Use of rehabilitation after hip and knee replacement in New Zealand: a national survey

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ABSTRACT

AIMS: Our objective was to describe rehabilitation used before and after joint replacement in New Zealand and evaluate variation based on geography and ethnicity.

METHODS: In this descriptive cross-sectional questionnaire-based study we recruited participants 45 years or older (n=608) from the New Zealand Joint Registry six months after primary total hip, total knee or uni-compartmental knee replacement.

RESULTS: The cohort was predominantly New Zealand European (89.9%). The average age of participants was 68.2 years. Less rehabilitation was used pre-operatively (31.0%) than post-operatively (79.6%) and total hip replacement participants reported using less rehabilitation (63.3%) than those after total knee (90.7%) or uni-compartmental knee (80.3%) replacement (p<0.01). There were trends towards more pre-operative rehabilitation for participants living in larger urban areas, most evident for total hip replacement (p<0.05).

CONCLUSIONS: Participants reported generally positive outcomes six months after primary total hip, knee and uni-compartmental knee replacement. However, differences in use of rehabilitation services before and after joint replacement were evident depending on joint replaced. Broadening setting options for rehabilitation might improve use of rehabilitation resources.

ong-term outcomes following primary hip and knee joint replacement are favourable with most patients experiencing positive functional outcomes over time.^{1,2} However, up to 30% of patients following knee replacement and a smaller number of those following hip replacement report little or no improvement with respect to ongoing pain, restricted range of motion and unsatisfactory function.²⁻⁴ There may be differences in recovery depending on type of joint replaced. For example, it is generally agreed that individuals take longer to recover and require more rehabilitation following total knee compared with total hip and uni-compartmental knee replacement.4-6 Various demographic and clinical factors may influence these outcomes. These include age, gender, general health and comorbidities, post-operative complications, surgical wait time and use of rehabilitation.^{1,4} The latter is the focus of this study.

Rehabilitation, particularly exercise-based physiotherapy is generally accepted as standard before and after hip and knee replacement^{7,8} and is a set of interventions designed to optimise functioning and reduce disability.9 However, protocols for rehabilitation before and after joint replacement vary widely across studies and countries and the optimal mix of setting, mode and intensity of rehabilitation remains unclear. 10,111 Pre-operative interventions include a focus on education and an opportunity to address physical and psychosocial issues that may impact on surgery outcomes, such as anxiety and depression, pain management, nutrition, smoking and exercise expectations. 4,12 Rehabilitation in the post-operative phase can include occupational therapy and physiotherapy to target pain management, levels of activity, participation and quality of life.4,13



There are a small number of published studies characterising rehabilitation services used by patients before and after joint replacements in some countries such as the US.14,15 However, in New Zealand little is known about the extent to which hip and knee replacement patients receive rehabilitation care and how use of rehabilitation varies on the basis of ethnicity. For example, while the issues are complex, differing rates of joint replacement uptake may be possible between Māori and non-Māori, consistent with two published studies we could find:16,17 however, no studies have considered whether there is variability in terms of use of rehabilitation before and after joint replacement on the basis of ethnicity. Use of rehabilitation services may also be impacted by economic barriers, 18,19 where access to health services might depend on where a person lives and access to funding for services.20

Study objectives

The objectives of this study are to: i) describe the extent to which New Zealanders use rehabilitation before and after joint replacement, and ii) to consider whether there is variation based on geography and ethnicity.

Methods

Study design and recruitment strategy

The role of rehabilitation (ROR) study is a cross-sectional questionnaire-based study investigating the use of rehabilitation before and during the first six months following primary total hip or knee, or uni-compartmental knee replacement in New Zealand.

Participants were recruited from the New Zealand Joint Registry (NZJR) in order to achieve a national sample with geographical diversity. Because of the large numbers of registered primary hip and knee replacements, NZJR obtains patient-reported outcome information from randomly selected patients across the country to achieve an annual response of 20%. This was the sampling frame for this study. Flyers for the study were included in six-month post-operative NZJR mail outs between June 2015 and July 2016, and all patients returning flyers with their contact information were approached as soon as flyers were returned and invited to participate in the study.

The study received ethical approval from the University of Otago Human Ethics Committee (ref H14/070).

Participant selection

Patients registered and followed by the NZJR after primary hip or knee joint replacement in either private or public systems in New Zealand were eligible to participate in the study. Patients who met the following criteria were included: i) age 45 years or older, ii) underwent an elective unilateral total hip or knee, or uni-compartmental knee replacement for osteoarthritis six months prior to recruitment, and iii) agreed to participate in the study. We excluded patients with any previous operation on the index joint and any non-elective joint replacements following fractures.

Data collection

Contact information was supplied monthly from the NZJR (name, preferred contact information) for potential participants meeting inclusion criteria who had agreed to being contacted by the study team. Potential participants were then contacted within one month of contact details being made available by a research assistant to discuss the study and invite participation.

Once recruited, ROR participants completed questions in booklet form regarding timing, type, intensity and duration of any rehabilitation following referral for joint replacement (pre- and post-operatively). Demographic and clinical questions were also included. Questionnaires were available for completion either online (eg, Survey Monkey™) or by mail depending on the preference of the participant. Additional clinical information (procedure type, date of surgery, body mass index, comorbidity classification) was collected from the NZJR. This minimised participant burden by avoiding duplication of data collection.

ROR study variables

Demographic variables included age, gender, ethnicity, education, work status, funder (public/private insurance/self). Clinical and surgical variables included other pre-existing medical conditions/ comorbidities (self-report/American Society of Anaesthesiologists (ASA) classification²¹); body mass index, procedure type (total hip, total knee, uni-compartmental knee) and time on surgical waiting list (weeks). Rehabilitation variables included time from surgery to first rehabilitation session (weeks); pre- and post-operative rehabilitation type (physiotherapy, occupational therapy, other), setting (home, outpatient, community centre, other),



frequency of sessions per week, total hours of rehabilitation); and number of post-operative follow-up reviews with the surgeon. Outcomes were evaluated using the six-month post-operative Oxford Hip and Knee scores^{22,23} accessed from NZJR and a brief measure of quality of life (WHOQOL-8).^{24,25}

Data analyses

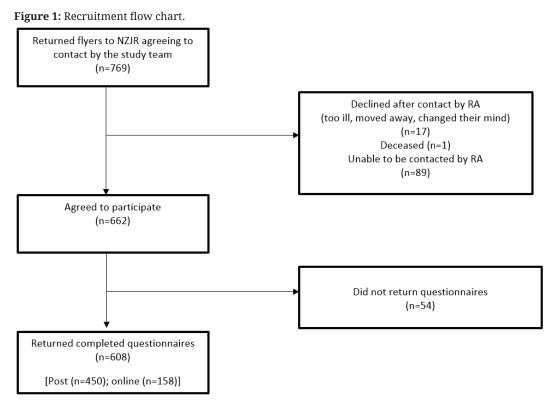
Data were analysed using SPSSv24.0.26 First, we characterised the sample in terms of demographic status, health (eg, comorbidities, body mass index), procedure type, geographic location, funding source, participation in pre- and/or post-operative rehabilitation therapies and outcomes, using descriptive statistics. Second, for those who obtained rehabilitation services, we identified the setting (eg, outpatient, at home, community centre), time from operation to first rehabilitation session, rehabilitation duration, frequency (times per week), and intensity (minutes per session x number of sessions per week/number of weeks of rehabilitation; total hours), and how rehabilitation services and practice patterns varied on the basis of geography and ethnicity.

Bivariate analyses tested relationships between demographic and clinical variables and rehabilitation pre- and post-operatively. For discrete variables, we created contingency tables (cross-tabs) and used chi-squared tests to determine the significance of two-way associations. For continuous variables with normal distributions, Pearson correlation, two-sample t-tests, or analysis of variance were used. For variables with non-normal distributions, non-parametric tests were used including Spearman correlation, Mann Whitney U or Kruskal-Wallis tests as appropriate.

The approach to missing data was to use list wise deletion, also the default SPSS approach. We believe this was appropriate because of the sample size and the limited amount of missing data (<3%) across variables. Data presented are unadjusted with no correction for confounding variables.

Results

Seven hundred and sixty-nine people meeting inclusion criteria returned flyers to the NZJR. Of these, n=608 were successfully recruited into the study and returned questionnaires (n=158 online and n=450 by post). Figure 1 shows recruitment flow into the study.



NZJR = New Zealand Joint Registry; RA = research assistant.



Description of study sample and outcomes

A summary of participant demographic, clinical and outcome characteristics is provided in Table 1. The average age of participants was 68.2 years. There were fewer men (45.2%) than women; the sample was predominantly New Zealand European (89.6%) and generally well educated, with 69.4% reporting high school- or tertiary-level

qualifications. The main funding sources for surgery were private insurance or public funding, and participants waited on average six months for surgery. Evaluation of outcomes indicated a majority of participants (51%) reported an excellent outcome on the basis of Oxford scores using the 4-category set of outcomes from poor to excellent recommended by the NZJR.²⁷ Mean level of quality of life was also high (mean WHOQOL-8 score 32.4, SD 4.9).

Table 1: Demographic and clinical characteristics of the ROR study sample (n=608).

	Total hip (n=219)	Total knee (n=313)	Uni-compartmental knee (n=76)†	Total sample (n=608)
Demographic characteristics	·			
Age [(y), mean ± SD] ^{2**}	67.6±8.0	68.7±8.2	65.2±8.5	68.2±7.9
Sex [male, n (%)]¹	91 (41.6)	150 (47.9)	34 (44.7)	275 (45.2)
Ethnicity [n (%)]¹				
- New Zealand European	197 (90.0)	276 (88.2)	72 (94.8)	545 (89.6)
- New Zealand Māori	16 (7.3)	16 (5.1)	1 (1.3)	33 (5.5)
- Other	6 (2.7)	21 (6.7)	3 (3.9)	30 (4.9)
Educational qualifications [n (%)] ¹				
- No formal qualifications	68 (31.1)	81 (25.9)	19 (25.6)	168 (27.7)
- High school qualifications	68 (31.1)	91 (29.1)	27 (36.5)	186 (30.6)
- Tertiary qualifications	79 (36.0)	129 (41.2)	27 (36.5)	235 (38.8)
- Other	4 (1.8)	12 (3.8)	1(1.4)	17 (2.8)
Work status at time of surgery [n (%)]1**				
- Employed full time	61 (27.9)	79 (25.2)	24 (31.6)	164 (27.0)
- Employed part time	25 (11.4)	49 (15.7)	19 (25.0)	93 (15.3)
- Not employed/retired	126 (57.5)	169 (54.0)	29 (38.2)	324 (53.3)
- Other	7 (3.2)	16 (5.1)	4 (5.2)	27 (4.5)
Funding [n (%)]¹				
- Accident Compensation Corporation	16 (7.3)	29 (9.3)	11 (14.7)	56 (9.2)
- Ministry of Health	121 (55.5)	156 (49.8)	32 (42.7)	309 (51.0)
- Private Insurance	68 (31.2)	117 (37.4)	28 (37.3)	213 (35.1)
- Self	12 (5.5)	9 (2.9)	4 (5.3)	25 (4.1)
- Other	1 (0.5)	2 (0.6)	0 (0)	3 (0.5)
Geographical variables [n (%)] ¹				
- Rural (town or area <10,000 people)	81 (37.7)	114 (36.7)	34 (45.3)	229 (38.1)
- Large town (10,000–50,000 people)	30 (14.0)	56 (18.0)	8 (10.7)	94 (15.6)
- Urban/city (>50,000 people)	104 (48.4)	141 (45.3)	33 (44.0)	278 (46.3)



Table 1: Demographic and clinical characteristics of the ROR study sample (n=608) (continued).

Clinical characteristics				
Wait list for surgery pre-op [weeks, mean \pm SD] ²	17.2±17.8	28.9±52.5	33.0±47.7	25.2±43.2
Comorbidities [n (%)] ¹				
- None	65 (33.2)	84 (29.8)	23 (34.8)	172 (31.6)
- Heart disease	51 (26.0)	71 (25.2)	13 (19.7)	135 (24.8)
- Respiratory disease	7 (3.6)	11 (3.9)	1 (1.5)	19 (3.5)
- Diabetes	6 (3.1)	13 (4.6)	5 (7.6)	24 (4.4)
- Depression or anxiety	4 (2.0)	18 (6.4)	3 (4.5)	25 (4.6)
- Other	63 (32.1)	85 (30.1)	21 (31.8)	169 (31.1)
Body Mass Index [mean ± SD] ^{2**}	27.8±4.4	30.8±5.1	28.8±4.6	29.4±5.0
ASA classification [n (%)]¹**				
- 1 (healthy)	32 (15.0)	34 (11.2)	21 (27.6)	87 (14.7)
- 2 (mild systemic disease)	141 (65.9)	214 (70.4)	46 (60.5)	401 (67.6)
- 3 (severe systemic disease—not incapacitating)	41 (19.2)	55 (18.1)	8 (10.5)	104 (17.5)
- 4 (life threatening disease—incapacitating)	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)
Oxford score 6-months post-surgery [M ± SD] ^{2**}	40.3±7.9	37.3±9.4	40.7±7.0	38.7±8.8
Oxford outcome categories3 [n (%)]1**				
- Poor (<27)	10 (4.7)	31 (10.0)	5 (6.7)	46 (7.6)
- Fair (27–33)	18 (8.4)	40 (12.9)	4 (5.3)	62 (10.3)
- Good (34–41)	69 (32.1)	96 (31.0)	21 (28.0)	186 (31.0)
- Excellent (>41)	118 (54.9)	143 (46.1)	45 (60.0)	306 (51.0)
WHOQOL-8 score 6-mths post-surgery [M ±SD] ²	32.2±6.0	30.6±4.5	32.9±4.9	31.4±5.2

^{**} p<0.05 (1 = Chi square; 2 = Kruskall-Wallis test). ASA = American Society for Anaesthesiologists; WHOQOL-8 = World Health Organization Quality of Life 8-item questionnaire. 95% CI = 95% confidence interval. 3. Categories from NZJR.²⁷ Where significant, data in **bold** delineates where the difference lies. †Bootstrapping not completed for unicompartmental knees due to low sample size.

When demographic and clinical variables were examined by procedure type, the analyses indicated participants undergoing uni-compartmental knee replacements were younger than total knee and total hip participants ($X^2(2)=7.96$, p=0.02) and more likely to be working at time of surgery (% in full- or part-time paid employment: uniknee 56.6; total knee 40.9; total hip 39.3; $X^2(8)=20.03$, p=0.01). Total knee replacement participants demonstrated higher mean body mass index than total hip and unicompartmental knee participants ($X^2(2)=8.61$, p=0.02). The only other significant difference across the three procedure groups was with respect to Oxford scores at six months after surgery with total knee participants reporting greater pain and functional difficulty than both other groups ($X^2(2)=7.96$, p=0.01).

Extent of rehabilitation used (intensity, duration, type)

Table 2 shows the breakdown of preand post-operative rehabilitation. These analyses indicated more participants used rehabilitation, mainly physiotherapy, post-operatively (79%) than they did pre-operatively (31.0%). Rehabilitation was mostly outpatient clinic-based compared with home- or community-based (pre-op clinic-based: 56.6%; post-op clinic-based: 68.9%). Of those using pre-operative rehabilitation, although there was wide variability, participants reported an average of 8.3 weeks of intervention, 2-3 sessions a week. Of those receiving post-operative rehabilitation, participants reported waiting on average 2.5 weeks before rehabilitation commenced, with an average of 7.1 weeks of follow up, 1-2 sessions a week.



Table 2: Pre- and post-rehabilitation characteristics (n=608).

	Total hip (n=219)	Total knee (n=313)	Uni-compartmental knee (n=76)†	Total sample (n=608)
Pre-op characteristics				
Any rehabilitation before surgery [yes, n (%)] ¹	72 (32.9)	98 (31.5)	18 (23.7)	188 (31.0)
Type of rehabilitation [n (%)] ¹				
- Occupational therapy	9 (12.3)	8 (7.9)	3 (15.0)	20 (10.3)
- Physiotherapy	39 (53.4)	56 (55.4)	9 (45.0)	104 (53.6)
- Other	73 (34.2)	36 (35.6)	8 (40.0)	69 (35.6)
Session venue [n (%)] ¹				
- Home-based	14 (19.4)	27 (27.6)	4 (21.1)	45 (23.8)
- Hospital or clinic based	42 (58.3)	55 (56.1)	10 (52.6)	107 (56.6)
- Community centre	11 (15.3)	14 (14.3)	4 (21.1)	29 (15.3
- Other	5 (6.9)	2 (2.0)	1 (5.3)	8 (4.2)
Pre-op sessions [weeks, mean ±SD] ²	10.4±22.7	6.9±10.1	7.0±5.9	8.3±15.5
Pre-op sessions [frequency per week, mean ±SD] ²	1.7±1.6	2.5±2.0	2.7±2.3	2.3±2.0
Total hours rehabilitation pre-op [mean ±SD] ^{2**}	8.1±22.1	4.6±6.7	5.3±5.1	6.0±14.0
Post-op characteristics				
Any rehab after surgery [yes, n (%)]1**	138 (63.3)	284 (90.7)	61 (80.3)	483 (79.6)
Type of rehab [n (%)] ¹				
- Occupational therapy	21 (14.6)	22 (7.7)	4 (6.5)	47 (9.6)
- Physiotherapy	105 (72.9)	237 (83.2)	49 (79.0)	391 (79.6)
- Other	18 (12.5)	26 (9.1)	9 (14.5)	53 (10.8)
Session venue [n (%)] ¹				
- Home-based	37 (25.9)	45 (16.1)	10 (16.1)	92 (19.0)
- Hospital or clinic based	90 (62.9)	198 (70.7)	46 (74.2)	334 (68.9)
- Community centre	14 (9.8)	34 (12.1)	5 (8.1)	53 (10.9)
- Other	2 (1.4)	3 (1.1)	1 (1.6)	6 (1.2)
Post-op sessions [weeks, mean \pm SD] ²	9.4±6.7	9.6±8.4	7.4±4.8	9.3±7.6
Post-op sessions [frequency per week, mean \pm SD] 2	1.6±1.2	1.5±0.7	1.5±0.9	1.6±1.0
Total hours rehabilitation post-op [mean ± SD] ²	6.2±5.0	7.9±9.8	5.6±5.7	7.1±8.1
Surgical reviews post-op [mean ± SD] ^{2**}	1.3±0.6	1.7±0.8	1.9±1.2	1.6±0.7
Time to rehab [weeks, mean ± SD] ²	2.8±2.4	2.5±2.5	2.1±2.4	2.5±2.4

^{**}p<0.05 using non parametric tests (1 = Chi square; 2 = Kruskall-Wallis tests). †Bootstrapping not done because of small sample size. Where significant, data in **bold** delineates where the difference lies.

There were no differences by procedure type regarding the intensity, location or duration of rehabilitation pre-operatively. Post-operatively, total hip replacement patients were less likely to use rehabilitation than those after total knee or a uni-compartmental knee replacement (total hip: 63.3%, total knee: 90.7%, uni-knee: 80.3%; $X^2(2)=59.5$, p<0.01). There were no differences in the intensity, location or duration

of rehabilitation used, but participants undergoing total hip replacement had fewer follow-up appointments with the surgeon than both knee replacement groups (mean number of surgeon visits post-surgery: total hip 1.5; total knee 1.9; uni-knee 1.9; $X^2(2)=16.86$, p<0.01). Finally, use of rehabilitation pre- and post-operatively were highly correlated. Participants who used rehabilitation pre-operatively were more likely to



have used rehabilitation post-operatively. Intensity of pre- and post-operative rehabilitation were also correlated in terms of number of hours, session duration, sessions per week and total hours of rehabilitation (total hours: r=0.34, p<0.01; session length: r=0.43, p<0.01; no of weeks of intervention: r=0.29, p<0.01; frequency of sessions per week: r=0.36, p<0.01).

Ethnicity and geographical location

There were no significant differences in use of rehabilitation pre- or post-operatively on the basis of ethnicity. However, nearly 90% of the sample was of New Zealand European ethnicity, with New Zealand Māori making up just 5.5%. The low numbers of non-New Zealand European participants prevented meaningful evaluation of these associations.

Although regional differences in access to surgery were suggested (data not shown), there were no significant differences in use of rehabilitation on the basis of geographical location when this was examined for the full sample. When this was broken down by procedure type the analyses suggested participants undergoing total hip replacement used more pre-operative rehabilitation if they lived in an urban area (60.6%) compared with those living in more rural areas (26.8%; X² (2)=6.73, p=0.04). There were no other significant associations between access to rehabilitation by geographical region.

Discussion

We characterised patterns of rehabilitation before and after hip and knee replacement and found differences in use of rehabilitation on the basis of procedure type and to a lesser extent, geography. More pre-operative rehabilitation was used by total hip and knee replacement participants compared with uni-compartmental knee replacement participants. Post-operatively those undergoing total hip replacement used less rehabilitation than the other two groups. There is a large body of evidence indicating those undergoing total knee replacements have slower recoveries with ongoing pain and functional impairment within the first 6-12 months compared with other joint replacement groups. 4-6,28 Thus it is perhaps unsurprising that total

knee participants used more rehabilitation. Our participants predominantly used clinic-based physiotherapy both pre- and post-operatively in keeping with findings in international literature.^{7,8} Other rehabilitation settings were used less frequently in our sample.

There were trends toward greater use of pre-operative rehabilitation by participants living in larger urban areas, most evident for those undergoing total hip replacement and to a lesser extent for those undergoing uni-compartmental knee replacement. We did not find any other differences in use of rehabilitation on the basis of geography. However, we noticed that a high proportion of participants in our sample live in rural New Zealand or in large urban areas, rather than smaller urban centres. The relationships between use of healthcare services and geography are understudied and depend on the ways these concepts are defined.29 We speculated, based on experiences of the research team, that people living in rural New Zealand may be more willing to travel to access health services. A percentage of people living in smaller towns adjacent to large urban centres may also use urban health services, although this may depend on the way smaller towns are defined or their location.29 The way geographical location was managed in the present study may have been too simplistic to capture such complexities in the joint replacement population.

Clinical and research implications

In the absence of data, it is unclear whether low ethnic diversity in our sample reflects poor uptake of joint replacement and use of rehabilitation among minority groups or a systematic response bias to completion of our survey. Potential inequities on the basis of ethnicity and geography may exist in the joint replacement population. Participants responding to our survey were predominantly New Zealand European and rates across ethnicity categories were inconsistent with general New Zealand population statistics. 16,30 Māori make up approximately 15% of New Zealand's population, however just over 5% of participants identified as Māori in the ROR study sample. Given our recruitment and sampling frame, we are not able



to determine whether lack of diversity in our sample reflected lower rates of access to joint replacement and/or use of rehabilitation among non-European groups or low rates of participation in health research. A first step towards resolving this issue would be for the NZJR to routinely report ethnicity information given that the Registry captures more than 95% of all joint replacement surgeries in New Zealand. This may provide helpful baseline information to motivate strategies to address any potential disparities. In addition, development of partnerships with Māori researchers and the Māori community, and more intentional recruitment strategies, may help to bridge the gap between Māori and non-Māori participation in health research.31

The ROR study also highlighted the predominance of rehabilitation provided via outpatient clinics. Such settings may inadvertently create geographic and socioeconomic barriers for access to rehabilitation, for example meeting transport costs and therapy surcharges. Services might consider increasing opportunities for home and community-based rehabilitation. There is mounting evidence that there is little difference in outcomes on the basis of setting^{10,11,32,33} but broadening options for accessing rehabilitation resources may have considerable benefits, especially for marginalised and minority groups. Other methods and venues, including telemedicine and community outreach have been debated as a means of improving equitable access to health resources more generally.19

Limitations

This study has limitations. One limitation is the representativeness of study participants. We were not able to analyse differences between responders and non-responders to determine this. The NZJR captures more than 95% of joint replacements in New Zealand²⁷ but only samples 20% of this larger group for follow-up collection of patient-reported outcome data. We sampled an even smaller proportion of this 20% taking into account NZJR response rates. However, when we considered demographic and clinical features of the wider NZJR population, our sample is similar

across variables such as age, gender, comorbidity levels and procedure type.

It is possible that our sampling method resulted in systematic bias relating to participation in rehabilitation research. Most importantly, our sample may under-represent the experiences of certain subsections of our target population, for example ethnic minority groups, and over-represent the views of those predisposed to do well. We were also not able to determine whether use of rehabilitation was associated with needs or function, or to determine if rehabilitation use described by participants matched that available by health services. Additionally, we asked participants to recall details regarding use of rehabilitation extending back many months and this raises a concern about recall bias. Nonetheless, this analysis drew on the experiences of 608 participants, which makes this one of the larger joint replacement rehabilitation studies. Future research evaluating rehabilitation before and after joint replacement using prospective methods is recommended to address these concerns.

Finally, we did not examine associations between use of rehabilitation and outcomes in this study as our objective was first to describe the landscape of rehabilitation use in the joint replacement population in New Zealand. More robust prospective methods would be recommended for confident examination of associations between these variables.

Conclusions

In this study participants reported generally positive outcomes six months after primary total hip, knee and uni-compartmental knee replacement consistent with the wider literature describing joint replacement outcomes. However, differences in use of rehabilitation were evident depending on procedure type and delays in starting rehabilitation were suggested. Our data also suggest that broadening setting options for rehabilitation before and after joint replacement by increasing use of home and community-based options, and other approaches such as telemedicine, could improve access to rehabilitation resources.



Competing interests:

Dr Snell reports grants from Canterbury Medical Research Foundation during the conduct of the study.

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