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Vaccination against COVID-19 reduced the mortality risk of COVID-positive hip fracture patients to baseline levels

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1 **Vaccination against COVID-19 reduced the mortality risk of COVID-positive hip fracture**
2 **patients to baseline levels: The nationwide data-linked IMPACT Protect study**

3

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39 **MINI ABSTRACT**

40 This nationwide study used data-linked records to assess the effect of COVID-19 vaccination in hip fracture
41 patients. Vaccination was associated with a lower risk of contracting COVID-19 and, among COVID-positive
42 patients, it reduced the mortality risk to that of COVID-negative patients. This provides essential data for future
43 communicable disease outbreaks.

44

45 **ABSTRACT**

46

47 *Purpose*

48 COVID-19 confers a three-fold increased mortality risk among hip fracture patients. The aims were to
49 investigate whether vaccination was associated with: i) lower mortality risk, and ii) lower likelihood of
50 contracting COVID-19 within 30 days of fracture.

51

52 *Methods*

53 This nationwide cohort study included all patients aged >50 years with a hip fracture between 01/03/20-
54 31/12/21. Data from the Scottish Hip Fracture Audit were collected and included: demographics, injury and
55 management variables, discharge destination, and 30-day mortality status. These variables were linked to
56 population-level records of COVID-19 vaccination and testing.

57

58 *Results*

59 There were 13,345 patients with a median age of 82.0 years (IQR 74.0-88.0), and 9329/13345 (69.9%) were
60 female. Of 3022/13345 (22.6%) patients diagnosed with COVID-19, 606/13345 (4.5%) were COVID-positive
61 within 30 days of fracture. Multivariable logistic regression demonstrated that vaccinated patients were less
62 likely to be COVID-positive (odds ratio (OR) 0.41, 95% confidence interval (CI) 0.34-0.48, $p<0.001$) than
63 unvaccinated patients. 30-day mortality rate was higher for COVID-positive than COVID-negative patients
64 (15.8% vs 7.9%, $p<0.001$). Controlling for confounders (age, sex, comorbidity, deprivation, pre-fracture
65 residence), unvaccinated patients with COVID-19 had a greater mortality risk than COVID-negative patients
66 (OR 2.77, CI 2.12-3.62, $p<0.001$), but vaccinated COVID-19-positive patients were not at increased risk (OR
67 0.93, CI 0.53-1.60, $p=0.783$).

68

69 *Conclusion*

70 Vaccination was associated with lower COVID-19 infection risk. Vaccinated COVID-positive patients had a
71 similar mortality risk to COVID-negative patients, suggesting a reduced severity of infection. This study
72 demonstrates the efficacy of vaccination in this vulnerable patient group, and presents data that will be valid in
73 the management of future outbreaks.

74

75 **KEYWORDS**

76 Hip fracture, COVID-19, vaccination, mortality, frailty

77

78 **INTRODUCTION**

79 Hip fracture patients are vulnerable to contracting and dying from COVID-19.[1–3] Unvaccinated patients that
80 have COVID-19 around the time of an acute hip fracture admission have an approximate three-fold increased
81 mortality risk compared to COVID-negative patients, are more likely to have longer hospital stays, higher post-
82 discharge care needs, increased frailty, and more frequent readmissions to hospital.[4–6]

83 The prevalence of COVID-19 among hip fracture patients has fluctuated in line with background
84 prevalence but this group of patients with high levels of frailty is likely to be at increased risk of transmission,
85 particularly in inpatient or residential care settings.[7] A systematic review of COVID-19 in hip fracture patients
86 conducted in the early stages of the pandemic reported a prevalence of 15% and demonstrated a 30-day mortality
87 rate of 35% among COVID-positive hip fracture patients.[4] A longer term study found that half of all hip
88 fracture patients affected by COVID-19 had died within a year of injury, with COVID-19 being a contributing
89 factor in a quarter of all deaths.[8] COVID-19 in the context of an acute hip fracture has been shown to be
90 associated with increased morbidity and a greater increase in frailty than those not affected by COVID-19.[6]

91 Strategies for mitigating the impact of COVID-19 on hip fracture patients and services have been
92 described, and include pre-emptive testing, isolation of high-risk patients, operating separate circuits in periods
93 of high disease prevalence, and ensuring adequate contact-tracing between inpatient and community-based
94 residential care settings.[9–12] The COVID-19 pandemic prompted the development of a rapid population-wide
95 vaccination programme and evidence suggests that this is effective in reducing transmission, morbidity, and
96 mortality from COVID-19 in the general population, and protection against more severe infections may be
97 particularly effective in frail or elderly groups.[13–16] In hip fracture patients specifically there is early evidence
98 to suggest that vaccination against COVID-19 may be associated with improved outcomes, but no population-
99 level studies have reported on the effects of vaccination against COVID-19 specifically in hip fracture
100 patients.[17–19]

101 The aims of this study were to investigate whether vaccination against COVID-19 was associated with:
102 (i) a lower risk of death within 30 days following hip fracture among COVID-positive patients, and ii) a lower
103 likelihood of having COVID-19 within 30 days of a hip fracture.

104

105 METHODS*106 Study design*

107 This nationwide cohort study collected and collated data from the Scottish Hip Fracture Audit (SHFA) and from
108 two COVID-specific nationwide healthcare databases.[20] It examined patients admitted with a hip fracture in
109 Scotland over a 21-month period between 1st March 2020 and 31st December 2021. The study was conducted
110 as part of the International Multicentre Project Auditing COVID-19 in Trauma & Orthopaedics (IMPACT),
111 which is a collaborative research group established in 2020 and has delivered a portfolio of original research
112 and audit studies into the effects of COVID-19 on hip fracture patients and the wider orthopaedic population.[21,
113 22]

114

115 Study population

116 The study included patients aged over 50 years that were admitted with an acute hip fracture between 01/03/20-
117 31/12/21. A hip fracture was defined as a fracture of the intracapsular or extracapsular portion of the proximal
118 femur up to the distal portion of the subtrochanteric region (defined as five centimetres distal to the lesser
119 trochanter). Patients were identified from the live dataset of the SHFA, which is a national registry administered
120 by Public Health Scotland (PHS).

121

122 Data collection & linkage

123 Patient-level data were collected prospectively as part of the routine SHFA activity by specialist audit
124 coordinators at each of the 17 hospitals that manage acute hip fractures and submitted to PHS where they were
125 collated into the central SHFA live dataset. Data pertaining to hip fracture patients admitted during the study
126 period were extracted, and variables were: a universal identifier (community health index [CHI]); demographics
127 (age, sex, pre-fracture residence level, postcode, American Society of Anesthesiologists (ASA) Physical
128 Classification System Grade [a five-level classification of current physical status based on the existence and
129 severity of systemic disease]); injury and treatment process factors (date of injury, date of surgery, length of
130 stay in acute hospital (acute LOS), total length of stay as an inpatient (total LOS)), and outcome measures
131 (discharge destination following the acute hospital stay, mortality status at 30 days post-fracture).[23] Postcode
132 was used to assign a quintile on the Scottish Index of Multiple Deprivation (SIMD), with patients in quintile 1
133 being most deprived, and those in quintile 5 being least deprived.[24] To account for patients that suffered more
134 than one hip fracture during the study period, SHFA episodes were categorised using a four-level ‘fracture
135 sequence’ variable: single fracture (for patients experiencing only one hip fracture during the study period); first
136 fracture (the first hip fracture in patients that had more than one in the study period); second fracture, and third
137 fracture.

138 The unique community health index (CHI) number of each included patient was used to identify and
139 extract relevant data from two national COVID-specific databases administered by PHS: the Electronic
140 Communication of Surveillance in Scotland (ECOSS) system, a component of the national Infection
141 Intelligence Platform (IIP) which collates all positive microbiology laboratory specimen results, and the Turas

142 Vaccination Management (TVM) tool, which is the web-based application used for point-of-care recording of
143 COVID-19 vaccination information in Scotland.[25, 26] Variables extracted from ECOSS were: CHI, postcode,
144 and date and time of all positive SARS-CoV-2 reverse transcription polymerase chain reaction (RT-PCR) swabs
145 between (18/03/20-03/07/22). Variables extracted from TVM were: CHI and the date and product name of any
146 vaccine doses administered (between 08/12/20-07/04/22). Patients were considered vaccinated if they had
147 received a vaccine dose prior to the acute hip fracture episode.

148 The three datasets were collated into a single dataset using the Power Query function, utilising CHI as
149 the common identifier to facilitate linkage of patient-level entries (Microsoft Excel, Microsoft Corporation,
150 Redmond, WA, USA). The common dataset was cleaned to remove duplicate records, those with missing
151 critical data, cases involving non-Scottish domiciled patients (where vaccination, microbiology, and follow-up
152 data may not be complete), and to ensure appropriate homogeneity of coding.

153

154 *Statistical methods*

155 Statistical analysis for this study was performed using RStudio (Integrated Development for R. Rstudio, PBC,
156 Boston, MA, USA) using the following packages: dplyr; tableone; mice, and finalfit.[27–30] Categorical
157 variables were assessed using Chi-square tests and continuous variables were assessed for inter-group
158 differences using independent samples t-tests for normally distributed data, and Mann-Whitney U tests for non-
159 normally distributed data. Linear and logistic regression analyses were used when continuous or discrete outputs
160 were required, respectively, and factors that demonstrated an association ($p < 0.1$) on unadjusted analysis were
161 included in multivariable regression models. A p-value of < 0.05 was considered statistically significant. Missing
162 data were assessed objectively for patterns of missingness.

163

164 *Missing data*

165 Missing data were analysed using the *finalfit* data science package, and multiple imputation by chained
166 equations was carried out using the *mice* package.[31] Analysis of missing data demonstrated that ASA Grade
167 was missing for 340/13345 (2.5%) and SIMD for 303/13345 (2.3%). ASA Grade is a core variable of the SHFA,
168 however an assessment of availability conducted as part of a previous study revealed that it is systematically
169 omitted from two participating centres and this accounted for 75% of missing values in this field. It was
170 therefore considered likely that the majority of missing ASA Grade values are missing completely at random
171 (MCAR), although some data may be missing due to patients not being assessed by an anaesthetist on account
172 of being unfit for surgery, in which case these data would be missing not at random (MNAR). SIMD was
173 unavailable for patients that did not have a complete postcode documented. Following analysis of the dataset it
174 is likely that this is a result of random omission from the data collection process, and the missing SIMD values
175 could be considered missing completely at random (MCAR). Missing data were modelled using multiple
176 imputation by chained equation (MICE), and the output of logistic regression analyses performed using imputed
177 data were presented alongside analyses performed with missing data.

178

179 *Ethical approval*

180 The study protocol was considered and approved by the SHFA Research Group on behalf of PHS, which is the
181 owner and controller of SHFA data. Access to the SHFA, ECOSS, and TVM data were provided by an
182 authorised PHS analyst to one author (AH) who is a PHS-affiliated research fellow. Data were handled in
183 accordance with UK Caldicott principles.

184 **RESULTS**185 *Patient characteristics*

186 There were 13,345 patients that were admitted with an acute hip fracture in Scotland between 01/03/20-
187 31/12/21. The median age was 82.0 years (IQR 74.0-88.0) and 9329/13345 (69.9%) were female. There were
188 6725/13345 (50.4%) patients that had been vaccinated before sustaining their hip fracture, and 6620/13345
189 (49.6%) patients were unvaccinated at the time of injury. Compared to the vaccinated group, the unvaccinated
190 group was slightly younger (median age 81.0 years [IQR 73.0-87.0] versus 83.0 years [IQR 75.0-88.0],
191 $p<0.001$), had a lower level of co-morbidity (more likely to have a lower ASA Grade), and had a slightly lower
192 level of socioeconomic deprivation (mean SIMD rank 3.27 (SD 1.39) versus 3.02 (SD 1.40), $p<0.001$). (Table
193 1) Patient cohort characteristics are described according to 30-day mortality status in Table 2, and according to
194 COVID-19 status and vaccination status in Table 3.

195

196 *Effect of vaccination on prevalence of COVID-19*

197 There were 3022/13345 (22.6%) patients diagnosed with COVID-19 at any time during the study period, and
198 606/13345 (4.5%) patients that were diagnosed with COVID-19 within 30 days of the fracture. The rate of
199 COVID-19 among unvaccinated patients was higher than among vaccinated patients (420/6620 [6.3%] versus
200 186/6725 [2.8%]).

201 Unadjusted logistic regression analysis demonstrated associations between an increased likelihood of
202 being COVID-positive and: older age (odds ratio (OR) 1.02, 1.01-1.03, $p<0.001$, for each increasing year); ASA
203 Grade 3 or 4 (OR 1.61, 1.28-2.04, $p<0.001$, and OR 1.52, 1.14-2.04, $p=0.005$, respectively compared to the
204 reference ASA Grade 2); pre-fracture residence in residential care (OR 1.29, 1.04-1.58, $p=0.017$), subacute
205 hospital (OR 1.86, 1.16-2.83, $p=0.006$), or acute hospital (OR 1.96, 1.37-2.72, $p<0.001$), and being unvaccinated
206 (OR 2.38, 2.00-2.85, $p<0.001$). (Table 4) When controlling for confounding factors (age, sex, ASA Grade,
207 socioeconomic deprivation, pre-fracture residence, fracture sequence), multivariable logistic regression
208 demonstrated that unvaccinated patients were more than twice as likely to be COVID-positive within 30 days
209 of a hip fracture (OR 2.47, 95% confidence interval (CI) 2.06-2.95, $p<0.001$) than vaccinated patients. (Table
210 4)

211

212 *Effect of vaccination on mortality risk*

213 There were 1108/13345 (8.3%) that died within 30 days of fracture. The 30-day mortality rate for COVID-
214 positive patients was twice as high as for COVID-negative patients (15.8% vs 7.9%, $p<0.001$), and when
215 considering only unvaccinated COVID-positive the 30-day mortality rate was 19.3%, whereas for vaccinated
216 COVID-positive patients it was 8.1% ($p<0.001$).

217 Unadjusted logistic regression analysis demonstrated associations between an increased 30-day
218 mortality risk and: older age (OR 1.04, 1.04-1.05, $p<0.001$, for each increasing year); male sex (OR 1.74, 1.53-
219 1.97, $p<0.001$); ASA Grade 3 (OR 2.57, 2.02-3.32, $p<0.001$), Grade 4 (OR 6.95, 5.39-9.08, $p<0.001$), or Grade
220 5 (OR 25.22, 17.72-36.05, $p<0.001$); pre-fracture residence in residential care (OR 2.65, 2.30-3.04, $p<0.001$),

221 subacute hospital (OR 2.19, 1.52-3.06, $p<0.001$), or acute hospital (OR 2.88, 2.22-3.68, $p<0.001$), and being
222 unvaccinated (OR 2.38, 2.00-2.85, $p<0.001$) (Table 5). When controlling for confounding factors, unvaccinated
223 COVID-positive patients had an almost three-fold greater mortality risk than COVID-negative patients (OR
224 2.77, CI 2.12-3.62, $p<0.001$), however the mortality risk of vaccinated COVID-positive patients was no higher
225 than that of COVID-negative patients (OR 0.93, CI 0.53-1.60, $p=0.783$). (Table 5)

226

227 *Sub-group analysis including patients on a time-dependent basis*

228 To control for the potential effects of hip fracture service variation over the course of the pandemic, all analyses
229 were repeated excluding patients admitted for a hip fracture within the first six months of the study period
230 (01/03/20-31/08/20). The patient characteristics and rate of COVID-19 were comparable between this sub-
231 group and the total study group (Supplementary Table 1). The main study findings were also replicated in this
232 sub-group. When controlling for confounders, unvaccinated patients had a higher likelihood of being diagnosed
233 with COVID-19 within 30 days of hip fracture than vaccinated patients (OR 3.68, CI 3.04-4.45, $p<0.001$;
234 Supplementary Table 2), unvaccinated COVID-positive patients were more likely to die than vaccinated
235 COVID-negative patients (OR 2.13, CI 1.52-2.98, $p<0.001$), and the mortality risk of vaccinated COVID-
236 positive patients was no higher than that of COVID-negative patients (OR 0.94, CI 0.54-1.62, $p=0.817$;
237 Supplementary Table 3).

238 **DISCUSSION**

239 This nationwide population-level data-linked cohort study assessed the association between vaccination on
240 COVID-19 prevalence and mortality risk among hip fracture patients. Patients that were vaccinated prior to
241 sustaining a hip fracture had a lower risk of being diagnosed with COVID-19 within 30 days of the injury.
242 Among patients that had COVID-19 within 30 days of fracture, unvaccinated patients had a three-fold increased
243 30-day mortality risk compared to COVID-negative patients, but COVID-19 affecting vaccinated patients was
244 not associated with an increased mortality risk. These findings support the hypothesis that vaccination is
245 effective at reducing the likelihood of both contracting and dying from COVID-19 among patients that sustain
246 a hip fracture. This study provides essential data on the effectiveness of such a vaccination programme for
247 future pandemics and highlights the importance of such programmes in this highly vulnerable patient group.

248 The study found an overall prevalence of COVID-19 of 22%, which is consistent with previous studies.
249 The 5% rate of COVID-19 diagnosed within 30 days of fracture reported by the current study is lower than in
250 the literature.[4] This could be due to this study considering only COVID-19 cases that were confirmed with
251 SARS-CoV-2 RT-PCR testing, whereas other studies had broader inclusion criteria, particularly those
252 conducted early in the pandemic (when background prevalence was highest), and included COVID-19
253 diagnoses based on radiological evidence or clinical suspicion.[12] Furthermore there is a recognised false-
254 negative rate associated with SARS-CoV-2 RT-PCR testing that varies according to the timing of the test in
255 relation to the course of the infection, the technique used to obtain the swab material, and other factors.[32, 33]
256 The three-fold increased mortality risk associated with COVID-19 in unvaccinated patients is consistent with
257 the magnitude of increase reported by studies conducted prior to the widespread availability of COVID-19
258 vaccines, and the reduction in mortality risk associated with vaccination reflects evidence of vaccination being
259 effective in the non-hip fracture population.[2, 9, 13, 16, 17, 34]

260 Prior to the COVID-19 pandemic the 30-day mortality rate of hip fracture patients in Scotland was
261 around 7.5%, with around 25% of patients dying within a year of the fracture.[35] The systematic review from
262 before the widespread availability of a vaccine against COVID-19 demonstrated a 30-day mortality rate of 35%
263 among COVID-positive hip fracture patients, and COVID-19 has been shown to be independently associated
264 with a three-fold increased 30-day mortality risk when controlling for confounding factors.[4] This is consistent
265 with the findings of the current study of an almost three-fold increased risk of death within 30 days for
266 unvaccinated COVID-positive patients. The majority of COVID-related deaths in hip fracture patients occur
267 within a month of diagnosis of COVID-19.[8] The current study found that vaccinated COVID-positive patients
268 were no more likely to be deceased within 30 days of fracture than COVID-negative patients, which suggests
269 that the lethal effects of COVID-19 in this frail group may be significantly diminished by vaccination, with
270 mortality risk being reduced to near pre-pandemic levels.

271 Previous studies have demonstrated that vaccination against COVID-19 may be associated with lower
272 rates of complications, admissions to intensive care, and overall mortality among hip fracture patients. [18, 19]
273 The findings of this study are important as they are the first to assess the protective effects of vaccination against
274 COVID-19 in hip fracture patients on a nationwide basis and appear to support the hypotheses that vaccination

275 against COVID-19 was effective at reducing the risk of this vulnerable patient group contracting COVID-19,
276 as well as dying within a month of an acute hip fracture episode complicated by COVID-19. Although this study
277 was not designed to assess for increased morbidity directly associated with vaccine administration, there is
278 overwhelming evidence to support safety and widespread use in the general and frail population.

279 There are several strengths to this study. The use of population-level health records provided a large
280 study sample that is generalisable to the whole hip fracture population. Furthermore, it is likely that these
281 findings may be generalisable to hip fracture patients in similar healthcare systems, as well as to the wider frail
282 population. This methodology is robust as data were collected prospectively at source, by trained clinical
283 auditors (SHFA data), technicians (ECOSS data), and clinicians (TVM data) and underwent validation and
284 collation by experience PHS analysts. Furthermore, the use of PHS-administered national health records ensured
285 maximal data coverage and validity. The SHFA is known to report >99% of hip fracture admissions in
286 Scotland.[35, 36] The ECOSS system is Scotland's nationwide infection surveillance system and draws directly
287 from live health records relating to any positive laboratory microbiological finding, and the TVM was
288 established as a bespoke system to record and monitor the administration of COVID-19 vaccinations in
289 Scotland. This study focused on COVID-19 within 30 days of fracture because it is reported that, when adjusting
290 for confounding factors, only a COVID-19 diagnosis made during the acute hip fracture period is associated
291 with an increased mortality risk – the so-called 'double-hit' effect in which patients are more vulnerable to
292 contracting and dying from COVID-19 during a period of acute illness and emergency surgery.[6] Mortality
293 status at 30 days following fracture was the primary outcome measure because it is collected using robust
294 methods by the SHFA local audit coordinators, and because the majority of deaths in COVID-positive patients
295 occur within the first month. Finally, hip fracture services in Scotland are standardised and delivered according
296 to the Scottish Standards of Care for Hip Fracture Patients (SSCHFP), which provides a consistent level of care
297 quality against which to measure outcomes.[37, 38]

298 There are several limitations to this study. The frequency of COVID-19 fluctuated throughout the study
299 period and public health data regarding disease prevalence relates to the general population, making it
300 challenging to interpret findings relating to the direct effects of vaccination on COVID-19 in this group. Further,
301 the vaccination programme prioritised the oldest and most vulnerable patients before being rolled out to younger
302 and less vulnerable groups. The impact of both these limitations may have been mitigated by comparing disease
303 prevalence between vaccinated and unvaccinated hip fracture patients, and by using multivariable logistic
304 regression analysis to assess the independent effect of vaccination status on the risk of being COVID-positive
305 within 30 days of injury. Secondly, the method of vaccination involved the use of different vaccine products
306 and a multi-dose strategy, and each product has been shown to confer different levels of protection against
307 contracting, transmitting, and dying from COVID-19. There were 12 distinct vaccine regimens administered to
308 patients in the current study, based around three products (Oxford-AstraZenica, Pfizer BioNTech, Moderna),
309 with patients receiving one, two or three doses. The study sample was insufficient to investigate the efficacy of
310 different vaccine regimens and control for confounding factors. Thirdly, the ease and consistency of access to
311 RT-PCR testing was limited in the early stages of the pandemic, and routine testing of all patients was not

312 introduced until around the height of the first wave of COVID-19 in the UK (and at different times according
313 to local protocols). Fourthly, it is a limitation of population-level studies of this scale that patient-level data
314 regarding specific comorbidities and medications are not routinely and/or robustly collected. In this study we
315 included all patient characteristics available in the national datasets that could influence the study findings,
316 including: age; sex; American Society of Anesthesiologists (ASA) grade (classifying pre-surgery medical
317 comorbidities); pre-fracture residence (a surrogate marker for performance status), and socioeconomic
318 deprivation (known to be associated with medical comorbidity and post-injury outcomes including mortality
319 and healthcare needs).[15, 23, 24] We did not have direct measurements of frailty, dementia, or delirium status,
320 which is a limitation common across national hip fracture registries, though controlling for ASA grade and pre-
321 fracture place of residence to some extent indirectly adjusts for these variables.[6, 15, 39–41] It was beyond the
322 scope of the study to collect and analyse patient-level data relating to pharmacological interventions for the
323 management of active COVID-19. There is a lack of robust evidence demonstrating a clear clinical benefit of
324 antiviral therapeutic regimens in the management of active COVID-19 in the geriatric orthopaedic population,
325 and the use of these therapies would have been highly uncommon among hip fracture patients in Scotland, hence
326 this was considered a minor limitation.[42]

327 A proportion of positive RT-PCR results will be false positives, representing a positive result despite
328 the absence of SARS-CoV-2 infection.[43] However, although the operational rate of false positive SARS-
329 CoV-2 RT-PCR tests is unknown, it is estimated to be <1% and is much smaller than the estimated false negative
330 rate. This ranged from 100% to 67% over the first four days of infection (the pre-symptomatic phase), is around
331 20% for the next four days (the symptomatic phase), and then increases steadily to around 66% after three weeks
332 of infection.[32, 33] These limitations in testing for SARS-CoV-2 infection means that the prevalence of
333 COVID-19, as well as the mortality rate of COVID-positive patients, is potentially underestimated by the
334 current study. It is therefore likely that the protective effects of vaccination against infection and mortality risk
335 may be greater than observed. Further work will investigate the effects of vaccination on broader outcome
336 measures in the hip fracture population including frailty, readmission to acute services, and post-discharge care
337 needs.

338

339

340 **CONCLUSION**

341 Vaccination against COVID-19 was independently associated with a lower risk of contracting COVID-19
342 within 30 days of a hip fracture. Among patients that had COVID-19 within 30 days of fracture, unvaccinated
343 patients had a three-fold increased 30-day mortality risk compared to COVID-negative patients, but COVID-
344 19 affecting vaccinated patients did not confer any increased mortality risk. The findings support the hypothesis
345 that vaccination was effective in reducing the likelihood of both contracting and dying from COVID-19 among
346 hip fracture patients, reducing the mortality risk back to near pre-pandemic levels. This provides a unique
347 perspective on the management of COVID-19, and presents data that will be valid in the management of future
348 outbreaks.

349

350

351 **Statements and Declarations:**

352 Andrew Hall, Nick Clement, Alasdair MacLulich, Tim White, and Andrew Duckworth declare that they have
353 no conflict of interest.

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477

478 TABLES

479 **Table 1.** Patient characteristics according to vaccination status.

		Vaccination Status		<i>p</i> -value*
		<i>Vaccinated</i> n= 6725	<i>Unvaccinated</i> n= 6620	
Age [median (IQR)]		83.0 [75.0, 88.0]	81.0 [73.0, 87.0]	<0.001+
Sex (%)				
	<i>Female</i>	4750 (70.6)	4579 (69.2)	0.068
	<i>Male</i>	1975 (29.4)	2041 (30.8)	
ASA Grade (%)				
	2	1352 (20.6)	1469 (22.8)	0.001
	1	94 (1.4)	116 (1.8)	
	3	3941 (60.1)	3785 (58.7)	
	4	1071 (16.3)	957 (14.8)	
	5	98 (1.5)	122 (1.9)	
SIMD Rank [mean (SD)]		3.02 (1.40)	3.27 (1.39)	<0.001
Pre-fracture Residence (%)				
	<i>Home</i>	5085 (75.6)	5103 (77.1)	0.086
	<i>Residential Care</i>	1223 (18.2)	1097 (16.6)	
	<i>Subacute</i>			
	<i>Hospital</i>	159 (2.4)	140 (2.1)	
	<i>Acute Hospital</i>	242 (3.6)	262 (4.0)	
	<i>Missing</i>	16 (0.2)	18 (0.3)	
Acute LOS [median (IQR)]		11.0 [8.0, 17.0]	10.0 [7.0, 16.0]	<0.001+
Total LOS [median (IQR)]		18.0 [9.0, 40.0]	16.0 [9.0, 36.0]	<0.001+
Discharge Destination (%)				
	<i>Home</i>	2505 (37.3)	2698 (40.8)	<0.001
	<i>Residential Care</i>	1045 (15.6)	958 (14.5)	
	<i>Subacute</i>			
	<i>Hospital</i>	2514 (37.4)	2295 (34.7)	
	<i>Acute Hospital</i>	279 (4.2)	293 (4.4)	
	<i>Deceased</i>	370 (5.5)	364 (5.5)	
Fracture Sequence (%)				
	<i>Single fracture</i>	6420 (95.5)	6332 (95.6)	<0.001
	<i>First fracture</i>	104 (1.5)	192 (2.9)	
	<i>Second fracture</i>	201 (3.0)	95 (1.4)	
	<i>Third fracture</i>	0 (0.0)	1 (0.0)	
COVID-19 Status (%)				
	<i>Negative</i>	6539 (97.2)	6200 (93.7)	<0.001
	<i>Positive within 30d</i>	186 (2.8)	420 (6.3)	
Vaccination Doses (%)				
	<i>Unvaccinated</i>	0 (0.0)	6620 (100.0)	<0.001
	<i>First dose</i>	1397 (20.8)	0 (0.0)	

30-day Mortality Status (%)	<i>Second dose</i>	5328 (79.2)	0 (0.0)	
	<i>Alive</i>	6183 (91.9)	6054 (91.5)	0.320
	<i>Deceased</i>	542 (8.1)	566 (8.5)	

480

481 IQR = interquartile range; ASA = American Society of Anesthesiologists; SIMD = Scottish Index of Multiple
 482 Deprivation; SD = standard deviation; LOS = length of stay; d = days

483 *Chi-square test for categorical variables with a normal distribution, independent pairs t-test for continuous
 484 variables, Mann-Whitney U test for continuous variables with a non-normal distribution (denoted with †)

485 **Table 2.** Patient characteristics according to mortality status at 30 days post-fracture.

	30-day Mortality Status		<i>p</i> -value*
	<i>Alive</i> <i>n</i> = 12237	<i>Deceased</i> <i>n</i> = 1108	
Age [median (IQR)]	82.0 (74.0-87.0)	85.0 (79.0-90.0)	<0.001 ⁺
Sex (%)			
<i>Female</i>	8682 (70.9)	647 (58.4)	<0.001
<i>Male</i>	3555 (29.1)	461 (41.6)	
ASA Grade (%)			
2	2747 (22.9)	74 (7.5)	<0.001
1	204 (1.7)	6 (0.6)	
3	7226 (60.1)	500 (50.6)	
4	1708 (14.2)	320 (32.4)	
5	131 (1.1)	89 (9.0)	
SIMD Rank [mean (SD)]	3.1 (1.4)	3.2 (1.4)	0.531
Pre-fracture Residence (%)			
<i>Home</i>	9552 (78.1)	636 (57.4)	<0.001
<i>Residential care</i>	1972 (16.1)	348 (31.4)	
<i>Subacute hospital</i>	261 (2.1)	38 (3.4)	
<i>Acute hospital</i>	423 (3.5)	81 (7.3)	
<i>Missing</i>	29 (0.2)	5 (0.5)	
Acute LOS [median (IQR)]	11.0 (8.0-17.0)	8.0 (5.0-13.0)	<0.001 ⁺
Total LOS [median (IQR)]	18.0 (9.0-41.0)	10.0 (6.0-18.0)	<0.001 ⁺
Discharge Destination (%)			
<i>Home</i>	5184 (42.4)	43 (3.9)	<0.001
<i>Residential care</i>	1825 (14.9)	178 (16.1)	
<i>Subacute hospital</i>	4658 (38.1)	151 (13.6)	
<i>Acute hospital</i>	490 (4.0)	82 (7.4)	
<i>Deceased</i>	80 (0.7)	654 (59.0)	
Fracture Sequence (%)			
<i>Single fracture</i>	11668 (95.4)	1084 (97.8)	<0.001
<i>First fracture</i>	293 (2.4)	3 (0.3)	
<i>Second fracture</i>	275 (2.2)	21 (1.9)	
<i>Third fracture</i>	1 (0.0)	0 (0.0)	

COVID-19 Status (%)				
	<i>Negative</i>	9381 (76.7)	942 (85.0)	<0.001
	<i>Positive within 30d</i>	510 (4.2)	96 (8.7)	
	<i>Positive outwith 30d</i>	2346 (19.2)	70 (6.3)	
Vaccination Status (%)				
	<i>Unvaccinated</i>	6054 (49.5)	566 (51.1)	0.273
	<i>Vaccinated</i>	6183 (50.5)	542 (48.9)	

486

487 IQR = interquartile range; ASA = American Society of Anesthesiologists; SIMD = Scottish Index of Multiple
 488 Deprivation; SD = standard deviation; LOS = length of stay; d = days

489 *Chi-square test for categorical variables with a normal distribution, independent pairs t-test for continuous
 490 variables, Mann-Whitney U test for continuous variables with a non-normal distribution (denoted with ⁺)

491 **Table 3.** Patient characteristics according to COVID-19 and vaccination status.

		COVID-19 Status (Vaccination Status)			<i>p</i> -value*
		<i>Negative</i> <i>n</i> = 12739	<i>Positive (Vaccinated)</i> <i>n</i> = 186	<i>Positive (Unvaccinated)</i> <i>n</i> = 420	
Age [median (IQR)]		82.0 [74.0, 88.0]	85.00 [79.0, 89.0]	83.0 [77.7, 88.0]	<0.001⁺
Sex (%)					
	<i>Female</i>	8909 (69.9)	135 (72.6)	285 (67.9)	0.478
	<i>Male</i>	3830 (30.1)	51 (27.4)	135 (32.1)	
ASA Grade (%)					
	2	2730 (22.0)	27 (14.8)	64 (15.5)	0.004
	1	206 (1.7)	1 (0.5)	3 (0.7)	
	3	7332 (59.1)	126 (69.2)	268 (65.0)	
	4	1930 (15.6)	27 (14.8)	71 (17.2)	
	5	213 (1.7)	1 (0.5)	6 (1.5)	
SIMD Rank [mean (SD)]		3.14 (1.40)	2.92 (1.47)	3.33 (1.40)	0.003
Pre-fracture Residence (%)					
	<i>Home</i>	9770 (76.7)	113 (60.8)	305 (72.6)	<0.001
	<i>Residential Care</i>	2199 (17.3)	45 (24.2)	76 (18.1)	
	<i>Subacute Hospital</i>	277 (2.2)	12 (6.5)	10 (2.4)	
	<i>Acute Hospital</i>	465 (3.7)	15 (8.1)	24 (5.7)	
	<i>Missing</i>	28 (0.2)	1 (0.5)	5 (1.2)	
Acute LOS [median (IQR)]		10.0 [7.0, 16.0]	13.0 [9.0, 24.0]	14.0 [8.0, 26.0]	<0.001⁺
Total LOS [median (IQR)]		16.0 [9.0, 37.0]	27.5 [13.2, 56.2]	30.0 [18.0, 53.0]	<0.001⁺
Discharge Destination (%)					
	<i>Home</i>	5063 (39.8)	38 (20.7)	102 (24.3)	<0.001
	<i>Residential Care</i>	1920 (15.1)	36 (19.6)	47 (11.2)	
	<i>Subacute Hospital</i>	4592 (36.1)	67 (36.4)	150 (35.8)	
	<i>Acute Hospital</i>	478 (3.8)	29 (15.8)	65 (15.5)	

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	<i>Deceased</i>	665 (5.2)	14 (7.6)	55 (13.1)	
Fracture Sequence (%)					
	<i>Single fracture</i>	12183 (95.6)	175 (94.1)	394 (93.8)	0.228
	<i>First fracture</i>	278 (2.2)	3 (1.6)	15 (3.6)	
	<i>Second fracture</i>	277 (2.2)	8 (4.3)	11 (2.6)	
	<i>Third fracture</i>	1 (0.0)	0 (0.0)	0 (0.0)	
30-day Mortality Status (%)					
	<i>Alive</i>	11727 (92.1)	171 (91.9)	339 (80.7)	<0.001
	<i>Deceased</i>	1012 (7.9)	15 (8.1)	81 (19.3)	

502

503 IQR = interquartile range; ASA = American Society of Anesthesiologists; SIMD = Scottish Index of Multiple Deprivation; SD = standard deviation; LOS =
 504 length of stay; d = days
 505 *Chi-square test for categorical variables with a normal distribution, independent pairs t-test for continuous variables, Mann-Whitney U test for continuous
 506 variables with a non-normal distribution (denoted with ⁺)

507 **Table 4.** Logistic regression analysis of factors associated with an increased likelihood of having COVID-19 within 30 days of hip fracture.

508

	<i>OR (Unadjusted)</i>	<i>OR (Multivariable)</i>	<i>OR (Multiple Imputation)</i>
Age	1.02 (1.01-1.03, p<0.001)	1.02 (1.01-1.03, p<0.001)	1.02 (1.01-1.03, p<0.001)
Sex			
<i>Female</i>	Reference	Reference	Reference
<i>Male</i>	1.03 (0.86-1.23, p=0.742)	1.04 (0.87-1.25, p=0.641)	1.04 (0.87-1.25, p=0.644)
ASA Grade			
2	Reference	Reference	Reference
1	0.58 (0.18-1.41, p=0.295)	0.64 (0.19-1.55, p=0.382)	0.63 (0.23-1.74, p=0.370)
3	1.61 (1.28-2.04, p<0.001)	1.44 (1.14-1.84, p=0.003)	1.44 (1.13-1.83, p=0.003)
4	1.52 (1.14-2.04, p=0.005)	1.28 (0.94-1.73, p=0.118)	1.27 (0.94-1.73, p=0.125)
5	0.99 (0.41-2.01, p=0.972)	0.79 (0.33-1.63, p=0.565)	0.79 (0.36-1.74, p=0.559)
SIMD Rank	1.03 (0.97-1.09, p=0.283)	-	1.01 (0.95-1.08, p=0.676)
Pre-fracture Residence			
<i>Home</i>	Reference	Reference	Reference
<i>Residential care</i>	1.29 (1.04-1.58, p=0.017)	1.08 (0.86-1.34, p=0.502)	1.10 (0.89-1.37, p=0.379)
<i>Subacute hospital</i>	1.86 (1.16-2.83, p=0.006)	1.76 (1.09-2.70, p=0.014)	1.64 (1.04-2.60, p=0.033)
<i>Acute hospital</i>	1.96 (1.37-2.72, p<0.001)	1.83 (1.27-2.57, p=0.001)	1.82 (1.28-2.57, p=0.001)
Fracture Sequence			
<i>Single fracture</i>	Reference	Reference	Reference
<i>First fracture</i>	1.39 (0.82-2.18, p=0.186)	-	1.17 (0.72-1.91, p=0.527)
<i>Second fracture</i>	1.47 (0.89-2.29, p=0.111)	-	1.49 (0.92-2.42, p=0.108)
<i>Third fracture</i>	0.00 (NA, p=0.966)		0.00 (NA, p=0.964)

Vaccination Status				
<i>Vaccinated</i>		Reference	Reference	Reference
<i>Unvaccinated</i>		2.38 (2.00-2.85, p<0.001)	2.47 (2.07-2.96, p<0.001)	2.47 (2.06-2.95, p<0.001)

509

510 OR = odds ratio; ASA = American Society of Anesthesiologists; SIMD = Scottish Index of Multiple Deprivation

511 **Table 5.** Logistic regression analysis of factors associated with an increased likelihood of death within 30 days of fracture.

	<i>OR (Unadjusted)</i>	<i>OR (Multivariable)</i>	<i>OR (Multiple Imputation)</i>
Age	1.04 (1.04-1.05, p<0.001)	1.03 (1.02-1.04, p<0.001)	1.03 (1.02-1.04, p<0.001)
Sex			
<i>Female</i>	Reference	Reference	Reference
<i>Male</i>	1.74 (1.53-1.97, p<0.001)	1.79 (1.55-2.06, p<0.001)	1.80 (1.58-2.06, p<0.001)
ASA Grade			
2	Reference	Reference	Reference
1	1.09 (0.42-2.34, p=0.838)	1.36 (0.52-2.92, p=0.482)	1.42 (0.60-3.34, p=0.423)
3	2.57 (2.02-3.32, p<0.001)	1.87 (1.46-2.42, p<0.001)	1.87 (1.44-2.43, p<0.001)
4	6.95 (5.39-9.08, p<0.001)	4.36 (3.35-5.76, p<0.001)	4.33 (3.29-5.70, p<0.001)
5	25.22 (17.72-36.05, p<0.001)	17.43 (12.11-25.18, p<0.001)	17.61 (12.06-25.72, p<0.001)
SIMD Rank	1.01 (0.97-1.06, p=0.531)	-	1.03 (0.98-1.08, p=0.237)
Pre-fracture Residence			
<i>Home</i>	Reference	Reference	Reference
<i>Residential care</i>	2.65 (2.30-3.04, p<0.001)	2.06 (1.76-2.42, p<0.001)	1.90 (1.64-2.22, p<0.001)
<i>Subacute hospital</i>	2.19 (1.52-3.06, p<0.001)	1.50 (0.99-2.20, p=0.045)	1.59 (1.10-2.31, p=0.014)
<i>Acute hospital</i>	2.88 (2.22-3.68, p<0.001)	1.95 (1.46-2.57, p<0.001)	1.96 (1.50-2.56, p<0.001)
Fracture Sequence			
<i>Single fracture</i>	Reference	Reference	Reference
<i>First fracture</i>	0.11 (0.03-0.29, p<0.001)	0.12 (0.03-0.31, p<0.001)	0.10 (0.03-0.32, p<0.001)
<i>Second fracture</i>	0.82 (0.51-1.25, p=0.391)	0.68 (0.41-1.06, p=0.106)	0.65 (0.41-1.03, p=0.068)
<i>Third fracture</i>	0.00 (NA, p=0.963)	0.00 (NA, p=0.964)	0.00 (NA, p=0.963)

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COVID-19 Status (%)			
<i>Negative</i>	Reference	Reference	Reference
<i>Positive [Vaccinated]</i>	1.02 (0.57-1.67, p=0.952)	0.98 (0.53-1.66, p=0.938)	0.93 (0.53-1.60, p=0.783)
<i>Positive [Unvaccinated]</i>	2.77 (2.14-3.54, p<0.001)	3.10 (2.35-4.04, p<0.001)	2.77 (2.12-3.62, p<0.001)

512

513 OR = odds ratio; ASA = Association of Anesthesiologists; SIMD = Scottish Index of Multiple Deprivation

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515 **SUPPLEMENTARY MATERIALS**

516 **Supplementary Table 1.** Patient characteristics according to COVID-19 and vaccination status for the reduced study period September 2020 to December
 517 2021 (i.e. excluding the first six months of total study period).

		COVID-19 Status (Vaccination Status)			<i>p</i> *
		<i>Negative</i> <i>n</i> = 9656	<i>Positive (Vaccinated)</i> <i>n</i> = 186	<i>Positive (Unvaccinated)</i> <i>n</i> = 319	
Age [median (IQR)]		82.00 [74.00, 88.00]	85.00 [79.00, 89.00]	83.00 [77.00, 88.00]	<0.001+
Sex (%)					
	<i>Female</i>	6731 (69.7)	135 (72.6)	221 (69.3)	0.688
	<i>Male</i>	2925 (30.3)	51 (27.4)	98 (30.7)	
ASA Grade (%)					
	2	2059 (21.9)	27 (14.8)	56 (17.8)	0.050
	1	156 (1.7)	1 (0.5)	2 (0.6)	
	3	5539 (58.9)	126 (69.2)	199 (63.4)	
	4	1486 (15.8)	27 (14.8)	51 (16.2)	
	5	171 (1.8)	1 (0.5)	6 (1.9)	
SIMD Rank [mean (SD)]		3.04 (1.40)	2.92 (1.47)	3.30 (1.41)	0.003
Pre-fracture Residence (%)					
	<i>Home</i>	7441 (77.1)	113 (60.8)	251 (78.7)	<0.001
	<i>Residential</i>				
	<i>Care</i>	1613 (16.7)	45 (24.2)	36 (11.3)	
	<i>Subacute</i>				
	<i>Hospital</i>	217 (2.2)	12 (6.5)	8 (2.5)	
	<i>Acute Hospital</i>	364 (3.8)	15 (8.1)	21 (6.6)	
	<i>Missing</i>	21 (0.2)	1 (0.5)	3 (0.9)	
Acute LOS [median (IQR)]		27.00 [8.00, 58.00]	23.00 [8.25, 56.50]	27.00 [11.00, 47.50]	<0.610+
Total LOS [median (IQR)]		17.00 [9.00, 39.00]	27.50 [13.25, 56.25]	32.00 [19.00, 55.00]	<0.001+
Discharge Destination (%)					
	<i>Home</i>	3824 (39.7)	38 (20.7)	96 (30.2)	<0.001
	<i>Residential</i>				
	<i>Care</i>	1396 (14.5)	36 (19.6)	22 (6.9)	

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	<i>Subacute Hospital</i>	3522 (36.5)	67 (36.4)	100 (31.4)	
	<i>Acute Hospital</i>	376 (3.9)	29 (15.8)	58 (18.2)	
	<i>Deceased</i>	521 (5.4)	14 (7.6)	42 (13.2)	
Fracture Sequence (%)					
	<i>Single fracture</i>	9231 (95.6)	175 (94.1)	296 (92.8)	0.052
	<i>First fracture</i>	176 (1.8)	3 (1.6)	12 (3.8)	
	<i>Second fracture</i>	249 (2.6)	8 (4.3)	11 (3.4)	
30-day Mortality Status (%)					
	<i>Alive</i>	8888 (92.0)	171 (91.9)	272 (85.3)	<0.001
	<i>Deceased</i>	768 (8.0)	15 (8.1)	47 (14.7)	

518

519 IQR = interquartile range; ASA = American Society of Anesthesiologists; SIMD = Scottish Index of Multiple Deprivation; SD = standard deviation; LOS =
520 length of stay; d = days

521 *Chi-square test for categorical variables with a normal distribution, independent pairs t-test for continuous variables, Mann-Whitney U test for continuous

522 variables with a non-normal distribution (denoted with ⁺)

523 **Supplementary Table 2.** Logistic regression analysis of factors associated with an increased likelihood of having COVID-19 within 30 days of hip fracture
 524 for the reduced study period September 2020 to December 2021 (i.e. excluding the first six months of total study period).

	<i>OR (Unadjusted)</i>	<i>OR (Multivariable)</i>	<i>OR (Multiple Imputation)</i>
Age	1.02 (1.01-1.03, p<0.001)	1.02 (1.01-1.03, p<0.001)	1.02 (1.01-1.03, p<0.001)
Sex			
<i>Female</i>	Reference	Reference	Reference
<i>Male</i>	1.03 (0.86-1.23, p=0.742)	0.97 (0.79-1.19, p=0.769)	0.97 (0.79-1.19, p=0.769)
ASA Grade			
2	Reference	Reference	Reference
1	0.58 (0.18-1.41, p=0.295)	0.53 (0.13-1.45, p=0.289)	0.53 (0.13-1.45, p=0.289)
3	1.61 (1.28-2.04, p<0.001)	1.33 (1.03-1.73, p=0.030)	1.33 (1.03-1.73, p=0.030)
4	1.52 (1.14-2.04, p=0.005)	1.11 (0.79-1.55, p=0.548)	1.11 (0.79-1.55, p=0.548)
5	0.99 (0.41-2.01, p=0.972)	0.76 (0.31-1.58, p=0.495)	0.76 (0.31-1.58, p=0.495)
SIMD Rank	1.03 (0.97-1.09, p=0.283)	1.04 (0.98-1.12, p=0.201)	1.04 (0.98-1.12, p=0.201)
Pre-fracture Residence			
<i>Home</i>	Reference	Reference	Reference
<i>Residential care</i>	1.29 (1.04-1.58, p=0.017)	0.90 (0.69-1.17, p=0.442)	0.90 (0.69-1.17, p=0.442)
<i>Subacute hospital</i>	1.86 (1.16-2.83, p=0.006)	1.68 (1.00-2.69, p=0.038)	1.68 (1.00-2.69, p=0.038)
<i>Acute hospital</i>	1.96 (1.37-2.72, p<0.001)	1.88 (1.28-2.69, p=0.001)	1.88 (1.28-2.69, p=0.001)
Fracture Sequence			
<i>Single fracture</i>	Reference	Reference	Reference
<i>First fracture</i>	1.39 (0.82-2.18, p=0.186)	1.27 (0.69-2.16, p=0.401)	1.27 (0.69-2.16, p=0.401)
<i>Second fracture</i>	1.47 (0.89-2.29, p=0.111)	1.48 (0.87-2.37, p=0.123)	1.48 (0.87-2.37, p=0.123)
Vaccination Status			
<i>Vaccinated</i>	Reference	Reference	Reference
<i>Unvaccinated</i>	2.38 (2.00-2.85, p<0.001)	3.68 (3.04-4.45, p<0.001)	3.68 (3.04-4.45, p<0.001)

525 OR = odds ratio; ASA = Association of Anesthesiologists; SIMD = Scottish Index of Multiple Deprivation

526 **Supplementary Table 3.** Logistic regression analysis of factors associated with an increased likelihood of death within 30 days of hip fracture for the
 527 reduced study period September 2020 to December 2021 (i.e. excluding the first six months of total study period).

	<i>OR (Unadjusted)</i>	<i>OR (Multivariable)</i>	<i>OR (Multiple Imputation)</i>
Age	1.03 (1.02-1.04, p<0.001)	1.03 (1.02-1.04, p<0.001)	1.03 (1.02-1.04, p<0.001)
Sex			
<i>Female</i>	Reference	Reference	Reference
<i>Male</i>	1.80 (1.54-2.09, p<0.001)	1.77 (1.50-2.09, p<0.001)	1.80 (1.54-2.09, p<0.001)
ASA Grade			
2	Reference	Reference	Reference
1	1.64 (0.65-4.15, p=0.295)	1.78 (0.61-4.15, p=0.231)	1.64 (0.65-4.15, p=0.295)
3	1.98 (1.48-2.66, p<0.001)	2.05 (1.52-2.82, p<0.001)	1.98 (1.48-2.66, p<0.001)
4	4.76 (3.48-6.50, p<0.001)	4.80 (3.48-6.73, p<0.001)	4.76 (3.48-6.50, p<0.001)
5	19.08 (12.69-28.70, p<0.001)	19.09 (12.49-29.40, p<0.001)	19.08 (12.69-28.70, p<0.001)
SIMD Rank	1.00 (0.95-1.06, p=0.881)	0.99 (0.93-1.04, p=0.647)	1.00 (0.95-1.06, p=0.881)
Pre-fracture Residence			
<i>Home</i>	Reference	Reference	Reference
<i>Residential care</i>	1.93 (1.61-2.31, p<0.001)	2.15 (1.78-2.59, p<0.001)	1.93 (1.61-2.31, p<0.001)
<i>Subacute hospital</i>	1.59 (1.05-2.41, p=0.027)	1.46 (0.91-2.26, p=0.098)	1.59 (1.05-2.41, p=0.027)
<i>Acute hospital</i>	2.09 (1.55-2.81, p<0.001)	1.98 (1.42-2.71, p<0.001)	2.09 (1.55-2.81, p<0.001)
Fracture Sequence			
<i>Single fracture</i>	Reference	Reference	Reference
<i>First fracture</i>	0.17 (0.05-0.54, p=0.003)	0.19 (0.05-0.52, p=0.005)	0.17 (0.05-0.54, p=0.003)
<i>Second fracture</i>	0.67 (0.41-1.10, p=0.113)	0.66 (0.38-1.07, p=0.116)	0.67 (0.41-1.10, p=0.113)
<i>Third fracture</i>	0.00 (NA, p=0.963)	0.00 (NA, p=0.964)	0.00 (NA, p=0.963)
COVID-19 Status (%)			
<i>Negative</i>	Reference	Reference	Reference
<i>Positive [Vaccinated]</i>	0.94 (0.54-1.62, p=0.817)	0.99 (0.54-1.69, p=0.981)	0.94 (0.54-1.62, p=0.817)
<i>Positive [Unvaccinated]</i>	2.13 (1.52-2.98, p<0.001)	2.46 (1.74-3.43, p<0.001)	2.13 (1.52-2.98, p<0.001)

528 OR = odds ratio; ASA = Association of Anesthesiologists; SIMD = Scottish Index of Multiple Deprivation

