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

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

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3 11 **ABSTRACT**
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6 12 **Objectives:** Determine whether patients who live in greener and more walkable neighborhoods live
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8 13 longer, and take fewer opioids, following hip or knee arthroplasty.
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11 14 **Design:** Retrospective cohort study
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14 15 **Setting:** Residential environment following surgery at one of 54 hospitals New Zealand hospitals
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16 16 **Participants:** All people who received a total hip or knee arthroplasty at a publicly-funded hospital in
17
18 17 New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties).
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22 18 **Primary and secondary outcome measure:** Time to all-cause mortality and number of post-surgical
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24 19 opioid prescriptions
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27 20 **Results:** Patients who lived in greener neighborhoods, as measured by the normalized difference
28
29 21 vegetation index (NDVI), lived longer following hip arthroplasty (standardized OR: 0.94 95% CI: 0.90-
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31 22 0.98), but no significant association was found for knee arthroplasty. Patients who lived in greener
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33 23 neighborhoods also took fewer opioids in the 12 months following surgery (standardized OR: 0.97 95%
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35 24 CI: 0.95-1.00). As with post-surgical mortality, the relationship between greenness and opioid use was
36
37 25 only significant for hip arthroplasty.
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41 26 **Conclusions:** Consistent with the literature on enhanced-recovery programs, people who lived in
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43 27 greener neighborhoods took fewer opioids, and lived longer, following hip arthroplasty. Improving
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45 28 access to the natural environment may therefore be an effective component of post-surgical recovery
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47 29 programs.
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51 30 **Keywords:** Normalized difference vegetation index, natural environment, surgical recovery, orthopedic
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3 32 **STRENGTHS AND LIMITATIONS OF THIS STUDY**
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- 6 33 • First study to examine the relationship between natural environment and surgical recovery
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8 34 outside of a hospital setting
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10 35 • Large cohort followed longitudinally for 9+ years
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12 36 • Observational study, so we couldn't establish a causal link between the natural environment
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14 37 and surgical recovery
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16 38 • Exposure was based on residential meshblock not residential address
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20 39 **Competing interests:** None declared
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23 40 **Funding:** No external funding was received
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25

26 41 **Data availability statement:** De-identified data are not publicly available but may be obtained from
27
28 42 Statistics New Zealand after gaining ethical approval and submitting a research proposal (contact:
29
30 43 access2microdata@stats.govt.nz). Note that, even with these approvals, data must be accessed via a
31
32 44 secure data lab in New Zealand. Exposure data, and code used for statistical analysis, are freely available
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34 45 from the authors.
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47 INTRODUCTION

48 Rates of hip and knee arthroplasty are rising globally. For example, in OECD countries, the incidence of
49 hip arthroplasty rose from 140/100,000 people in 2005 to 164/100,000 in 2011 [1]. Similarly, the
50 incidence of knee arthroplasty in OECD countries rose from 114/100,000 in 2005 to 150/100,000 in 2011
51 [2]. Increases in life expectancy and obesity rates suggest that this trend is likely to continue [3]. Given
52 this increased demand, and constrained healthcare budgets, research has focused on identifying
53 approaches that improve post-surgical health outcomes, shorten length of stay, and reduce costs. For
54 example, enhanced-recovery programs that emphasize rapid mobilization and rehabilitation following
55 hip or knee arthroplasty, can reduce length of hospital stay [4] and decrease mortality [5]. However, no
56 research has focused on the effect of patients' residential environment, despite the well-established link
57 between exposure to the natural environment and increased physical activity [6-9], and research
58 showing that viewing a natural scene while recovering from surgery can reduce both length of hospital
59 stay and post-surgical opioid use [10]. We address this gap in the literature by evaluating the
60 relationship between exposure to the built and natural environment and recovery from hip or knee
61 arthroplasty in a large New Zealand cohort.

62 Literature review

63 Numerous studies have examined how different elements of enhanced-recovery programs affect post-
64 operative outcomes (also known as fast-track or rapid-recovery programs). These programs use
65 coordinated multimodal techniques to reduce recovery times and improve post-operative outcomes [3].
66 For example, pre-operative education can shorten hospital stays [11] and reduce post-operative pain
67 [12]. Several studies have found that pre-emptive analgesia allows more rapid mobilization and return
68 of function [13, 14]. Multiple studies have found that rapid mobilization on the day of surgery (typically
69 2-6 hours after surgery) reduces length of stay and improves function [15-17]. Similarly, aggressive

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3 70 physical therapy (extending beyond the day of surgery) can reduce length of stay and improve function
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5 71 [18-20]. Finally, in a prospective study of 4,500 patients in the UK, enhanced recovery was associated
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7 72 with improved two-year survival rates when compared to traditional post-surgical protocols, which
8
9 73 suggests that post-operative mobility may have long-term benefits [5].
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13 74 Several studies have found that exposure to the natural environment is associated with increased
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15 75 physical activity. For example, using survey data in Chicago (n=1,544), Fan et al. [21] found that
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17 76 respondents with a greater area of public parks within 0.5 miles of their home were more likely to
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19 77 engage in physical activity. A survey of 1,895 people in Adelaide, Australia [9] found that respondents
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21 78 who perceived their neighborhood as greener were more likely to engage in recreational walking.
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23 79 Similarly, a study in 1,803 people in Perth, Australia [22] found that people who lived nearer to
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25 80 recreational amenities, including public parks, were more likely to meet minimum physical-activity
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27 81 requirements.
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31 **METHODS**

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34 **Study sample**

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37 84 Our sample consisted of all people who received a total hip or knee arthroplasty at a publicly-funded
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39 85 hospital in New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties). We
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41 86 obtained individual-level hospital and pharmaceutical records via Statistics New Zealand's Integrated
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43 87 Data Infrastructure (IDI), which is a large database of routinely-collected individual-level data [23]. The
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45 88 IDI is structured around a central spine designed to identify all New Zealand residents. Datasets
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47 89 describing health, education, benefits, criminal justice, population (births, deaths, and immigration),
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49 90 income and work, and housing are linked to this central spine.
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53 91 As this study was based on routinely-collected health data, and did not involve contacting individual
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55 92 patients, the study was classified as minimal risk by the New Zealand Health and Disabilities Ethics
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3 93 Committee and was approved by Statistics New Zealand (MAA-2017-57). In addition, our research
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5 94 conformed to the Declaration of Helsinki guidelines.
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8 95 *Patient and Public Involvement statement:* There was no patient recruitment.
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10 11 96 **Outcomes**

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14 97 We used two outcomes to measure recovery: time to all-cause mortality and number of opioid
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16 98 prescriptions 3, 12, and 24 months post-surgery. We chose these outcomes, as they are important
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18 99 metrics of post-surgical recovery, and previous research has shown that rapid mobilization and
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20 100 rehabilitation can reduce two-year mortality rates following hip or knee arthroplasty [24], and exposure
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22 101 to the natural environment, in a hospital setting, is associated with reduced perioperative use of opioids
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24 102 [10].
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28 103 By the end of 2016, 2,263 of the 7,449 people who had received a hip arthroplasty had died as had
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30 104 1,741 of the 6,558 people who received knee arthroplasties.
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33 105 The number of opioid prescriptions received was calculated by linkage to pharmacy records. We did not
34
35 106 include prescriptions for methadone or buprenorphine, as in New Zealand these are primarily used to
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37 107 treat addiction. To control for pre-surgical pain, we calculated the number of opioid prescriptions each
38
39 108 participant received in the 12 months before surgery. Finally, to account for opioid potency, we
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41 109 categorized each opioid prescription as either strong (potency equal to or greater than morphine) or
42
43 110 weak (potency less than morphine). On average, study participants received 3.04 (SD=9.38) opioid
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45 111 prescriptions in the 12 months before surgery (0.68 strong and 2.36 weak) and 2.72 (SD=7.06) opioid
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47 112 prescriptions in the 12 months after surgery (0.75 strong and 1.98 weak).
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51 52 113 **Exposures**

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54 114 All exposures are based on a participant's residential meshblock, which is the smallest geographic unit at
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56 115 which Statistics New Zealand reports data. On average, 95 people live in a meshblock.
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3 116 Linking to address history in the IDI allowed us to estimate exposures for each year of the study (2005-
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5 117 2016). From these annual values, we calculated mean post-surgical exposure, which we defined as the
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7 118 mean exposure from the year of surgery to death or 2016, whichever came first.

119 Walkability

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

124 Land-use mix is defined as:

$$125 \quad \text{Land - use mix} = \frac{\sum_{i=1}^n (LC_i * \ln(LC_i))}{\ln(N)}$$

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

130 Greenness

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

137 **Covariates**

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

145 **Statistical analysis**

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

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

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

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3 160 the regression model. When choosing between two collinear variables, we included the variable with
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5 161 the lowest p-value when individually regressed against the dependent variable.
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8 162 We also conducted stratified analyses to see whether the relationship between the natural environment
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10 163 and health outcomes was the same across different strata of the sample. Analyses were conducted for
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12 164 hip and knee arthroplasty combined as well as for each outcome separately.
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15 165 **RESULTS**

16 166 Table 1 provides descriptive statistics for our sample.
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19 167 In the frailty model, specifying the survival function using a Weibull distribution gave the best model fit.
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22 168 Being older, male, European New Zealander, or Māori (the indigenous people of New Zealand) were all
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24 169 mortality risk factors (Table 2). Similarly, people who received more pre-surgery opioids, or had a longer
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26 170 hospital stay, were at greater risk of mortality. Six chronic conditions were risk factors as was higher
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28 171 neighborhood deprivation, although this relationship was only significant for hip arthroplasty.
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31 172 People who lived in greener neighborhoods (defined as mean post-surgical NDVI) were at lower risk of
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33 173 mortality, although this relationship was only significant in the hip-and-knee arthroplasty and hip-
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35 174 arthroplasty-only models (Table 2). To better elucidate the dose-response function linking NDVI and
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37 175 mortality, we re-estimated the hip-and-knee-arthroplasty frailty model splitting NDVI into quartiles
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39 176 (Table 3). Only the highest quartile was statistically significant, although NDVI remained protective in the
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41 177 second and third quartiles.
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47 178 Figure 1 shows the odds-ratio for mean lifetime NDVI for different strata of the sample. Stratifying the
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49 179 sample resulted in some loss of significance, due to lower numbers in each stratum. Notably, the
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51 180 protective effect of NDVI was higher for men than women. The protective effect of NDVI was also
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53 181 modestly higher for people who lived in higher SES neighborhoods (NZDep 1-5) compared to lower SES
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3 182 neighborhoods (NZDep 6-10). Similarly, NDVI was somewhat more protective for people who were
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5 183 younger than average (mean age at surgery=68).
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8 184 In the opioid model (Table 4), women, European New Zealanders, and people who were prescribed
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10 185 more pre-surgery opioid prescriptions received significantly more post-surgical opioid scripts in all three
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12 186 time periods with the exception of European New Zealanders in the 24 months post-surgery model
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14 187 (Table 4). Those who received a knee arthroplasty (as opposed to a hip arthroplasty), or stayed longer in
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16 188 hospital, also received more post-surgical opioids, as did people who had COPD, coronary heart disease,
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18 189 or traumatic brain injury. In contrast, older people received fewer opioid prescriptions, although the
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20 190 significance of this relationship varied across the three time periods. Separating opioids into weak and
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22 191 strong was not revealing and reduced the significance of variables of interest (data not shown). Mean
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24 192 post-surgical greenness was associated with significantly fewer post-surgical opioid prescriptions in all
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26 193 three time periods (Table 4). Living in a rural area, walkability, and land cover were not significantly
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28 194 associated with the number of post-surgical opioid prescriptions or post-surgical longevity (data not
29
30 195 shown). In addition, consistent with the frailty model, NDVI was not significant, when the analysis was
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32 196 restricted to knee-arthroplasty (results not shown). Finally, when we split NDVI into quartiles, none
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34 197 were significant (results not shown).
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40 198 In the stratified analysis (figure 2), greenness was more protective for men than women, which is
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42 199 consistent with the frailty model.
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45 200 **DISCUSSION**

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48 201 In a cohort of people who received a total hip or knee arthroplasty at a publicly-funded hospital in New
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50 202 Zealand in 2006 or 2007, we found that residents of greener neighborhoods received fewer post-surgical
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52 203 opioid prescriptions and lived longer, with the strongest results for hip arthroplasty. Our results are
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54 204 consistent with those reported by Ulrich [10], who found that, after gall-bladder surgery, patients
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3 205 recovered faster, and took fewer opioids, if they were in a room with a view of a natural scene. Our
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5 206 results were also consistent with a previous study [5], which found that rapid mobilization following hip
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7 207 or knee arthroplasty was associated with better two-year survival rates. Our study suggests that the
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9 208 benefits of mobilization (assuming this plays a role in the observed association between green space and
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11 209 mortality or opioid-use) extend beyond the immediate post-surgical period.
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15 210 In both the opioid and survival models, we found that greenness was more protective for men than
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17 211 women. This differential association may be because women's life expectancy is greater than men, so
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19 212 they are less likely to have a live-in partner who could encourage them to be physically active, and
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21 213 accompany them while they engage in outdoor activity that they might otherwise find too daunting. This
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23 214 possible mechanism is consistent with multiple studies showing that having a live-in partner is
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25 215 protective of a range of health outcomes [29]. In addition, this suggests that women, or indeed men,
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27 216 who live alone may benefit from additional post-surgical support.
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31 217 Greenness was associated with lower post-surgical opioid use, and lower mortality, in people recovering
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33 218 from hip arthroplasty but not those recovering from knee arthroplasty. This may be because knee
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35 219 arthroplasty is a more difficult and painful surgery to recover from (post-surgical opioid use was higher
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37 220 for knee-arthroplasty patients), and the protective effect of neighborhood greenness is insufficient to
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39 221 induce a clinically significant increase in post-surgical mobilization. However, other mechanism may also
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41 222 be involved (see below), so results should be interpreted with care.
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45 223 There was modest evidence that younger people, and those living in less deprived neighborhoods,
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47 224 derived greater benefit from exposure to greenness. This may be because younger people are more
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49 225 physically able to engage in outdoor activity, and that greenspace in higher SES neighborhoods may be
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51 226 better maintained and more appealing because of lower crime.
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3 227 When we split NDVI into quartiles in the frailty model, we found that only the top quartile was
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5 228 protective at conventional significance levels. This suggests that there may be a minimum threshold
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7 229 below which greenness offers no health benefits. However, it is important to note that NDVI is a coarse
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9 230 measure of overall greenness. It does not reveal which elements of the natural environment provide the
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11 231 greatest health benefits. Identifying the most protective elements would help inform the design of
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13 232 landscapes that are not in the top quartile of NDVI, but nonetheless provide health benefits.
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17 233 The magnitude of the protective effect of neighborhood greenness is not trivial. For example, in the 3-
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19 234 months post-surgery model of opioid use, a 2-SD decrease in NDVI is roughly equivalent to the risk of
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21 235 having chronic heart disease at the time of surgery. In the hip-only frailty model, a 2-SD decrease in
22
23 236 NDVI is roughly equivalent to the risk of being two years older.
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27 237 Physical activity is likely not the only mechanism linking greenness and improved post-surgical
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29 238 outcomes. For example, exposure to the natural environment can reduce short-term markers of stress
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31 239 such as heart rate, blood pressure, and salivary cortisol [30, 31]. In turn, stress is a well-documented risk
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33 240 factor for premature mortality [32] and can also trigger opioid cravings [33]. Similarly, exposure to the
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35 241 natural environment is associated with increased social connectivity [34], and social isolation can
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37 242 increase individual reactivity to opioids [35] as well as being a risk factor for premature mortality [36].
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39 243 More recently, research suggests that exposure to the natural environment may increase the microbial
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41 244 diversity of the human microbiome [37], and protect against adverse health outcomes [38] through
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43 245 improved immune function. In addition, improved immune function is associated with improved surgical
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45 246 recovery [39] and better orthopedic outcomes in elderly patients [40].
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50 247 Our study has several limitations. This is an observational study, so we were not able to establish a
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52 248 causal relationship between exposure to the natural environment, opioid use, and surgical recovery. In
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54 249 addition, our metrics of exposure to the natural environment were coarse. In particular, meshblock-level
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3 250 NDVI is an imperfect measure of a person's exposure to the natural environment. This is especially true
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5 251 in larger, rural meshblocks, where mean NDVI may not optimally represent a person's residential
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7 252 exposure to the natural environment. In addition, our outcome measures do not fully capture all
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9 253 elements of surgical recovery. For example, we did not have access to data on post-surgical physical
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11 254 activity levels or weight.
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256 **TABLES**

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

Variable	HIP		KNEE	
	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

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

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262

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

Variable	HIP AND KNEE		HIP		KNEE	
	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	

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

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

271 **Table 3:** Frailty model of time to all-cause mortality following hip or knee arthroplasty with NDVI quartiles (number of participants=14,010;
 272 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

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

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

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276

277 **Table 4:** Mixed negative-binomial model of number of opioid prescriptions 3 months, 12 months, and 24 months after hip or knee arthroplasty
 278 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

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

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

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2
3 283 **FIGURE LEGENDS**
4

5 284 **Figure 1:** Odds-ratio plot of standardized mean post-surgical NDVI for time to all-cause mortality
6 285 following hip or knee arthroplasty (number of participants=14,010, number of observations= 149,523)¹.
7 286 Low/high SES denotes participants whose lifetime NZ Deprivation Index is above/below average.
8 287 Old/young denote participants who are older/younger than the sample mean. The ethnicity reference
9 288 group is a composite of all ethnicities other than European NZ or Māori (figures 1 and 2 were created
10 289 with the user-written Stata command COEFPLOT)

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13 290 ¹ Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three
14 291

15 292
16 293 **Figure 2:** Odds-ratio plot of standardized mean post-surgical NDVI for number of opioid prescriptions 3
17 294 months post-surgery (n=14,010)¹. For definitions and reference groups see figure 1.

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19 295 ¹ Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three
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297 **Contributorship statement:** GHD designed the study, conducted the analysis, and wrote the majority of
298 the manuscript. DG created the exposure metrics and edited the manuscript. JD wrote parts of the
299 manuscript and edited multiple drafts.

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301 **LITERATURE CITED**

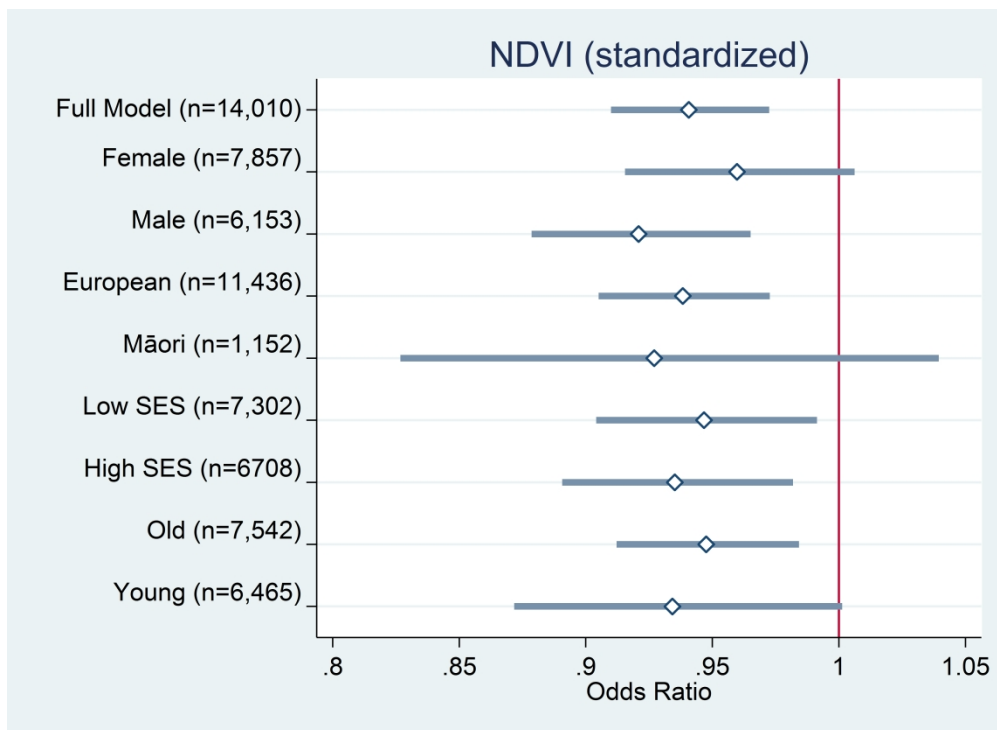
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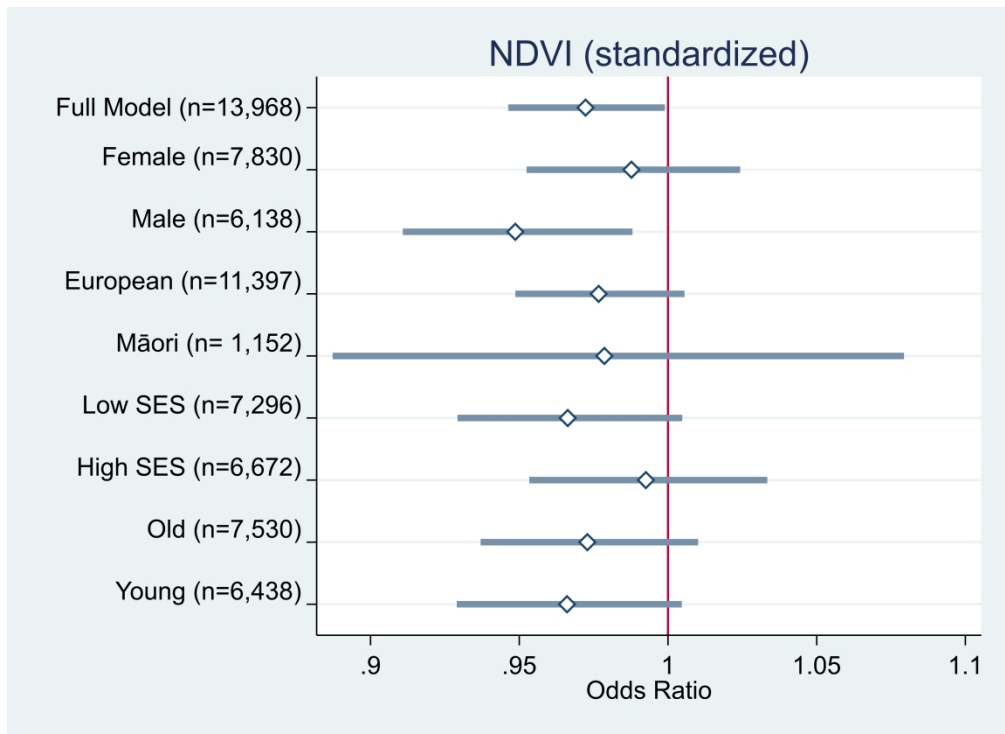
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1763x1282mm (72 x 72 DPI)

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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A

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(e) Describe any sensitivity analyses

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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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	14-16
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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	6
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-029522.R1
Article Type:	Original research
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Complete List of Authors:	Donovan, Geoffrey; USDA Forest Service, PNW Research Station Gatzolis, Demetrios; USDA Forest Service Pacific Northwest Research Station Douwes, Jeroen; Massey University, Centre for Public Health Research
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLOGY, Hip < ORTHOPAEDIC & TRAUMA SURGERY, Knee < ORTHOPAEDIC & TRAUMA SURGERY

SCHOLARONE™
Manuscripts

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3 1 **The relationship between exposure to the natural environment and recovery from hip or knee**
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5 2 **arthroplasty: a New Zealand retrospective cohort study**
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8 3 Geoffrey H. Donovan,^{a,*} Demetrios Gatzliolis,^b and Jeroen Douwes^a
9

10 4 ^aCenter for Public Health Research, Massey University, PO Box 756, Wellington 6140, New Zealand

11 5 ^bUSDA Forest Service, PNW Research Station, 620 SW Main, Suite 502, Portland, Oregon, USA

12 6 *Corresponding author ORCID: 0000-0002-1624-3440
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14 8 **Word count: 3,000**
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56 USA +1 503-808-2043, geoffrey.donovan@usda.gov
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3 12 **ABSTRACT**
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6 13 **Objectives:** Determine whether patients who live in greener and more walkable neighborhoods live
7
8 14 longer, and take fewer opioids, following hip or knee arthroplasty.
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10
11 15 **Design:** Retrospective cohort study.
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14 16 **Setting:** Residential environment following surgery at one of 54 New Zealand hospitals.
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17 17 **Participants:** All people who received a total hip or knee arthroplasty at a publicly-funded hospital in
18
19 18 New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties).
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21
22 19 **Primary and secondary outcome measure:** Time to all-cause mortality and number of post-surgical
23
24 20 opioid prescriptions.
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27 21 **Results:** Patients who lived in greener neighborhoods, as measured by the normalized difference
28
29 22 vegetation index (NDVI), lived longer following hip or knee arthroplasty (standardized OR: 0.95 95% CI:
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31 23 0.92-0.99). However, when we estimated separate hip-arthroplasty-only and knee-arthroplasty-only
32
33 24 models, greenness was only significantly associated with greater longevity following hip arthroplasty.
34
35 25 Similarly, patients who lived in greener neighborhoods took fewer opioids in the 12 months following
36
37 26 hip or knee arthroplasty (standardized OR: 0.97 95% CI: 0.95-0.99), but in separate hip-arthroplasty-only
38
39 27 and knee-arthroplasty-only models, greenness was only significantly associated with lower opioid use
40
41 28 following hip arthroplasty. Walkability was not significantly associated with post-surgical opioid use or
42
43 29 post-surgical longevity. All odds ratios were adjusted for sex, ethnicity, age, pre-surgical chronic health
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45 30 conditions, pre-surgical opioid use, social deprivation, and length of hospital stay.
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50 31 **Conclusions:** Consistent with the literature on enhanced-recovery programs, people who lived in
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52 32 greener neighborhoods took fewer opioids, and lived longer, following hip arthroplasty. Improving
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33 access to the natural environment may therefore be an effective component of post-surgical recovery
34 programs.

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

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3 37 **STRENGTHS AND LIMITATIONS OF THIS STUDY**
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- 6 38 • First study to examine the relationship between natural environment and surgical recovery
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8 39 outside of a hospital setting
9
10 40 • Large cohort followed longitudinally for 9+ years
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12 41 • Observational study, so a causal link between the natural environment and surgical recovery
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14 42 couldn't be established
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16 43 • Exposure was based on residential meshblock not residential address
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20 44 **Competing interests:** None declared
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22

23 45 **Funding:** No external funding was received
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25

26 46 **Data availability statement:** De-identified data are not publicly available but may be obtained from
27
28 47 Statistics New Zealand after gaining ethics approval and submitting a research proposal (contact:
29
30 48 access2microdata@stats.govt.nz). Note that, even with these approvals, data must be accessed via a
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32 49 secure data lab in New Zealand. Exposure data, and code used for statistical analysis, are freely available
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34 50 from the authors.
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52 INTRODUCTION

53 Rates of hip and knee arthroplasty are rising globally. For example, in Organization for Economic
54 Cooperation and Development (OECD) countries, the incidence of hip arthroplasty rose from
55 140/100,000 people in 2005 to 164/100,000 in 2011 [1]. Similarly, the incidence of knee arthroplasty in
56 OECD countries rose from 114/100,000 in 2005 to 150/100,000 in 2011 [2]. Increases in life expectancy
57 and obesity rates suggest that this trend is likely to continue [3]. Given this increased demand, and
58 constrained healthcare budgets, research has focused on identifying approaches that improve post-
59 surgical health outcomes, shorten length of stay, and reduce costs. For example, enhanced-recovery
60 programs that emphasize rapid mobilization and rehabilitation following hip or knee arthroplasty can
61 reduce length of hospital stay [4] and decrease mortality [5]. However, no research has focused on the
62 effect of patients' residential environments, despite the well-established link between exposure to the
63 natural environment and increased physical activity [6-9], and research showing that passively viewing a
64 natural scene while recovering from surgery can reduce both length of hospital stay and post-surgical
65 opioid use [10]. We address this gap in the literature by evaluating the relationship between exposure to
66 the built and natural environment and recovery from hip or knee arthroplasty in a large New Zealand
67 cohort.

68 Literature review

69 Numerous studies have examined how different elements of enhanced-recovery programs affect post-
70 operative outcomes (also known as fast-track or rapid-recovery programs). These programs use
71 coordinated multimodal techniques to reduce recovery times and improve post-operative outcomes [3].
72 For example, pre-operative education can shorten hospital stays [11] and reduce post-operative pain
73 [12]. Several studies have found that pre-emptive analgesia allows more rapid mobilization and return
74 of function [13, 14]. Multiple studies have found that rapid mobilization on the day of surgery (typically

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3 75 2-6 hours after surgery) reduces length of stay and improves function [15-17]. Similarly, aggressive
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5 76 physical therapy (extending beyond the day of surgery) can reduce length of stay and improve function
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7 77 [18-20]. Finally, in a prospective study of 4,500 patients in the UK, enhanced recovery was associated
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10 78 with improved two-year survival rates when compared to traditional post-surgical protocols, which
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12 79 suggests that post-operative mobility may have long-term benefits [5].
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15 80 Several studies have found that exposure to the natural environment is associated with increased
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17 81 physical activity. For example, using survey data in Chicago (n=1,544), Fan et al. [21] found that
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19 82 respondents with a greater area of public parks within 0.5 miles of their home were more likely to
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21 83 engage in physical activity. A survey of 1,895 people in Adelaide, Australia [9] found that respondents
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23 84 who perceived their neighborhoods as greener were more likely to engage in recreational walking.
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25 85 Similarly, a study in 1,803 people in Perth, Australia [22] found that people who lived nearer to
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27 86 recreational amenities, including public parks, were more likely to meet minimum physical-activity
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29 87 requirements.
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33 88 Passive exposure to the natural environment can also produce health benefits. In particular, several
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35 89 studies have found that greenness exposure can reduce perceived pain in a range of settings.
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37 90 Specifically, a RCT of 46 healthy volunteers [23] found that participants who had just watched a video of
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39 91 a natural scene had significantly higher pain threshold and tolerance than participants who had watched
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41 92 a blank screen. Similarly, a RCT of adults undergoing flexible bronchoscopy found that participants who
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43 93 viewed a natural scene reported significantly less pain [24]. Finally, an RCT of a two-day forestry-therapy
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45 94 program in Korea found that participants in the program (n=33) had significantly lower levels of pain and
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47 95 depression than controls (n=25). In addition, participants had significantly higher heart-rate variability
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49 96 and natural-killer cell activity.
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53 54 97 **METHODS** 55 56 57

98 **Study sample**

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

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

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

113 **Outcomes**

114 We used two outcomes to measure recovery: time to all-cause mortality and number of opioid
115 prescriptions 3, 12, and 24 months post-surgery. We chose these outcomes as they are important
116 metrics of post-surgical recovery. In addition, previous research has shown that rapid mobilization and
117 rehabilitation can reduce two-year mortality rates following hip or knee arthroplasty [26], and exposure
118 to the natural environment, in a hospital setting, is associated with reduced perioperative use of opioids
119 [10].

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3 120 By the end of 2016, 2,263 (30.0%) of the 7,449 people who had received a hip arthroplasty had died as
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5 121 had 1,741 (26.5%) of the 6,558 people who received knee arthroplasties.
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8 122 The number of opioid prescriptions received was calculated by linkage to pharmacy records. We did not
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10 123 include prescriptions for methadone or buprenorphine, as in New Zealand these are primarily used to
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12 124 treat addiction. To control for pre-surgical pain, we calculated the number of opioid prescriptions each
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14 125 participant received in the 12 months before surgery. Finally, to account for opioid potency, we
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16 126 categorized each opioid prescription as either strong (potency equal to or greater than morphine) or
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18 127 weak (potency less than morphine). On average, study participants received 3.04 (SD=9.38) opioid
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20 128 prescriptions in the 12 months before surgery (0.68 strong and 2.36 weak) and 2.72 (SD=7.06) opioid
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22 129 prescriptions in the 12 months after surgery (0.75 strong and 1.98 weak).
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27 130 **Exposures**

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30 131 All exposures are based on a participant's residential meshblock, which is the smallest geographic unit at
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32 132 which Statistics New Zealand reports data. On average, 95 people live in a meshblock.
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35 133 Linking to address history in the IDI allowed us to estimate exposures for each year of the study (2005-
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37 134 2016). From these annual values, we calculated mean post-surgical exposure, which we defined as the
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39 135 mean exposure from the year of surgery to death or 2016, whichever came first.
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42 136 We had no information on participants' pre- or post-surgical physical activity. Therefore, exposure
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44 137 metrics describe the physical environment that a participant is exposed to, but they do not describe how
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46 138 a participant physically interacts with different environments.
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49 139 **Walkability**

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52 140 We used a previously validated walkability index [27] with three components: number of households per
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54 141 hectare (data source: 2006 New Zealand Census), number of road intersections per square kilometer
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3 142 (data source: Land Information New Zealand), and land-use mix (data source: 2008 New Zealand Land
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5 143 Cover Database v4.1). In all three cases, we used the version of each data source that was closest to
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7 144 baseline. Land-cover data were available from 2001, 2008, and 2012. However, the classification
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10 145 schemes were not consistent across the three years. In addition, when we compared 2008 and 2012
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12 146 data, we found that the net area of New Zealand that changed from one land class to another was only
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14 147 0.903%. Therefore, we used 2008 data for our analysis.

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17 148 Land-use mix is defined as:

$$19 \quad 20 \quad 21 \quad 22 \quad 23 \quad 24 \quad 25 \quad 26 \quad 27 \quad 28 \quad 29 \quad 30 \quad 31 \quad 32 \quad 33 \quad 34 \quad 35 \quad 36 \quad 37 \quad 38 \quad 39 \quad 40 \quad 41 \quad 42 \quad 43 \quad 44 \quad 45 \quad 46 \quad 47 \quad 48 \quad 49 \quad 50 \quad 51 \quad 52 \quad 53 \quad 54 \quad 55 \quad 56 \quad 57 \quad 58 \quad 59 \quad 60$$
$$Land - use\ mix = \frac{\sum_{i=1}^n (LC_i * \ln(LC_i))}{\ln(N)}$$

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

154 Greenness

155 We used two measures of exposure to the natural environment: land-cover data (see above) and the
156 Normalized Difference Vegetation Index (NDVI), which is a greenness index derived from satellite
157 imagery. Specifically, for each year from 2005 to 2016, we used maximum annual NDVI derived from
158 30m-resolution Landsat imagery that was calculated at the top of the atmosphere, which normalized all
159 atmospheric effects. We standardized NDVI values to make regression coefficients easier to interpret.
160 From these annual values, we calculated mean post-surgical greenness exposure.

161 **Covariates**

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3 162 Using data from the IDI, we controlled for sex, ethnicity, and age. In addition, we controlled for
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5 163 neighborhood deprivation using the New Zealand Deprivation Index (NZDep), which is a well-validated
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7 164 index calculated from nine census variables [28]. NZDep ranges from 1 to 10 with higher values denoting
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10 165 higher levels of social deprivation. Finally, we controlled for eight chronic conditions at time of surgery:
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12 166 coronary heart disease, gout, chronic obstructive pulmonary disease (COPD), diabetes, cancer, stroke,
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14 167 acute myocardial infarction, and traumatic brain injury. We chose to account for these conditions as
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16 168 they are major health outcomes that could affect surgical recovery, and they were pre-defined by
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19 169 Statistics New Zealand based on hospital-admissions and pharmacy data [29]. Note that we did not have
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21 170 access to data on physical activity, BMI, or diet.

171 **Statistical analysis**

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

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

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

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3 185 each independent variable. If any variable had a variance-inflation factor over two, we dropped it from
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5 186 the regression model. When choosing between two collinear variables, we included the variable with
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7 187 the lowest p-value when individually regressed against the dependent variable.
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10 188 We also conducted stratified analyses to see whether the relationship between the natural environment
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12 189 and health outcomes was the same across different strata of the sample. Analyses were conducted for
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14 190 hip and knee arthroplasty combined as well as for each outcome separately.
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18 191 **RESULTS**

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21 192 Table 1 provides descriptive statistics for our sample.
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24 193 In the frailty model, specifying the survival function using a Weibull distribution gave the best model fit.
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26 194 Being older, male, European New Zealander, or Māori (the indigenous people of New Zealand) were all
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28 195 mortality risk factors (Table 2) (The reference ethnic group was Pacific, Asian, MELAA, or other).
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30 196 Similarly, people who received more pre-surgery opioids, or had a longer hospital stay, were at greater
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32 197 risk of mortality. Six chronic conditions were risk factors as was higher neighborhood deprivation,
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34 198 although this relationship was only significant for hip arthroplasty.
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38 199 People who lived in greener neighborhoods (defined as mean post-surgical NDVI) were at lower risk of
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40 200 mortality, although this relationship was only significant in the hip-and-knee arthroplasty and hip-
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42 201 arthroplasty-only models (Table 2). To better elucidate the dose-response function linking NDVI and
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44 202 mortality, we re-estimated the hip-and-knee-arthroplasty frailty model splitting NDVI into quartiles
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47 203 (Table 3). Only the highest quartile was statistically significant, in the combined and hip-only models,
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49 204 although NDVI remained protective in the second and third quartiles. In the knee-only model, the
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51 205 second quartile of NDVI was protective although only at the 10% level. In addition, the third and fourth
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53 206 quartiles of NDVI did not show a consistent protective effect.
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3 207 Figure 1 shows the odds ratio for mean lifetime NDVI for different strata of the sample. Stratifying the
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5 208 sample resulted in some loss of significance, due to lower numbers in each stratum. Notably, the
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7 209 protective effect of NDVI was higher for men than women. The protective effect of NDVI was also
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10 210 modestly higher for people who lived in higher SES neighborhoods (NZDep 1-5) compared to lower SES
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12 211 neighborhoods (NZDep 6-10). Similarly, NDVI was somewhat more protective for people who were
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14 212 younger than average (mean age at surgery=68).

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17 213 In the opioid model (Table 4), women, European New Zealanders, and people who were prescribed
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19 214 more pre-surgery opioid prescriptions received significantly more post-surgical opioid scripts in all three
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21 215 time periods with the exception of European New Zealanders in the 24 months post-surgery model
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23 216 (Table 4). Those who received a knee arthroplasty (as opposed to a hip arthroplasty) or stayed longer in
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25 217 hospital also received more post-surgical opioids, as did people who had COPD, coronary heart disease,
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27 218 or traumatic brain injury. In contrast, older people received fewer opioid prescriptions, although the
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29 219 significance of this relationship varied across the three time periods. Separating opioids into weak and
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31 220 strong was not revealing and reduced the significance of variables of interest (data not shown). Mean
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33 221 post-surgical greenness was associated with significantly fewer post-surgical opioid prescriptions in all
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35 222 three time periods (Table 4). Living in a rural area and land cover were not significantly associated with
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37 223 the number of post-surgical opioid prescriptions or time to all-cause mortality (data not shown). In
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39 224 addition, walkability was not significantly associated with either opioid use or mortality. For example,
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41 225 the odds ratio on walkability in the 3-month post-surgical opioid model was 1.043 (95% CI: 0.966-1.127),
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43 226 and the odds ratio in the hip-only frailty model was 1.035 (95% CI: 0.971-1.104). Even when the analysis
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45 227 was restricted to only-hip or only-knee arthroplasties, the relationship between walkability and
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47 228 mortality or opioid use remained insignificant.
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3 229 In addition, consistent with the frailty model, NDVI was not significant, when the analysis was restricted
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5 230 to knee-arthroplasty (results not shown). Finally, when we split NDVI into quartiles, none were
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7 231 significant (results not shown).
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10 232 In the stratified analysis (figure 2), greenness was more protective for men than women, which is
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13 233 consistent with the frailty model.
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15 234 **DISCUSSION**

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18 235 In a cohort of people who received a total hip or knee arthroplasty at a publicly-funded hospital in New
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20 236 Zealand in 2006 or 2007, we found that residents of greener neighborhoods received fewer post-surgical
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22 237 opioid prescriptions and lived longer, with the strongest results for hip arthroplasty. Our results are
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24 238 consistent with those reported by Ulrich [10], who found that, after gall-bladder surgery, patients
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26 239 recovered faster and took fewer opioids if they were in a room with a view of a natural scene. Our
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28 240 results are also consistent with a previous study [5], which found that rapid mobilization following hip or
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30 241 knee arthroplasty was associated with better two-year survival rates. Finally, results suggests that the
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32 242 benefits of exposure to the natural environment extend beyond the immediate post-surgical period.
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37 243 In both the opioid and survival models, we found that greenness was more protective for men than
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39 244 women. This differential association may be because women's life expectancy is greater than men, so
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41 245 they are less likely to have a live-in partner who could encourage them to be physically active, and
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43 246 accompany them while they engage in outdoor activity that they might otherwise find too daunting (we
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45 247 have no evidence that women in our sample had fewer live-in partners). This possible mechanism is
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47 248 consistent with multiple studies showing that having a live-in partner is protective of a range of health
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49 249 outcomes [31]. In addition, this suggests that women, or indeed men, who live alone may benefit from
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51 250 additional post-surgical support. However, other mechanisms may also be involved. For example,
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3 251 women may be more active or may have more social support at baseline, which might reduce the
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5 252 protective effect of exposure to the natural environment.
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8 253 Greenness was associated with lower post-surgical opioid use, and lower mortality, in people recovering
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10 254 from hip arthroplasty but not those recovering from knee arthroplasty. This may be because knee
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12 255 arthroplasty is a more difficult and painful surgery to recover from [32] (post-surgical opioid use was
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14 256 65% higher for knee-arthroplasty patients in our sample), and the protective effect of neighborhood
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16 257 greenness is insufficient to induce a clinically significant increase in post-surgical mobilization.
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20 258 There was modest evidence that younger people, and those living in less deprived neighborhoods,
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22 259 derived greater benefit from exposure to greenness. This may be because younger people are more
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24 260 physically able to engage in outdoor activity, and that greenspace in higher SES neighborhoods may be
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26 261 better maintained and more appealing because of lower crime [33].
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30 262 When we split NDVI into quartiles in the frailty model, we found that only the top quartile was
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32 263 protective at conventional significance levels. This suggests that there may be a minimum threshold
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34 264 below which greenness offers no health benefits. However, it is important to note that NDVI is a coarse
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36 265 measure of overall greenness. It does not reveal which elements of the natural environment provide the
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38 266 greatest health benefits. Identifying the most protective elements would help inform the design of
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40 267 landscapes that are not in the top quartile of NDVI, but nonetheless provide health benefits.
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44 268 The magnitude of the protective effect of neighborhood greenness is not trivial. For example, in the 3-
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46 269 months post-surgery model of opioid use, a 2-SD decrease in NDVI is roughly equivalent to the risk of
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48 270 having chronic heart disease at the time of surgery. In the hip-only frailty model, a 2-SD decrease in
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50 271 NDVI is roughly equivalent to the risk of being two years older.
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53 272 Physical activity is likely not the only mechanism linking greenness and improved post-surgical
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55 273 outcomes. For example, exposure to the natural environment can reduce short-term markers of stress
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3 274 such as heart rate, blood pressure, and salivary cortisol [34, 35]. In turn, stress is a well-documented risk
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5 275 factor for premature mortality [36] and can also trigger opioid cravings [37]. Similarly, exposure to the
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7 276 natural environment is associated with increased social connectivity [38], and social isolation can
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10 277 increase individual reactivity to opioids [39] as well as being a risk factor for premature mortality [40].
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12 278 More recently, research suggests that exposure to the natural environment may increase the microbial
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14 279 diversity of the human microbiome [41], and protect against adverse health outcomes [42] through
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16 280 improved immune function. In addition, improved immune function is associated with improved surgical
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18 281 recovery [43] and better orthopedic outcomes in elderly patients [44].
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22 282 Our study has several limitations. This is an observational study, so we were not able to establish a
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24 283 causal relationship between exposure to the natural environment, opioid use, and surgical recovery. In
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26 284 addition, our metrics of exposure to the natural environment were coarse. In particular, meshblock-level
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28 285 NDVI is an imperfect measure of a person's exposure to the natural environment. This is especially true
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30 286 in larger, rural meshblocks, where mean NDVI may not optimally represent a person's residential
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33 287 exposure to the natural environment.
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36 288 **Conclusions**

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39 289 In a large (n=14,010) cohort of participants who received a hip or knee arthroplasty at a publicly-funded
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41 290 New Zealand hospital in 2006 or 2007, we found that exposure to the natural environment was
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43 291 associated with fewer post-surgical opioid prescriptions, and increased time to all-cause mortality, in
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45 292 hip-arthroplasty patients only. Results suggest that clinicians should consider a patient's home
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47 293 environment when designing post-operative care plans. In particular, clinicians may wish to explicitly
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49 294 incorporate neighborhood greenspace. When a patient doesn't have access to greenspace, additional
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52 295 support may be warranted to encourage at-home mobilization.
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297 **TABLES**

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

Variable	HIP		KNEE	
	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

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

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

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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.

Variable	HIP AND KNEE		HIP		KNEE	
	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.

Variables	HIP AND KNEE		HIP		KNEE	
	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

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3 326 **FIGURE LEGENDS**
4

5 327 **Figure 1:** Odds-ratio plot of standardized mean post-surgical NDVI for time to all-cause mortality
6 328 following hip or knee arthroplasty (number of participants=14,010, number of observations= 149,523)¹.
7 329 Low/high SES denotes participants whose lifetime NZ Deprivation Index is above/below average.
8 330 Old/young denote participants who are older/younger than the sample mean. The ethnicity reference
9 331 group is a composite of all ethnicities other than European NZ or Māori (figures 1 and 2 were created
10 332 with the user-written Stata command COEFPLOT)

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13 333 ¹ Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three
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15 335
16 336 **Figure 2:** Odds-ratio plot of standardized mean post-surgical NDVI for number of opioid prescriptions 3
17 337 months post-surgery (n=14,010)¹. For definitions and reference groups see figure 1.

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19 338 ¹ Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three
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340 **Contributorship statement:** GHD designed the study, conducted the analysis, and wrote the majority of
341 the manuscript. DG created the exposure metrics and edited the manuscript. JD wrote parts of the
342 manuscript and edited multiple drafts.
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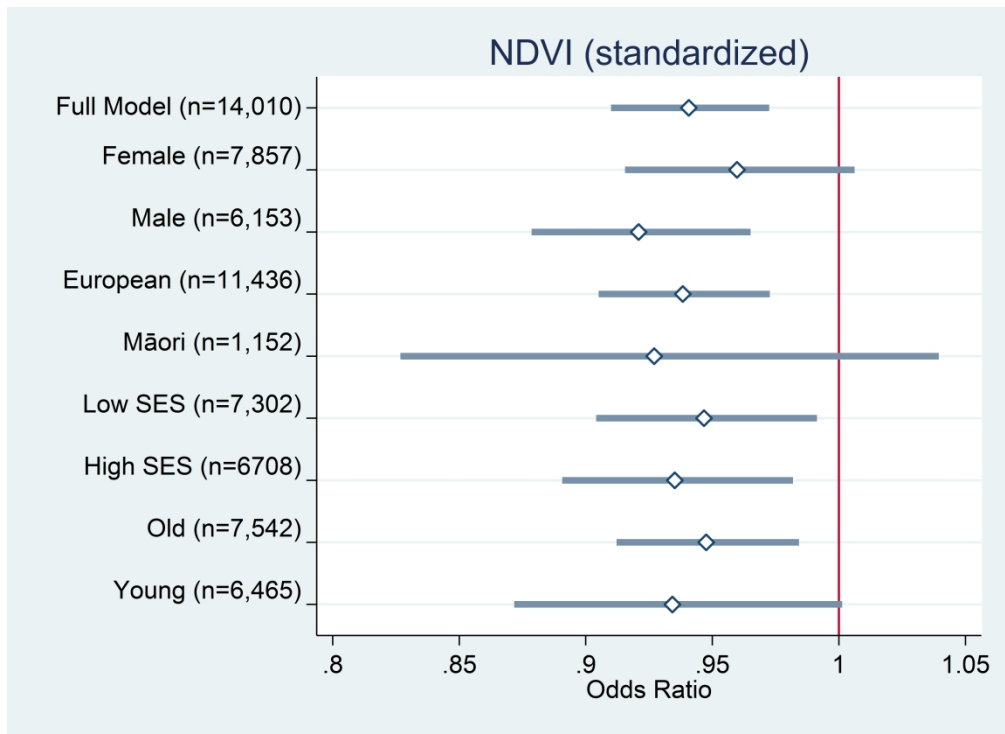
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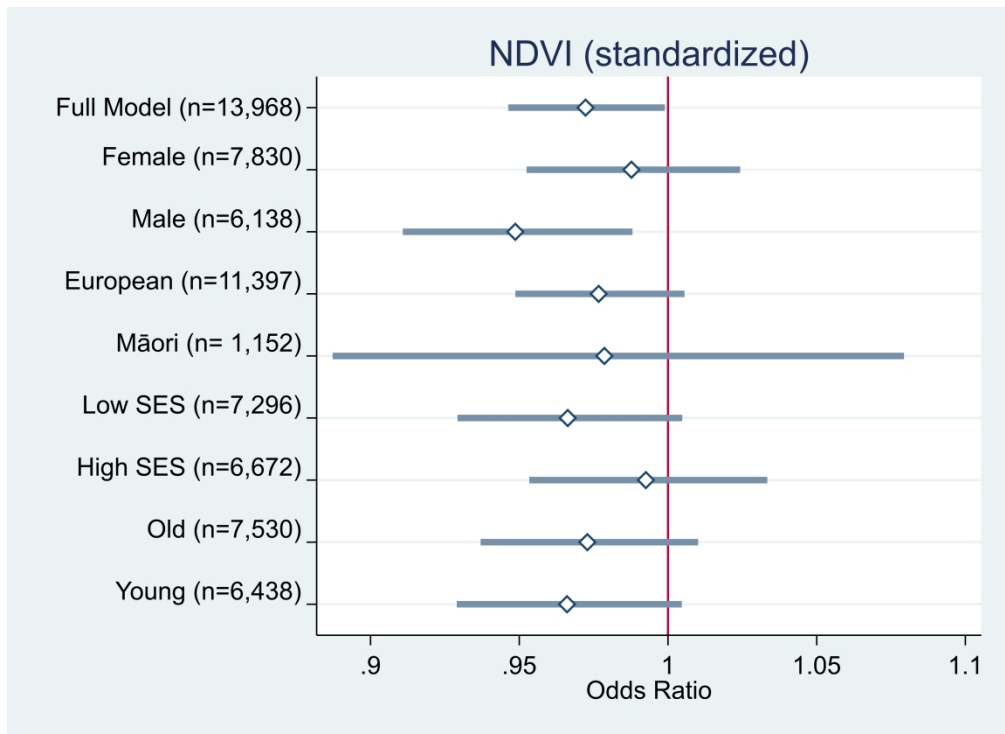
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1763x1282mm (72 x 72 DPI)

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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A

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(e) Describe any sensitivity analyses

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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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	14-16
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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	6
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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

Journal:	<i>BMJ Open</i>
Manuscript ID	bmjopen-2019-029522.R2
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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Epidemiology
Keywords:	EPIDEMIOLGY, Hip < ORTHOPAEDIC & TRAUMA SURGERY, Knee < ORTHOPAEDIC & TRAUMA SURGERY

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Manuscripts

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3 1 **The relationship between exposure to the natural environment and recovery from hip or knee**
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5 2 **arthroplasty: a New Zealand retrospective cohort study**
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8 3 Geoffrey H. Donovan,^{a,*} Demetrios Gatzliolis,^b and Jeroen Douwes^a
9

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14 8 **Word count: 3,000**
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56 USA +1 503-808-2043, geoffrey.donovan@usda.gov
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3 12 **ABSTRACT**
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6 13 **Objectives:** Determine whether patients who live in greener and more walkable neighborhoods live
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8 14 longer, and take fewer opioids, following hip or knee arthroplasty.
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11 15 **Design:** Retrospective cohort study.
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14 16 **Setting:** Residential environment following surgery at one of 54 New Zealand hospitals.
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17 17 **Participants:** All people who received a total hip or knee arthroplasty at a publicly-funded hospital in
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19 18 New Zealand in 2006 and 2007 (7,449 hip arthroplasties and 6,558 knee arthroplasties).
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21
22 19 **Primary and secondary outcome measure:** Time to all-cause mortality and number of post-surgical
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24 20 opioid prescriptions.
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27 21 **Results:** Patients who lived in greener neighborhoods, as measured by the normalized difference
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29 22 vegetation index (NDVI), lived longer following hip or knee arthroplasty (standardized OR: 0.95 95% CI:
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31 23 0.92-0.99). However, when we estimated separate hip-arthroplasty-only and knee-arthroplasty-only
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33 24 models, greenness was only significantly associated with greater longevity following hip arthroplasty.
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35 25 Similarly, patients who lived in greener neighborhoods took fewer opioids in the 12 months following
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37 26 hip or knee arthroplasty (standardized OR: 0.97 95% CI: 0.95-0.99), but in separate hip-arthroplasty-only
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39 27 and knee-arthroplasty-only models, greenness was only significantly associated with lower opioid use
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41 28 following hip arthroplasty. Walkability was not significantly associated with post-surgical opioid use or
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43 29 post-surgical longevity. All odds ratios were adjusted for sex, ethnicity, age, pre-surgical chronic health
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45 30 conditions, pre-surgical opioid use, social deprivation, and length of hospital stay.
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50 31 **Conclusions:** Consistent with the literature on enhanced-recovery programs, people who lived in
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52 32 greener neighborhoods took fewer opioids, and lived longer, following hip arthroplasty. Improving
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33 access to the natural environment may therefore be an effective component of post-surgical recovery
34 programs.

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

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For peer review only

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3 37 **STRENGTHS AND LIMITATIONS OF THIS STUDY**
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- 6 38 • First study to examine the relationship between natural environment and surgical recovery
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8 39 outside of a hospital setting
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10 40 • Large cohort followed longitudinally for 9+ years
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12 41 • Observational study, so a causal link between the natural environment and surgical recovery
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14 42 couldn't be established
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16 43 • Exposure was based on residential meshblock not residential address
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20 44 **Competing interests:** None declared
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23 45 **Funding:** No external funding was received
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26 46 **Data availability statement:** De-identified data are not publicly available but may be obtained from
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28 47 Statistics New Zealand after gaining ethics approval and submitting a research proposal (contact:
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30 48 access2microdata@stats.govt.nz). Note that, even with these approvals, data must be accessed via a
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32 49 secure data lab in New Zealand. Exposure data, and code used for statistical analysis, are freely available
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35 50 from the authors.
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52 INTRODUCTION

53 Rates of hip and knee arthroplasty are rising globally. For example, in Organization for Economic
54 Cooperation and Development (OECD) countries, the incidence of hip arthroplasty rose from
55 140/100,000 people in 2005 to 164/100,000 in 2011 [1]. Similarly, the incidence of knee arthroplasty in
56 OECD countries rose from 114/100,000 in 2005 to 150/100,000 in 2011 [2]. Increases in life expectancy
57 and obesity rates suggest that this trend is likely to continue [3]. Given this increased demand, and
58 constrained healthcare budgets, research has focused on identifying approaches that improve post-
59 surgical health outcomes, shorten length of stay, and reduce costs. For example, enhanced-recovery
60 programs that emphasize rapid mobilization and rehabilitation following hip or knee arthroplasty can
61 reduce length of hospital stay [4] and decrease mortality [5]. However, no research has focused on the
62 effect of patients' residential environments, despite the well-established link between exposure to the
63 natural environment and increased physical activity [6-9], and research showing that passively viewing a
64 natural scene while recovering from surgery can reduce both length of hospital stay and post-surgical
65 opioid use [10]. We address this gap in the literature by evaluating the relationship between exposure to
66 the built and natural environment and recovery from hip or knee arthroplasty in a large New Zealand
67 cohort.

68 Literature review

69 Numerous studies have examined how different elements of enhanced-recovery programs affect post-
70 operative outcomes (also known as fast-track or rapid-recovery programs). These programs use
71 coordinated multimodal techniques to reduce recovery times and improve post-operative outcomes [3].
72 For example, pre-operative education can shorten hospital stays [11] and reduce post-operative pain
73 [12]. Several studies have found that pre-emptive analgesia allows more rapid mobilization and return
74 of function [13, 14]. Multiple studies have found that rapid mobilization on the day of surgery (typically

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3 75 2-6 hours after surgery) reduces length of stay and improves function [15-17]. Similarly, aggressive
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5 76 physical therapy (extending beyond the day of surgery) can reduce length of stay and improve function
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7 77 [18-20]. Finally, in a prospective study of 4,500 patients in the UK, enhanced recovery was associated
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10 78 with improved two-year survival rates when compared to traditional post-surgical protocols, which
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12 79 suggests that post-operative mobility may have long-term benefits [5].
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15 80 Several studies have found that exposure to the natural environment is associated with increased
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17 81 physical activity. For example, using survey data in Chicago (n=1,544), Fan et al. [21] found that
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19 82 respondents with a greater area of public parks within 0.5 miles of their home were more likely to
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21 83 engage in physical activity. A survey of 1,895 people in Adelaide, Australia [9] found that respondents
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23 84 who perceived their neighborhoods as greener were more likely to engage in recreational walking.
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25 85 Similarly, a study in 1,803 people in Perth, Australia [22] found that people who lived nearer to
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27 86 recreational amenities, including public parks, were more likely to meet minimum physical-activity
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29 87 requirements.
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33 88 Passive exposure to the natural environment can also produce health benefits. In particular, several
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35 89 studies have found that greenness exposure can reduce perceived pain in a range of settings.
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38 90 Specifically, a RCT of 46 healthy volunteers [23] found that participants who had just watched a video of
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40 91 a natural scene had significantly higher pain threshold and tolerance than participants who had watched
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42 92 a blank screen. Similarly, a RCT of adults undergoing flexible bronchoscopy found that participants who
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44 93 viewed a natural scene reported significantly less pain [24]. Finally, an RCT of a two-day forestry-therapy
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46 94 program in Korea found that participants in the program (n=33) had significantly lower levels of pain and
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48 95 depression than controls (n=25). In addition, participants had significantly higher heart-rate variability
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50 96 and natural-killer cell activity.
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54 97 **METHODS**

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98 Study sample

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

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

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

113 Outcomes

114 We used two outcomes to measure recovery: time to all-cause mortality and number of opioid
115 prescriptions 3, 12, and 24 months post-surgery. We chose these outcomes as they are important
116 metrics of post-surgical recovery. In addition, previous research has shown that rapid mobilization and
117 rehabilitation can reduce two-year mortality rates following hip or knee arthroplasty [26], and exposure
118 to the natural environment, in a hospital setting, is associated with reduced perioperative use of opioids
119 [10].

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3 120 By the end of 2016, 2,263 (30.0%) of the 7,449 people who had received a hip arthroplasty had died as
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5 121 had 1,741 (26.5%) of the 6,558 people who received knee arthroplasties.
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8 122 The number of opioid prescriptions received was calculated by linkage to pharmacy records. We did not
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10 123 include prescriptions for methadone or buprenorphine, as in New Zealand these are primarily used to
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12 124 treat addiction. To control for pre-surgical pain, we calculated the number of opioid prescriptions each
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14 125 participant received in the 12 months before surgery. Finally, to account for opioid potency, we
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16 126 categorized each opioid prescription as either strong (potency equal to or greater than morphine) or
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18 127 weak (potency less than morphine). On average, study participants received 3.04 (SD=9.38) opioid
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20 128 prescriptions in the 12 months before surgery (0.68 strong and 2.36 weak) and 2.72 (SD=7.06) opioid
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22 129 prescriptions in the 12 months after surgery (0.75 strong and 1.98 weak).
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27 130 **Exposures**

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30 131 All exposures are based on a participant's residential meshblock, which is the smallest geographic unit at
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32 132 which Statistics New Zealand reports data. On average, 95 people live in a meshblock.
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35 133 Linking to address history in the IDI allowed us to estimate exposures for each year of the study (2005-
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37 134 2016). From these annual values, we calculated mean post-surgical exposure, which we defined as the
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39 135 mean exposure from the year of surgery to death or 2016, whichever came first.
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42 136 We had no information on participants' pre- or post-surgical physical activity. Therefore, exposure
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44 137 metrics describe the physical environment that a participant is exposed to, but they do not describe how
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46 138 a participant physically interacts with different environments.
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49 139 **Walkability**

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52 140 We used a previously validated walkability index [27] with three components: number of households per
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54 141 hectare (data source: 2006 New Zealand Census), number of road intersections per square kilometer
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3 142 (data source: Land Information New Zealand), and land-use mix (data source: 2008 New Zealand Land
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5 143 Cover Database v4.1). In all three cases, we used the version of each data source that was closest to
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7 144 baseline. Land-cover data were available from 2001, 2008, and 2012. However, the classification
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10 145 schemes were not consistent across the three years. In addition, when we compared 2008 and 2012
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12 146 data, we found that the net area of New Zealand that changed from one land class to another was only
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14 147 0.903%. Therefore, we used 2008 data for our analysis.

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17 148 Land-use mix is defined as:

$$19 \quad \text{Land-use mix} = \frac{\sum_{i=1}^n (LC_i * \ln(LC_i))}{\ln(N)}$$

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25 150 Where LC_i denotes the proportion of each meshblock that is covered by the i th land-cover type and N
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27 151 denotes the total number of land-cover types. Following Frank et al., we standardized household
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29 152 density, intersection density, and land-use mix (by subtracting the mean and dividing by the standard
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31 153 deviation), and summed the three standardized scores into a single walkability index.

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34 154 Greenness

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37 155 We used two measures of exposure to the natural environment: land-cover data (see above) and the
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39 156 Normalized Difference Vegetation Index (NDVI), which is a greenness index derived from satellite
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41 157 imagery. Specifically, for each year from 2005 to 2016, we used maximum annual NDVI derived from
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43 158 30m-resolution Landsat imagery that was calculated at the top of the atmosphere, which normalized all
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45 159 atmospheric effects. We standardized NDVI values to make regression coefficients easier to interpret.
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48 160 From these annual values, we calculated mean post-surgical greenness exposure.

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51 161 **Covariates**

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3 162 Using data from the IDI, we controlled for sex, ethnicity, and age. In addition, we controlled for
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5 163 neighborhood deprivation using the New Zealand Deprivation Index (NZDep), which is a well-validated
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7 164 index calculated from nine census variables [28]. NZDep ranges from 1 to 10 with higher values denoting
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10 165 higher levels of social deprivation. Finally, we controlled for eight chronic conditions at time of surgery:
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12 166 coronary heart disease, gout, chronic obstructive pulmonary disease (COPD), diabetes, cancer, stroke,
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14 167 acute myocardial infarction, and traumatic brain injury. We chose to account for these conditions as
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16 168 they are major health outcomes that could affect surgical recovery, and they were pre-defined by
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19 169 Statistics New Zealand based on hospital-admissions and pharmacy data [29]. Note that we did not have
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21 170 access to data on physical activity, BMI, or diet.
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24 171 **Statistical analysis**

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27 172 We analyzed time-to-death data using a frailty model that included hospital-level random effects. We
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29 173 were particularly careful to account for the hospital where the surgery was performed, because smaller
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31 174 hospitals that may not be able to provide the specialist care of a larger hospital are more likely to be in
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33 175 rural areas that are greener. We evaluated five different functional forms for the survival function
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35 176 (Weibull, exponential, log-logistic, log-normal, and gamma) and chose between them using the Akaike
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37 177 information criterion. We analyzed the number of post-operative opioid scripts using a mixed negative-
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39 178 binomial regression that included hospital-level random effects.
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43 179 A backwards-selection procedure was used for all model selection: variables were dropped from the
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45 180 analysis using progressively smaller p-value thresholds (final threshold: $p < 0.1$). Insignificant variables can
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47 181 still be confounders [30], so we systematically re-introduced dropped variables and retained them if the
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49 182 coefficients on variables of interest changed by more than 10%.

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53 183 To avoid including highly collinear combinations of variables, we estimated ordinary least squares
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55 184 versions of each model (results not shown), which allowed us to calculate variance-inflation factors for
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3 185 each independent variable. If any variable had a variance-inflation factor over two, we dropped it from
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5 186 the regression model. When choosing between two collinear variables, we included the variable with
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7 187 the lowest p-value when individually regressed against the dependent variable.
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10 188 We also conducted stratified analyses to see whether the relationship between the natural environment
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12 189 and health outcomes was the same across different strata of the sample. Analyses were conducted for
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14 190 hip and knee arthroplasty combined as well as for each outcome separately.
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18 191 **RESULTS**

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21 192 Table 1 provides descriptive statistics for our sample.
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24 193 In the frailty model, specifying the survival function using a Weibull distribution gave the best model fit.
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26 194 Being older, male, European New Zealander, or Māori (the indigenous people of New Zealand) were all
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28 195 mortality risk factors (Table 2) (The reference ethnic group was Pacific, Asian, MELAA, or other).
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30 196 Similarly, people who received more pre-surgery opioids, or had a longer hospital stay, were at greater
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32 197 risk of mortality. Six chronic conditions were risk factors as was higher neighborhood deprivation,
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34 198 although this relationship was only significant for hip arthroplasty.
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38 199 People who lived in greener neighborhoods (defined as mean post-surgical NDVI) were at lower risk of
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40 200 mortality, although this relationship was only significant in the hip-and-knee arthroplasty and hip-

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42 201 arthroplasty-only models (Table 2). To better elucidate the dose-response function linking NDVI and
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44 202 mortality, we re-estimated the hip-and-knee-arthroplasty frailty model splitting NDVI into quartiles
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47 203 (Table 3). Only the highest quartile was statistically significant, in the combined and hip-only models,
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49 204 although NDVI remained protective in the second and third quartiles. In the knee-only model, the
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51 205 second quartile of NDVI was protective although only at the 10% level. In addition, the third and fourth
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53 206 quartiles of NDVI did not show a consistent protective effect.
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3 207 Figure 1 shows the odds ratio for mean lifetime NDVI for different strata of the sample. Stratifying the
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5 208 sample resulted in some loss of significance, due to lower numbers in each stratum. Notably, the
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7 209 protective effect of NDVI was higher for men than women. The protective effect of NDVI was also
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9 210 modestly higher for people who lived in higher SES neighborhoods (NZDep 1-5) compared to lower SES
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11 211 neighborhoods (NZDep 6-10). Similarly, NDVI was somewhat more protective for people who were
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13 212 younger than average (mean age at surgery=68).
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17 213 In the opioid model (Table 4), women, European New Zealanders, and people who were prescribed
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19 214 more pre-surgery opioid prescriptions received significantly more post-surgical opioid scripts in all three
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21 215 time periods with the exception of European New Zealanders in the 24 months post-surgery model
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23 216 (Table 4). Those who received a knee arthroplasty (as opposed to a hip arthroplasty) or stayed longer in
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25 217 hospital also received more post-surgical opioids, as did people who had COPD, coronary heart disease,
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27 218 or traumatic brain injury. In contrast, older people received fewer opioid prescriptions, although the
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29 219 significance of this relationship varied across the three time periods. Separating opioids into weak and
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31 220 strong was not revealing and reduced the significance of variables of interest (data not shown). Mean
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33 221 post-surgical greenness was associated with significantly fewer post-surgical opioid prescriptions in all
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35 222 three time periods (Table 4). Living in a rural area and land cover were not significantly associated with
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37 223 the number of post-surgical opioid prescriptions or time to all-cause mortality (data not shown). In
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39 224 addition, walkability was not significantly associated with either opioid use or mortality. For example,
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41 225 the odds ratio on walkability in the 3-month post-surgical opioid model was 1.043 (95% CI: 0.966-1.127),
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43 226 and the odds ratio in the hip-only frailty model was 1.035 (95% CI: 0.971-1.104). Even when the analysis
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45 227 was restricted to only-hip or only-knee arthroplasties, the relationship between walkability and
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47 228 mortality or opioid use remained insignificant.
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3 229 In addition, consistent with the frailty model, NDVI was not significant, when the analysis was restricted
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5 230 to knee-arthroplasty (results not shown). Finally, when we split NDVI into quartiles, none were
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7 231 significant (results not shown).
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10 232 In the stratified analysis (figure 2), greenness was more protective for men than women, which is
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13 233 consistent with the frailty model.
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15 234 **DISCUSSION**

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18 235 In a cohort of people who received a total hip or knee arthroplasty at a publicly-funded hospital in New
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20 236 Zealand in 2006 or 2007, we found that residents of greener neighborhoods received fewer post-surgical
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22 237 opioid prescriptions and lived longer, with the strongest results for hip arthroplasty. Our results are
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24 238 consistent with those reported by Ulrich [10], who found that, after gall-bladder surgery, patients
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26 239 recovered faster and took fewer opioids if they were in a room with a view of a natural scene. Our
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28 240 results are also consistent with a previous study [5], which found that rapid mobilization following hip or
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30 241 knee arthroplasty was associated with better two-year survival rates. Finally, results suggests that the
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32 242 benefits of exposure to the natural environment extend beyond the immediate post-surgical period.
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37 243 Greenness was associated with lower post-surgical opioid use, and lower mortality, in people recovering
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39 244 from hip arthroplasty but not those recovering from knee arthroplasty. This may be because knee
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41 245 arthroplasty is a more difficult and painful surgery to recover from [31] (post-surgical opioid use was
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43 246 65% higher for knee-arthroplasty patients in our sample), and the protective effect of neighborhood
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45 247 greenness is insufficient to induce a clinically significant increase in post-surgical mobilization.
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49 248 There was modest evidence that younger people, and those living in less deprived neighborhoods,
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51 249 derived greater benefit from exposure to greenness. This may be because younger people are more
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53 250 physically able to engage in outdoor activity, and that greenspace in higher SES neighborhoods may be
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55 251 better maintained and more appealing because of lower crime [32].
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3 252 When we split NDVI into quartiles in the frailty model, we found that only the top quartile was
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5 253 protective at conventional significance levels. This suggests that there may be a minimum threshold
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7 254 below which greenness offers no health benefits. However, it is important to note that NDVI is a coarse
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9 255 measure of overall greenness. It does not reveal which elements of the natural environment provide the
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11 256 greatest health benefits. Identifying the most protective elements would help inform the design of
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13 257 landscapes that are not in the top quartile of NDVI, but nonetheless provide health benefits.

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17 258 The magnitude of the protective effect of neighborhood greenness is not trivial. For example, in the 3-
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19 259 months post-surgery model of opioid use, a 2-SD decrease in NDVI is roughly equivalent to the risk of
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21 260 having chronic heart disease at the time of surgery. In the hip-only frailty model, a 2-SD decrease in
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23 261 NDVI is roughly equivalent to the risk of being two years older.

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27 262 Physical activity is likely not the only mechanism linking greenness and improved post-surgical
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29 263 outcomes. For example, exposure to the natural environment can reduce short-term markers of stress
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31 264 such as heart rate, blood pressure, and salivary cortisol [33, 34]. In turn, stress is a well-documented risk
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33 265 factor for premature mortality [35] and can also trigger opioid cravings [36]. Similarly, exposure to the
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35 266 natural environment is associated with increased social connectivity [37], and social isolation can
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37 267 increase individual reactivity to opioids [38] as well as being a risk factor for premature mortality [39].
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39 268 More recently, research suggests that exposure to the natural environment may increase the microbial
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41 269 diversity of the human microbiome [40], and protect against adverse health outcomes [41] through
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43 270 improved immune function. In addition, improved immune function is associated with improved surgical
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45 271 recovery [42] and better orthopedic outcomes in elderly patients [43].

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50 272 Our study has several limitations. This is an observational study, so we were not able to establish a
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52 273 causal relationship between exposure to the natural environment, opioid use, and surgical recovery. In
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54 274 addition, our metrics of exposure to the natural environment were coarse. In particular, meshblock-level
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3 275 NDVI is an imperfect measure of a person's exposure to the natural environment. This is especially true
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5 276 in larger, rural meshblocks, where mean NDVI may not optimally represent a person's residential
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8 277 exposure to the natural environment.
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10 278 **Conclusions**

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13 279 In a large (n=14,010) cohort of participants who received a hip or knee arthroplasty at a publicly-funded
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15 280 New Zealand hospital in 2006 or 2007, we found that exposure to the natural environment was
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17 281 associated with fewer post-surgical opioid prescriptions, and increased time to all-cause mortality, in
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19 282 hip-arthroplasty patients only. Results suggest that clinicians should consider a patient's home
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21 283 environment when designing post-operative care plans. In particular, clinicians may wish to explicitly
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23 284 incorporate neighborhood greenspace. When a patient doesn't have access to greenspace, additional
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25 285 support may be warranted to encourage at-home mobilization.
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287 **TABLES**

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

Variable	HIP		KNEE	
	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

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

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

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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.

Variable	HIP AND KNEE		HIP		KNEE	
	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.

Variables	HIP AND KNEE		HIP		KNEE	
	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

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3 316 **FIGURE LEGENDS**
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5 317 **Figure 1:** Odds-ratio plot of standardized mean post-surgical NDVI for time to all-cause mortality
6 318 following hip or knee arthroplasty (number of participants=14,010, number of observations= 149,523)¹.
7 319 Low/high SES denotes participants whose lifetime NZ Deprivation Index is above/below average.
8 320 Old/young denote participants who are older/younger than the sample mean. The ethnicity reference
9 321 group is a composite of all ethnicities other than European NZ or Māori (figures 1 and 2 were created
10 322 with the user-written Stata command COEFPLOT)

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13 323 ¹ Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three
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16 326 **Figure 2:** Odds-ratio plot of standardized mean post-surgical NDVI for number of opioid prescriptions 3
17 327 months post-surgery (n=14,010)¹. For definitions and reference groups see figure 1.
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19 328 ¹ Following IDI protocols, all sample sizes have been rounded to the nearest multiple of three
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330 **Contributorship statement:** GHD designed the study, conducted the analysis, and wrote the majority of
331 the manuscript. DG created the exposure metrics and edited the manuscript. JD wrote parts of the
332 manuscript and edited multiple drafts.
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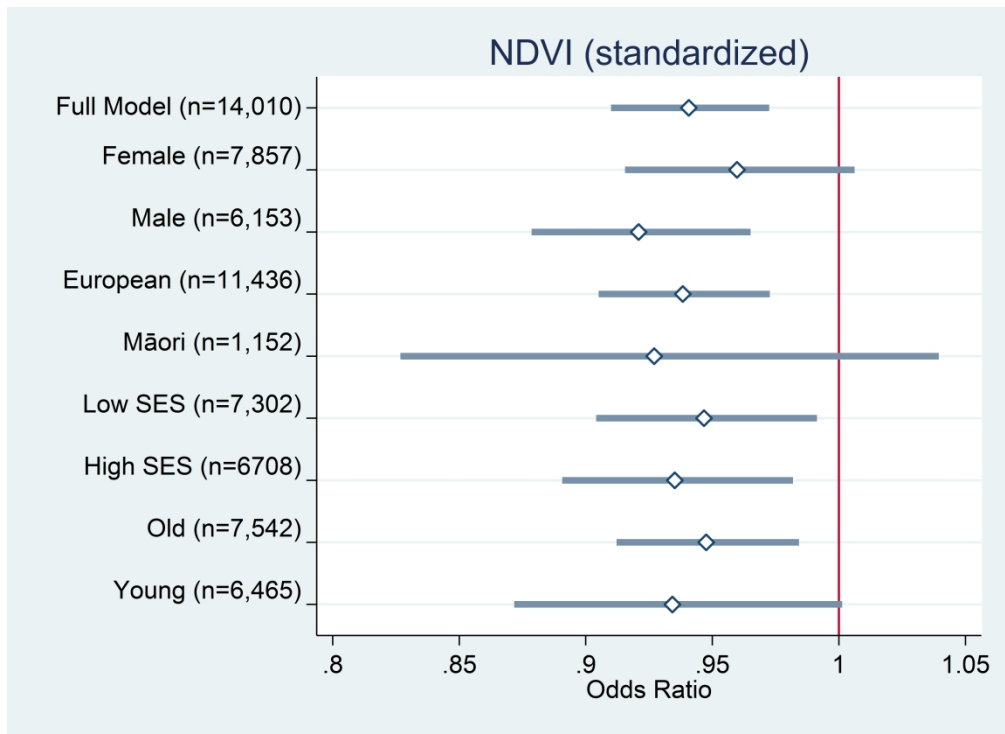
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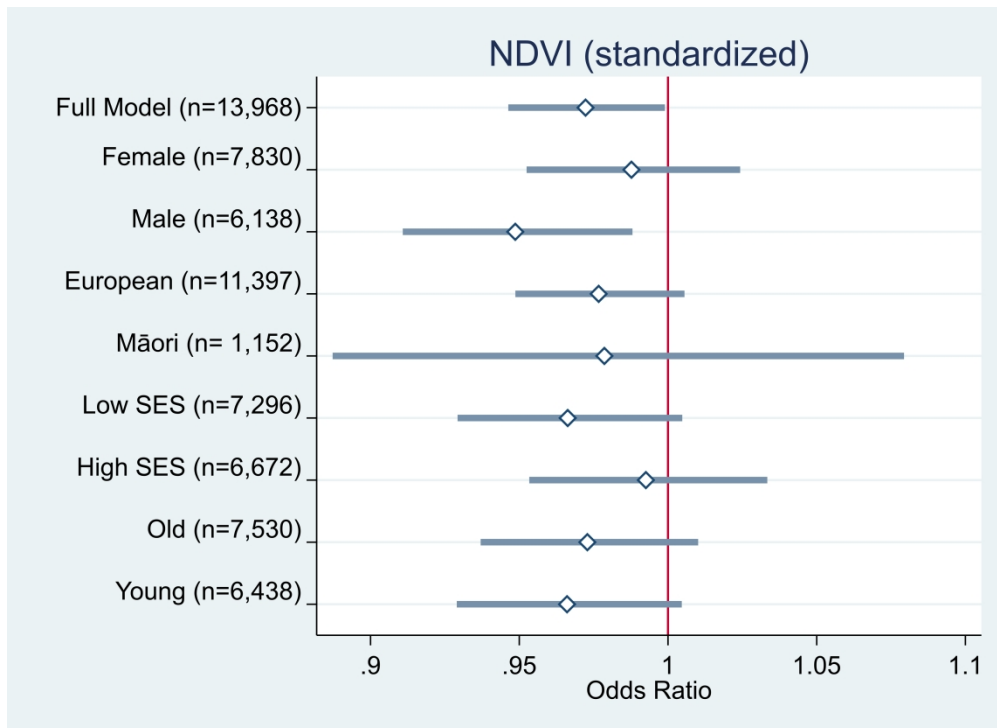
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STROBE Statement—checklist of items that should be included in reports of observational studies

	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) <i>Cohort study</i> —Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up <i>Case-control study</i> —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 <i>Cross-sectional study</i> —Give the eligibility criteria, and the sources and methods of selection of participants	5-6
		(b) <i>Cohort study</i> —For matched studies, give matching criteria and number of exposed and unexposed <i>Case-control study</i> —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) <i>Cohort study</i> —If applicable, explain how loss to follow-up was addressed <i>Case-control study</i> —If applicable, explain how matching of cases and controls was addressed <i>Cross-sectional study</i> —If applicable, describe analytical methods taking account of sampling strategy	N/A

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(e) Describe any sensitivity analyses

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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 (b) Give reasons for non-participation at each stage (c) Consider use of a flow diagram	14-16
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) <i>Cohort study</i> —Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	<i>Cohort study</i> —Report numbers of outcome events or summary measures over time	6
		<i>Case-control study</i> —Report numbers in each exposure category, or summary measures of exposure	
		<i>Cross-sectional study</i> —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.