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BMJ Open Influence of social support on return to work after total hip or total knee arthroplasty: a prospective multicentre cohort study

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To cite: Kamp T, Stevens M, Van Beveren J. et al. Influence of social support on return to work after total hip or total knee arthroplasty: a prospective multicentre cohort study. BMJ Open 2022;12:e059225. doi:10.1136/ bmjopen-2021-059225

Prepublication history and additional supplemental material for this paper are available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/ bmjopen-2021-059225).

Received 11 November 2021 Accepted 13 May 2022



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ABSTRACT

Objectives There is strong evidence that social support is an important determinant of return to work (RTW). Little is known about the role of social support in RTW after total hip or knee arthroplasty (THA/TKA). Objective was to examine the influence of preoperative and postoperative perceived social support on RTW status 6 months postoperatively.

Design A prospective multicentre cohort study was conducted.

Setting Orthopaedic departments of four Dutch medical centres; a tertiary university hospital, two large teaching hospitals and a general hospital.

Participants Patients planned to undergo THA/TKA, aged 18-63 and employed preoperatively were included.

Main outcome measures Questionnaires were filled out preoperatively and 3 and 6 months postoperatively and included questions to assess patients' perceived social support targeting three sources of social support: from home (friends, family), from work (coworkers, supervisors) and from healthcare (occupational physician, general practitioner, other caregivers). Control variables included age, gender, education, type of arthroplasty and comorbidities. RTW was defined as having fully returned to work 6 months postoperatively. Univariate and multivariate logistic regression analyses were conducted.

Results Enrolled were 190 patients (n=77THA, n=113TKA, median age was 56 years, 56% women). The majority returned to work (64%). Preoperatively, social support from the occupational physician was associated with RTW (OR 2.53, 95% CI 1.15 to 5.54). Postoperatively, social support from the occupational physician (OR 3.04, 95% CI 1.43 to 6.47) and the supervisor (OR 2.56, 95% CI 1.08 to 6.06) was associated with RTW.

Conclusions This study underscores the importance of work-related social support originating from the occupational physician and supervisor in facilitating RTW after primary THA/TKA, both preoperatively and postoperatively. Further research is needed to confirm our results and to understand the facilitating role of social support in RTW, as arthroplasty is being performed on a younger population for whom work participation is critical.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Prospective multicentre design with a relatively large number of patients and a follow-up of 6 months.
- ⇒ Generalisability of the outcomes as a result of the representative sample.
- ⇒ Multivariate analyses on three different sources of social support, investigating both preoperative and postoperative data.
- ⇒ Due to limited power, our study only focused on preoperative and postoperative data separately.
- ⇒ We only focused on the first time workers fully returned to work.

INTRODUCTION

Adequate social support is known to have positive effects on health status and health behaviors, well-being and work participation. 2 3 Social support has been defined as the assistance and protection given to an individual, ¹ which can come from a variety of sources such as friends, family, coworkers, organisations and healthcare professionals. There are different dimensions of social support instrumental, informational, appraisal and emotional, wherethe former two are known as instrumental support and the latter two as perceived social support. 4-7

There is strong evidence that perceived social support from home, work and occupational healthcare is an important determinant in the return to work (RTW) process and work disability among a variety of working populations. ^{2 3 8-13} Social support within and outside the workplace has shown to contribute to the RTW process.² 8-12 In a recent systematic review about the influence of social support and social integration on RTW outcomes among individuals with work-related injuries, receiving support from family, regular contact and good communication with the employer and genuine concern and support



from coworkers and supervisors were identified as facilitators of RTW,² whereas perceived lack of emotional support, especially lack of on-going support from supervisors, was seen as a barrier to the RTW process.² Regarding healthcare support, positive RTW recommendations from healthcare professionals showed to be associated with a 60% higher RTW rate in a cohort of 325 patients with low back injury.¹⁴ Multiple qualitative studies conducted among different patient groups showed the important role of perceived support from healthcare professionals in the RTW process. 15-17 Although these studies emphasise the importance of social support from home, work and healthcare, so far little is known about the role of social support in the RTW process among the rapidly growing patient group undergoing a total hip arthroplasty (THA) or total knee arthroplasty (TKA).

The number of THA and TKA procedures performed annually in the Netherlands continues to increase steadily, most rapidly among working-age patients. 18 In 2018, 14768 primary THAs and 12777 primary TKAs were performed among working-age adults in the Netherlands, a 56% and 32% increase compared with 2010, respectively.¹⁹ Similar trends, with the largest increase among working-age patients, are seen in the USA and other Western countries.²⁰ This increase is mainly due to increased prosthetic survivorship and the fact that particularly the severity of the osteoarthritis (OA) and patients' preferences, instead of age, have become a major criteria when deciding whether to undergo THA or TKA.^{22 23} On the one hand, the rise in THA and TKA procedures performed in younger patients and on the other hand the increase in retirement age results in higher numbers of patients expecting to remain in paid employment after surgery. 18 24 Previous studies show that 59%–85% of patients RTW within 6 months, 25–27 so the absolute number of patients who have not returned to work within 6 months is substantial.

Our previous study, which also used data from the 'Work participation In Patients with Osteoarthritis' (WIPO) cohort, showed the importance of psychosocial working conditions in time to RTW after THA or TKA.²⁸ However, little research has been conducted among THA and TKA patients on the effect of social support on RTW outcomes. Some qualitative studies have shown that absence of workplace support by the supervisor was associated with a negative experience of returning to work in arthroplasty patients.²⁹ It was also found that a supportive environment at home and at work, as well as supportive care from healthcare professionals might be helpful in facilitating successful RTW, rehabilitation, and postoperative satisfaction.^{29–31} No quantitative studies have been found so far that examined the effect of different types of social support on RTW among THA and TKA patients. No evidence exists either on the timing of social support, that is, the effect of social support immediately before or after surgery compared to later postoperatively. The aim of this study was therefore to investigate the influence of perceived social support from different sources (home,

work, healthcare) on RTW status 6 months postoperatively in a sample of THA and TKA patients.

MATERIALS AND METHODS

Design and procedure

A prospective multicentre cohort study was conducted among patients who underwent THA or TKA for primary OA. This study was part of the 'WIPO' cohort (WIPO, Trial-ID NTR3497). 28 32-34 Between March 2012 and July 2014, patients were recruited at the orthopaedic departments of the following Dutch medical centres: (1) University Medical Center Groningen (tertiary university hospital), (2) Martini Hospital Groningen (large teaching hospital), (3) Medical Center Leeuwarden (large teaching hospital) and (4) Röpcke-Zweers Hospital Hardenberg (general hospital), all in the northern Netherlands. Patients waiting for THA or TKA were contacted by phone and invited to participate. Preoperative questionnaires were filled in approximately 1 month before surgery. Postoperative follow-up data, for this study, were collected after 3 and 6 months. If applicable, missing answers were added later to the questionnaire after retrieving them by telephone. Informed consent was assumed as being obtained when patients returned finished questionnaires and thereby granting our request to participate in the study. If patients did not want to participate in the study, they were asked to return a blank questionnaire. Patients were informed of this consent method by mail, in an information letter that also communicated the voluntary nature of the study and the anonymous nature of all the data to be processed.

Study population

Patients with primary hip and knee OA undergoing THA or TKA, aged 18–63 and employed preoperatively, were included. Excluded were patients who in the previous 6 months received another joint arthroplasty, THA or TKA due to secondary OA, unicompartmental knee arthroplasty, THA or TKA revision and with inadequate understanding of the Dutch language. A dropout was defined as a patient leaving the study preterm by not filling in the 6-month postoperative questionnaire for any reason.

MEASURES

Dependent variable

RTW (yes/no) was measured at the 6-month postoperative follow-up. Patients were asked whether they returned to work, with the following answering possibilities: no RTW, partial RTW, full RTW. RTW was defined as participants who answered that they fully returned to work after surgery, no RTW was defined as participants who answered that they did not or partially RTW.

Independent variables

Perceived social support was measured preoperatively (baseline) and 3 months postoperatively using three

questionnaires targeting support from home, work and healthcare.

Social support from home, that is, friends and family, was assessed with the Groningen Orthopaedic Social Support Scale (GO-SSS). The GO-SSS consists of 12 questions divided into two subscales: perceived social support (seven items) and instrumental social support (five items). This study focused on the perceived social support subscale. On a Likert scale, four answers were possible (never or rarely, occasionally, regularly and often). A sum score was computed, where higher scores indicated more perceived social support. The GO-SSS showed to be a reliable and valid instrument to assess social support for patients following arthroplasty, with a 0.89 Cronbach alpha for the entire questionnaire and 0.86 internal consistency for the perceived social support (PSS) subscale. ³⁵

Social support from work was assessed with a self-constructed scale focusing on perceived social support. The questionnaire consisted of two questions about perceived support from co-workers and the supervisor. Each item is preceded by the question 'How much support did you receive during your period of recuperation from...' with responses on a 1–3 point scale (no support, little support, ample support). Dichotomous variables were computed, distinguishing between no perceived support and perceived support (consisting of little or ample support). The two questions were analysed separately.

Social support from healthcare was measured with a self-constructed scale focusing on perceived social support regarding work. The questionnaire included three questions about perceived support from an occupational physician (OP), a general practitioner (GP) and other caregivers. Each item is preceded by the question 'How much support regarding work did you receive during your period of recuperation from...' with responses on a 1–3 point scale (no support, little support, ample support). Dichotomous variables were computed, distinguishing between no perceived support and perceived support (consisting of a little or ample support). The three questions were analysed separately.

Covariates

Data about the following sociodemographic characteristics were collected preoperatively: age (years), gender, education (categorised into elementary, secondary and higher), being breadwinner (yes/no). Disease-related information was gathered by inquiring about type of arthroplasty (THA or TKA), body mass index (BMI) divided into normal (<25 kg/m²) and overweight or obese (>25 kg/m²) and comorbidity measured with a 27-item chronic conditions questionnaire (Statistics Netherlands. Health questionnaire 1989).³6 Amount of comorbidities was divided into none, one or two, or more than two. Data about work-related characteristics included questions about self-employment (yes/no), company size (number of employees: 1–9, 10–99, more than 100), contractual hours (h), working hours (h), type of job (executive/

administrative/advisory/management/policy) and type of tasks (physical/mental/combination). Executive jobs cover blue collar workers, that is, requiring manual labour. Physical work demands were measured by asking whether patients had to perform physical activities like standing, sitting, walking, kneeling or squatting during work (yes/no).

Statistical analysis

Descriptive statistics—mean (SD), n (%)—were used to describe baseline characteristics of the study population. Univariate and multivariate logistic regression analyses were used to study the prognostic factors for RTW 6 months postoperatively. Separate analyses were conducted for perceived social support measured preoperatively and 3 months postoperatively.

The association between each potential prognostic factor and RTW was univariately assessed. All prognostic factors with a p value ≤ 0.20 in the univariate analyses were included in the multivariate regression analyses,³⁷ after checking for multicollinearity. Variables were omitted by backward selection, depending on their level of statistical significance (p<0.05). Control variables for the analyses included sex, age, education, type of surgery, comorbidities and work tasks.^{38–41} Control variables were based on previous literature and were defined a priori. Sensitivity analyses were conducted for THA and TKA groups separately, since previous literature suggests that postoperative recovery and RTW differ between these groups. 42 43 ORs were calculated, including 95% CI. A non-response analysis was performed. Statistical analyses were performed with IBM Statistical Package for the Social Sciences (SPSS) V.25.0 and Mplus V.7.1.

Patient and public involvement statement

Neither patients nor the public were involved in the design, conduct, reporting or dissemination plans of our research.

RESULTS

From the 311 patients who had undergone a primary THA or TKA, 190 (n=77THA, n=113TKA) were included in the study. Figure 1 is a flowchart showing the total number of patients at baseline and the drop-outs to follow-up. The characteristics of the study sample are presented in table 1 and online supplemental table 1. Median age was 56 years (IQR 52-60 years). The sample consisted of 84 (44%) men and 106 (56%) women, 77 (41%) patients with THA and 113 (59%) patients with TKA. For educational level, 33% had completed elementary school, 44% secondary school and 21% higher education. BMI of 77% was above $25 \,\mathrm{kg/m^2}$ and 46% had two or more comorbidities. Patients worked on average 32 hours per week. Our cohort had mostly executive jobs (55%; blue collar). A combination of physically and mentally challenging tasks was performed by 39% of patients; the remaining patients were divided equally into performing either physical or

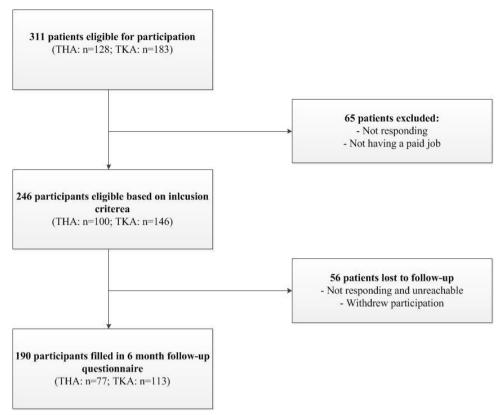


Figure 1 Flowchart study enrolment and follow-up. THA, total hip arthroplasty. TKA, total knee arthroplasty;

mental work tasks. Work demands of the majority included sitting and/or walking, and a quarter of the patients had to perform kneeling or squatting work demands. The majority of patients returned to work (64%) by 6 months postsurgery. To correct for the drop-out rate during follow-up, we conducted a non-response analysis, which showed no significant differences on baseline characteristics or independent variables.

Univariate and multivariate logistic regression analyses

In the *preoperative* univariate analyses, social support from the OP was the only variable below the cut-off value of p<0.2, therefore, no multivariate analyses were performed. Preoperative social support from the OP was univariately significantly associated with RTW (OR 2.53, 95% CI 1.15 to 5.54; table 2). In the postoperative univariate analyses, social support from the supervisor, the OP, the GP and other caregivers was below the cut-off value of p<0.2 and were, therefore, used in the multivariate analyses. In the multivariate model perceived social support from the OP (OR 3.04, 95% CI 1.43 to 6.47) and from the supervisor (OR 2.56, 95% CI 1.08 to 6.06) showed statistically significant associations with RTW. The odds of an individual having returned to work 6 months postsurgery increased by 3.04 and 2.56 for those patients who perceived social support from the OP and from the supervisor, respectively (table 2).

Sensitivity analyses

Analysing the THA and TKA groups separately, the *preoperative* multivariate model showed no association between

social support and RTW in both subgroups (table 3). The *postoperative* multivariate model of patients with THA showed that perceived social support from the supervisor was significantly associated with RTW (OR 1.90, 95% CI 1.12 to 21.53; table 3). The *postoperative* multivariate model of TKA patients showed a significant association between perceived social support from the OP and RTW (OR 5.14, 95% CI 1.84 to 14.36; table 3).

DISCUSSION

This study aimed to investigate the influence of preoperative and postoperative perceived social support from home, work and healthcare on RTW status 6 months postoperatively in a sample of patients with THA and TKA. We found that patients who perceived social support from the OP preoperatively had 2.5 times higher odds of RTW within 6 months postoperatively compared with patients who perceived no support. Patients who perceived social support from the OP and from the supervisor 3 months postoperatively had 3.0 and 2.6 times higher odds of RTW, respectively. These results imply the important role of workplace support in the RTW process, as both the OP and supervisor are linked to the workplace.

In our study, the majority of patients (64%) returned to work within 6 months postoperatively, which is in line with previous studies.^{25–27} Our findings that perceived social support from the OP is important, both preoperatively and postoperatively, is in line with previous quantitative studies on social support from the OP in other



Table 1 Baseline study population char	acteristics			
Variables	Total (N=190)			
Age, median (IQR)	56 (52–60)			
Male/female, n (%)	84 (44)/106 (56)			
Highest educational level (n (%))				
Lower (elementary school, vocational education)	62 (33)			
Secondary (high school, intermediate vocational education)	84 (44)			
Higher (higher professional education university)	39 (21)			
Wage earner, n (%)	106 (56)			
THA/TKA, n (%)	77 (41) / 113 (59)			
BMI (kg/m ²), n (%)				
<25	40 (21)			
>25	147 (77)			
Number of comorbidities, n (%)				
No	19 (10)			
One or two	62 (33)			
More than two	88 (46)			
Self-employed, n (%)	22 (12)			
Company size (number of employees), n (%)				
1–9	28 (15)			
10–99	50 (26)			
>100	112 (59)			
Contractual hours (median, IQR)	32 (21 to 37)			
Working hours (median, IQR)	32 (22 to 40)			
Job type, n (%)				
Executive	105 (55)			
Administrative	22 (12)			
Advisory	11 (6)			
Management	27 (14)			
Policy	23 (12)			
Work tasks n (%)				
Physical	57 (30)			
Mental	57 (30)			
Both	74 (39)			
Work demands, n (%)				
Standing	100 (47)			
Sitting	107 (56)			
Walking	104 (55)			
Kneeling or squatting	52 (27)			
All numbers are represented as median with loand percentages (%). THA, total hip arthroplasty; TKA, total knee art				

populations. ¹³ ¹⁴ ¹⁷ In qualitative studies among patients with THA and TKA, employers and clinicians also indicated the added value of OPs, especially if there, already, was contact before surgery. ²⁹ ⁴⁴

Our findings that social support from the supervisor was associated with RTW are also in line with previous studies conducted among other population groups. ^{2 45 46} Supervisors play a considerable role in initiating effective support strategies ^{47–49}: they are expected to communicate the process of RTW with the employee and the OP and implement accommodations, both in agreement with the OP. ^{2 11} In our multivariate analyses, we only found an association between postoperative and not preoperative social support from the supervisor and RTW, leaving questions about optimal timing. An explanation might be that the supervisor is better able to perform specific actions postoperatively to facilitate RTW.

In contrast to previous studies, we did not find an association between social support from home or coworkers and RTW in our study population. A possible explanation for this absence in our study might relate to the duration of sickness absence: other studies that found an association between social support from home or coworkers and RTW were mainly conducted among population groups with long-term absence (>6 months), 3 13 whereas a THA or TKA often lead to a short-term work absence (<3–6 months) for most patients. Disease chronicity and long-term absence may influence the necessity and contributing value of social support from home and coworkers for RTW outcomes.

In our study, we did not find an effect of perceived social support from other caregivers (eg, physiotherapists) on RTW. This might be because we did not further specify the question and patients could have experienced it as implicit. The role of social support from a physiotherapist on RTW warrants further research, since our particular subsample has frequent contact with these specific healthcare professionals. Value of a physiotherapist is illustrated by Lysaght *et al*, who reported in their qualitative research that half of the workers experienced support by a physiotherapist. ¹¹ More research is needed to evaluate the role of physiotherapists and their contribution to the RTW process.

Our sensitivity analyses showed some differences in factors associated with RTW between patients with THA and TKA. Postoperative perceived social support from the supervisor was associated with RTW of THA patients and postoperative perceived social support from the OP was associated with RTW of patients with TKA. This dissimilarity in findings may be explained by differences in the rehabilitation process. It is known that for patients with THA, rehabilitation is easier than for patients with TKA. However, it must be kept in mind that the wide 95% CI indicated that our sample size is too small. These results need to be replicated with a larger sample size before definitive conclusions can be drawn.

Finally, our non-response analyses did not show significant differences on baseline characteristics or



Table 2 Preoperative and 3 months postoperative univariate and multivariate logistic regression analyses of perceived social support variables on return to work (RTW) status

	Univaria	ate		Multiva	Multivariate		
Variables	OR	Р	95% CI	OR	Р	95% CI	
Preoperative							
Support from home	1.04	0.40	0.95 to 1.14				
Support from co-workers (ref=no)	1.26	0.64	0.48 to 3.31				
Support from supervisor (ref=no)	1.57	0.30	0.68 to 3.62				
Support from OP (ref=no)	2.53	0.02*	1.15 to 5.54				
Support from GP (ref=no)	1.46	0.30	0.71 to 2.98				
Support from other caregivers (ref=no)	1.24	0.57	0.59 to 2.63				
Three months postoperative							
Support from home	1.01	0.92	0.92 to 1.10				
Support from co-workers (ref=no)	1.28	0.56	0.56 to 2.93				
Support from supervisor (ref=no)	2.71	0.02†	1.18 to 6.23	2.56	0.03*	1.08 to 6.06	
Support from OP (ref=no)	3.17	0.00†	1.51 to 6.66	3.04	0.00*	1.43 to 6.47	
Support from GP (ref=no)	2.51	0.02†	1.19 to 5.29				
Support from other caregivers (ref=no)	1.64	0.17†	0.81 to 3.32				

Adjusted for sex, age, education, comorbidities, type of surgery and work tasks.

CI, confidence interval; GP, general practitioner; OP, occupational physician; OR, odds ratio.

independent variables. However, it might be that non-response could partly be explained by unfavourable RTW outcomes.

Strengths and limitations

An important strength of this study is its prospective multicentre design with a relatively large number of patients and a follow-up of 6 months. Another strength is the representative sample of patients and, therefore, the generalisability of the outcomes. We provided multivariate analysis on three different sources of social support, plus investigated both preoperative and postoperative data, in contrast to previous research on social support among other patient groups.² This study does have some limitations. Due to limited power, our study only focused on preoperative and postoperative data separately. The sample sizes of our subgroups (THA and TKA) in the sensitivity analyses lacked power to draw definitive conclusions, and we only focused on the first time workers fully returned to work. Future research should also include sustainable RTW to assess the impact of social support on these RTW trajectories.

Finally, another limitation was the self-reported measurements, which are generally susceptible to the effects of reporting bias.

Implications

Changing workforce dynamics and trends towards THA or TKA, surgery among working-age employees propel an urgent need to understand the facilitators and barriers for RTW, besides those of pain and function.³³ There are

still many uncertainties about the potential influence of psychosocial work factors (including social support), timing of interventions designed to facilitate RTW and engagement of clinicians and employers as key actors in the RTW process.

To our knowledge, this is the first quantitative study to examine the role of social support among this specific population. The differences in predicting factors between patients with THA and TKA might imply a need for group-specific approaches. Further research on social support is needed to confirm our results and to understand the facilitating role of social support on RTW. The optimal timing to implement contact, that is, social support, the course (change over time) of social support from different sources and their effect on RTW should also be investigated. Therefore, studies among THA and TKA patients specifically focused at social support, and using validated questionnaires to measure social support from different sources, ^{50.51} would be very valuable.

CONCLUSION

This study showed that, in particular, perceived social support from OPs and supervisors may predict RTW after THA and TKA. Both preoperative and postoperative social support were associated with RTW, which may suggest that perceived work-related social support from OPs and supervisors are important factors over an extended period of time. Some differences in factors were found between patients with THA and TKA, where postoperative

^{*}p<0.05.

[†]p<0.2.



Table 3 Preoperative and 3 months postoperative univariate and multivariate logistic regression analyses of perceived social support variables on return to work (RTW) status among subsamples of patients with THA and TKA

Variables	Univari	ate		Multivariate			
	OR	95% CI	Р	OR	95% CI	Р	
Preoperative							
THA (n=77)							
Support from home	1.03	0.88 to 1.20	0.76				
Support from co-workers (ref=no)	2.04	0.35 to 11.90	0.43				
Support from supervisor (ref=no)	2.79	0.55 to 14.07	0.21				
Support from OP (ref=no)	3.33	0.81 to 13.69	0.10†				
Support from GP (ref=no)	1.15	0.34 to 3.90	0.83				
Support from other caregivers (ref=no)	0.67	0.19 to 2.33	0.53				
TKA (n=113)							
Support from home	1.05	0.94 to 1.18	0.38				
Support from co-workers (ref=no)	1.10	0.32 to 3.76	0.88				
Support from supervisor (ref=no)	1.25	0.45 to 3.48	0.67				
Support from OP (ref=no)	2.06	0.76 to 5.57	0.15†				
Support from GP (ref=no)	1.64	0.64 to 4.21	0.31				
Support from other caregivers (ref=no)	1.64	0.60 to 4.49	0.33				
Three months postoperative							
THA (n=77)							
Support from home	1.09	0.93 to 1.27	0.29				
Support from co-workers (ref=no)	3.13	0.55 to 17.80	0.20				
Support from supervisor (ref=no)	1.90	1.12 to 21.53	0.04†	1.90	1.12 to 21.53	0.04*	
Support from OP (ref=no)	1.85	0.51 to 6.81	0.35				
Support from GP (ref=no)	3.24	0.77 to 13.61	0.11†				
Support from other caregivers (ref=no)	0.65	0.18 to 2.39	0.52				
TKA (n=113)							
Support from home	0.97	0.87 to 1.08	0.60				
Support from co-workers (ref=no)	1.26	0.46 to 3.43	0.66				
Support from supervisor (ref=no)	2.65	0.87 to 8.07	0.09†				
Support from OP (ref=no)	5.14	1.84 to 14.36	0.00†	5.14	1.84 to 14.36	0.00*	
Support from GP (ref=no)	2.40	0.94 to 6.11	0.07†				
Support from other caregivers (ref=no)	2.32	0.91 to 5.90	0.08†				

Adjusted for sex, age, education, comorbidities, and work tasks.

Cl, confidence interval; GP, general practitioner; OP, occupational physician; OR, odds ratio; THA, total hip arthroplasty; TKA, total knee arthroplasty.

Netherlands

social support from the supervisor predicted RTW of patients with THA and postoperative social support from the OP-predicted RTW of patients with TKA. Further research on the role of social support in returning to work after THA and TKA is needed, as arthroplasty is being performed on an increasingly younger population for whom work participation is of critical importance.

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Contributors TK conceived and designed the study, wrote the manuscript, performed statistical analysis, prepared the figures. MS conceived and designed the study, supervised the work, made substantial changes to the manuscript, arranged

^{*}p<0.05

[†]p<0.2



the data. JVB arranged the data, critically assessed and corrected the manuscript. PCR arranged the data, critically assessed and corrected the manuscript. RB arranged the data, critically assessed and corrected the manuscript. SjB conceived and designed the study, arranged the data. SaB conceived and designed the study, supervised the work, made substantial changes to the manuscript, arranged the data. Guarantor: TK

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval This study was approved by the Medical Ethics Board of University Medical Center Groningen (METc 2012.153). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request. The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

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