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Published in:
BMJ Open

DOI:
10.1136/bmjopen-2018-021742

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Document Version
Final author's version (accepted by publisher, after peer review)

Publication date:
2019

Link to publication in University of Groningen/UMCG research database

Citation for published version (APA):

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Influence of significant others on work participation of individuals with chronic diseases: a systematic review

Nicole C Snippen,1 Haitze J de Vries,1 Sylvia J van der Burg-Vermeulen,2 Mariët Hagedoorn,3 Sandra Brouwer1

ABSTRACT

Objective It is widely recognised that significant others (SOs), such as a partner, family member or friend, can influence health outcomes of individuals with a chronic disease. However, not much is known about which specific cognitions (ie, illness perceptions and expectation of work ability) and behaviours (eg, emotional and practical support) of SOs influence work participation. Therefore, we aimed to identify cognitions and behaviours of SOs that are related to work participation of individuals with a chronic disease.

Design A systematic review and thematic synthesis.

Data sources PubMed, Embase, PsycINFO, SocINDEX and Web of Science were searched until 28 March 2017.

Eligibility criteria for selecting studies We included studies reporting on cognitions and behaviours of SOs related to work participation in populations with various chronic diseases.

Data extraction and synthesis Two independent reviewers extracted the data and performed a quality assessment using the Quality Assessment Tool for Quantitative Studies from the Effective Public Health Practice Project 2007 and a checklist for assessment of qualitative studies derived from the Cochrane Supplemental Handbook Guidance. Evidence was thematically synthesised.

Results Out of 5168 articles, 18 were included (15 qualitative and 3 quantitative) of moderate to high quality. Studies were on cancer, chronic pain, brain injuries and mental health disorders. After thematic synthesis 27 factors could be distinguished. Consistent evidence was found that SOs’ positive and encouraging attitudes towards sickness absence and advise, encouragement or pressure to refrain from work.

Conclusions Our findings show that several cognitions and behaviours of SOs can facilitate or hinder work participation of individuals with a chronic disease. Intervening on these factors by involving SOs in disability prevention and return to work intervention strategies may be beneficial. More prognostic studies are needed, as the current evidence is mostly based on qualitative studies.

Strengths and limitations of this study

To our knowledge, this is the first systematic review that has investigated cognitions and behaviours of significant others that may influence work participation of individuals with a chronic disease.

The present systematic review was based on a comprehensive search of the literature in five relevant databases, with an additional reference check.

We used quality assessment tools recommended by Cochrane to assess the quality of the evidence.

This review is limited to English articles; articles in languages other than English were excluded.

The small number of quantitative studies rendered a meta-analysis impossible; therefore, no statistical analyses were performed.

INTRODUCTION

Cognitions and behaviours of significant others (SOs) in the personal environment, such as a partner, family member or friend, can play an important role in health outcomes of individuals with a chronic disease.1–6 In the clinical setting, it has been shown that the behaviour of SOs can have either detrimental or favourable effects on perceived symptoms and behaviour of individuals with a chronic disease, thereby influencing recovery, treatment effects, quality of life and disability.3–5 Although it is widely recognised that SOs can also influence work participation of individuals with a chronic disease, for instance, through social support,7–11 research on the influence of SOs on work outcomes is scarce. Despite increasing evidence that beliefs and behaviours of SOs are important for work outcomes,7–11 not much is known about which specific cognitions or behaviours of SOs influence work participation of their relatives and friends.

A rationale for the influence of SOs on work participation can be found in cognitive behavioural models, which propose that a person’s cognitions with regard to
the disease and work, that is, thoughts, beliefs, attitudes and expectations, generate behavioural and emotional responses to illness events and guide coping strategies. There is evidence that behaviours of SOs influence the behaviour and consequently health and work outcomes of individuals with a chronic disease. Illness perceptions held by SOs—consisting of perceptions and beliefs concerning the disease—have been proposed to be a mechanism through which SOs may influence work participation. In this context, several studies have described that SOs can reinforce an individual’s unhelpful cognitions about the illness, such as beliefs about limitations due to the disease, mistaken beliefs about the nature of illness, pessimistic beliefs regarding the outcome of treatment and the unlikelihood of returning to work.

In occupational healthcare, there is a growing notion that the social context plays an important role in return-to-work (RTW) processes and that it can be beneficial to address social factors such as responses of SOs. As there is evidence that clinical healthcare interventions in which SOs are involved are more effective than care as usual where SOs are not involved, this may also prove to be beneficial in occupational healthcare. Consequently, various multidisciplinary guidelines recommend (occupational) health professionals to address social factors and involve SOs such as family members in treatment and care.

In recent years, the focus in healthcare has shifted to self-management and adapting to a disease, which requires a more supportive role for (occupational) health professionals. Aside from facilitating and supporting the RTW process of sick-listed workers, occupational health professionals have the responsibility to support workers to cope with problems due to disease and to empower them to manage their own health and well-being to prevent sickness absence. In this context, professionals should support workers to use their own resources to successfully adapt to a disease and to enable them to work. One resource that may be used to support individuals with a chronic disease to participate in work is their network of SOs.

Although it is recognised that SOs can influence workers’ recovery and work outcome, more research is needed to determine which specific cognitivebehavioural factors in the social environment influence work participation and should therefore be taken into account in occupational healthcare. Therefore, in this systematic review we aim to identify cognitions and behaviours of SOs that are related to work participation of individuals with a chronic disease. Investigating which SO-related factors are associated with work participation of individuals with a chronic disease may increase our understanding of staying at work and RTW processes, which can be applied in occupational health interventions to facilitate work participation.

**METHOD**

**Search strategy**

We conducted a search in PubMed, Embase, PsycINFO, SocINDEX and Web of Science (inception of databases until 28 March 2017). When available, subject headings such as MeSH terms in PubMed were used, in addition to free text words. Four main categories (chronic illness, work participation, SOs and SOs’ cognitions and behaviours) were combined with the Boolean operator ‘AND’ to identify studies (online supplementary text S1). We included terms on the following chronic diseases: diabetes mellitus, cancer, chronic pain, chronic fatigue, cardiovascular diseases, pulmonary diseases, musculoskeletal disorders, brain injuries and depressive disorder. Additionally, we included broader search terms such as ‘chronic disease’ and ‘disabled persons’. In addition to the search, we conducted a reference check to identify additional studies not retrieved through database searching.

**Selection of studies**

The article selection was performed in three phases by two independent reviewers (NCS, HJdV). In the first phase, articles were excluded based on title. Second, articles were excluded based on abstract. In the third phase, the reviewers selected articles for final inclusion based on full-text appraisal. To be included, articles had to meet the following criteria: (i) the study population consisted of subjects with a chronic illness or their SOs; (ii) the subjects were aged 18–67 years (working population); (iii) the study examined sickness absence, work disability, unemployment, RTW or staying at work as the outcome; (iv) at least one of the independent variables investigated concerned cognitions or behaviour of a SO (a family member, close friend, spouse or partner) and (v) the article was written in English.

In this study, we were interested in SOs’ cognitions such as their perceptions and interpretations of the causes and consequences of their close other’s illness and work ability, in this study defined as thoughts, beliefs, attitudes and expectations. Furthermore, with regard to behaviour, studies were included if they reported on specific supportive or obstructive behaviours of SOs (eg, giving advice, showing empathy, taking over household chores, pressuring their close other to rest). As we aimed to find specific behaviours of SOs related to work outcomes, only studies in which constructs such as social support or emotional support were defined as actual provided or received behaviour were included. Studies reporting on satisfaction with support or experienced support from SOs, without providing information on specific provided or received behaviours of SOs, were excluded. Finally, we included both self-reported cognitions and behaviours by SOs and cognitions and behaviours of SOs as perceived by individuals with a chronic disease, as both perspectives are relevant for the research question in this review.

Studies were excluded when both reviewers considered that these did not fulfil the inclusion criteria.
Disagreements regarding inclusion were resolved by consensus. If no consensus was reached or in case of doubt, the article was screened by the other authors and discussed to reach consensus.

**Data extraction**

Two reviewers (NCS, HJdV) independently extracted the data from all selected studies using an adapted version of the Cochrane Data collection form for intervention reviews on randomised controlled trials (RCTs) and non-RCTs. The following information was extracted from every included study: study design; study objectives; diagnosed condition; general description of subjects including age, gender and additional details; outcome measures; type of SO; investigated or identified cognitions or behaviour of SOs and relation with the studied work outcome.

**Assessment of quality**

The quality of included quantitative studies was assessed using the Quality Assessment Tool for Quantitative Studies from the Effective Public Health Practice Project 2007, recommended by Cochrane. This tool is suitable for assessment of studies of any quantitative design. Two reviewers (NCS, HJdV) used this tool to rate studies on selection bias, study design, confounders, blinding, data collection method and withdrawals and dropouts (online supplementary table S1). Based on these criteria, quality was rated as low when two or more components had weak ratings, moderate when one component had a weak rating and strong if there were no weak ratings.

The quality of included qualitative studies was independently assessed by two reviewers (NCS, HJdV) using a checklist with criteria for assessment of qualitative studies derived from the Cochrane Supplemental Handbook Guidance. This checklist identified credibility, transferability, dependability and confirmability (online supplementary table S2). Based on these criteria, studies were rated as having high quality if all criteria were met; moderate if flaws were identified in one or more criteria that raised some doubt about the results and low when flaws were identified in one or more criteria that seriously weakened confidence in the results.

**Evidence grading**

For each individual outcome, the body of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach. In grading the evidence, qualitative studies were not considered. The initial level of evidence was determined by study design, after which the level of evidence may have been downgraded depending on the presence of five factors or upgraded depending on the effect size (online supplementary box S1).

**Data synthesis**

As it was expected that most studies would be of qualitative nature, a thematic synthesis was conducted, with a separate synthesis of results for quantitative and qualitative studies. This method is often used to analyse data in primary qualitative research to integrate the findings of multiple qualitative studies. The thematic analysis consisted of three stages: line-by-line extraction of the data, developing descriptive themes and generating analytical themes. In the first stage, the relevant findings of the studies were extracted, including the association with the studied work outcome. In the second stage, the findings were grouped together to form various descriptive themes. Finally, in the third stage, the descriptive themes were grouped together by type of factor, based on whether it concerns SOs’ cognitions or behaviours. Furthermore, as prior research has found moderate correlations between self-reports and informant reporting, a distinction was made between self-reported cognitions and behaviours versus cognitions and behaviours of SOs as perceived by individuals with a chronic disease.

To give an overall overview of the results, we summarised for each factor: (i) the total number of studies reporting on the factor, (ii) the number of studies of low, moderate and high quality reporting on the factor and (iii) whether the factor was consistently reported as either a facilitator or barrier for work participation of individuals with a chronic disease across studies.

**Patient involvement**

In this systematic review, no patients were involved in setting the research question, the outcome measures, the design or conduct of the study. No patients were asked to advise on interpretation of results or to contribute to the writing or editing of this document. An advisory work group consisting of a patient representative and occupational health professionals will be consulted on dissemination of the study results.

**RESULTS**

**Selection of studies**

The search of the databases identified 5168 articles, excluding duplicates (figure 1). After screening on titles and abstracts, 117 articles remained for possible inclusion. Reference checks identified 18 additional studies, resulting in a total of 135 articles for full-text assessment. After full-text screening, 117 studies were excluded. The main reason for exclusion was that no cognitions or behaviours of SOs were identified or discussed. Other reasons for exclusion were that studies did not examine any work outcome; did not focus on workers with a chronic disease or the study population was not of working age. Five articles were discussed within the team in order to reach consensus. The first author of one article was contacted for additional information to allow making a decision. Finally, 18 articles met the criteria for inclusion and were assessed for quality.
The main characteristics of the included quantitative and qualitative studies are respectively presented in table 1 and online supplementary table S3. The reported cognitions and behaviours of SOs are presented with the direction of its association with the studied work outcome. We aimed to provide a comprehensive overview of participant characteristics of each study, including information on age, gender, ethnicity, education and chronic disease(s). Unfortunately, not all the desired information was available across articles and could therefore not be consistently reported in table 1 and online supplementary table S3. For example, as most studies did not include information about participants’ ethnicity, this information is only included for the studies that did report on participants’ ethnicity.

Studies with various populations were included, mostly involving somatic diseases including various types of cancer, chronic pain and brain injuries. However, one study focused on individuals with severe and persistent mental illnesses. Within the included studies, participants’ age ranged from their early 20s to their late 60s.

Three quantitative studies (one cross-sectional, one retrospective and one prospective cohort study) and 15 qualitative studies were included. One quantitative study focused primarily on the influence of behaviours of SOs on work participation of individuals with a chronic disease, while in the other two studies the influence of behaviours and cognitions of SOs on work participation was one of several factors being investigated. In all three studies, the study population consisted of individuals with a chronic disease, in which participants reported about perceived cognitions and behaviours of their SOs. Of the qualitative studies, seven studies focused primarily on the role of SOs regarding work participation of individuals with a chronic disease. In four of these studies, interviews were conducted with both SOs who reflected on their own behaviour and individuals with a chronic disease who

Figure 1  Flow diagram of the search process. SO, significant others.
Table 1  Characteristics of included quantitative studies

<table>
<thead>
<tr>
<th>Author, year (ref no.)</th>
<th>Country</th>
<th>Study design</th>
<th>Aim of the study</th>
<th>Sample</th>
<th>Involved significant other(s)</th>
<th>Work outcome</th>
<th>Identified cognitions or behaviours of significant other(s)</th>
<th>Association with work outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balswick 1970(50)</td>
<td>USA, Iowa</td>
<td>Cross-sectional</td>
<td>To examine the relationship between spouse companionship support and the degree of vocational rehabilitation success on the part of a handicapped spouse</td>
<td>245 predominantly white participants diagnosed with physical or learning disabilities, a mean age of 38 years and an average education of 12 years</td>
<td>Spouse</td>
<td>Employment success (proportion of time that the patient was employed fulltime during the previous year)</td>
<td>Participation of the spouse in the patient’s life outside the job (only for those patients having had 12 or more years of education) ( \chi^2=6.34 (p&lt;0.01)^* ) + More ‘dubious’ support from the spouse: expressing concern about the handicap, encouraging the patient in work, talking with the patient about goals and plans (among those subjects with an education under 12 years) ( \chi^2=4.57 (p&lt;0.05)^* ) -</td>
<td></td>
</tr>
<tr>
<td>Kong et al 2012(48)</td>
<td>China</td>
<td>Retrospective cohort study</td>
<td>To predict the RTW outcome and optimise the intervention scheme of a case management programme initiated in China</td>
<td>335 participants with work-related injuries—mostly fractures (61.8%) or another limb injury (75.8%)—with a mean age of 36.3 years (SD=9.7 years). Most participant were male (86.0%), married (75.8%), migrant workers (60.3%), with middle school education (82.7%)</td>
<td>Family members</td>
<td>Successful return to work (sustained work for at least 3 months during follow-up period) and shorter absence duration (period between discharge from the rehabilitation centre and resuming work)</td>
<td>Positive family attitude towards return to work (RTW: ( p&lt;0.05 ), HR=4.0, absence duration: ( p&lt;0.01 ))^* +</td>
<td></td>
</tr>
<tr>
<td>Sandström and Esbjornsson 1986(40)</td>
<td>Sweden</td>
<td>Prospective cohort study with follow-up at 1 and 4 years</td>
<td>To determine the significance of the patient’s own prediction as to whether he/she would, or would not, return to work after vocational rehabilitation</td>
<td>52 participants with non-specific low back pain. Male participants (n=35) had a mean age of 41 years (range 27–49) and female participants (n=17) had a mean age of 38 years (range 29–49)</td>
<td>Close relatives</td>
<td>Return to work (study I: sick listed for 25 days or less, study II: sick listed for 6 months or less)</td>
<td>Opinion of closest relatives that the patient is too ill to return to work (( p&lt;0.05 ))^* -</td>
<td></td>
</tr>
</tbody>
</table>

*Reported by individuals with a chronic disease. +, facilitator for studied work outcome; –, barrier for studied work outcome. RTW, return to work.
reported about perceived cognitions and behaviours of their SOs. In one study, the study population consisted of SOs only and in two studies the study population consisted only of individuals with a chronic disease. Aside from those studies with a primary focus on the influence of SOs on work outcome, eight qualitative studies did include findings on this topic, but did not primarily focus on the influence of SOs on work outcomes. In these studies, only interviews with individuals with a chronic disease were conducted.

Quality assessment

The results of the quality assessment of quantitative studies are presented in table 2. In all studies, the data collection method was rated as weak because the data collection tools were not shown to be reliable and/or valid or this was unclear. However, as this was the only weak rating in every study, the overall quality was moderate for all studies.

The results of the quality assessment of qualitative studies are presented in table 3. The quality of the included qualitative studies ranged from moderate to high. The agreement of the two reviewers was high on credibility, transferability and dependability and moderate on confirmability. The confirmability was unclear for multiple studies, often due to lack of information; however, we considered it unlikely that this would seriously alter the results.

Grading the evidence of SO factors in quantitative studies

The results of the level of evidence assessment of quantitative studies are presented in table 4. All three studies were observational; therefore, all studied factors initially had a low level of evidence. We found no reasons to downgrade the level of evidence of any of the factors. The level of evidence of one factor (positive family attitude towards RTW) was upgraded to moderate because a large effect was found (HR=4.0). The five factors assessed for level of evidence were each found in only one quantitative study. Although many factors were not studied in quantitative studies and could therefore not be graded, various factors were reported in multiple qualitative studies (table 5).

Synthesis of quantitative studies

In the three quantitative studies five SO factors were reported, which are described in the sections below. In these studies, all factors were reported by individuals with a chronic disease.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Selection bias</th>
<th>Study design</th>
<th>Confounders</th>
<th>Blinding</th>
<th>Data collection method</th>
<th>Withdrawals and dropouts</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balswick, 1970</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Kong et al 2012</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Sandström and Esbjornsson, 1986</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>1</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

1, strong rating; 2, moderate rating; 3, weak rating; 4, not applicable.

<table>
<thead>
<tr>
<th>Author(s)</th>
<th>Credibility</th>
<th>Transferability</th>
<th>Dependability</th>
<th>Confirmability</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Auerbach and Richardson, 2005</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Brooks et al 2013</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Dorland et al 2016</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Duijts et al 2016</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Frederiksen et al 2015</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Gagnon et al 2016</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Main et al 2005</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>McCluskey et al 2011</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>McCluskey et al 2014</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>McCluskey et al 2015</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Nilsson et al 2011</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rubenson et al 2007</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
<tr>
<td>Svensson et al 2010</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tamminga et al 2012</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Tan et al 2012</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>?</td>
<td>2</td>
</tr>
</tbody>
</table>

1, high; 2, moderate; 3, low; ?, unclear.
Significant others’ cognitions

Beliefs of SOs regarding the consequences of the disease and RTW were found to be related to RTW. The opinion of close relatives that patients were too ill to return to work and worries that the condition would deteriorate if patients would return to work were both negatively related to RTW.49 Additionally, positive attitudes of family towards RTW was found to be strongly related to a shorter duration of sickness absence and a higher chance of RTW.48

Significant others’ behaviours

Participatory support from a spouse—measured by a combination of engaging in relaxing activities together, attending events together and sharing meals—was found to be significantly associated with more employment success (the proportion of time the patient was employed full-time during the past year).50 However, this only held true for patients with 12 or more years of education.50 On the other hand, the degree of what the authors defined as ‘dubious support’ from a spouse had a negative relationship with employment success among lower educated patients.50 In that study, dubious support was measured with three questions in which participants had to indicate how much their spouse was concerned about the participant’s handicap, how much their spouses encouraged them in their work and the number of times participants talked over their goals and plans with their spouses.50 The authors reasoned that spouses should be less concerned about the handicap when participants were more adjusted in their work, and that more adjusted participants would need less encouragement and had less need to talk over life goals and plans. The authors state that positive responses on dubious support could therefore not only be a sign of healthy companionship support, but could also be an indication of over support.50

Synthesis of qualitative studies

The 15 qualitative studies reported on 60 factors (including duplicate factors). After thematic synthesis, 26 factors remained of which are described below. Of these factors, 13 were reported by SOs, 5 by workers with a chronic disease and 8 by both workers with a chronic disease and SOs.

Table 4: Level of evidence of significant others factors studied in quantitative studies

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participating in the patient’s life outside the job</td>
<td>1</td>
<td>Cross-sectional study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>‘Dubious’ support</td>
<td>1</td>
<td>Cross-sectional study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Positive family attitude towards return to work</td>
<td>1</td>
<td>Retrospective cohort study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Strong association</td>
<td>Moderate</td>
</tr>
<tr>
<td>Opinion of closest relatives that the patient is too ill to return to work</td>
<td>1</td>
<td>Prospective cohort study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Worries of closest relatives regarding deterioration of the patient’s condition if returning to work</td>
<td>1</td>
<td>Prospective cohort study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
</tbody>
</table>

Significant others’ cognitions

Significant others’ behaviours

Participatory support from a spouse—measured by a combination of engaging in relaxing activities together, attending events together and sharing meals—was found to be significantly associated with more employment success (the proportion of time the patient was employed full-time during the past year).50 However, this held true only for patients with 12 or more years of education.50

Significant others’ cognitions

Beliefs of SOs regarding the consequences of the disease and RTW were found to be related to RTW. The opinion of close relatives that patients were too ill to return to work and worries that the condition would deteriorate if patients would return to work were both negatively related to RTW.49 Additionally, positive attitudes of family towards RTW was found to be strongly related to a shorter duration of sickness absence and a higher chance of RTW.48

Significant others’ behaviours

Participatory support from a spouse—measured by a combination of engaging in relaxing activities together, attending events together and sharing meals—was found to be significantly associated with more employment success (the proportion of time the patient was employed full-time during the past year).50 However, this only held true for patients with 12 or more years of education.50 On the other hand, the degree of what the authors defined as ‘dubious support’ from a spouse had a negative relationship with employment success among lower educated patients.50 In that study, dubious support was measured with three questions in which participants had to indicate how much their spouse was concerned about the participant’s handicap, how much their spouses encouraged them in their work and the number of times participants talked over their goals and plans with their spouses.50 The authors reasoned that spouses should be less concerned about the handicap when participants were more adjusted in their work, and that more adjusted participants would need less encouragement and had less need to talk over life goals and plans. The authors state that positive responses on dubious support could therefore not only be a sign of healthy companionship support, but could also be an indication of over support.50

Synthesis of qualitative studies

The 15 qualitative studies reported on 60 factors (including duplicate factors). After thematic synthesis, 26 factors remained of which are described below. Of these factors, 13 were reported by SOs, 5 by workers with a chronic disease and 8 by both workers with a chronic disease and SOs.

Table 4: Level of evidence of significant others factors studied in quantitative studies

<table>
<thead>
<tr>
<th>Factor</th>
<th>Number of studies</th>
<th>Study design</th>
<th>Risk of bias</th>
<th>Inconsistency</th>
<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participating in the patient’s life outside the job</td>
<td>1</td>
<td>Cross-sectional study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>‘Dubious’ support</td>
<td>1</td>
<td>Cross-sectional study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Positive family attitude towards return to work</td>
<td>1</td>
<td>Retrospective cohort study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Strong association</td>
<td>Moderate</td>
</tr>
<tr>
<td>Opinion of closest relatives that the patient is too ill to return to work</td>
<td>1</td>
<td>Prospective cohort study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
<tr>
<td>Worries of closest relatives regarding deterioration of the patient’s condition if returning to work</td>
<td>1</td>
<td>Prospective cohort study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
</tbody>
</table>

Significant others’ cognitions

Beliefs of SOs regarding the consequences of the disease and RTW were found to be related to RTW. The opinion of close relatives that patients were too ill to return to work and worries that the condition would deteriorate if patients would return to work were both negatively related to RTW.49 Additionally, positive attitudes of family towards RTW was found to be strongly related to a shorter duration of sickness absence and a higher chance of RTW.48

Significant others’ behaviours

Participatory support from a spouse—measured by a combination of engaging in relaxing activities together, attending events together and sharing meals—was found to be significantly associated with more employment success (the proportion of time the patient was employed full-time during the past year).50 However, this only held true for patients with 12 or more years of education.50 On the other hand, the degree of what the authors defined as ‘dubious support’ from a spouse had a negative relationship with employment success among lower educated patients.50 In that study, dubious support was measured with three questions in which participants had to indicate how much their spouse was concerned about the participant’s handicap, how much their spouses encouraged them in their work and the number of times participants talked over their goals and plans with their spouses.50 The authors reasoned that spouses should be less concerned about the handicap when participants were more adjusted in their work, and that more adjusted participants would need less encouragement and had less need to talk over life goals and plans. The authors state that positive responses on dubious support could therefore not only be a sign of healthy companionship support, but could also be an indication of over support.50

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<th>Indirectness</th>
<th>Imprecision</th>
<th>Other considerations</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participating in the patient’s life outside the job</td>
<td>1</td>
<td>Cross-sectional study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
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<td>1</td>
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<td>Not serious</td>
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<td>None</td>
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</tr>
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<td>Worries of closest relatives regarding deterioration of the patient’s condition if returning to work</td>
<td>1</td>
<td>Prospective cohort study</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>Not serious</td>
<td>None</td>
<td>Low</td>
</tr>
</tbody>
</table>
### Table 5: Overview of evidence found for significant others factors associated with work participation

<table>
<thead>
<tr>
<th>Type of factor</th>
<th>Factors investigated</th>
<th>Number and type of articles</th>
<th>High quality</th>
<th>Moderate quality</th>
<th>Consistency</th>
<th>Reported by</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cognitions</strong></td>
<td>Work as cause of the disease&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>1 QS, 1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Working is not possible due to disease (ability to work depends on a cure)&lt;sup&gt;3-9&lt;/sup&gt;</td>
<td>1 PCS, 1 QS</td>
<td>1 QS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Consequences of the disease are permanent&lt;sup&gt;19,51&lt;/sup&gt;</td>
<td>2 QS, 1 QS</td>
<td>1 QS</td>
<td>+</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Believing that return to work will lead to deterioration of condition&lt;sup&gt;19,51&lt;/sup&gt;</td>
<td>1 PCS, 1 QS, 1 QS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Perceiving that patient has no rights with regard to previous employment&lt;sup&gt;19&lt;/sup&gt;</td>
<td>1 QS, 1 QS, 1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Perceived low level of control over the patient's employment&lt;sup&gt;1&lt;/sup&gt;</td>
<td>2 QS</td>
<td>2 QS</td>
<td>+</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive and encouraging attitudes/outlook in general and with regard to return to work&lt;sup&gt;48-53,99&lt;/sup&gt;</td>
<td>1 RCS, 3 QS, 2 QS, 1 RCS, 1 QS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive attitude about the patient and his abilities (viewing the patient as not being disabled or a victim)&lt;sup&gt;10,22&lt;/sup&gt;</td>
<td>2 QS</td>
<td>2 QS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Negative attitudes about the availability of suitable work&lt;sup&gt;21&lt;/sup&gt;</td>
<td>1 QS, 1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Distrust towards the patient and the severity of the complaints and disease&lt;sup&gt;20&lt;/sup&gt;</td>
<td>1 QS, 1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exaggerated protective attitude&lt;sup&gt;10&lt;/sup&gt;</td>
<td>1 QS</td>
<td>1 QS</td>
<td>n/a</td>
<td>Individuals with a chronic disease</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Positive attitudes towards sickness absence&lt;sup&gt;37-60&lt;/sup&gt;</td>
<td>4 QS, 2 QS, 2 QS, 2 QS</td>
<td>+</td>
<td>Individuals with a chronic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Behaviours</strong></td>
<td>Enabling discussion about return to work, talking with and listening to the patient&lt;sup&gt;31,53,95,61&lt;/sup&gt;</td>
<td>4 QS, 2 QS, 2 QS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sharing information&lt;sup&gt;61&lt;/sup&gt;</td>
<td>1 QS, 1 QS</td>
<td>n/a</td>
<td>Individuals with a chronic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Giving feedback, advice and guidance with regard to future planning&lt;sup&gt;32,95&lt;/sup&gt;</td>
<td>2 QS, 1 QS, 1 QS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Showing understanding and empathy&lt;sup&gt;31,53,95,58&lt;/sup&gt;</td>
<td>4 QS, 2 QS</td>
<td>2 QS</td>
<td>–</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Emphasising what a patient can still do&lt;sup&gt;19&lt;/sup&gt;</td>
<td>1 QS</td>
<td>1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Highlighting beneficial consequences of employment&lt;sup&gt;59&lt;/sup&gt;</td>
<td>1 QS</td>
<td>1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Encouraging and motivating the patient&lt;sup&gt;10,52,53,95,57,61,62&lt;/sup&gt;</td>
<td>7 QS, 4 QS, 3 QS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Emphasising the negative consequences of the disease&lt;sup&gt;19&lt;/sup&gt;</td>
<td>1 QS</td>
<td>1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Waiting on a cure&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1 QS</td>
<td>1 QS</td>
<td>n/a</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Validating patients' statements of incapacity and self-limiting behaviour&lt;sup&gt;19,51&lt;/sup&gt;</td>
<td>2 QS, 1 QS</td>
<td>1 QS</td>
<td>+</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Advising, encouraging and pressuring the patients to refrain from work or not return to work&lt;sup&gt;59,57-60&lt;/sup&gt;</td>
<td>5 QS, 2 QS, 3 QS</td>
<td>+</td>
<td>Individuals with a chronic disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Helping with daily activities, household tasks and transportation&lt;sup&gt;51,54-56,60,61&lt;/sup&gt;</td>
<td>6 QS, 5 QS, 1 QS</td>
<td>–</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Exploring and accessing beneficial services and resources (both at and outside of work)&lt;sup&gt;19,55&lt;/sup&gt;</td>
<td>2 QS, 1 QS</td>
<td>1 QS</td>
<td>+</td>
<td>SOs</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Participation in the patient's life, doing joint activities/initiating activities&lt;sup&gt;50,53&lt;/sup&gt;</td>
<td>1 CSS, 2 QS, 1 QS, 1 CSS</td>
<td>+</td>
<td>Individuals with a chronic disease and SOs</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Providing dubious support&lt;sup&gt;50&lt;/sup&gt;</td>
<td>1 CSS</td>
<td>1 CSS</td>
<td>n/a</td>
<td>Individuals with a chronic disease</td>
<td></td>
</tr>
</tbody>
</table>

+ Consistently reported as either a facilitator or barrier for work participation across studies; –, not consistently reported as either a facilitator or barrier for work participation across studies; n/a, not applicable (reported in only one study); CSS, cross-sectional study; PCS, prospective cohort study; QS, qualitative study; RCS, retrospective cohort study; SO, significant other.
control over patients’ illness, recovery, work situation and employment were reported to be barriers for patients’ ability to remain in employment and RTW. However, factors concerning SOs’ perceived negative consequences of the disease (for work) and lack of control over the disease and employment were only mentioned by SOs, not by individuals with a chronic disease.

Additionally, positive, encouraging and supportive attitudes from SOs were reported as a determinant of patients’ ability to remain in employment, job retention, staying at work and productive occupations. In these cases, SOs remained positive both about patients and their abilities and viewed patients as not being disabled or victims. On the other hand, negative and pessimistic attitudes of SOs were reported to negatively affect patients’ ability to stay at work and return to work. SOs’ negative attitudes were directed at the availability of suitable work and consisted of distrust towards the severity of patients’ complaints and disease. Finally, exaggerated protective attitudes and expressing positive attitudes towards sickness absence were reported to be barriers for work functioning and RTW. Although SOs’ positive attitudes towards sickness absence was frequently reported as a barrier for work participation by individuals with a chronic disease, it was not mentioned by SOs.

Significant others’ behaviours
Maintaining open communication with patients was reported as a behavioural determinant of job retention, staying at work and productive occupations. This communication included talking with and actively listening to patients; sharing information; enabling discussion about return to work and giving feedback, advice and guidance.

There are contradicting findings with regard to showing understanding and empathy. On the one hand, patients and SOs emphasised the importance of understanding and sympathy from SOs with regard to patients’ ability to stay at work and return to work and productive activities. On the other hand, in one study patients who had not successfully returned to work reported a high degree of sympathy from their SOs in combination with SOs validating their incapacity and self-limiting behaviour. The authors hypothesised that these behaviours may have acted as obstacles for RTW, as SOs reinforced patients’ unhelpful beliefs concerning the chance of re-injury or the likelihood of RTW.

Empowering, encouraging and motivating behaviour from SOs was also reported as a behavioural determinant of a patient’s ability to remain in employment, job retention, staying at work, work functioning and return to work and productive occupations. SOs emphasised what patients could still do despite their illness and highlighted beneficial consequences of employment. Furthermore, they encouraged and motivated patients to have a positive outlook and to keep active or return to activities and work. On the other hand, SOs of patients who were not able to remain in employment or return to work emphasised the negative consequences of the disease and seemed to validate patients’ statements of incapacity and self-limiting behaviour. Furthermore, SOs of patients with a disability claim expressed that they were waiting on a cure in order for the patient to be able to return to work. Additionally, advising, encouraging and pressuring patients to refrain from working or returning to work were reported as barriers for work functioning and RTW, and could lead patients to take sickness absence days. Although pressure from SOs not to (return to) work was frequently reported as a barrier for work participation by individuals with a chronic disease, this was not mentioned by SOs.

Furthermore, practical support was reported to be a facilitator for patients’ ability to remain in employment and for RTW and productive occupations. Practical support in this context varied from providing practical help with daily activities, household tasks and transportation, to exploring and accessing beneficial services and resources. However, one study reported that help with everyday activities and high levels of routine dependency could be a barrier for RTW.

Finally, initiating activities and doing joint activities were seen as facilitators of returning to productive occupations and staying at work by patients and SOs.

Synthesis of overall results
After thematic synthesis, a total of 27 factors were distinguished (table 5). Ten out of 27 (37%) factors were reported both by individuals with a chronic disease and SOs, of which 8 were consistently reported as either a facilitator or barrier for work participation. The results indicate that SOs’ cognitions and behaviours potentially can facilitate or hinder work participation of workers with a chronic disease. A positive attitude of SOs towards RTW, and activity participation outside work were found to be facilitators for work participation in both qualitative and quantitative studies. Overall, there is consistent evidence that positive, encouraging and supportive attitudes; maintaining open communication and encouraging and motivating behaviour of SOs were facilitators for work participation (ie, staying at work, a shorter duration of sickness absence, job retention and RTW). There is also consistent evidence that negative perceptions, beliefs and attitudes regarding the causes and consequences of the disease and overprotective behaviour were barriers for work participation (ie, employment success, work functioning, ability to remain in employment and RTW). Evidence regarding the influence of practical support and showing understanding and empathy on work participation is inconsistent.

DISCUSSION
Within our knowledge, this is the first systematic review that aims to identify cognitions and behaviours of SOs, like relatives and friends, that are related to work
participation of individuals with a chronic disease. Although the possible influence of SOs on work participation is recognised in occupational healthcare, research focusing primarily on relevant cognitions and behaviours of SOs in the context of work participation is scarce. This review aimed to address this research gap, with some promising results.

We included 18 studies with various populations, consisting of patients with cancer, chronic pain, brain injuries and in one study patients with severe and persistent mental illnesses. Seven qualitative studies focused primarily on the role of SOs regarding work participation of individuals with a chronic disease. The findings show that cognitions and behaviours of SOs may influence work participation of their relative or friend. Of the 27 identified factors, 7 factors were reported in at least four studies.

First, there was consistent evidence that positive and encouraging attitudes of SOs regarding returning to work or staying at work can facilitate these outcomes. Second, there was consistent evidence that encouragement and motivating behaviour from SOs may facilitate job retention, work functioning, staying at work and RTW. Maintaining open communication—for example, to enable discussion on return to work and have conversations with patients about the illness and (return to) work—was also reported to be a facilitator for job retention, staying at work and RTW. On the other hand, SOs’ positive attitudes towards sickness absence and their advice, encouragement or pressure to refrain from work were consistently found to be barriers for staying at work, work functioning and RTW. Finally, there is some evidence that practical help with daily activities and empathy and understanding from SOs can facilitate work participation. However, the evidence for these factors is not consistent, as each factor has once been reported as a possible barrier for staying at work and RTW. These contrasting findings can be explained by underlying processes, such as interaction between cognitions and behaviours of patients and SOs. For example, practical help from SOs could enable patients to stay at or return to work, which would otherwise not be possible due to fatigue or pain. On the other hand, practical help could also be indicative of overprotection in which SOs may reinforce patients’ unhelpful beliefs and encourage or pressure patients to limit activities and not to return to work.

The findings in this review are consistent with findings of studies on the influence of cognitions and behaviours of SOs on other patient outcomes (e.g. health outcomes, symptom severity, quality of life, self-management behaviour, functioning). For instance, SOs’ beliefs on the causes and consequences of the disease and symptoms and their own and patients’ personal control of the disease have been shown to be related to patient outcomes. Furthermore, various behaviours of SOs—such as encouraging patients to rest, discouraging patients from activities, expressing concern, encouraging activities, initiating and participating in activities, taking over tasks, maintaining open communication and talking with patients—have also been found to be related to various outcomes.

With regard to the results of this systematic review it should be noted that, with the exception of one study, all included studies focused on populations with somatic chronic diseases, that is, cancer, chronic pain and brain injuries. It remains unclear whether the processes involved are similar for populations with other somatic or mental diseases, as the role of SOs—for example, concerning beliefs and type of support—may differ between these groups. Research on illness perceptions about health outcomes has shown that the respective importance of the five dimensions of patients’ illness representations—causes, duration, consequences, symptoms and controllability or curability of the disease—differ between diseases. Thus, instead of a generic importance of cognitions and behaviours, specific maladaptive cognitions and behaviours may be more common or of more importance in some diseases than in others. Finally, as work outcome studied in the included studies varied widely, it was impossible to determine whether cognitions and behaviours of SOs differ across work outcomes. The majority of studies focused on RTW, while research on other work outcomes such as staying at work, job retention and work functioning is scarce.

**Limitations**

A limitation of this study is that articles in languages other than English were excluded. As a consequence, some useful and relevant studies might have been missed. In addition, all included studies were from high-income countries except for two studies from upper middle-income countries, restricting the generalisability of the results. Generalisability of results is also restricted due to the limited amount of quantitative studies that were available on this topic. Most of the included studies were of qualitative design, with relatively small study samples. Thus, although various cognitions and behaviours of SOs were reported as being important with respect to work participation, most of these factors were not confirmed in quantitative studies. In addition, the small number of quantitative studies rendered a meta-analysis impossible. Therefore, no statistical analyses were performed.

Finally, we identified multiple qualitative studies exploring facilitators and/or barriers for work performance or RTW that did not report on any cognitions or behaviours of SOs. Thus, not all individuals with a chronic disease report their social environment as being a relevant factor for work participation. There are various possible explanations why individuals may not mention their SOs when discussing facilitators and barriers for work participation. For instance, participants may not relate their disease and ability to work to circumstances...
in their social environment or they may be unaware of how SOs may influence their cognitions, behaviours and work participation.

Implications and recommendations for future research

Our findings support the hypothesis that cognitions and behaviours of SOs can influence work participation of individuals with chronic diseases such as cancer, chronic pain, brain injuries and mental health disorders. As there is growing evidence that clinical healthcare interventions in which SOs are involved in treatment are more effective than care as usual where SOs are not involved in treatment, this may also prove to be beneficial in the work context of occupational healthcare. However, with the limited amount of studies on this topic with regard to work participation more research is needed for which several recommendations can be made.

First, our review shows that quantitative research on cognitions and behaviours of SOs with regard to work participation of individuals with a chronic disease is scarce. We identified only three quantitative studies in which specific cognitions or behaviours of SOs were investigated in relation to work participation. More qualitative research is available in this context, in which cognitions and behaviours of SOs are identified that may be important with regard to work participation. Therefore, future research should focus on quantitatively confirming these findings, thus providing a higher level of evidence.

Second, future studies should explore which cognitions and behaviours of SOs are most strongly related to work participation and determine if these relationships are disease generic or disease specific. This could result in valuable insights into which of these factors would be most promising to take into account in occupational healthcare to facilitate RTW of workers on sick leave and prevent work disability of individuals with a chronic disease.

Finally, future prognostic studies may focus on the relationship between dyadic agreement of patients with a chronic disease and their SOs and work participation, as dyadic agreement has been shown to influence other patient outcomes such as well-being and may also influence work participation.

CONCLUSIONS

In this review, we identified 27 cognitions and behaviours of SOs that were reported as determinants for work participation of individuals with a chronic disease. Our findings show that several cognitive behavioural factors of SOs can facilitate or hinder work participation. Aside from one factor (positive family attitude towards return to work) for which moderate-level evidence was found, all factors were of low-level evidence. Despite the overall low level of evidence, our review indicates that involving SOs in occupational healthcare and intervening on these factors may be beneficial. High-quality prognostic studies are needed that investigate cognitive behavioural factors of SOs in relation to work participation to confirm our findings. Future studies could focus on exploring which cognitions and behaviours of SOs are most strongly related to duration of sick leave and RTW.

Acknowledgements

The authors would like to thank Truus van Ittersum, for her contribution in the search strategy.

Contributors

All authors contributed to the conception and design of the study. NCS developed the search strategy with support from an information specialist (acknowledged); all authors reviewed the search terms. NCS and HJvdP performed the literature search, study selection, data extraction and interpretation of the data and drafted the manuscript. NCS, HJvdP, SJvdB-V, MH and SB have contributed to revising the article critically for important intellectual content. The final version of this manuscript has been approved by all the authors.

Funding

This work was supported by Instituut Gak, grant number 2016755.

Competing interests

NCS, HJvdP and SB report grants from Instituut Gak, during the conduct of the study; SJvdB-V and MH have nothing to disclose.

Patient consent for publication

Not required.

Provenance and peer review

Not commissioned; externally peer reviewed.

Data sharing statement

Extra information concerning the methods and results is available by emailing NCS.

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REFERENCES


