick leave in employed cancer survivors are presented. The study targeted factors present at short-term sick leave, i.e., 10 months. Timely knowledge of prognostic factors of work disability may support cancer survivors in their trajectory of vocational rehabilitation. A cohort of sick-listed employed cancer survivors was followed for 24 months. Included participants were aged between 20

and 63 years. Data were collected, using questionnaires, at 10 months after reporting sick. The level of work disability was assessed by an IP and a labour expert at 24-month sick leave. Univariate and multiple logistic regression analyses were performed. Analysis showed that, at 10-month sick leave, negative perception of health care providers on cancer survivors' work ability and little experienced influence on RTW, both as reported by respondents, were associated with increased risk for work disability at 24 months.

In Chapter 4, the results of a cross-sectional study on factors associated with work disability in employed cancer survivors at 24-month sick leave are presented. Identification of factors associated with work disability in cancer survivors on long-term sick leave may support these survivors in choosing effective measures to facilitate vocational rehabilitation and RTW. Therefore, this study aimed to disclose factors associated with work disability in cancer survivors at 24-month sick leave. The study population consisted of employed sick-listed cancer survivors, aged between 18 and 64 years. They received a questionnaire at 24-month sick leave, the maximum period of sick leave allowed by Dutch social security legislation. Data were linked with the outcome of work disability assessments, as performed by the Dutch Social Security Agency. A hierarchical multivariate logistic regression analysis was performed to identify factors associated with work disability. At 24-month sick leave, increased risk for work disability was associated with Dutch nationality, higher education, hormone therapy, metastatic disease, high level of sickness impact, and low work ability.

Chapter 5 targets the third research question, in which the results of a prospective cohort study on predictive factors for CRF and work ability in cancer survivors beyond 24-month sick leave are discussed. The aim of this study was to identify prognostic factors related to both CRF and work ability in cancer survivors on long-term sick leave. Participants were between 18 and 64 years of age, had a first diagnosis of cancer, applied for a work disability benefit, and approached a 24-month sick leave term. Questionnaire data with a baseline measurement at 24-month sick leave with a follow-up measurement after 12 months, and register data of the Dutch Social Security Agency, were used. Univariate and multivariate linear regression analyses were applied to identify predictors. A higher level of fatigue

was associated with being divorced or widowed, a higher level of sickness impact, having depressive symptoms, and working in health care. A lower level of fatigue was associated with having received chemotherapy and lower fatigue at baseline. A higher score on work ability was associated with having received chemotherapy, better global health and better work ability at baseline. A lower work ability was associated with being principal wage earner, uncertainty related to being free of disease, a higher level of sickness impact, and higher level of wage loss.

In Chapter 6, the results of a study describing the mediating role of coping between self-reported health complaints and functional limitations, self-assessed work ability and work status of long-term sick-listed cancer survivors are presented. The purpose was to investigate the possible mediating role of active and passive coping between self-reported health complaints and functional limitations, as assessed by an IP, self-assessed work ability, and work status in cancer survivors on long-term sick leave. Validated questionnaires were used for self-reported health complaints, work ability and work status. The functional limitations of the respondents were transformed into scales for mental and physical limitations, and limitations in working hours. Using Lisrel, a structural model was tested, in which only for active coping a mediating role was found.

Finally, in Chapter 7, the fourth research question was addressed. In this chapter, the results of a qualitative study, that describes IPs' perspectives related to the work disability assessment of cancer survivors, are discussed. Work disability assessment of cancer survivors is a complex decision making process. In the Netherlands, IPs play a key role in assessing work disability of cancer survivors on long-term sick leave. In this study, the aspects IPs consider in assessing work disability of cancer survivors and their experiences related to the use of guidelines are described. The study also addresses IPs' needs related to the use of a prediction rule that targets to support work disability assessments in cancer survivors. A total of 29 IPs participated in this qualitative study. Three consecutive focus group interviews were held, using a predetermined topic list. The interviews were recorded, transcribed, and then independently analysed using standard procedures of thematic analysis. The IPs felt responsible for correct assessment of cancer survivors' work disability, in which predominantly medical factors were investigated. Next, non-medical factors

related to the person, work and/or social environment were considered. Guideline adherence, e.g., to the guidelines on colorectal cancer and breast cancer, proved to be diverse. Related to the use of a prediction rule, its influence on communication with other stakeholders was addressed as an important issue. Furthermore, IPs thought a prediction rule should be valid, reliable and easy to use.

In Chapter 8, the main findings of the separate studies are discussed and linked in order to meet the two objectives of the thesis, i.e., to both enhance work participation of cancer survivors and support IPs in assessing work disability of cancer survivors. Results related to the research questions show that factors, such as job demands, health condition, RTW expectations and support from other stakeholders, are factors associated with work participation of cancer survivors. Some of the identified factors, e.g., poor health, older age, RTW expectations, or low education, seem generic, applicable to all sick-listed workers, irrespective of diagnosis. However, in the work disability assessment of cancer survivors, IPs initially seem to address disease-related aspects, and next question aspects of role functioning, in order to decide on functional abilities and their durability. A diagnosis of cancer may come along with a wide range of limitations in functional abilities, depending on site, stage, side-effects of treatment, and course of the disease. Therefore, next to generic factors that relate to work participation, IPs should specifically question disease-related factors, in which the use of evidence-based guidelines may be supportive. Related to the course of fatigue and work ability beyond 24-month sick leave, socio-demographics, health characteristics and job demands showed to be relevant predictive factors. Based on this information, a prediction rule that targets work ability in cancer survivors beyond 24-month sick leave may support the choice of initiating a vocational rehabilitation trajectory and/or plan a future reassessment.

IMPLICATIONS FOR RESEARCH, PRACTICE AND POLICY

Results of this thesis stress the need for large scale RTW intervention studies in cancer survivors. Also, researchers should make an effort to converge the

design of studies, and consider using uniform outcome measures. Next, validation and development of prediction rules in insurance medicine need more attention, and research on vocational rehabilitation in cancer survivors should also address unemployed workers. During the first year of sick leave, early identification of factors associated with work participation may support a timely and adequate vocational rehabilitation of cancer survivors. Knowledge of these factors is also a necessary condition to, at later stage, assess work disability claims of cancer survivors correctly and judge durability of functional abilities. Related to work disability assessments in cancer survivors, the use of guidelines, prediction rules and continuing education of all IPs should be advocated. It may enhance uniformity of assessments and add to the quality of care. The consequence of using a prediction rule that targets work ability, would be to develop a policy that offers vocational rehabilitation for those in need for support. Cancer survivors may benefit if, in clinical medicine, more attention is given to their working life.

S

Samenvatting

De afgelopen decennia is het aantal mensen met kanker toegenomen, maar is tevens veel vooruitgang geboekt op het gebied van vroegdiagnostiek en behandeling van kanker. Hiermee is de kans op genezing ten opzichte van het verleden duidelijk toegenomen. Ook in de Nederlandse beroepsbevolking is gedurende de afgelopen decennia sprake geweest van een geleidelijke toename van het aantal werknemers met kanker. Als gevolg van deze beide ontwikkelingen zal de komende jaren het aantal werknemers dat na behandeling van kanker het werk weer wil hervatten, dan ook toenemen. De meerderheid van de werknemers die behandeld zijn voor kanker weet binnen twee jaar na ziekmelding te hervatten in werk. Toch ontvangt het Uitvoeringsinstituut Werknemersverzekeringen (UWV), de organisatie die in Nederland belast is met de uitvoering van de werknemersverzekeringen (zoals de WW, WIA en Ziektewet) ieder jaar meer dan 4200 nieuwe aanvragen voor een arbeidsongeschiktheidsuitkering vanwege de diagnose kanker. Het lukt een werknemer niet altijd terug te keren op de werkvloer omdat, ook na een succesvolle behandeling voor kanker, restklachten aanwezig kunnen blijven. Deze restklachten kunnen gepaard gaan met langdurige lichamelijke, psychische en/of cognitieve beperkingen. In dit geval kan een WIA uitkering worden aangevraagd. WIA staat voor: Wet werk en inkomen naar arbeidsvermogen, het betreft de publieke arbeidsongeschiktheidsverzekering voor werknemers. Een WIA uitkering wordt gewoonlijk aangevraagd indien iemand door ziekte niet of minder kan werken, na een ziekteverzuimperiode van maximaal twee jaar (de zogenaamde einde wachttijd WIA aanvraag). Bij een WIA aanvraag beoordeelt de verzekeringsarts de belastbaarheid van de werknemer welke, indien van toepassing, omschreven wordt met een functionele mogelijkheden lijst. Tevens dient de verzekeringsarts een uitspraak te doen over de duurzaamheid van eventuele beperkingen. De praktijk leert dat de beoordeling van de belastbaarheid bij iemand die behandeld is voor kanker niet altijd eenvoudig is. Zeker indien sprake is van moeilijk te objectiveren klachten, zoals vermoeidheid, of problemen met de aandacht en/of concentratie aanwezig blijven. Voor de werknemer die behandeld is voor kanker kan werkhervatting een gunstig effect hebben, zowel ten aanzien van gezondheid als welzijn. Werkhervatting biedt naast inkomen ook dag invulling en structuur, kan een gunstig effect hebben op het zelfvertrouwen en kan leiden tot een afname van ervaren restverschijnselen. Voor

de werkgever gaat werkhervatting vaak gepaard met afname van zowel de kosten van loondoorbetaling bij ziekteverzuim, als productieverlies. Zowel vanuit het perspectief van de werknemer als vanuit maatschappelijk oogpunt is er dan ook een belang om werkhervatting voor werknemers die behandeld zijn voor kanker te ondersteunen.

De focus van dit proefschrift richt zich daarom op (1) het stimuleren van de werkhervatting van de werknemer die behandeld is voor kanker, en (2) het ondersteunen van de verzekeringsarts die de belastbaarheid van deze werknemer beoordeelt.

In dit kader is onderzocht welke factoren verbonden zijn met werkhervatting, ziekteverzuim en arbeidsongeschiktheid bij werknemers die behandeld zijn voor kanker. Tevens is onderzocht welke factoren verzekeringsartsen gebruiken bij hun onderzoek naar de belastbaarheid van deze werknemers.

Na een algemene inleiding (Hoofdstuk 1) gaat Hoofdstuk 2 over factoren die werkhervatting en arbeidsparticipatie voorspellen bij werknemers met langdurig ziekteverzuim die behandeld zijn voor kanker. Het doel van dit onderzoek was om een overzicht van prognostische factoren voor werkhervatting en arbeidsparticipatie te verkrijgen. Het betreft een literatuuronderzoek waarbij werd gezocht naar relevante Engelstalige artikelen. Longitudinale prospectieve cohortstudies werden geselecteerd als de populatie bestond uit patiënten met kanker tussen de 18 en 65 jaar oud. Ook de kwaliteit van de geïncludeerde studies werd beoordeeld (als hoog, gemiddeld of laag) op grond van het risico op bias. Bias betekent kort gezegd “een vertekende weergave van de daadwerkelijke associatie”. Prognostische factoren werden vervolgens ingedeeld op basis van kenmerken gerelateerd aan de persoon (bijvoorbeeld leeftijd, geslacht), de ziekte (bijvoorbeeld soort tumor) of werk (bijvoorbeeld belasting in werk). Aansluitend werd ook per prognostische factor de sterkte van het gevonden bewijs bepaald, op basis van de kwaliteit van de artikelen én van het aantal artikelen over deze factoren.

Achtentwintig cohort studies voldeden aan de inclusiecriteria. Zwaar werk en chemotherapie waren negatief geassocieerd met werkhervatting, terwijl minder invasieve chirurgie positief was geassocieerd met werkhervatting. Werknemers die behandeld waren voor borstkanker hadden de grootste kans op werkhervatting.

Hogere leeftijd, lage opleiding en een laag inkomen waren negatief geassocieerd met arbeidsparticipatie.

Factoren die na twee jaar ziekteverzuim geassocieerd zijn met arbeidsongeschiktheid worden besproken in Hoofdstuk 3 en 4. In Hoofdstuk 3 staan de resultaten van een longitudinale cohort studie beschreven. Er is onderzocht welke factoren de mate van arbeidsongeschiktheid na twee jaar ziekteverzuim voorspellen. Het onderzoek betrof 131 werknemers in vaste dienst, die na ziekmelding met de diagnose kanker twee jaar werden gevolgd. Bij tien maanden ziekteverzuim ontvingen zij een vragenlijst, tevens werd na de beoordeling van de WIA aanvraag de mate van arbeidsongeschiktheid genoteerd. Als onafhankelijke variabelen werden socio-demografische, gezondheid- en werk-gerelateerde kenmerken en ook verwachtingen ten aanzien van werkhervatting gekozen. De vastgestelde mate van arbeidsongeschiktheid per einde wachttijd diende als afhankelijke variabele. De mate van arbeidsongeschiktheid werd ingedeeld in twee groepen, namelijk loonverlies ≤80% versus >80%. Univariate en multivariate analyses werden verricht, de laatste volgens een hiërarchisch model. In de multivariate analyse bleek dat het ontbreken van invloed op de reïntegratie en een negatieve visie van zorgverleners ten aanzien van de werkhervatting geassocieerd waren met een grotere mate van arbeidsongeschiktheid.

In Hoofdstuk 4 wordt een onderzoek naar determinanten van arbeidsongeschiktheid bij werknemers met kanker die twee jaar verzuimen beschreven. Het betreft een cross-sectioneel onderzoek bij 351 werknemers. Zij kregen voorafgaand aan de WIA beoordeling een vragenlijst thuisgestuurd en tevens werden gegevens bij het UWV opgevraagd. Als onafhankelijke variabelen werden wederom socio-demografische, gezondheids- en werk-gerelateerde kenmerken gekozen. De vastgestelde mate van arbeidsongeschiktheid, weer ingedeeld volgens loonverlies ≤80% versus >80%, werd als afhankelijke variabele gebruikt. Ook hier werden univariate en multivariate analyses (volgens hiërarchisch model) verricht. In de multivariate analyse bleek dat Nederlandse nationaliteit, hogere opleiding, hormoontherapie, metastasering, veel ervaren belemmeringen en laag ervaren werkvermogen geassocieerd waren met een grotere mate van arbeidsongeschiktheid.

In Hoofdstuk 5 worden de resultaten besproken van een prospectieve cohort studie naar voorspellende factoren van werkvermogen en vermoeidheid bij werknemers die behandeld zijn voor kanker. Het doel van deze studie was om prognostische factoren voor werkvermogen en vermoeidheid te identificeren. Voor dit onderzoek werden werknemers geselecteerd die behandeld waren voor kanker, twee jaar verzuimden, en een aanvraag voor een WIA uitkering hadden ingediend. Bij de WIA aanvraag en één jaar later werden gegevens verzameld met een vragenlijst. Ook werden gegevens bij het UWV opgevraagd. Univariate en multivariate lineaire regressie analyse werd gebruikt om voorspellers te identificeren. Vervolgens werden twee predictiemodellen gemaakt, een om werkvermogen en een om vermoeidheid één jaar na de WIA beoordeling te voorspellen. Uit het predictiemodel voor werkvermogen blijkt dat een hoger werkvermogen één jaar na de WIA beoordeling wordt voorspeld door behandeling met chemotherapie, een algemeen beter ervaren gezondheid, en het oorspronkelijk rond de WIA beoordeling gerapporteerde werkvermogen. Een lager werkvermogen één jaar na de WIA beoordeling wordt voorspeld door kostwinnerschap, of iemand ziektevrij is, de ervaren fysieke belemmeringen, en de mate van loonverlies. Uit het predictiemodel voor vermoeidheid blijkt dat grotere vermoeidheid één jaar na de WIA beoordeling voorspeld wordt door burgerlijke staat (bijvoorbeeld meer vermoeidheid bij gescheiden werknemers of wier partner was overleden), de ervaren fysieke belemmeringen, depressieve symptomen, en werken in de gezondheidszorg. Een lagere vermoeidheid wordt voorspeld door behandeling met chemotherapie en het niveau van vermoeidheid bij de WIA beoordeling.

Hoofdstuk 6 gaat over de rol van coping bij werknemers die behandeld zijn voor kanker. Het doel was om de mogelijke mediërende rol van actieve en passieve coping te onderzoeken tussen enerzijds zelf-gerapporteerde gezondheidsklachten en anderzijds functionele beperkingen, zoals beoordeeld door een verzekeringsarts, zelf gerapporteerd werkvermogen, en werkstatus. Met gevalideerde vragenlijsten werden gegevens met betrekking tot gezondheid, werkvermogen en werkstatus verzameld. De functionele beperkingen van de respondenten werden getransformeerd in schalen voor psychische en lichamelijke beperkingen, en beperkingen van

de werktijden. Met behulp van een LISREL analyse werd een model ontworpen en getest. Hierin werd alleen voor actieve coping een mediërende rol gevonden.

De bevindingen van een kwalitatief onderzoek worden in Hoofdstuk 7 gepresenteerd. Dit hoofdstuk gaat over factoren die verzekeringsartsen gebruiken bij het beoordelen van de belastbaarheid van kankerpatiënten na twee jaar ziekteverzuim. Hiertoe werden focusgroep interviews verricht, waaraan 29 verzekeringsartsen deelnamen. Zij werden groepsgewijs bevraagd naar de wijze waarop zij de belastbaarheid van werknemers die behandeld zijn voor kanker beoordelen, in het bijzonder met betrekking tot vermoeidheidsklachten. Ook het gebruik van de functionele mogelijkheden lijst en verzekeringsgeneeskundige protocollen werd besproken. Tenslotte was er aandacht voor de behoefte onder de verzekeringsartsen aan een prognostisch instrument van werkvermogen. Uit het onderzoek blijkt dat verzekeringsartsen grote verantwoordelijkheid voelen om de belastbaarheid van deze werknemers zo goed mogelijk te beoordelen. Hierbij worden in eerste aanleg argumenten van medische aard en inhoud gebruikt. Naar mate deze medische argumenten minder uitgesproken zijn, wordt meer belang gehecht aan niet medische factoren ter onderbouwing van het oordeel. Ook blijkt dat het gebruik van de bestaande verzekeringsgeneeskundige protocollen verdere aandacht verdient, en dat bij de invoering van een prognostisch instrument van werkvermogen een implementatiestrategie gewenst is.

In hoofdstuk 8 volgt de discussie, waarin de belangrijkste resultaten van dit proefschrift worden besproken, in onderling verband én in perspectief worden geplaatst. Hierbij worden de bevindingen ook gespiegeld aan de resultaten van eerder onderzoek waarna aanbevelingen voor verder onderzoek en voor de praktijk volgen. Als belangrijke punten kunnen worden genoemd dat:

– diverse voorspellers (zoals functie-eisen, gezondheid, verwachtingen en sociale steun) van invloed zijn op de arbeidsparticipatie van werknemers die behandeld zijn voor kanker;
– de verzekeringsarts deze voorspellers dient te betrekken bij zijn/haar onderzoek, bij voorkeur in een vroeg stadium;

– de verzekeringsarts zich hierbij bewust moet zijn van eigen attitude, niet louter aandacht dient te schenken aan gepresenteerde gezondheidsklachten, en dat gebruik van beschikbare protocollen tot meer uniformiteit kan leiden;
– op basis van de resultaten van dit onderzoek een prognostisch instrument voor werkvermogen is ontwikkeld, hetgeen de verzekeringsarts kan ondersteunen bij de beoordeling van de belastbaarheid en/of het plannen van een heronderzoek.

Als aanbeveling voor verder onderzoek is het gewenst om te kijken naar langetermijn effecten van behandeling voor kanker op deelname in arbeid en naar het effect van vroege interventies op arbeidsongeschiktheid na twee jaar ziekteverzuim bij kankerpatiënten. Maar ook onderzoek naar langdurige arbeidsongeschiktheid na behandeling voor kanker verdient verdere aandacht. In het bijzonder lijkt het gewenst hierbij aandacht te schenken aan de kwetsbare positie van werknemers zonder vast dienstverband, de zogenaamde vangnetters.

Als aanbeveling voor de praktijk wordt verzekeringsartsen bij de beoordeling van de belastbaarheid van werknemers die behandeld zijn voor kanker, geadviseerd rekening te houden met de verwachtingen en perceptie van de werknemer, het ervaren werkvermogen en sociale steun. Beleidsmakers binnen de verzekeringsgeneeskunde wordt geadviseerd om de verdere ontwikkeling en validering van predictieregels te faciliteren en ter hand te nemen, waarbij actieve participatie van verzekeringsartsen gewenst is. Tot slot lijkt het noodzakelijk dat, zowel in de eerste als tweedelijns geneeskunde, (nog) meer aandacht komt voor arbeidsparticipatie van werknemers die behandeld zijn voor kanker.

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D

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