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Patients living in greener neighborhoods live longer and take fewer opioids following hip arthroplasty

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ABSTRACT

Objectives: Determine whether patients who live in greener and more walkable neighborhoods live longer, and take fewer opioids, following hip or knee arthroplasty.

Design: Retrospective cohort study

Setting: Residential environment following surgery at one of 54 hospitals New Zealand hospitals

Participants: All people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties).

Primary and secondary outcome measure: Time to all-cause mortality and number of post-surgical opioid prescriptions

Results: Patients who lived in greener neighborhoods, as measured by the normalized difference vegetation index (NDVI), lived longer following hip arthroplasty (standardized OR: 0.94 95% CI: 0.90-0.98), but no significant association was found for knee arthroplasty. Patients who lived in greener neighborhoods also took fewer opioids in the 12 months following surgery (standardized OR: 0.97 95% CI: 0.95-1.00). As with post-surgical mortality, the relationship between greenness and opioid use was only significant for hip arthroplasty.

Conclusions: Consistent with the literature on enhanced-recovery programs, people who lived in greener neighborhoods took fewer opioids, and lived longer, following hip arthroplasty. Improving access to the natural environment may therefore be an effective component of post-surgical recovery programs.

Keywords: Normalized difference vegetation index, natural environment, surgical recovery, orthopedic

STRENGHTS AND LIMITATIONS OF THIS STUDY

- First study to examine the relationship between natural environment and surgical recovery outside of a hospital setting
- Large cohort followed longitudinally for 9+ years
- Observational study, so we couldn't establish a causal link between the natural environment and surgical recovery
- Exposure was based on residential meshblock not residential address

Competing interests: None declared

Funding: No external funding was received

Data availability statement: De-identified data are not publicly available but may be obtained from Statistics New Zealand after gaining ethical approval and submitting a research proposal (contact: access2microdata@stats.govt.nz). Note that, even with these approvals, data must be accessed via a secure data lab in New Zealand. Exposure data, and code used for statistical analysis, are freely available from the authors.

INTRODUCTION

Rates of hip and knee arthroplasty are rising globally. For example, in OECD countries, the incidence of hip arthroplasty rose from 140/100,000 people in 2005 to 164/100,000 in 2011 [1]. Similarly, the incidence of knee arthroplasty in OECD countries rose from 114/100,000 in 2005 to 150/100,000 in 2011 [2]. Increases in life expectancy and obesity rates suggest that this trend is likely to continue [3]. Given this increased demand, and constrained healthcare budgets, research has focused on identifying approaches that improve post-surgical health outcomes, shorten length of stay, and reduce costs. For example, enhanced-recovery programs that emphasize rapid mobilization and rehabilitation following hip or knee arthroplasty, can reduce length of hospital stay [4] and decrease mortality [5]. However, no research has focused on the effect of patients' residential environment, despite the well-established link between exposure to the natural environment and increased physical activity [6-9], and research showing that viewing a natural scene while recovering from surgery can reduce both length of hospital stay and post-surgical opioid use [10]. We address this gap in the literature by evaluating the relationship between exposure to the built and natural environment and recovery from hip or knee arthroplasty in a large New Zealand cohort.

Literature review

Numerous studies have examined how different elements of enhanced-recovery programs affect post-operative outcomes (also known as fast-track or rapid-recovery programs). These programs use coordinated multimodal techniques to reduce recovery times and improve post-operative outcomes [3]. For example, pre-operative education can shorten hospital stays [11] and reduce post-operative pain [12]. Several studies have found that pre-emptive analgesia allows more rapid mobilization and return of function [13, 14]. Multiple studies have found that rapid mobilization on the day of surgery (typically 2-6 hours after surgery) reduces length of stay and improves function [15-17]. Similarly, aggressive

physical therapy (extending beyond the day of surgery) can reduce length of stay and improve function [18-20]. Finally, in a prospective study of 4,500 patients in the UK, enhanced recovery was associated with improved two-year survival rates when compared to traditional post-surgical protocols, which suggests that post-operative mobility may have long-term benefits [5].

Several studies have found that exposure to the natural environment is associated with increased physical activity. For example, using survey data in Chicago (n=1,544), Fan et al. [21] found that respondents with a greater area of public parks within 0.5 miles of their home were more likely to engage in physical activity. A survey of 1,895 people in Adelaide, Australia [9] found that respondents who perceived their neighborhood as greener were more likely to engage in recreational walking. Similarly, a study in 1,803 people in Perth, Australia [22] found that people who lived nearer to recreational amenities, including public parks, were more likely to meet minimum physical-activity requirements.

METHODS

Study sample

Our sample consisted of all people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties). We obtained individual-level hospital and pharmaceutical records via Statistics New Zealand's Integrated Data Infrastructure (IDI), which is a large database of routinely-collected individual-level data [23]. The IDI is structured around a central spine designed to identify all New Zealand residents. Datasets describing health, education, benefits, criminal justice, population (births, deaths, and immigration), income and work, and housing are linked to this central spine.

As this study was based on routinely-collected health data, and did not involve contacting individual patients, the study was classified as minimal risk by the New Zealand Health and Disabilities Ethics

Committee and was approved by Statistics New Zealand (MAA-2017-57). In addition, our research conformed to the Declaration of Helsinki guidelines.

Patient and Public Involvement statement: There was no patient recruitment.

Outcomes

We used two outcomes to measure recovery: time to all-cause mortality and number of opioid prescriptions 3, 12, and 24 months post-surgery. We chose these outcomes, as they are important metrics of post-surgical recovery, and previous research has shown that rapid mobilization and rehabilitation can reduce two-year mortality rates following hip or knee arthroplasty [24], and exposure to the natural environment, in a hospital setting, is associated with reduced perioperative use of opioids [10].

By the end of 2016, 2,263 of the 7,449 people who had received a hip arthroplasty had died as had 1,741 of the 6,558 people who received knee arthroplasties.

The number of opioid prescriptions received was calculated by linkage to pharmacy records. We did not include prescriptions for methadone or bruprenorphine, as in New Zealand these are primarily used to treat addiction. To control for pre-surgical pain, we calculated the number of opioid prescriptions each participant received in the 12 months before surgery. Finally, to account for opioid potency, we categorized each opioid prescription as either strong (potency equal to or greater than morphine) or weak (potency less than morphine). On average, study participants received 3.04 (SD=9.38) opioid prescriptions in the 12 months before surgery (0.68 strong and 2.36 weak) and 2.72 (SD=7.06) opioid prescriptions in the 12 months after surgery (0.75 strong and 1.98 weak).

Exposures

All exposures are based on a participant's residential meshblock, which is the smallest geographic unit at which Statistics New Zealand reports data. On average, 95 people live in a meshblock.

Linking to address history in the IDI allowed us to estimate exposures for each year of the study (2005-2016). From these annual values, we calculated mean post-surgical exposure, which we defined as the mean exposure from the year of surgery to death or 2016, whichever came first.

Walkability

We used a previously validated walkability index [25] with three components: number of households per hectare (data source: 2006 New Zealand Census), number of road intersections per square kilometer (data source: Land Information New Zealand), and land-use mix (data source: 2008 New Zealand Land Cover Database v4.1).

Land-use mix is defined as:

$$Land-use\ mix = \frac{\sum_{i=1}^{n}(LC_i * ln(LC_i))}{ln(N)}$$

Where LC_i denotes the proportion of each meshblock that is covered by the *i*th land-cover type and *N* denotes the total number of land-cover types. Following Frank et al., we standardized household density, intersection density, and land-use mix (by subtracting the mean and dividing by the standard deviation), and summed the three standardized scores into a single walkability index.

Greenness

We used two measures of exposure to the natural environment: land-cover data (see above) and the Normalized Difference Vegetation Index (NDVI), which is a greenness index derived from satellite imagery. Specifically, we used maximum annual NDVI derived from 30m-resolution Landsat imagery that was calculated at the top of the atmosphere, which normalized all atmospheric effects. We standardized NDVI values to make regression coefficients easier to interpret. From these annual values, we calculated mean post-surgical greenness exposure.

Covariates

Using data from the IDI, we controlled for sex, ethnicity, and age. In addition, we controlled for neighborhood deprivation using the New Zealand Deprivation Index (NZDep), which is a well-validated index calculated from nine census variables [26]. NZDep ranges from 1 to 10 with higher values denoting higher levels of social deprivation. Finally, we controlled for eight chronic conditions at time of surgery: coronary heart disease, gout, chronic obstructive pulmonary disease (COPD), diabetes, cancer, stroke, acute myocardial infarction, and traumatic brain injury. Conditions were pre-defined by Statistics New Zealand based on hospital-admissions and pharmacy data [27].

Statistical analysis

We analyzed time-to-death data using a frailty model that included hospital-level random effects. We were particularly careful to account for the hospital where the surgery was performed, because smaller hospitals that may not be able to provide the specialist care of a larger hospital are more likely to be in rural areas that are greener. We evaluated five different functional forms for the survival function (Weibull, exponential, log-logistic, log-normal, and gamma) and chose between them using the Akaike information criterion. We analyzed the number of post-operative opioid scripts using a mixed negative-binomial regression that included hospital-level random effects.

A backwards-selection procedure was used for all model selection: variables were dropped from the analysis using progressively smaller p-value thresholds (final threshold: $p<0.1$). Insignificant variables can still be confounders [28], so we systematically re-introduced dropped variables and retained them if the coefficients on variables of interest changed by more than 10%.

To avoid including highly collinear combinations of variables, we estimated ordinary least squares versions of each model (results not shown), which allowed us to calculate variance-inflation factors for each independent variables. If any variable had a variance-inflation factor over two, we dropped it from

the regression model. When choosing between two collinear variables, we included the variable with the lowest p-value when individually regressed against the dependent variable.

We also conducted stratified analyses to see whether the relationship between the natural environment and health outcomes was the same across different strata of the sample. Analyses were conducted for hip and knee arthroplasty combined as well as for each outcome separately.

RESULTS

Table 1 provides descriptive statistics for our sample.

In the frailty model, specifying the survival function using a Weibull distribution gave the best model fit. Being older, male, European New Zealander, or Māori (the indigenous people of New Zealand) were all mortality risk factors (Table 2). Similarly, people who received more pre-surgery opioids, or had a longer hospital stay, were at greater risk of mortality. Six chronic conditions were risk factors as was higher neighborhood deprivation, although this relationship was only significant for hip arthroplasty.

People who lived in greener neighborhoods (defined as mean post-surgical NDVI) were at lower risk of mortality, although this relationship was only significant in the hip-and-knee arthroplasty and hip-arthroplasty-only models (Table 2). To better elucidate the dose-response function linking NDVI and mortality, we re-estimated the hip-and-knee-arthroplasty frailty model splitting NDVI into quartiles (Table 3). Only the highest quartile was statistically significant, although NDVI remained protective in the second and third quartiles.

Figure 1 shows the odds-ratio for mean lifetime NDVI for different strata of the sample. Stratifying the sample resulted in some loss of significance, due to lower numbers in each stratum. Notably, the protective effect of NDVI was higher for men than women. The protective effect of NDVI was also modestly higher for people who lived in higher SES neighborhoods (NZDep 1-5) compared to lower SES

neighborhoods (NZDep 6-10). Similarly, NDVI was somewhat more protective for people who were younger than average (mean age at surgery=68).

In the opioid model (Table 4), women, European New Zealanders, and people who were prescribed more pre-surgery opioid prescriptions received significantly more post-surgical opioid scripts in all three time periods with the exception of European New Zealanders in the 24 months post-surgery model (Table 4). Those who received a knee arthroplasty (as opposed to a hip arthroplasty), or stayed longer in hospital, also received more post-surgical opioids, as did people who had COPD, coronary heart disease, or traumatic brain injury. In contrast, older people received fewer opioid prescriptions, although the significance of this relationship varied across the three time periods. Separating opioids into weak and strong was not revealing and reduced the significance of variables of interest (data not shown). Mean post-surgical greenness was associated with significantly fewer post-surgical opioid prescriptions in all three time periods (Table 4). Living in a rural area, walkability, and land cover were not significantly associated with the number of post-surgical opioid prescriptions or post-surgical longevity (data not shown). In addition, consistent with the frailty model, NDVI was not significant, when the analysis was restricted to knee-arthroplasty (results not shown). Finally, when we split NDVI into quartiles, none were significant (results not shown).

In the stratified analysis (figure 2), greenness was more protective for men than women, which is consistent with the frailty model.

DISCUSSION

In a cohort of people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 or 2007, we found that residents of greener neighborhoods received fewer post-surgical opioid prescriptions and lived longer, with the strongest results for hip arthroplasty. Our results are consistent with those reported by Ulrich [10], who found that, after gall-bladder surgery, patients

recovered faster, and took fewer opioids, if they were in a room with a view of a natural scene. Our results were also consistent with a previous study [5], which found that rapid mobilization following hip or knee arthroplasty was associated with better two-year survival rates. Our study suggests that the benefits of mobilization (assuming this plays a role in the observed association between green space and mortality or opioid-use) extend beyond the immediate post-surgical period.

In both the opioid and survival models, we found that greenness was more protective for men than women. This differential association may be because women's life expectancy is greater than men, so they are less likely to have a live-in partner who could encourage them to be physically active, and accompany them while they engage in outdoor activity that they might otherwise find too daunting. This possible mechanism is consistent with multiple studies showing that having a live-in partner is protective of a range of health outcomes [29]. In addition, this suggests that women, or indeed men, who live alone may benefit from additional post-surgical support.

Greenness was associated with lower post-surgical opioid use, and lower mortality, in people recovering from hip arthroplasty but not those recovering from knee arthroplasty. This may be because knee arthroplasty is a more difficult and painful surgery to recover from (post-surgical opioid use was higher for knee-arthroplasty patients), and the protective effect of neighborhood greenness is insufficient to induce a clinically significant increase in post-surgical mobilization. However, other mechanism may also be involved (see below), so results should be interpreted with care.

There was modest evidence that younger people, and those living is less deprived neighborhoods, derived greater benefit from exposure to greenness. This may be because younger people are more physically able to engage in outdoor activity, and that greenspace in higher SES neighborhoods may be better maintained and more appealing because of lower crime.

When we split NDVI into quartiles in the frailty model, we found that only the top quartile was protective at conventional significance levels. This suggests that there may be a minimum threshold below which greenness offers no health benefits. However, it is important to note that NDVI is a coarse measure of overall greenness. It does not reveal which elements of the natural environment provide the greatest health benefits. Identifying the most protective elements would help inform the design of landscapes that are not in the top quartile of NDVI, but nonetheless provide health benefits.

The magnitude of the protective effect of neighborhood greenness is not trivial. For example, in the 3-months post-surgery model of opioid use, a 2-SD decrease in NDVI is roughly equivalent to the risk of having chronic heart disease at the time of surgery. In the hip-only frailty model, a 2-SD decrease in NDVI is roughly equivalent to the risk of being two years older.

Physical activity is likely not the only mechanism linking greenness and improved post-surgical outcomes. For example, exposure to the natural environment can reduce short-term markers of stress such as heart rate, blood pressure, and salivary cortisol [30, 31]. In turn, stress is a well-documented risk factor for premature mortality [32] and can also trigger opioid cravings [33]. Similarly, exposure to the natural environment is associated with increased social connectivity [34], and social isolation can increase individual reactivity to opioids [35] as well as being a risk factor for premature mortality [36]. More recently, research suggests that exposure to the natural environment may increase the microbial diversity of the human microbiome [37], and protect against adverse health outcomes [38] through improved immune function. In addition, improved immune function is associated with improved surgical recovery [39] and better orthopedic outcomes in elderly patients [40].

Our study has several limitations. This is an observational study, so we were not able to establish a causal relationship between exposure to the natural environment, opioid use, and surgical recovery. In addition, our metrics of exposure to the natural environment were coarse. In particular, meshblock-level

NDVI is an imperfect measure of a person's exposure to the natural environment. This is especially true in larger, rural meshblocks, where mean NDVI may not optimally represent a person's residential exposure to the natural environment. In addition, our outcome measures do not fully capture all elements of surgical recovery. For example, we did not have access to data on post-surgical physical activity levels or weight.

TABLES

Table 1: Descriptive statistics for study participants who received a hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 or 2007 (hip: n=7,449; knee: n=6,558)[1]

	HIP		*KNEE*	
Variable	**Mean**	**SD**	**Mean**	**SD**
Male (%)	43.2	-	44.9	-
Ethnicity: NZ European (%)	82.0	-	81.1	-
Ethnicity: Māori (%)	9.9	-	6.4	-
Ethnicity: Pacific Islander (%)	0.99	-	3.2	-
Chronic condition: COPD (%)	8.8	-	9.8	-
Chronic condition: acute MI (%)	5.8	-	5.1	-
Chronic condition: CHD (%)	10.6	-	12.1	-
Chronic condition: stroke (%)	2.3	-	2.6	-
Chronic condition: diabetes (%)	12.4	-	15.5	-
Chronic condition: traumatic brain injury (%)	1.5	-	1.1	-
Length of hospital stay (days)	6.4	4.5	6.2	3.0
Opioid scripts (12 month pre-surgery)	3.2	6.8	2.4	5.2
Opioid scripts (12 month post-surgery)	2.1	4.9	2.8	5.1
Age on day of surgery	68.2	12.0	69.5	9.9
Mean post-surgical NDVI	0.527	0.123	0.526	0.121

[1] Following IDI protocols, all sample sizes (including the number of hospitals) have been rounded to the nearest multiple of three

Table 2: Frailty model of time to all-cause mortality (Hip and knee: number of participants=14,010, number of observations= 149,523; hip: number of participants=7,449, number of observations=78,501; knee: number of participants=6,558, number of observations= 71,022)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori.

	HIP AND KNEE		*HIP*		*KNEE*	
Variable	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Age (years)	1.090***	1.086 - 1.094	1.084***	1.078 - 1.089	1.098***	1.091 - 1.105
Female	0.711***	0.667 - 0.758	0.730***	0.670 - 0.796	0.665***	0.604 - 0.732
Ethnicity: European NZ	1.309***	1.151 - 1.490	1.279***	1.063 - 1.538	1.284***	1.072 - 1.537
Ethnicity: Māori	2.137***	1.806 - 2.528	1.910***	1.516 - 2.406	2.286***	1.778 - 2.939
Mean post-surgical NZDep	1.010*	0.998 - 1.023	1.018**	1.002 - 1.035	0.999	0.980 - 1.017
Chronic condition: COPD	1.448***	1.325 - 1.583	1.410***	1.250 - 1.591	1.478***	1.294 - 1.688
Chronic condition: acute MI	1.442***	1.293 - 1.607	1.384***	1.199 - 1.597	1.476***	1.249 - 1.744
Chronic condition: cancer	1.485***	1.357 - 1.625	1.592***	1.417 - 1.790	1.333***	1.157 - 1.536
Chronic condition: Stroke	1.567***	1.346 - 1.825	1.702***	1.394 - 2.078	1.385***	1.094 - 1.755
Chronic condition: diabetes	1.306***	1.203 - 1.417	1.278***	1.142 - 1.430	1.342***	1.191 - 1.513
Chronic condition: Traumatic brain injury	1.299*	0.994 - 1.697	1.193	0.835 - 1.703	1.452*	0.968 - 2.177
Opioid scripts 12 months pre-surgery	1.005***	1.004 - 1.006	1.018***	1.014 - 1.022	1.004***	1.002 - 1.006
Mean post-surgical NDVI (standardized)	0.954***	0.922 - 0.987	0.936***	0.895 - 0.979	0.978	0.929 - 1.029
Length of hospital stay	1.034***	1.029 - 1.039	1.030***	1.025 - 1.036	1.052***	1.040 - 1.063
Variance of hospital random effect	0.01404		0.011138		0.006208	
Number of Hospitals[1]	54		51		51	

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes (including the number of hospitals) have been rounded to the nearest multiple of three

Table 3: Frailty model of time to all-cause mortality following hip or knee arthroplasty with NDVI quartiles (number of participants=14,010; number of observations= 149,523)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori.

Variables	HR	95% CI
Age (years)	1.090***	1.086 - 1.094
Female	0.714***	0.670 - 0.761
Ethnicity: European NZ	1.305***	1.147 - 1.484
Ethnicity: Māori	2.124***	1.796 - 2.513
NZDep	1.012*	1.000 - 1.024
Chronic condition: COPD	1.448***	1.325 - 1.583
Chronic condition: acute MI	1.443***	1.295 - 1.608
Chronic condition: cancer	1.489***	1.361 - 1.629
Chronic condition: Stroke	1.568***	1.347 - 1.826
Chronic condition: diabetes	1.307***	1.204 - 1.418
Chronic condition: Traumatic brain injury	1.300*	0.995 - 1.699
Opioid scripts 12 months pre-surgery	1.005***	1.004 - 1.006
NDVI (standardized) quartile 2	0.933	0.856 - 1.017
NDVI (standardized) quartile 3	0.953	0.873 - 1.041
NDVI (standardized) quartile 4	0.884**	0.804 - 0.971
Length of hospital stay	1.034***	1.029 - 1.039

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes (including the number of hospitals) have been rounded to the nearest multiple of three

Table 4: Mixed negative-binomial model of number of opioid prescriptions 3 months, 12 months, and 24 months after hip or knee arthroplasty including a hospital-level random effect (n=14,010)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ.

	3 MONTHS POST SURGERY		*12 MONTHS POST SURGERY*		*24 MONTHS POST SURGERY*	
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Opioid scripts 12 months pre-surgery	1.083***	1.079 - 1.087	1.136***	1.130 - 1.141	1.147***	1.141 - 1.154
Female	1.124***	1.072 - 1.177	1.177***	1.121 - 1.237	1.195***	1.134 - 1.259
Ethnicity: European NZ	1.247***	1.171 - 1.329	1.121***	1.051 - 1.196	1.01	0.944 - 1.080
Age	0.994***	0.992 - 0.996	0.998	0.996 - 1.001	0.998*	0.995 - 1.000
Mean post-surgical NDVI (standardized)	0.969***	0.947 - 0.992	0.971**	0.947 - 0.995	0.969**	0.944 - 0.994
Knee	1.653***	1.578 - 1.731	1.594***	1.519 - 1.673	1.547***	1.471 - 1.627
COPD	1.219***	1.133 - 1.311	1.272***	1.175 - 1.378	1.374***	1.262 - 1.496
CHD	1.133***	1.057 - 1.214	1.091**	1.012 - 1.175	1.069*	0.988 - 1.157
Traumatic Brain Injury	1.197*	0.992 - 1.444	1.335***	1.088 - 1.637	1.448***	1.166 - 1.799
Days in Hospital	1.015***	1.009 - 1.022	1.035***	1.027 - 1.043	1.037***	1.029 - 1.045
Variance of hospital random effect	1.164***	1.064 - 1.272	1.072***	1.020 - 1.127	1.071**	1.009 - 1.137

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

FIGURE LEGENDS

Figure 1: Odds-ratio plot of standardized mean post-surgical NDVI for time to all-cause mortality following hip or knee arthroplasty (number of participants=14,010, number of observations= 149,523)[1]. Low/high SES denotes participants whose lifetime NZ Deprivation Index is above/below average. Old/young denote participants who are older/younger than the sample mean. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori (figures 1 and 2 were created with the user-written Stata command COEFPLOT)

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

Figure 2: Odds-ratio plot of standardized mean post-surgical NDVI for number of opioid prescriptions 3 months post-surgery (n=14,010)[1]. For definitions and reference groups see figure 1.

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

Contributorship statement: GHD designed the study, conducted the analysis, and wrote the majority of the manuscript. DG created the exposure metrics and edited the manuscript. JD wrote parts of the manuscript and edited multiple drafts.

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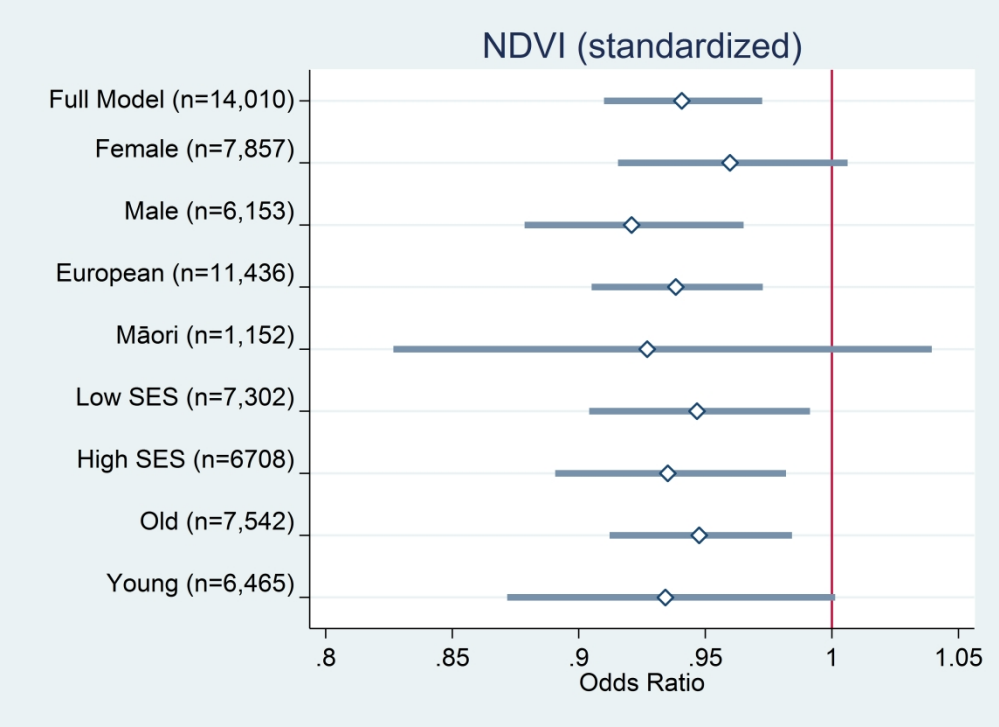

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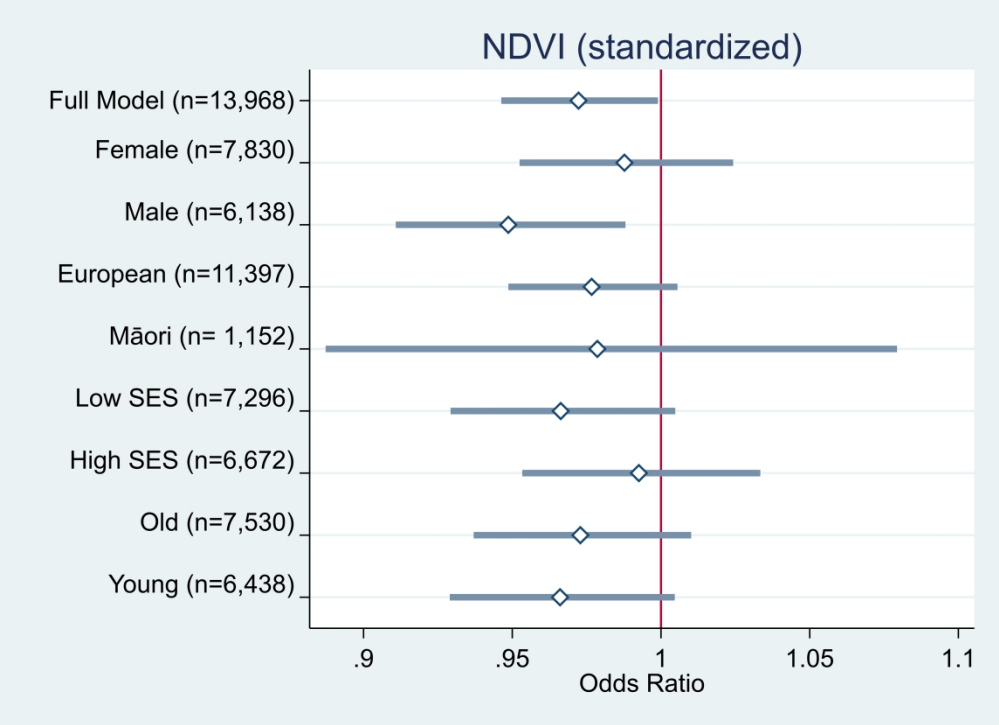

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-8*
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	N/A
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A

	(*e*) Describe any sensitivity analyses	9

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14-16
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*6*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15-17
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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The relationship between exposure to the natural environment and recovery from hip or knee arthroplasty: a New Zealand retrospective cohort study

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ABSTRACT

Objectives: Determine whether patients who live in greener and more walkable neighborhoods live longer, and take fewer opioids, following hip or knee arthroplasty.

Design: Retrospective cohort study.

Setting: Residential environment following surgery at one of 54 New Zealand hospitals.

Participants: All people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties).

Primary and secondary outcome measure: Time to all-cause mortality and number of post-surgical opioid prescriptions.

Results: Patients who lived in greener neighborhoods, as measured by the normalized difference vegetation index (NDVI), lived longer following hip or knee arthroplasty (standardized OR: 0.95 95% CI: 0.92-0.99). However, when we estimated separate hip-arthroplasty-only and knee-arthroplasty-only models, greenness was only significantly associated with greater longevity following hip arthroplasty. Similarly, patients who lived in greener neighborhoods took fewer opioids in the 12 months following hip or knee arthroplasty (standardized OR: 0.97 95% CI: 0.95-0.99), but in separate hip-arthroplasty-only and knee-arthroplasty-only models, greenness was only significantly associated with lower opioid use following hip arthroplasty. Walkability was not significantly associated with post-surgical opioid use or post-surgical longevity. All odds ratios were adjusted for sex, ethnicity, age, pre-surgical chronic health conditions, pre-surgical opioid use, social deprivation, and length of hospital stay.

Conclusions: Consistent with the literature on enhanced-recovery programs, people who lived in greener neighborhoods took fewer opioids, and lived longer, following hip arthroplasty. Improving

access to the natural environment may therefore be an effective component of post-surgical recovery programs.

Keywords: Normalized difference vegetation index, natural environment, surgical recovery, orthopedic

STRENGTHS AND LIMITATIONS OF THIS STUDY

- First study to examine the relationship between natural environment and surgical recovery outside of a hospital setting
- Large cohort followed longitudinally for 9+ years
- Observational study, so a causal link between the natural environment and surgical recovery couldn't be established
- Exposure was based on residential meshblock not residential address

Competing interests: None declared

Funding: No external funding was received

Data availability statement: De-identified data are not publicly available but may be obtained from Statistics New Zealand after gaining ethics approval and submitting a research proposal (contact: access2microdata@stats.govt.nz). Note that, even with these approvals, data must be accessed via a secure data lab in New Zealand. Exposure data, and code used for statistical analysis, are freely available from the authors.

INTRODUCTION

Rates of hip and knee arthroplasty are rising globally. For example, in Organization for Economic Cooperation and Development (OECD) countries, the incidence of hip arthroplasty rose from 140/100,000 people in 2005 to 164/100,000 in 2011 [1]. Similarly, the incidence of knee arthroplasty in OECD countries rose from 114/100,000 in 2005 to 150/100,000 in 2011 [2]. Increases in life expectancy and obesity rates suggest that this trend is likely to continue [3]. Given this increased demand, and constrained healthcare budgets, research has focused on identifying approaches that improve post-surgical health outcomes, shorten length of stay, and reduce costs. For example, enhanced-recovery programs that emphasize rapid mobilization and rehabilitation following hip or knee arthroplasty can reduce length of hospital stay [4] and decrease mortality [5]. However, no research has focused on the effect of patients' residential environments, despite the well-established link between exposure to the natural environment and increased physical activity [6-9], and research showing that passively viewing a natural scene while recovering from surgery can reduce both length of hospital stay and post-surgical opioid use [10]. We address this gap in the literature by evaluating the relationship between exposure to the built and natural environment and recovery from hip or knee arthroplasty in a large New Zealand cohort.

Literature review

Numerous studies have examined how different elements of enhanced-recovery programs affect post-operative outcomes (also known as fast-track or rapid-recovery programs). These programs use coordinated multimodal techniques to reduce recovery times and improve post-operative outcomes [3]. For example, pre-operative education can shorten hospital stays [11] and reduce post-operative pain [12]. Several studies have found that pre-emptive analgesia allows more rapid mobilization and return of function [13, 14]. Multiple studies have found that rapid mobilization on the day of surgery (typically

2-6 hours after surgery) reduces length of stay and improves function [15-17]. Similarly, aggressive physical therapy (extending beyond the day of surgery) can reduce length of stay and improve function [18-20]. Finally, in a prospective study of 4,500 patients in the UK, enhanced recovery was associated with improved two-year survival rates when compared to traditional post-surgical protocols, which suggests that post-operative mobility may have long-term benefits [5].

Several studies have found that exposure to the natural environment is associated with increased physical activity. For example, using survey data in Chicago (n=1,544), Fan et al. [21] found that respondents with a greater area of public parks within 0.5 miles of their home were more likely to engage in physical activity. A survey of 1,895 people in Adelaide, Australia [9] found that respondents who perceived their neighborhoods as greener were more likely to engage in recreational walking. Similarly, a study in 1,803 people in Perth, Australia [22] found that people who lived nearer to recreational amenities, including public parks, were more likely to meet minimum physical-activity requirements.

Passive exposure to the natural environment can also produce health benefits. In particular, several studies have found that greenness exposure can reduce perceived pain in a range of settings. Specifically, a RCT of 46 healthy volunteers [23] found that participants who had just watched a video of a natural scene had significantly higher pain threshold and tolerance than participants who had watched a blank screen. Similarly, a RCT of adults undergoing flexible bronchoscopy found that participants who viewed a natural scene reported significantly less pain [24]. Finally, an RCT of a two-day forestry-therapy program in Korea found that participants in the program (n=33) had significantly lower levels of pain and depression than controls (n=25). In addition, participants had significantly higher heart-rate variability and natural-killer cell activity.

METHODS

Study sample

Our sample consisted of all people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties). We obtained individual-level hospital and pharmaceutical records via Statistics New Zealand's Integrated Data Infrastructure (IDI), which is a large database of routinely-collected individual-level data [25]. The IDI is structured around a central spine designed to identify all New Zealand residents. Datasets describing health, education, benefits, criminal justice, population (births, deaths, and immigration), income and work, and housing are linked to this central spine.

As this study was based on routinely-collected health data, and did not involve contacting individual patients, the study was classified as minimal risk by the New Zealand Health and Disabilities Ethics Committee and was approved by Statistics New Zealand (MAA-2017-57). Before we were granted access, all data were anonymized by Statistics New Zealand. In addition, our research conformed to the Declaration of Helsinki guidelines.

Patient and Public Involvement statement: Neither patients, nor the public, were involved in the design or conduct of this study.

Outcomes

We used two outcomes to measure recovery: time to all-cause mortality and number of opioid prescriptions 3, 12, and 24 months post-surgery. We chose these outcomes as they are important metrics of post-surgical recovery. In addition, previous research has shown that rapid mobilization and rehabilitation can reduce two-year mortality rates following hip or knee arthroplasty [26], and exposure to the natural environment, in a hospital setting, is associated with reduced perioperative use of opioids [10].

By the end of 2016, 2,263 (30.0%) of the 7,449 people who had received a hip arthroplasty had died as had 1,741 (26.5%) of the 6,558 people who received knee arthroplasties.

The number of opioid prescriptions received was calculated by linkage to pharmacy records. We did not include prescriptions for methadone or buprenorphine, as in New Zealand these are primarily used to treat addiction. To control for pre-surgical pain, we calculated the number of opioid prescriptions each participant received in the 12 months before surgery. Finally, to account for opioid potency, we categorized each opioid prescription as either strong (potency equal to or greater than morphine) or weak (potency less than morphine). On average, study participants received 3.04 (SD=9.38) opioid prescriptions in the 12 months before surgery (0.68 strong and 2.36 weak) and 2.72 (SD=7.06) opioid prescriptions in the 12 months after surgery (0.75 strong and 1.98 weak).

Exposures

All exposures are based on a participant's residential meshblock, which is the smallest geographic unit at which Statistics New Zealand reports data. On average, 95 people live in a meshblock.

Linking to address history in the IDI allowed us to estimate exposures for each year of the study (2005-2016). From these annual values, we calculated mean post-surgical exposure, which we defined as the mean exposure from the year of surgery to death or 2016, whichever came first.

We had no information on participants' pre- or post-surgical physical activity. Therefore, exposure metrics describe the physical environment that a participant is exposed to, but they do not describe how a participant physically interacts with different environments.

Walkability

We used a previously validated walkability index [27] with three components: number of households per hectare (data source: 2006 New Zealand Census), number of road intersections per square kilometer

(data source: Land Information New Zealand), and land-use mix (data source: 2008 New Zealand Land Cover Database v4.1). In all three cases, we used the version of each data source that was closest to baseline. Land-cover data were available from 2001, 2008, and 2012. However, the classification schemes were not consistent across the three years. In addition, when we compared 2008 and 2012 data, we found that the net area of New Zealand that changed from one land class to another was only 0.903%. Therefore, we used 2008 data for our analysis.

Land-use mix is defined as:

$$Land-use\ mix = \frac{\sum_{i=1}^{n}(LC_i * ln(LC_i))}{ln(N)}$$

Where LC_i denotes the proportion of each meshblock that is covered by the *i*th land-cover type and *N* denotes the total number of land-cover types. Following Frank et al., we standardized household density, intersection density, and land-use mix (by subtracting the mean and dividing by the standard deviation), and summed the three standardized scores into a single walkability index.

Greenness

We used two measures of exposure to the natural environment: land-cover data (see above) and the Normalized Difference Vegetation Index (NDVI), which is a greenness index derived from satellite imagery. Specifically, for each year from 2005 to 2016, we used maximum annual NDVI derived from 30m-resolution Landsat imagery that was calculated at the top of the atmosphere, which normalized all atmospheric effects. We standardized NDVI values to make regression coefficients easier to interpret. From these annual values, we calculated mean post-surgical greenness exposure.

Covariates

Using data from the IDI, we controlled for sex, ethnicity, and age. In addition, we controlled for neighborhood deprivation using the New Zealand Deprivation Index (NZDep), which is a well-validated index calculated from nine census variables [28]. NZDep ranges from 1 to 10 with higher values denoting higher levels of social deprivation. Finally, we controlled for eight chronic conditions at time of surgery: coronary heart disease, gout, chronic obstructive pulmonary disease (COPD), diabetes, cancer, stroke, acute myocardial infarction, and traumatic brain injury. We chose to account for these conditions as they are major health outcomes that could affect surgical recovery, and they were pre-defined by Statistics New Zealand based on hospital-admissions and pharmacy data [29]. Note that we did not have access to data on physical activity, BMI, or diet.

Statistical analysis

We analyzed time-to-death data using a frailty model that included hospital-level random effects. We were particularly careful to account for the hospital where the surgery was performed, because smaller hospitals that may not be able to provide the specialist care of a larger hospital are more likely to be in rural areas that are greener. We evaluated five different functional forms for the survival function (Weibull, exponential, log-logistic, log-normal, and gamma) and chose between them using the Akaike information criterion. We analyzed the number of post-operative opioid scripts using a mixed negative-binomial regression that included hospital-level random effects.

A backwards-selection procedure was used for all model selection: variables were dropped from the analysis using progressively smaller p-value thresholds (final threshold: $p<0.1$). Insignificant variables can still be confounders [30], so we systematically re-introduced dropped variables and retained them if the coefficients on variables of interest changed by more than 10%.

To avoid including highly collinear combinations of variables, we estimated ordinary least squares versions of each model (results not shown), which allowed us to calculate variance-inflation factors for

each independent variable. If any variable had a variance-inflation factor over two, we dropped it from the regression model. When choosing between two collinear variables, we included the variable with the lowest p-value when individually regressed against the dependent variable.

We also conducted stratified analyses to see whether the relationship between the natural environment and health outcomes was the same across different strata of the sample. Analyses were conducted for hip and knee arthroplasty combined as well as for each outcome separately.

RESULTS

Table 1 provides descriptive statistics for our sample.

In the frailty model, specifying the survival function using a Weibull distribution gave the best model fit. Being older, male, European New Zealander, or Māori (the indigenous people of New Zealand) were all mortality risk factors (Table 2) (The reference ethnic group was Pacific, Asian, MELAA, or other). Similarly, people who received more pre-surgery opioids, or had a longer hospital stay, were at greater risk of mortality. Six chronic conditions were risk factors as was higher neighborhood deprivation, although this relationship was only significant for hip arthroplasty.

People who lived in greener neighborhoods (defined as mean post-surgical NDVI) were at lower risk of mortality, although this relationship was only significant in the hip-and-knee arthroplasty and hip-arthroplasty-only models (Table 2). To better elucidate the dose-response function linking NDVI and mortality, we re-estimated the hip-and-knee-arthroplasty frailty model splitting NDVI into quartiles (Table 3). Only the highest quartile was statistically significant, in the combined and hip-only models, although NDVI remained protective in the second and third quartiles. In the knee-only model, the second quartile of NDVI was protective although only at the 10% level. In addition, the third and fourth quartiles of NDVI did not show a consistent protective effect.

Figure 1 shows the odds ratio for mean lifetime NDVI for different strata of the sample. Stratifying the sample resulted in some loss of significance, due to lower numbers in each stratum. Notably, the protective effect of NDVI was higher for men than women. The protective effect of NDVI was also modestly higher for people who lived in higher SES neighborhoods (NZDep 1-5) compared to lower SES neighborhoods (NZDep 6-10). Similarly, NDVI was somewhat more protective for people who were younger than average (mean age at surgery=68).

In the opioid model (Table 4), women, European New Zealanders, and people who were prescribed more pre-surgery opioid prescriptions received significantly more post-surgical opioid scripts in all three time periods with the exception of European New Zealanders in the 24 months post-surgery model (Table 4). Those who received a knee arthroplasty (as opposed to a hip arthroplasty) or stayed longer in hospital also received more post-surgical opioids, as did people who had COPD, coronary heart disease, or traumatic brain injury. In contrast, older people received fewer opioid prescriptions, although the significance of this relationship varied across the three time periods. Separating opioids into weak and strong was not revealing and reduced the significance of variables of interest (data not shown). Mean post-surgical greenness was associated with significantly fewer post-surgical opioid prescriptions in all three time periods (Table 4). Living in a rural area and land cover were not significantly associated with the number of post-surgical opioid prescriptions or time to all-cause mortality (data not shown). In addition, walkability was not significantly associated with either opioid use or mortality. For example, the odds ratio on walkability in the 3-month post-surgical opioid model was 1.043 (95% CI: 0.966-1.127), and the odds ratio in the hip-only frailty model was 1.035 (95% CI: 0.971-1.104). Even when the analysis was restricted to only-hip or only-knee arthroplasties, the relationship between walkability and mortality or opioid use remained insignificant.

In addition, consistent with the frailty model, NDVI was not significant, when the analysis was restricted to knee-arthroplasty (results not shown). Finally, when we split NDVI into quartiles, none were significant (results not shown).

In the stratified analysis (figure 2), greenness was more protective for men than women, which is consistent with the frailty model.

DISCUSSION

In a cohort of people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 or 2007, we found that residents of greener neighborhoods received fewer post-surgical opioid prescriptions and lived longer, with the strongest results for hip arthroplasty. Our results are consistent with those reported by Ulrich [10], who found that, after gall-bladder surgery, patients recovered faster and took fewer opioids if they were in a room with a view of a natural scene. Our results are also consistent with a previous study [5], which found that rapid mobilization following hip or knee arthroplasty was associated with better two-year survival rates. Finally, results suggests that the benefits of exposure to the natural environment extend beyond the immediate post-surgical period.

In both the opioid and survival models, we found that greenness was more protective for men than women. This differential association may be because women's life expectancy is greater than men, so they are less likely to have a live-in partner who could encourage them to be physically active, and accompany them while they engage in outdoor activity that they might otherwise find too daunting (we have no evidence that women in our sample had fewer live-in partners). This possible mechanism is consistent with multiple studies showing that having a live-in partner is protective of a range of health outcomes [31]. In addition, this suggests that women, or indeed men, who live alone may benefit from additional post-surgical support. However, other mechanisms may also be involved. For example,

women may be more active or may have more social support at baseline, which might reduce the protective effect of exposure to the natural environment.

Greenness was associated with lower post-surgical opioid use, and lower mortality, in people recovering from hip arthroplasty but not those recovering from knee arthroplasty. This may be because knee arthroplasty is a more difficult and painful surgery to recover from [32] (post-surgical opioid use was 65% higher for knee-arthroplasty patients in our sample), and the protective effect of neighborhood greenness is insufficient to induce a clinically significant increase in post-surgical mobilization.

There was modest evidence that younger people, and those living in less deprived neighborhoods, derived greater benefit from exposure to greenness. This may be because younger people are more physically able to engage in outdoor activity, and that greenspace in higher SES neighborhoods may be better maintained and more appealing because of lower crime [33].

When we split NDVI into quartiles in the frailty model, we found that only the top quartile was protective at conventional significance levels. This suggests that there may be a minimum threshold below which greenness offers no health benefits. However, it is important to note that NDVI is a coarse measure of overall greenness. It does not reveal which elements of the natural environment provide the greatest health benefits. Identifying the most protective elements would help inform the design of landscapes that are not in the top quartile of NDVI, but nonetheless provide health benefits.

The magnitude of the protective effect of neighborhood greenness is not trivial. For example, in the 3-months post-surgery model of opioid use, a 2-SD decrease in NDVI is roughly equivalent to the risk of having chronic heart disease at the time of surgery. In the hip-only frailty model, a 2-SD decrease in NDVI is roughly equivalent to the risk of being two years older.

Physical activity is likely not the only mechanism linking greenness and improved post-surgical outcomes. For example, exposure to the natural environment can reduce short-term markers of stress

such as heart rate, blood pressure, and salivary cortisol [34, 35]. In turn, stress is a well-documented risk factor for premature mortality [36] and can also trigger opioid cravings [37]. Similarly, exposure to the natural environment is associated with increased social connectivity [38], and social isolation can increase individual reactivity to opioids [39] as well as being a risk factor for premature mortality [40]. More recently, research suggests that exposure to the natural environment may increase the microbial diversity of the human microbiome [41], and protect against adverse health outcomes [42] through improved immune function. In addition, improved immune function is associated with improved surgical recovery [43] and better orthopedic outcomes in elderly patients [44].

Our study has several limitations. This is an observational study, so we were not able to establish a causal relationship between exposure to the natural environment, opioid use, and surgical recovery. In addition, our metrics of exposure to the natural environment were coarse. In particular, meshblock-level NDVI is an imperfect measure of a person's exposure to the natural environment. This is especially true in larger, rural meshblocks, where mean NDVI may not optimally represent a person's residential exposure to the natural environment.

Conclusions

In a large (n=14,010) cohort of participants who received a hip or knee arthroplasty at a publicly-funded New Zealand hospital in 2006 or 2007, we found that exposure to the natural environment was associated with fewer post-surgical opioid prescriptions, and increased time to all-cause mortality, in hip-arthroplasty patients only. Results suggest that clinicians should consider a patient's home environment when designing post-operative care plans. In particular, clinicians may wish to explicitly incorporate neighborhood greenspace. When a patient doesn't have access to greenspace, additional support may be warranted to encourage at-home mobilization.

TABLES

Table 1: Descriptive statistics for study participants who received a hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 or 2007 (hip: n=7,449; knee: n=6,558)[1]

	HIP		*KNEE*	
Variable	**Mean**	**SD**	**Mean**	**SD**
Male (%)	43.2	-	44.9	-
Race: NZ European (%)	82.0	-	81.1	-
Race: Māori (%)	9.9	-	6.4	-
Race: Pacific Islander (%)	0.99	-	3.2	-
Race: Asian (%)	1.53	-	1.56	-
Race MELAA[2] (%)	2.67	-	2.84	-
Race: Other/Unspecified (5)	2.91	-	4.9	-
Chronic condition: COPD (%)	8.8	-	9.8	-
Chronic condition: acute MI (%)	5.8	-	5.1	-
Chronic condition: CHD (%)	10.6	-	12.1	-
Chronic condition: stroke (%)	2.3	-	2.6	-
Chronic condition: diabetes (%)	12.4	-	15.5	-
Chronic condition: traumatic brain injury (%)	1.5	-	1.1	-
Length of hospital stay (days)	6.4	4.5	6.2	3.0
Opioid scripts (12 month pre-surgery)	3.2	6.8	2.4	5.2
Opioid scripts (12 month post-surgery)	2.1	4.9	2.8	5.1
Age on day of surgery	68.2	12.0	69.5	9.9
Mean post-surgical NDVI	0.527	0.123	0.526	0.121

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

[2] Aggregate category used by Statistics New Zealand to describe Middle Eastern, Latin American, or African ethnicity

Table 2: Frailty model of time to all-cause mortality (Hip and knee: number of participants=14,010, number of observations= 149,523; hip: number of participants=7,449, number of observations=78,501; knee: number of participants=6,558, number of observations= 71,022)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori.

	HIP AND KNEE		*HIP*		*KNEE*	
Variable	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Age (years)	1.090***	1.086 - 1.094	1.084***	1.078 - 1.089	1.098***	1.091 - 1.105
Female	0.711***	0.667 - 0.758	0.730***	0.670 - 0.796	0.665***	0.604 - 0.732
Ethnicity: European NZ	1.309***	1.151 - 1.490	1.279***	1.063 - 1.538	1.284***	1.072 - 1.537
Ethnicity: Māori	2.137***	1.806 - 2.528	1.910***	1.516 - 2.406	2.286***	1.778 - 2.939
Mean post-surgical NZDep	1.010*	0.998 - 1.023	1.018**	1.002 - 1.035	0.999	0.980 - 1.017
Chronic condition: COPD	1.448***	1.325 - 1.583	1.410***	1.250 - 1.591	1.478***	1.294 - 1.688
Chronic condition: acute MI	1.442***	1.293 - 1.607	1.384***	1.199 - 1.597	1.476***	1.249 - 1.744
Chronic condition: cancer	1.485***	1.357 - 1.625	1.592***	1.417 - 1.790	1.333***	1.157 - 1.536
Chronic condition: stroke	1.567***	1.346 - 1.825	1.702***	1.394 - 2.078	1.385***	1.094 - 1.755
Chronic condition: diabetes	1.306***	1.203 - 1.417	1.278***	1.142 - 1.430	1.342***	1.191 - 1.513
Chronic condition: traumatic brain injury	1.299*	0.994 - 1.697	1.193	0.835 - 1.703	1.452*	0.968 - 2.177
Opioid scripts 12 months pre-surgery	1.005***	1.004 - 1.006	1.018***	1.014 - 1.022	1.004***	1.002 - 1.006
Mean post-surgical NDVI (standardized)	0.954***	0.922 - 0.987	0.936***	0.895 - 0.979	0.978	0.929 - 1.029
Length of hospital stay	1.034***	1.029 - 1.039	1.030***	1.025 - 1.036	1.052***	1.040 - 1.063
Variance of hospital random effect	0.01404		0.011138		0.006208	
Number of hospitals[1]	54		51		51	

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes (including the number of hospitals) have been rounded to the nearest multiple of three

Table 3: Frailty model of time to all-cause mortality following hip or knee arthroplasty with NDVI quartiles (Hip and knee: number of participants=14,010, number of observations= 149,523; hip: number of participants=7,449, number of observations=78,501; knee: number of participants=6,558, number of observations= 71,022)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori.

	HIP AND KNEE		*HIP*		*KNEE*	
Variables	**HR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age (years)	1.090***	1.086 - 1.094	1.083***	1.078-1.089	1.098***	1.091-1.105
Female	0.714***	0.670 - 0.761	0.735***	0.674-0.801	0.666***	0.605-0.734
Ethnicity: European NZ	1.305***	1.147 - 1.484	1.272**	1.058-1.529	1.277***	1.066-1.53
Ethnicity: Māori	2.124***	1.796 - 2.513	1.895***	1.504-2.386	2.276***	1.771-2.926
NZDep	1.012*	1.000 - 1.024	1.021**	1.005-1.038	0.998	0.98-1.016
Chronic condition: COPD	1.448***	1.325 - 1.583	1.41***	1.249-1.591	1.476***	1.292-1.686
Chronic condition: acute MI	1.443***	1.295 - 1.608	1.383***	1.199-1.596	1.476***	1.249-1.744
Chronic condition: cancer	1.489***	1.361 - 1.629	1.602***	1.425-1.8	1.33***	1.154-1.532
Chronic condition: stroke	1.568***	1.347 - 1.826	1.702***	1.394-2.079	1.384***	1.092-1.753
Chronic condition: diabetes	1.307***	1.204 - 1.418	1.275***	1.139-1.427	1.348***	1.196-1.519
Chronic condition: traumatic brain injury	1.300*	0.995 - 1.699	1.194	0.836-1.705	1.464*	0.976-2.195
Opioid scripts 12 months pre-surgery	1.005***	1.004 - 1.006	1.018***	1.014-1.023	1.004***	1.002-1.006
NDVI (standardized) quartile 2	0.933	0.856 - 1.017	0.988	0.881-1.107	0.852*	0.747-0.971
NDVI (standardized) quartile 3	0.953	0.873 - 1.041	0.926	0.823-1.042	0.974	0.854-1.111
NDVI (standardized) quartile 4	0.884**	0.804 - 0.971	0.863**	0.762-0.978	0.902	0.784-1.038
Length of hospital stay	1.034***	1.029 - 1.039	1.03	1.024-1.035	1.052***	1.041-1.064

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes (including the number of hospitals) have been rounded to the nearest multiple of three

Table 4: Mixed negative-binomial model of number of opioid prescriptions 3 months, 12 months, and 24 months after hip or knee arthroplasty including a hospital-level random effect (n=14,010)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ.

	3 MONTHS POST SURGERY		*12 MONTHS POST SURGERY*		*24 MONTHS POST SURGERY*	
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Opioid scripts 12 months pre-surgery	1.083***	1.079 - 1.087	1.136***	1.130 - 1.141	1.147***	1.141 - 1.154
Female	1.124***	1.072 - 1.177	1.177***	1.121 - 1.237	1.195***	1.134 - 1.259
Ethnicity: European NZ	1.247***	1.171 - 1.329	1.121***	1.051 - 1.196	1.01	0.944 - 1.080
Age	0.994***	0.992 - 0.996	0.998	0.996 - 1.001	0.998*	0.995 - 1.000
Mean post-surgical NDVI (standardized)	0.969***	0.947 - 0.992	0.971**	0.947 - 0.995	0.969**	0.944 - 0.994
Knee	1.653***	1.578 - 1.731	1.594***	1.519 - 1.673	1.547***	1.471 - 1.627
COPD	1.219***	1.133 - 1.311	1.272***	1.175 - 1.378	1.374***	1.262 - 1.496
CHD	1.133***	1.057 - 1.214	1.091**	1.012 - 1.175	1.069*	0.988 - 1.157
Traumatic brain Injury	1.197*	0.992 - 1.444	1.335***	1.088 - 1.637	1.448***	1.166 - 1.799
Days in hospital	1.015***	1.009 - 1.022	1.035***	1.027 - 1.043	1.037***	1.029 - 1.045
Variance of hospital random effect	1.164***	1.064 - 1.272	1.072***	1.020 - 1.127	1.071**	1.009 - 1.137

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

FIGURE LEGENDS

Figure 1: Odds-ratio plot of standardized mean post-surgical NDVI for time to all-cause mortality following hip or knee arthroplasty (number of participants=14,010, number of observations= 149,523)[1]. Low/high SES denotes participants whose lifetime NZ Deprivation Index is above/below average. Old/young denote participants who are older/younger than the sample mean. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori (figures 1 and 2 were created with the user-written Stata command COEFPLOT)

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

Figure 2: Odds-ratio plot of standardized mean post-surgical NDVI for number of opioid prescriptions 3 months post-surgery (n=14,010)[1]. For definitions and reference groups see figure 1.

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

Contributorship statement: GHD designed the study, conducted the analysis, and wrote the majority of the manuscript. DG created the exposure metrics and edited the manuscript. JD wrote parts of the manuscript and edited multiple drafts.

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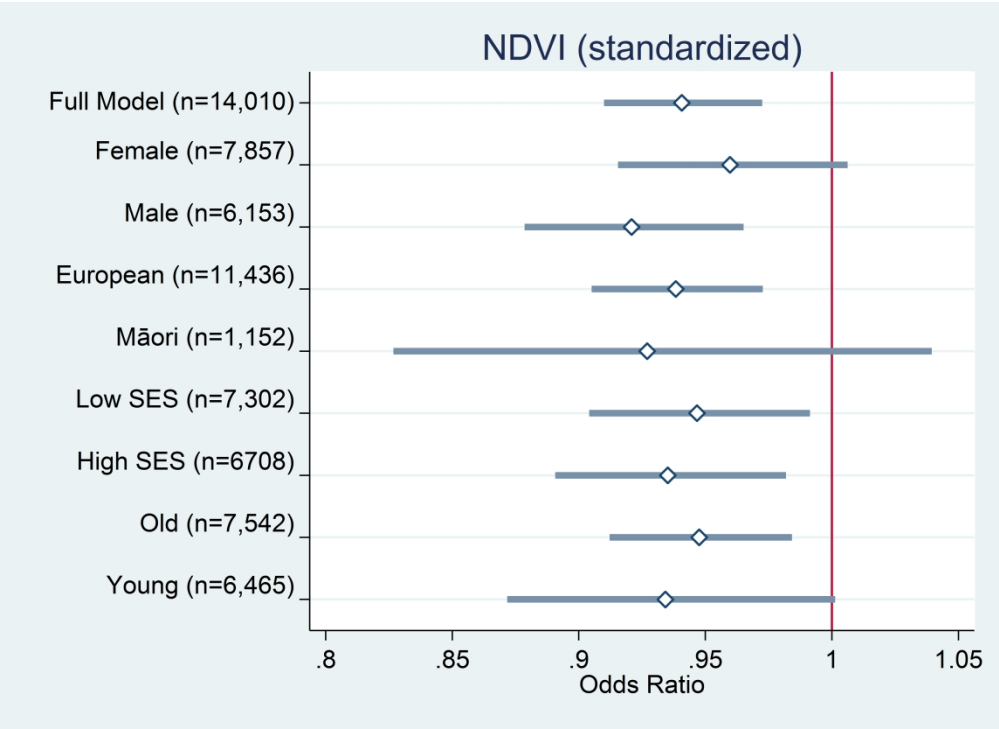

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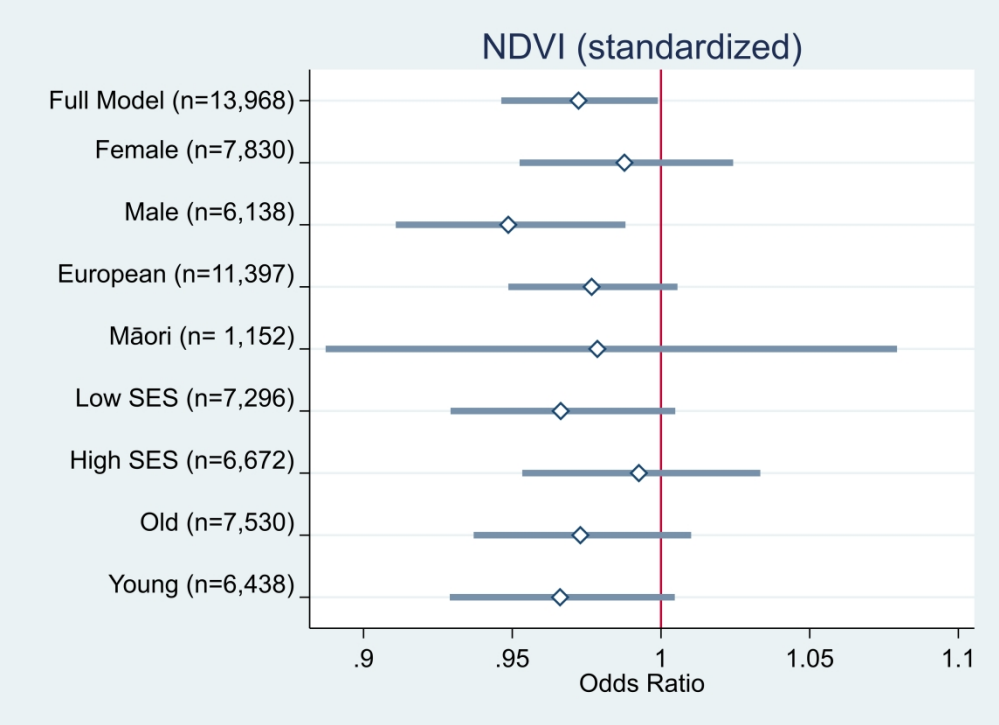

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-8*
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	N/A
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A

	(*e*) Describe any sensitivity analyses	9

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14-16
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*6*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15-17
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

The relationship between exposure to the natural environment and recovery from hip or knee arthroplasty: a New Zealand retrospective cohort study

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The relationship between exposure to the natural environment and recovery from hip or knee arthroplasty: a New Zealand retrospective cohort study

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ABSTRACT

Objectives: Determine whether patients who live in greener and more walkable neighborhoods live longer, and take fewer opioids, following hip or knee arthroplasty.

Design: Retrospective cohort study.

Setting: Residential environment following surgery at one of 54 New Zealand hospitals.

Participants: All people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties).

Primary and secondary outcome measure: Time to all-cause mortality and number of post-surgical opioid prescriptions.

Results: Patients who lived in greener neighborhoods, as measured by the normalized difference vegetation index (NDVI), lived longer following hip or knee arthroplasty (standardized OR: 0.95 95% CI: 0.92-0.99). However, when we estimated separate hip-arthroplasty-only and knee-arthroplasty-only models, greenness was only significantly associated with greater longevity following hip arthroplasty. Similarly, patients who lived in greener neighborhoods took fewer opioids in the 12 months following hip or knee arthroplasty (standardized OR: 0.97 95% CI: 0.95-0.99), but in separate hip-arthroplasty-only and knee-arthroplasty-only models, greenness was only significantly associated with lower opioid use following hip arthroplasty. Walkability was not significantly associated with post-surgical opioid use or post-surgical longevity. All odds ratios were adjusted for sex, ethnicity, age, pre-surgical chronic health conditions, pre-surgical opioid use, social deprivation, and length of hospital stay.

Conclusions: Consistent with the literature on enhanced-recovery programs, people who lived in greener neighborhoods took fewer opioids, and lived longer, following hip arthroplasty. Improving

access to the natural environment may therefore be an effective component of post-surgical recovery programs.

Keywords: Normalized difference vegetation index, natural environment, surgical recovery, orthopedic

STRENGTHS AND LIMITATIONS OF THIS STUDY

- First study to examine the relationship between natural environment and surgical recovery outside of a hospital setting
- Large cohort followed longitudinally for 9+ years
- Observational study, so a causal link between the natural environment and surgical recovery couldn't be established
- Exposure was based on residential meshblock not residential address

Competing interests: None declared

Funding: No external funding was received

Data availability statement: De-identified data are not publicly available but may be obtained from Statistics New Zealand after gaining ethics approval and submitting a research proposal (contact: access2microdata@stats.govt.nz). Note that, even with these approvals, data must be accessed via a secure data lab in New Zealand. Exposure data, and code used for statistical analysis, are freely available from the authors.

INTRODUCTION

Rates of hip and knee arthroplasty are rising globally. For example, in Organization for Economic Cooperation and Development (OECD) countries, the incidence of hip arthroplasty rose from 140/100,000 people in 2005 to 164/100,000 in 2011 [1]. Similarly, the incidence of knee arthroplasty in OECD countries rose from 114/100,000 in 2005 to 150/100,000 in 2011 [2]. Increases in life expectancy and obesity rates suggest that this trend is likely to continue [3]. Given this increased demand, and constrained healthcare budgets, research has focused on identifying approaches that improve post-surgical health outcomes, shorten length of stay, and reduce costs. For example, enhanced-recovery programs that emphasize rapid mobilization and rehabilitation following hip or knee arthroplasty can reduce length of hospital stay [4] and decrease mortality [5]. However, no research has focused on the effect of patients' residential environments, despite the well-established link between exposure to the natural environment and increased physical activity [6-9], and research showing that passively viewing a natural scene while recovering from surgery can reduce both length of hospital stay and post-surgical opioid use [10]. We address this gap in the literature by evaluating the relationship between exposure to the built and natural environment and recovery from hip or knee arthroplasty in a large New Zealand cohort.

Literature review

Numerous studies have examined how different elements of enhanced-recovery programs affect post-operative outcomes (also known as fast-track or rapid-recovery programs). These programs use coordinated multimodal techniques to reduce recovery times and improve post-operative outcomes [3]. For example, pre-operative education can shorten hospital stays [11] and reduce post-operative pain [12]. Several studies have found that pre-emptive analgesia allows more rapid mobilization and return of function [13, 14]. Multiple studies have found that rapid mobilization on the day of surgery (typically

2-6 hours after surgery) reduces length of stay and improves function [15-17]. Similarly, aggressive physical therapy (extending beyond the day of surgery) can reduce length of stay and improve function [18-20]. Finally, in a prospective study of 4,500 patients in the UK, enhanced recovery was associated with improved two-year survival rates when compared to traditional post-surgical protocols, which suggests that post-operative mobility may have long-term benefits [5].

Several studies have found that exposure to the natural environment is associated with increased physical activity. For example, using survey data in Chicago (n=1,544), Fan et al. [21] found that respondents with a greater area of public parks within 0.5 miles of their home were more likely to engage in physical activity. A survey of 1,895 people in Adelaide, Australia [9] found that respondents who perceived their neighborhoods as greener were more likely to engage in recreational walking. Similarly, a study in 1,803 people in Perth, Australia [22] found that people who lived nearer to recreational amenities, including public parks, were more likely to meet minimum physical-activity requirements.

Passive exposure to the natural environment can also produce health benefits. In particular, several studies have found that greenness exposure can reduce perceived pain in a range of settings. Specifically, a RCT of 46 healthy volunteers [23] found that participants who had just watched a video of a natural scene had significantly higher pain threshold and tolerance than participants who had watched a blank screen. Similarly, a RCT of adults undergoing flexible bronchoscopy found that participants who viewed a natural scene reported significantly less pain [24]. Finally, an RCT of a two-day forestry-therapy program in Korea found that participants in the program (n=33) had significantly lower levels of pain and depression than controls (n=25). In addition, participants had significantly higher heart-rate variability and natural-killer cell activity.

METHODS

Study sample

Our sample consisted of all people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties). We obtained individual-level hospital and pharmaceutical records via Statistics New Zealand's Integrated Data Infrastructure (IDI), which is a large database of routinely-collected individual-level data [25]. The IDI is structured around a central spine designed to identify all New Zealand residents. Datasets describing health, education, benefits, criminal justice, population (births, deaths, and immigration), income and work, and housing are linked to this central spine.

As this study was based on routinely-collected health data, and did not involve contacting individual patients, the study was classified as minimal risk by the New Zealand Health and Disabilities Ethics Committee and was approved by Statistics New Zealand (MAA-2017-57). Before we were granted access, all data were anonymized by Statistics New Zealand. In addition, our research conformed to the Declaration of Helsinki guidelines.

Patient and Public Involvement statement: Neither patients, nor the public, were involved in the design or conduct of this study.

Outcomes

We used two outcomes to measure recovery: time to all-cause mortality and number of opioid prescriptions 3, 12, and 24 months post-surgery. We chose these outcomes as they are important metrics of post-surgical recovery. In addition, previous research has shown that rapid mobilization and rehabilitation can reduce two-year mortality rates following hip or knee arthroplasty [26], and exposure to the natural environment, in a hospital setting, is associated with reduced perioperative use of opioids [10].

By the end of 2016, 2,263 (30.0%) of the 7,449 people who had received a hip arthroplasty had died as had 1,741 (26.5%) of the 6,558 people who received knee arthroplasties.

The number of opioid prescriptions received was calculated by linkage to pharmacy records. We did not include prescriptions for methadone or buprenorphine, as in New Zealand these are primarily used to treat addiction. To control for pre-surgical pain, we calculated the number of opioid prescriptions each participant received in the 12 months before surgery. Finally, to account for opioid potency, we categorized each opioid prescription as either strong (potency equal to or greater than morphine) or weak (potency less than morphine). On average, study participants received 3.04 (SD=9.38) opioid prescriptions in the 12 months before surgery (0.68 strong and 2.36 weak) and 2.72 (SD=7.06) opioid prescriptions in the 12 months after surgery (0.75 strong and 1.98 weak).

Exposures

All exposures are based on a participant's residential meshblock, which is the smallest geographic unit at which Statistics New Zealand reports data. On average, 95 people live in a meshblock.

Linking to address history in the IDI allowed us to estimate exposures for each year of the study (2005-2016). From these annual values, we calculated mean post-surgical exposure, which we defined as the mean exposure from the year of surgery to death or 2016, whichever came first.

We had no information on participants' pre- or post-surgical physical activity. Therefore, exposure metrics describe the physical environment that a participant is exposed to, but they do not describe how a participant physically interacts with different environments.

Walkability

We used a previously validated walkability index [27] with three components: number of households per hectare (data source: 2006 New Zealand Census), number of road intersections per square kilometer

(data source: Land Information New Zealand), and land-use mix (data source: 2008 New Zealand Land Cover Database v4.1). In all three cases, we used the version of each data source that was closest to baseline. Land-cover data were available from 2001, 2008, and 2012. However, the classification schemes were not consistent across the three years. In addition, when we compared 2008 and 2012 data, we found that the net area of New Zealand that changed from one land class to another was only 0.903%. Therefore, we used 2008 data for our analysis.

Land-use mix is defined as:

$$Land-use\ mix = \frac{\sum_{i=1}^{n}(LC_i * ln(LC_i))}{ln(N)}$$

Where LC_i denotes the proportion of each meshblock that is covered by the *i*th land-cover type and *N* denotes the total number of land-cover types. Following Frank et al., we standardized household density, intersection density, and land-use mix (by subtracting the mean and dividing by the standard deviation), and summed the three standardized scores into a single walkability index.

Greenness

We used two measures of exposure to the natural environment: land-cover data (see above) and the Normalized Difference Vegetation Index (NDVI), which is a greenness index derived from satellite imagery. Specifically, for each year from 2005 to 2016, we used maximum annual NDVI derived from 30m-resolution Landsat imagery that was calculated at the top of the atmosphere, which normalized all atmospheric effects. We standardized NDVI values to make regression coefficients easier to interpret. From these annual values, we calculated mean post-surgical greenness exposure.

Covariates

Using data from the IDI, we controlled for sex, ethnicity, and age. In addition, we controlled for neighborhood deprivation using the New Zealand Deprivation Index (NZDep), which is a well-validated index calculated from nine census variables [28]. NZDep ranges from 1 to 10 with higher values denoting higher levels of social deprivation. Finally, we controlled for eight chronic conditions at time of surgery: coronary heart disease, gout, chronic obstructive pulmonary disease (COPD), diabetes, cancer, stroke, acute myocardial infarction, and traumatic brain injury. We chose to account for these conditions as they are major health outcomes that could affect surgical recovery, and they were pre-defined by Statistics New Zealand based on hospital-admissions and pharmacy data [29]. Note that we did not have access to data on physical activity, BMI, or diet.

Statistical analysis

We analyzed time-to-death data using a frailty model that included hospital-level random effects. We were particularly careful to account for the hospital where the surgery was performed, because smaller hospitals that may not be able to provide the specialist care of a larger hospital are more likely to be in rural areas that are greener. We evaluated five different functional forms for the survival function (Weibull, exponential, log-logistic, log-normal, and gamma) and chose between them using the Akaike information criterion. We analyzed the number of post-operative opioid scripts using a mixed negative-binomial regression that included hospital-level random effects.

A backwards-selection procedure was used for all model selection: variables were dropped from the analysis using progressively smaller p-value thresholds (final threshold: $p<0.1$). Insignificant variables can still be confounders [30], so we systematically re-introduced dropped variables and retained them if the coefficients on variables of interest changed by more than 10%.

To avoid including highly collinear combinations of variables, we estimated ordinary least squares versions of each model (results not shown), which allowed us to calculate variance-inflation factors for

each independent variable. If any variable had a variance-inflation factor over two, we dropped it from the regression model. When choosing between two collinear variables, we included the variable with the lowest p-value when individually regressed against the dependent variable.

We also conducted stratified analyses to see whether the relationship between the natural environment and health outcomes was the same across different strata of the sample. Analyses were conducted for hip and knee arthroplasty combined as well as for each outcome separately.

RESULTS

Table 1 provides descriptive statistics for our sample.

In the frailty model, specifying the survival function using a Weibull distribution gave the best model fit. Being older, male, European New Zealander, or Māori (the indigenous people of New Zealand) were all mortality risk factors (Table 2) (The reference ethnic group was Pacific, Asian, MELAA, or other). Similarly, people who received more pre-surgery opioids, or had a longer hospital stay, were at greater risk of mortality. Six chronic conditions were risk factors as was higher neighborhood deprivation, although this relationship was only significant for hip arthroplasty.

People who lived in greener neighborhoods (defined as mean post-surgical NDVI) were at lower risk of mortality, although this relationship was only significant in the hip-and-knee arthroplasty and hip-arthroplasty-only models (Table 2). To better elucidate the dose-response function linking NDVI and mortality, we re-estimated the hip-and-knee-arthroplasty frailty model splitting NDVI into quartiles (Table 3). Only the highest quartile was statistically significant, in the combined and hip-only models, although NDVI remained protective in the second and third quartiles. In the knee-only model, the second quartile of NDVI was protective although only at the 10% level. In addition, the third and fourth quartiles of NDVI did not show a consistent protective effect.

Figure 1 shows the odds ratio for mean lifetime NDVI for different strata of the sample. Stratifying the sample resulted in some loss of significance, due to lower numbers in each stratum. Notably, the protective effect of NDVI was higher for men than women. The protective effect of NDVI was also modestly higher for people who lived in higher SES neighborhoods (NZDep 1-5) compared to lower SES neighborhoods (NZDep 6-10). Similarly, NDVI was somewhat more protective for people who were younger than average (mean age at surgery=68).

In the opioid model (Table 4), women, European New Zealanders, and people who were prescribed more pre-surgery opioid prescriptions received significantly more post-surgical opioid scripts in all three time periods with the exception of European New Zealanders in the 24 months post-surgery model (Table 4). Those who received a knee arthroplasty (as opposed to a hip arthroplasty) or stayed longer in hospital also received more post-surgical opioids, as did people who had COPD, coronary heart disease, or traumatic brain injury. In contrast, older people received fewer opioid prescriptions, although the significance of this relationship varied across the three time periods. Separating opioids into weak and strong was not revealing and reduced the significance of variables of interest (data not shown). Mean post-surgical greenness was associated with significantly fewer post-surgical opioid prescriptions in all three time periods (Table 4). Living in a rural area and land cover were not significantly associated with the number of post-surgical opioid prescriptions or time to all-cause mortality (data not shown). In addition, walkability was not significantly associated with either opioid use or mortality. For example, the odds ratio on walkability in the 3-month post-surgical opioid model was 1.043 (95% CI: 0.966-1.127), and the odds ratio in the hip-only frailty model was 1.035 (95% CI: 0.971-1.104). Even when the analysis was restricted to only-hip or only-knee arthroplasties, the relationship between walkability and mortality or opioid use remained insignificant.

In addition, consistent with the frailty model, NDVI was not significant, when the analysis was restricted to knee-arthroplasty (results not shown). Finally, when we split NDVI into quartiles, none were significant (results not shown).

In the stratified analysis (figure 2), greenness was more protective for men than women, which is consistent with the frailty model.

DISCUSSION

In a cohort of people who received a total hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 or 2007, we found that residents of greener neighborhoods received fewer post-surgical opioid prescriptions and lived longer, with the strongest results for hip arthroplasty. Our results are consistent with those reported by Ulrich [10], who found that, after gall-bladder surgery, patients recovered faster and took fewer opioids if they were in a room with a view of a natural scene. Our results are also consistent with a previous study [5], which found that rapid mobilization following hip or knee arthroplasty was associated with better two-year survival rates. Finally, results suggests that the benefits of exposure to the natural environment extend beyond the immediate post-surgical period.

Greenness was associated with lower post-surgical opioid use, and lower mortality, in people recovering from hip arthroplasty but not those recovering from knee arthroplasty. This may be because knee arthroplasty is a more difficult and painful surgery to recover from [31] (post-surgical opioid use was 65% higher for knee-arthroplasty patients in our sample), and the protective effect of neighborhood greenness is insufficient to induce a clinically significant increase in post-surgical mobilization.

There was modest evidence that younger people, and those living in less deprived neighborhoods, derived greater benefit from exposure to greenness. This may be because younger people are more physically able to engage in outdoor activity, and that greenspace in higher SES neighborhoods may be better maintained and more appealing because of lower crime [32].

When we split NDVI into quartiles in the frailty model, we found that only the top quartile was protective at conventional significance levels. This suggests that there may be a minimum threshold below which greenness offers no health benefits. However, it is important to note that NDVI is a coarse measure of overall greenness. It does not reveal which elements of the natural environment provide the greatest health benefits. Identifying the most protective elements would help inform the design of landscapes that are not in the top quartile of NDVI, but nonetheless provide health benefits.

The magnitude of the protective effect of neighborhood greenness is not trivial. For example, in the 3-months post-surgery model of opioid use, a 2-SD decrease in NDVI is roughly equivalent to the risk of having chronic heart disease at the time of surgery. In the hip-only frailty model, a 2-SD decrease in NDVI is roughly equivalent to the risk of being two years older.

Physical activity is likely not the only mechanism linking greenness and improved post-surgical outcomes. For example, exposure to the natural environment can reduce short-term markers of stress such as heart rate, blood pressure, and salivary cortisol [33, 34]. In turn, stress is a well-documented risk factor for premature mortality [35] and can also trigger opioid cravings [36]. Similarly, exposure to the natural environment is associated with increased social connectivity [37], and social isolation can increase individual reactivity to opioids [38] as well as being a risk factor for premature mortality [39]. More recently, research suggests that exposure to the natural environment may increase the microbial diversity of the human microbiome [40], and protect against adverse health outcomes [41] through improved immune function. In addition, improved immune function is associated with improved surgical recovery [42] and better orthopedic outcomes in elderly patients [43].

Our study has several limitations. This is an observational study, so we were not able to establish a causal relationship between exposure to the natural environment, opioid use, and surgical recovery. In addition, our metrics of exposure to the natural environment were coarse. In particular, meshblock-level

NDVI is an imperfect measure of a person's exposure to the natural environment. This is especially true in larger, rural meshblocks, where mean NDVI may not optimally represent a person's residential exposure to the natural environment.

Conclusions

In a large (n=14,010) cohort of participants who received a hip or knee arthroplasty at a publicly-funded New Zealand hospital in 2006 or 2007, we found that exposure to the natural environment was associated with fewer post-surgical opioid prescriptions, and increased time to all-cause mortality, in hip-arthroplasty patients only. Results suggest that clinicians should consider a patient's home environment when designing post-operative care plans. In particular, clinicians may wish to explicitly incorporate neighborhood greenspace. When a patient doesn't have access to greenspace, additional support may be warranted to encourage at-home mobilization.

TABLES

Table 1: Descriptive statistics for study participants who received a hip or knee arthroplasty at a publicly-funded hospital in New Zealand in 2006 or 2007 (hip: n=7,449; knee: n=6,558)[1]

	HIP		*KNEE*	
Variable	**Mean**	**SD**	**Mean**	**SD**
Male (%)	43.2	-	44.9	-
Race: NZ European (%)	82.0	-	81.1	-
Race: Māori (%)	9.9	-	6.4	-
Race: Pacific Islander (%)	0.99	-	3.2	-
Race: Asian (%)	1.53	-	1.56	-
Race MELAA[2] (%)	2.67	-	2.84	-
Race: Other/Unspecified (5)	2.91	-	4.9	-
Chronic condition: COPD (%)	8.8	-	9.8	-
Chronic condition: acute MI (%)	5.8	-	5.1	-
Chronic condition: CHD (%)	10.6	-	12.1	-
Chronic condition: stroke (%)	2.3	-	2.6	-
Chronic condition: diabetes (%)	12.4	-	15.5	-
Chronic condition: traumatic brain injury (%)	1.5	-	1.1	-
Length of hospital stay (days)	6.4	4.5	6.2	3.0
Opioid scripts (12 month pre-surgery)	3.2	6.8	2.4	5.2
Opioid scripts (12 month post-surgery)	2.1	4.9	2.8	5.1
Age on day of surgery	68.2	12.0	69.5	9.9
Mean post-surgical NDVI	0.527	0.123	0.526	0.121

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

[2] Aggregate category used by Statistics New Zealand to describe Middle Eastern, Latin American, or African ethnicity

Table 2: Frailty model of time to all-cause mortality (Hip and knee: number of participants=14,010, number of observations= 149,523; hip: number of participants=7,449, number of observations=78,501; knee: number of participants=6,558, number of observations= 71,022)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori.

	HIP AND KNEE		*HIP*		*KNEE*	
Variable	**HR**	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Age (years)	1.090***	1.086 - 1.094	1.084***	1.078 - 1.089	1.098***	1.091 - 1.105
Female	0.711***	0.667 - 0.758	0.730***	0.670 - 0.796	0.665***	0.604 - 0.732
Ethnicity: European NZ	1.309***	1.151 - 1.490	1.279***	1.063 - 1.538	1.284***	1.072 - 1.537
Ethnicity: Māori	2.137***	1.806 - 2.528	1.910***	1.516 - 2.406	2.286***	1.778 - 2.939
Mean post-surgical NZDep	1.010*	0.998 - 1.023	1.018**	1.002 - 1.035	0.999	0.980 - 1.017
Chronic condition: COPD	1.448***	1.325 - 1.583	1.410***	1.250 - 1.591	1.478***	1.294 - 1.688
Chronic condition: acute MI	1.442***	1.293 - 1.607	1.384***	1.199 - 1.597	1.476***	1.249 - 1.744
Chronic condition: cancer	1.485***	1.357 - 1.625	1.592***	1.417 - 1.790	1.333***	1.157 - 1.536
Chronic condition: stroke	1.567***	1.346 - 1.825	1.702***	1.394 - 2.078	1.385***	1.094 - 1.755
Chronic condition: diabetes	1.306***	1.203 - 1.417	1.278***	1.142 - 1.430	1.342***	1.191 - 1.513
Chronic condition: traumatic brain injury	1.299*	0.994 - 1.697	1.193	0.835 - 1.703	1.452*	0.968 - 2.177
Opioid scripts 12 months pre-surgery	1.005***	1.004 - 1.006	1.018***	1.014 - 1.022	1.004***	1.002 - 1.006
Mean post-surgical NDVI (standardized)	0.954***	0.922 - 0.987	0.936***	0.895 - 0.979	0.978	0.929 - 1.029
Length of hospital stay	1.034***	1.029 - 1.039	1.030***	1.025 - 1.036	1.052***	1.040 - 1.063
Variance of hospital random effect	0.01404		0.011138		0.006208	
Number of hospitals[1]	54		51		51	

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes (including the number of hospitals) have been rounded to the nearest multiple of three

Table 3: Frailty model of time to all-cause mortality following hip or knee arthroplasty with NDVI quartiles (Hip and knee: number of participants=14,010, number of observations= 149,523; hip: number of participants=7,449, number of observations=78,501; knee: number of participants=6,558, number of observations= 71,022)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori.

	HIP AND KNEE		*HIP*		*KNEE*	
Variables	**HR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age (years)	1.090***	1.086 - 1.094	1.083***	1.078-1.089	1.098***	1.091-1.105
Female	0.714***	0.670 - 0.761	0.735***	0.674-0.801	0.666***	0.605-0.734
Ethnicity: European NZ	1.305***	1.147 - 1.484	1.272**	1.058-1.529	1.277***	1.066-1.53
Ethnicity: Māori	2.124***	1.796 - 2.513	1.895***	1.504-2.386	2.276***	1.771-2.926
NZDep	1.012*	1.000 - 1.024	1.021**	1.005-1.038	0.998	0.98-1.016
Chronic condition: COPD	1.448***	1.325 - 1.583	1.41***	1.249-1.591	1.476***	1.292-1.686
Chronic condition: acute MI	1.443***	1.295 - 1.608	1.383***	1.199-1.596	1.476***	1.249-1.744
Chronic condition: cancer	1.489***	1.361 - 1.629	1.602***	1.425-1.8	1.33***	1.154-1.532
Chronic condition: stroke	1.568***	1.347 - 1.826	1.702***	1.394-2.079	1.384***	1.092-1.753
Chronic condition: diabetes	1.307***	1.204 - 1.418	1.275***	1.139-1.427	1.348***	1.196-1.519
Chronic condition: traumatic brain injury	1.300*	0.995 - 1.699	1.194	0.836-1.705	1.464*	0.976-2.195
Opioid scripts 12 months pre-surgery	1.005***	1.004 - 1.006	1.018***	1.014-1.023	1.004***	1.002-1.006
NDVI (standardized) quartile 2	0.933	0.856 - 1.017	0.988	0.881-1.107	0.852*	0.747-0.971
NDVI (standardized) quartile 3	0.953	0.873 - 1.041	0.926	0.823-1.042	0.974	0.854-1.111
NDVI (standardized) quartile 4	0.884**	0.804 - 0.971	0.863**	0.762-0.978	0.902	0.784-1.038
Length of hospital stay	1.034***	1.029 - 1.039	1.03	1.024-1.035	1.052***	1.041-1.064

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes (including the number of hospitals) have been rounded to the nearest multiple of three

Table 4: Mixed negative-binomial model of number of opioid prescriptions 3 months, 12 months, and 24 months after hip or knee arthroplasty including a hospital-level random effect (n=14,010)[1]. The ethnicity reference group is a composite of all ethnicities other than European NZ.

	3 MONTHS POST SURGERY		*12 MONTHS POST SURGERY*		*24 MONTHS POST SURGERY*	
	HR	**95% CI**	**HR**	**95% CI**	**HR**	**95% CI**
Opioid scripts 12 months pre-surgery	1.083***	1.079 - 1.087	1.136***	1.130 - 1.141	1.147***	1.141 - 1.154
Female	1.124***	1.072 - 1.177	1.177***	1.121 - 1.237	1.195***	1.134 - 1.259
Ethnicity: European NZ	1.247***	1.171 - 1.329	1.121***	1.051 - 1.196	1.01	0.944 - 1.080
Age	0.994***	0.992 - 0.996	0.998	0.996 - 1.001	0.998*	0.995 - 1.000
Mean post-surgical NDVI (standardized)	0.969***	0.947 - 0.992	0.971**	0.947 - 0.995	0.969**	0.944 - 0.994
Knee	1.653***	1.578 - 1.731	1.594***	1.519 - 1.673	1.547***	1.471 - 1.627
COPD	1.219***	1.133 - 1.311	1.272***	1.175 - 1.378	1.374***	1.262 - 1.496
CHD	1.133***	1.057 - 1.214	1.091**	1.012 - 1.175	1.069*	0.988 - 1.157
Traumatic brain Injury	1.197*	0.992 - 1.444	1.335***	1.088 - 1.637	1.448***	1.166 - 1.799
Days in hospital	1.015***	1.009 - 1.022	1.035***	1.027 - 1.043	1.037***	1.029 - 1.045
Variance of hospital random effect	1.164***	1.064 - 1.272	1.072***	1.020 - 1.127	1.071**	1.009 - 1.137

***p<0.01, **p<0.05, *p<0.1

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

FIGURE LEGENDS

Figure 1: Odds-ratio plot of standardized mean post-surgical NDVI for time to all-cause mortality following hip or knee arthroplasty (number of participants=14,010, number of observations= 149,523)[1]. Low/high SES denotes participants whose lifetime NZ Deprivation Index is above/below average. Old/young denote participants who are older/younger than the sample mean. The ethnicity reference group is a composite of all ethnicities other than European NZ or Māori (figures 1 and 2 were created with the user-written Stata command COEFPLOT)

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

Figure 2: Odds-ratio plot of standardized mean post-surgical NDVI for number of opioid prescriptions 3 months post-surgery (n=14,010)[1]. For definitions and reference groups see figure 1.

[1] Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three

Contributorship statement: GHD designed the study, conducted the analysis, and wrote the majority of the manuscript. DG created the exposure metrics and edited the manuscript. JD wrote parts of the manuscript and edited multiple drafts.

LITERATURE CITED

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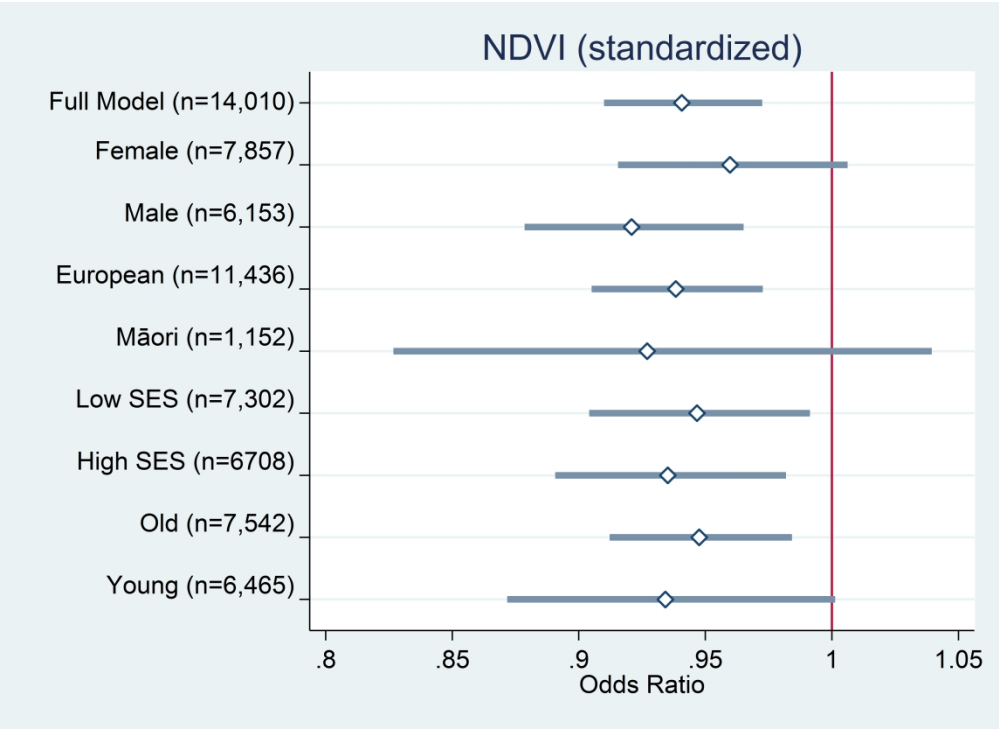

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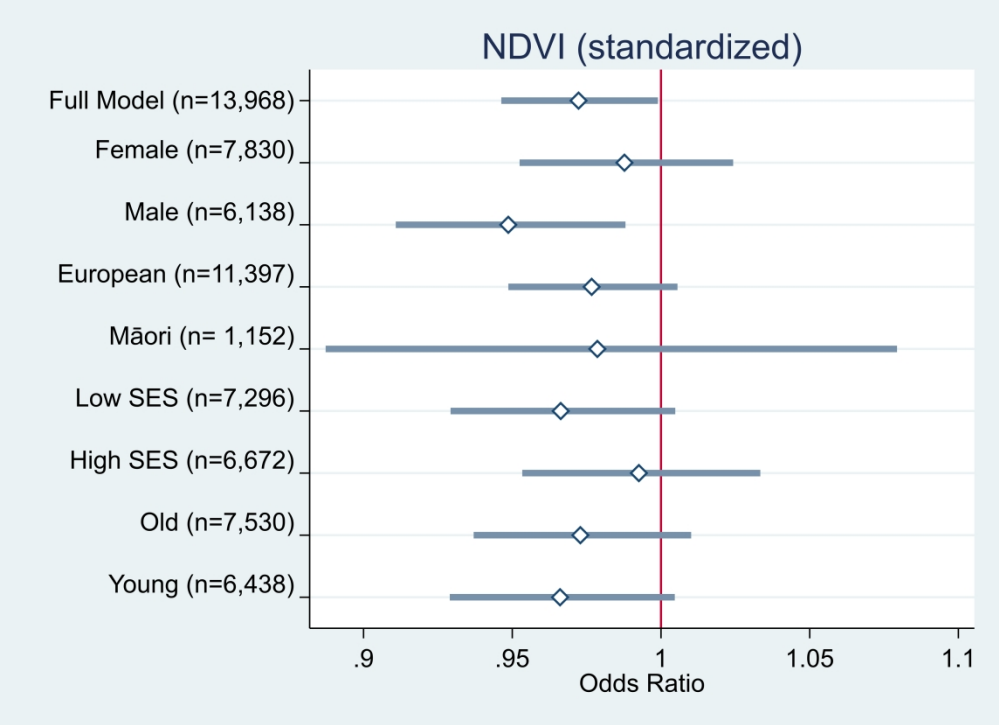

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4-5
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5-9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-9
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*6-8*
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6-9
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	8-9
		(*b*) Describe any methods used to examine subgroups and interactions	8-9
		(*c*) Explain how missing data were addressed	N/A
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A

	(*e*) Describe any sensitivity analyses	9

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	14-16
		(b) Give reasons for non-participation at each stage	
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	14
		(b) Indicate number of participants with missing data for each variable of interest	N/A
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*6*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	15-17
		(*b*) Report category boundaries when continuous variables were categorized	
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	
Discussion			
Key results	18	Summarise key results with reference to study objectives	11-12
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	12-13
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11-12
Generalisability	21	Discuss the generalisability (external validity) of the study results	
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	3

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.