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Fay M. Manning[1,2], Faraz Mughal[1,3], Hazem Ahmed Saad Mohamed Ismail[4], Libby M Baines[1], Carolyn A. Chew-Graham[1], Zoe Paskins[1,5] and James A. Prior[1,5]

Affiliations

[1]School of Medicine, Keele University

[2]School of Medicine, University of Exeter

[3]Centre for Mental Health and Safety, Division of Psychology and Mental Health, University of Manchester

[4]School of Medicine, Royal College of Surgeons, Bahrain

[5]Haywood Academic Rheumatology Centre, Midlands Partnership Foundation Trust

Corresponding Author

Dr James Prior, Research Fellow in Epidemiology, School of Medicine, Keele University, j.a.prior@keele.ac.uk

Authors information and affiliation:

Fay M. Manning, Lecturer, Department of Medical Imaging, University of Exeter, UK f.manning2@exeter.ac.uk ORCID: 0000-0002-9768-1695 - BSc, MSc, PhD

Faraz Mughal, GP and National Institute for Health and Care Research (NIHR) doctoral fellow, School of Medicine, Keele University, UK. Honorary clinical research fellow, Warwick Medical School, UK F.mughal@keele.ac.uk ORCID: 0000-0002-5437-5962 - DCH, MPhil, FRCGP.

Hazem Ahmed Saad Mohamed Ismail, Medical Student, 18202063@rcsi-mub.com - Student

Libby Marie Baines – Research placement student, Keele University Stoke-on-Trent, UK libbyybaines@icloud.com - Student

Carolyn A. Chew-Graham, Professor of General Practice Research, School of Medicine, Keele University - c.a.chew-graham@keele.ac.uk ORCID: 0000-0002-9722-9981 - BSc MB ChB MD FRCGP OBE

Zoe Paskins, Reader and Honorary Consultant in Rheumatology, School of Medicine, Keele University & Haywood Academic Rheumatology Centre, Stoke-on-Trent, UK - z.paskins@keele.ac.uk ORCID: 0000-0002-7783-2986 - MBChB MMedED FRCP PhD

James A. Prior, Research Fellow in Epidemiology, Keele University - j.a.prior@keele.ac.uk ORCID: 0000-0001-9213-2796 – BSc (Hons), MSc, PhD

Abstract

Background: Increase in presentations of self-harm to primary care, a risk factor of suicide has led to a growing interest in identifying at-risk populations.

Aim: To examine whether osteoporosis or fractures are risk factors for self-harm, suicidal ideation, and suicide.

Design and Setting: Systematic review of observational studies in adults (18> years) which had examined the role of osteoporosis and/or fractures in subsequent self-harm, suicidal ideation, and/or suicide.

*Method: S*ix databases were searched from inception to July 2019. Additional citation tracking of eligible studies was done in November 2022. Screening, data extraction and quality assessment of full-text articles were performed independently by at least two authors. Where possible, meta-analysis was run on comparable risk estimates.

Results and Conclusion: Fifteen studies were included, two examined the outcome of self-harm, three suicidal ideation and 10 suicide. In approximately half of studies on osteoporosis, the risk of suicidal ideation and suicide remained significant. However, pooling of adjusted odds ratios from three studies indicated no association between osteoporosis and suicide (1.14(95% confidence interval 0.88-1.49)). Nine studies examined the risk of a mixture of fracture types across different outcomes, limiting comparisons. However, all studies examining vertebral fracture (n=3) reported a significant adjusted negative association for self-harm and suicide. In conclusion, Patients with vertebral fractures may benefit from case-finding for mood disorders in primary care, which are risk factors for suicide, and the subsequent management. However, due to the limited number and quality of studies and mixed findings, further examination of these associations is warranted.

64

How this fits in?

66 An increased risk of self-harm and suicide has been identified in people with physical health

67 conditions, such as fibromyalgia and osteoporosis. This is the first study to synthesise the

68 evidence on osteoporosis and fractures as risk factors for self-harm, suicidal ideation, and

69 suicide (including suicidal behaviours). We found that though there was no association between

70 osteoporosis and suicide, vertebral fractures appeared to increase the risk of self-harm and

71 suicide. Patients with vertebral fractures therefore may benefit from clinical case-finding for

72 mood disorders with personalised primary care management.

73

Introduction

Rates of suicide in the UK have risen since 2017, with a 9% increase by 2019 (1). Similarly, there has been an increase in presentations of self-harm to primary care (2), with the risk of suicide increasing fifty-fold in the year after self-harm compared to the general population (3). Such increases have led to a growing interest in identifying at-risk populations. Though a history of mental ill-health, notably depressive disorders, is an understood risk factor for self-harm (4); pain, and more specifically back pain, are also independent risk factors for self-harm (5, 6) and suicide, specifically in older adults (7).

Recent studies have demonstrated increased risk of self-harm in people with physical health conditions such as fibromyalgia and osteoarthritis (5, 8). Although pain is not a symptom of osteoporosis, pain frequently occurs because of subsequent fractures (9, 10), and with 1 in 3 women and 1 in 5 men > 50 years experiencing an osteoporotic fracture in their lifetime, osteoporosis has been suggested as a risk factor for self-harm and suicide (5, 11). Furthermore, common outcomes of fractures, including osteoporotic fractures, such as isolation and depression are risk factors for suicide (12)

Previous research examining the risk of self-harm or suicide in older adults with osteoporosis or fractures has yielded conflicting results (5, 13, 14, 15), possibly due to a lack of consensus on diagnosis definitions, population variations, and study limitations. We aimed to examine whether osteoporosis and/or fractures are risk factors for self-harm, suicidal ideation, or suicide.

Methods

We conducted a systematic review and meta-analysis. The protocol was registered on PROSPERO (CRD42017056011) and adhered to PRISMA guidance (16).

Ethics Approval

Ethics approval was not required for this study.

4

Search Methods

The population of interest were adults with osteoporosis and/or fracture. The outcomes of interest were risk estimates of self-harm, suicidal ideations (including suicidal behaviours) and suicide.

Exclusion criteria:

i)   studies with a population of <18 years old

ii)   studies that could not be translated

iii)   Systematic reviews, case reports, or case series studies

Searches were tailored and conducted in six electronic databases: MEDLINE, psycARTICLES, AMED, CINAHLPlus, PsycINFO, and Web of Science from inception to August 2019. Search strategies utilised database subject headings and text word searching in title, abstract or keywords, combining terms for: 1) Osteoporosis and fractures; and 2) self-harm, suicidal ideation (including suicidal behaviours) and suicide (**Supplementary Box 1**). In addition, the reference lists of included studies and relevant systematic reviews were checked and key studies citation tracked. To account for the delay in publication due to COVID-19, citation tracking was conducted on all included papers in November 2022 to ensure relevant new studies were identified.

Study Screening and Selection

A two-stage screening of articles against pre-defined eligibility criteria was implemented. First, by titles and abstracts; second by full text. At each stage, screening was conducted by two reviewers independently (FMM, JAP, HASMI) and articles were excluded by consensus. Arising disagreements were resolved through discussion.

129 *Quality Assessment*

130 The Quality In Prognosis Studies (QUIPS) tool was used to assess included articles (17). It

131 examines the risk of bias across six domains: study population, study attrition, prognostic factor

132 measurement, outcome measurement, study confounding and statistical analysis and reporting.

133 All included articles were assessed for their quality independently by two pairs of assessors

134 (FMM and JAP or FM and ZP). Any disagreement on scoring was initially discussed and

135 arbitrated by a different reviewer if required.

136

137 *Data extraction*

138 Data were extracted by two authors (HASMI, LMB) on demographic information (age, sex,

139 country of origin etc.) and size of the study sample, numbers of patients with condition of

140 interest, study setting (e.g., primary care), exposures (e.g., osteoporosis or fracture), exposure

141 definition, outcome (e.g., self-harm, suicidal ideation and suicide), and method of risk estimates

142 regarding the association between exposure and outcome.

143 Findings were tabulated by their exposure category, i.e., articles examining either osteoporosis

144 or fracture were compared separately. Within each of these exposure categories, outcomes were

145 subcategorized by either self-harm, suicidal ideation/behaviour or suicide. Risk estimates, 95%

146 confidence intervals (CI) and statistical significance were extracted and reported for each study,

147 and where available separately for males and females. Specifically for fractures, risk estimates

148 were tabulated by location of fracture where reported. We did not contact authors if we were

149 unable to identify certain required information in their publication.

150

151 *Meta-analysis*

152 Where enough studies (≥3) examining comparable factors were identified, a random-effects

153 meta-analysis was used to pool reported risk of any of the examined exposures along with their

154 95% CI. Heterogeneity was assessed by I^2. Analysis was undertaken in STATA (version 14) (18).

155

156 *Patient and Public Involvement*

157 Keele Research User Group consists of a diverse group of people with lived experience of

158 osteoporosis, or of caring for people with osteoporosis. In a series of meetings to discuss

159 research, public contributors talked about the significant psychological and social sequalae of

160 osteoporotic fractures. However, there was no direct public and patient involvement in the

161 conduct or interpretation of this study.

162

163 **Results**

164 Searches identified 325 unique articles, of which 306 were excluded and 18 underwent full

165 review (1 article could not be retrieved). Citation tracking identified a further three eligible

166 studies resulting in a total of 15 included studies (**Figure 1**).

167

168 The included studies were categorised into two groups by risk factor, osteoporosis, and

169 fracture. Eight studies reported osteoporosis as a risk factor (11, 13, 14, 19, 20, 21, 22, 23), ten

170 studies examined fractures as a risk factor (13, 14, 15, 21, 24, 25, 26, 27, 28, 29) and three

171 studies examined both (13, 14, 21). Of the studies reporting osteoporosis, three reported

172 suicidal ideation as the outcome (19, 20, 21), and five reported suicide as the outcome (11, 13,

173 14, 22, 23). Of the studies examining fractures, one reported the outcome of self-harm (24), two

174 of suicidal ideation (15, 21), four of suicide (13, 14, 25, 26), and one included the outcome of

175 self-harm and suicide (27). In the three studies examining both population groups of

176 osteoporosis and fractures, one reported the outcome suicidal ideation (21), and two reported

177 on the risk of suicide (13, 14). Most studies included a relatively even sample of male and female

178 participants, but only three stratified risk estimates by gender (13, 20, 24) (**Table 1**). The

179 majority of studies showed moderate to high risk of bias (**Supplementary Table 1**).

180

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182

7

183 *Characteristics of osteoporosis studies*

184 Studies were conducted in a range of countries, predominantly Europe (11, 13, 21) and East

185 Asia (14, 19, 20). Study settings included primary care (11), primary and secondary/specialist

186 care (14, 22) and general populations (13, 19, 20, 21, 23). Four studies did not report average

187 age and/or standard deviation (SD) (11, 13, 20, 22), with two only reporting the age ranges

188 used to group participants (13, 20). Three studies included participants below the age of 45

189 years (11, 20, 22) and four included participants over the age of 80 (11, 13, 20, 23).

190 Osteoporosis was predominantly identified utilising disease codes in a range of health record

191 databases (**Supplementary table 1)**. In terms of outcomes, suicidal ideation was recorded via

192 patient self-report (14, 20, 21), whilst papers reporting numbers of suicide utilised health care

193 records (11, 13, 14, 22, 23).

194

195 *Osteoporosis as a risk factor for suicidal ideation*

196 Two of the three studies reported significant crude estimates (Odds ratios (ORc)), ranging from

197 1.90 (95%CI 1.38-2.62) to 2.13 (1.34-3.39) (19, 20). Only one of these reported adjusted odds

198 ratios, (ORa) and they remained significant (2.07 (1.19-3.59 p<0.05)) (20). The third study did

199 not report a crude ratio; however, reported a significant adjusted estimate (1.19 (1.04-1.36)

200 (21). Two studies stratified risk by gender. Erlangsen et al., (2015) reported significant crude

201 and adjusted risk ratios (RRa) for both men (1.67(1.1-2.51) and women (1.88(1.5-2.35) (13).

202 Kim et al., reported crude and adjusted risk estimates for suicidal ideation in men and women;

203 however, only risk estimates for males were significant in crude and adjusted ratios (ORa

204 2.07(1.19-3.59)) (20).

205

206 *Osteoporosis as a risk factor for suicide*

207 Five of the seven studies relating to osteoporosis as a risk factor for suicide found significant

208 crude results (11, 13, 14, 22, 23), with estimates ranging from 1.28 (ORc 95%CI 1.23-1.33) (14)

209 to 3.12 (ORc 1.56-6.21) (23). Four studies also reported adjusted risk ratios, with two retaining

8

210   significance (males RRa 1.67 (1.1-2.51); females RRa 1.88 (1.5-2.35) (13). Adjusted odds ratio

211   data from a total of 4123 primary and secondary care patients across three studies was pooled

212   and found no association between osteoporosis and subsequent suicide (1.14 (95% confidence

213   interval 0.88-1.49) (**Figure 2**).

214

215   *Characteristics of fracture studies*

216   Ten studies, mostly conducted in East Asia (14, 15, 25, 28, 29) and Europe (13, 21, 24) examined

217   fracture as a risk factor. Study settings included primary care (24), a retirement community

218   (26), secondary care (25), across primary and secondary care (15), and the general population

219   (13, 21) (**Table 1**). Most studies included a balanced sample of men and women, or a higher

220   percentage of females (as expected in osteoporotic studies). Four studies reported mean ages

221   (SD) ranging from 59.8 (±14.3) to 75.0 (±6.8) years (14, 21, 25, 27). Five studies included

222   participants aged over 80 years (13, 25, 26, 28, 29), and one included participants below ≤35

223   years (15) (**Table 1**).

224   Fractures were defined inconsistently between studies. Five of the ten studies (examining

225   outcomes self-harm (13), suicidal ideation (15, 21), suicide (14, 26)) reported a grouped

226   fracture risk estimate; however, each utilised a different grouping definition; 'all fractures',

227   'pathological fractures', 'fractures >50yrs' and other fractures', 'any fracture in last 5 years'

228   (**Table 1** and expanded in **Supplementary Table 2**). Chang et al., reported the greatest detail

229   with 11 bodily regions (14), whereas Tsai et al., grouped fractures into just two groups of 'trunk'

230   and 'lower-limb' (15) (**Supplementary Table 2**). Hip and vertebral fractures were the most

231   consistently reported fracture sites, reported in five and four studies respectively (13, 14, 21,

232   24, 26, 29). However, these studies utilised a range of risk estimate types (**Table 3**).

233

234   *Fracture as a risk factor for self-harm*

235   Erlangsen et al., (2021) investigated 'any fractures in the prior 5 years' as a risk factor for self-

236   harm, whilst Prior et al., examined the relationship between vertebral fractures and self-harm.

237   Crude and adjusted hazard ratios were significant in both men and women. Erlangsen et al.,

238   (2021) found a significant adjusted incidence ratio (aIR) of 1.38 (95% CI 1.12-1.71) (27). Prior

239   et al found that men and women with vertebral fractures, were almost four and two times more

240   at risk of self-harm than those without such fractures (adjusted Hazard Ratio (aHR) of 3.90

241   (95% CI 1.80-8.50 and 1.90 (1.10-3.20) respectively) (24) (**Supplementary Table 3**).

242

243   *Fracture as a risk factor for suicidal ideation/behaviour*

244   Tsai et al., reported significant crude (2.37 (95%CI 1.93-2.91)) and adjusted Hazard Ratio

245   (2.21(1.8-2.71)) estimates for fractures as a risk factor for suicidal ideation (15) (**Table 2**).

246   However, when this data was dichotomised by fracture location (trunk or leg/lower limb), no

247   adjusted associations were retained. Lutz et al., reported a significant adjusted association

248   between experiencing any fractures (defined as anything other than hip/femoral neck) and

249   suicidal ideation (OR 1.3 (1.1-1.54)) (21) (**Table 1**).

250

251   *Fracture as a risk factor for suicide*

252   Six studies examined fractures as a risk factor for suicide. All of these examined one or more

253   specific fracture locations, with three examining the role of 'grouped' fractures. Of the grouped

254   fractures, Chang et al & Turvey et al reported significant crude associations ('Pathological

255   fracture' (ORc 1.74 (1.52-1.98) (14), 'fractures in those over 50 years of age' (ORc 3.39 (1.16-

256   9.4)) (26)), but only Chang adjusted for confounders, finding significance to be retained (OR

257   1.49(1.28-1.73) Erlangsen et al., (2021) examined the adjusted association between self-

258   reported 'fractures in last five years' and suicide but found no significant association (**Table 2**).

259   Three studies examining the role of vertebral fractures on suicide found significant associations

260   in all, with risk estimates ranging from 1.40 (1.07-1.82) by Chang et al to 2.20 (1.79-2.70) by

261   Erlangsen et al (in women) (13, 14, 29). Four studies examined the association between

262   hip/femoral neck fracture and suicide (14, 26, 27, 28) two of these found a significant crude

263   association. Significant associations in the two studies were retained after adjustment (13, 14).

264 Though several other fracture sites were examined, conflicting or infrequent examination of

265 these means that no consensus on an association with suicide can be drawn (**Table 3)**. Studies

266 examining the risk of self-harm and suicidal ideation in populations with fractures at specific

267 sites were also limited (**Supplementary Table 3)**.

268

269 **Discussion**

270 *Summary*

271 This systematic review included all identified studies examining osteoporosis and fracture as

272 risk factors for self-harm, suicidal ideation, and suicide. Though data is limited, particularly for

273 self-harm, we found that for approximately half of osteoporosis and fracture studies, there

274 remained significant risks of suicidal ideation or suicide after adjustment. All three studies

275 which examined the role of vertebral fracture as a risk factor for suicide found a significant

276 association, even after adjustment (though data pooling was not possible). This was also

277 supported by the one study to have examined the role of vertebral fractures on self-harm (30).

278 Pooled analysis of three studies found that people with osteoporosis were no more likely to die

279 from suicide than patients without osteoporosis.

280

281 *Strengths and limitations*

282 This is the first paper to assemble literature on osteoporosis and fractures as risk factors for

283 self-harm, suicidal ideation, and suicide. Despite only 15 studies included we were able to

284 conduct a meta-analysis which provides greater reliability of risk estimates. Another strength is

285 the analysis of fracture as a risk factor by bodily location, which highlighted vertebral fractures

286 as a potentially important risk factor. There are, however, several limitations that need to be

287 recognised. We characterised papers primarily by population group of either osteoporosis or

288 fractures and though the poor coding of osteoporosis and fractures in primary care data has

289 previously been noted [54(31)(31)], we undertook quality assurance to assess such variations

290 (**Supplementary Figure 1**). A further limitation of this study is that due to the variety of

11

291 definitions, populations and risk estimates used, we were only able to pool three studies, which

292 varied widely in quality. However, the fact that meta-analysis included the study by Chang et al

293 that was a very large study, and, that all estimates were adjusted, adds some credibility to these

294 findings and an opportunity for others to build on.

295

296 *Comparison with existing literature*

297 Vertebral fractures have significant long-term physical, psychological and social sequelae. Pain

298 is a likely mechanism for fractures associated with self-harm, suicidal ideation, and suicide;

299 especially as osteoporotic fractures have been reported to induce both acute and chronic

300 nociceptive and neuropathic pain (32, 33). The presence of fractures has social implications due

301 to the fear of falling or of recurrent fracture (34, 35), with osteoporotic fracture increasing the

302 odds of functional decline by 48% (36). Further poor osteoporotic fracture outcomes include

303 increased social support requirements and diminished quality of life, including depression and

304 deterioration in perceived health. (37, 38). Although suicide risk is multifactorial, depression,

305 anxiety, and other mood disorders are major risk factors, and thus the impact of fractures

306 towards such conditions could in part explain the risk identified related to vertebral fractures

307 (39). Furthermore, the effects of fractures last long beyond incidence. Hallberg et al., reported

308 that two years post fracture, the social function and mental health components of health-related

309 quality of life were still significantly lower than controls in those with vertebral and hip

310 fractures [15]. Though this aligns with spinal, and to a lesser extent hip, fractures being

311 significantly associated with suicide in this review, it does not align with the temporal nature of

312 suicide risk post-fracture as reported by Jang et al., (28). They found that risk of suicide was

313 highest in the first 180 days after hip fracture (HR 2.97 (95% CI 1.32-6.69), and then reduced

314 (25), with similar patterns in pelvic and spinal fractures (28, 29).

315

316 This lack of association with osteoporosis and suicide may relate to the fact that osteoporosis

317 without fracture is primarily asymptomatic and though low trauma fracture is an indicator of

318 osteoporosis, not all those who have low bone density have broken a bone. As such,

319 osteoporosis is often referred to as 'silent' (9). Despite this common label, a diagnosis of

320 osteoporosis can cause changes in the perception of one's self which may result in social

321 isolation, low mood, and anxiety (35).

322

323 *Implications for Research and/or practice.*

324 This study indicates that patients diagnosed with vertebral fractures might benefit from case-

325 finding for mood disorders, such as depression, a risk factor for suicide, and enquiring about

326 suicide and self-harm (40). Osteoporosis is commonly diagnosed, and patients seek help for

327 fracture care, in primary care which may be an important setting to identify patients at risk of

328 self-harm and suicide and intervene early. New research would enable the assessment of the

329 feasibility, acceptability, and effectiveness of such approaches. Early intervention studies have

330 shown that physical exercise programs that focus on physical anxiety can decrease fear of falls

331 in those with osteoporosis, and potentially lead to lower rates of isolation (41, 42), which might

332 be a causative factor in self-harm and suicide. Such programs have been shown to be effectively

333 implemented through primary care (43).

334

335 **Conclusion**

336 Though studies were typically too diverse for pooling of data, one meta-analysis of three studies

337 showed no association between osteoporosis and suicide, across several individual studies,

338 vertebral fractures were shown to be potential risk factors for suicide. Our review demonstrates

339 the potential importance of teasing apart the role of osteoporosis and fracture in research and

340 provides strong justification for further research around vertebral fracture in this area. Primary

341 care clinicians are well placed to implement case-finding for mood disorders and suicide risk

342 assessment in patients with vertebral fractures and undertake subsequent management.

343

344

Declarations

Contribution Statement

Conceptualisation: FMM, JAP and ZP. Protocol: FMM, JAP and ZP. Search Implementation:
HASMI, FMM and JAP. Data extraction and Quality: HASMI, FMM, LB, ZP, FM and JAP
Synthesis: FMM, FM, ZP, CCG and JAP Writing- Original draft: FMM and JAP Writing- Review
and Editing: FMM, HASMI, LB, FM, CCG, ZP and JAP.

Data Sharing Statement

Full search criteria for MEDLINE is included in Supplementary file 1.

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Table 1. Characteristics of Included Studies

Author	Year	Country	Study design	Setting	Sample size (% females)	Age (years, mean ± SD)	Disease Definition
Osteoporosis & Suicidal Ideation							
Chan	2011	Taiwan	Cross-sectional study	General Population	3596 (47.4)	73.5 ± 5.8	Pt recall of physicians' diagnosis
Kim	2016	Korea	Cross-sectional study	General population	19,243 (64.8)	Age groups 19-44, 45-64, 64-74, and ≥75‡	Self-reported diagnosis
Lutz*	2016	Europe	Cross-sectional	General Population	38,670 (55.8)	64.88 ± 10.27	Pt recall of physicians' diagnosis
Osteoporosis & Suicide							
Ahmedani	2017	USA	Case-control	Primary and Specialist Care	270,074 (52.5)	39.4‡	VDW code
Voaklander	2007	Canada	Population based case-control	General Population	3601 (28.3)	76.3 ± 7.08	Hospital or community record†
Webb	2012	UK	Nested case-control study	Primary care	18,333 (33)	17-98‡	GPRD codes
Chang*	2018	Taiwan	Population based case control	Primary and secondary health care	173,970 (32)	59.8 ± 14.3	Database code (733.0x)
Erlangsen*	2015	Denmark	Register based cohort study	General Population	1,849,110 (77.7)	Age groups 65-79 and ≥80‡	NRP database

Author	Year	Country	Study Design	Setting	Sample size (% females)	Age (years, mean ± SD)	Fracture Location
Fracture & Self-harm							
Prior	2020	UK	Respective Cohort	Primary Care	32,586 (70.1)	74.81‡	Vertebrae
Erlangsen b¥	2021	Australia	Cohort design	General population	266,324 (53.6)	62.7 ± 11.2	Bone fracture in last 5 years
Fracture & Suicidal behaviour/ideation							
Tsai	2019	Taiwan	Retrospective cohort	Inpatient/outpatient care	165,608 (43.9)	<35 and >65‡	Trunk, lower limbs and multiple locations
Lutz*	2016	Europe	Cross-sectional	General Population	38,670 (55.8)	64.88 ± 10.27	Hip/femoral, other

Fracture & Suicide

Chang*	2018	Taiwan	Population based case control	Primary and secondary health care	173,970 (32)	59.8 ± 14.3	Pathological, spine, clavicle, humerus, forearm, wrist, radius/ulna/hand, femoral neck/shaft, patella/tibia/fibula, ankle/foot and pelvis
Erlangsen a*	2015	Denmark	Register based cohort study	General Population	1,849,110 (77.7)	Age groups 65-79 and ≥80‡	Spinal, hip, leg, foot, shoulder/arm and hand
Jang a	2020	South Korea	Nationwide Cohort	Secondary Care	34,431 (73.81)	75.0 ± 6.8	Hip
Jang b	2021	South Korea	Register based cohort study	NHIS-Senior cohort	18,420 (66.8)	65 - >85	Hip, spine, radius and humorous
Jang c	2022	South Korea	Nested Case Control	NHIS-Senior cohort	5198 (65.56)	65 - >85	Pelvic fracture
Turvey	2002	USA	Nested case-control	Retirement Community	420 (4.76)	78.6 (76-90) ‡	Hip
Erlangsen b¥	2021	Australia	Cohort design	General population	266,324 (53.6)	62.7 ± 11.2	Bone fracture

*Papers reporting on both osteoporosis and fractures

¥Papers reporting on both self-harm and suicide

VDW- Virtual data warehouse.

†Hospital classified a hospitalisation record showing osteoporosis as a primary or contributing diagnoses. Community classified as least two episodes of care recorded for osteoporosis in the Physician Claim File

GPRD- General Practice Research Database

NRP- National Registry of Patients

‡No mean and/or standard deviation age of participants provided

Table 2. Reported crude and adjusted risk estimates for Osteoporosis and fractures as a risk factor for self-harm, suicidal ideation/behaviour and suicide

Author	Type of risk estimate	Crude			Adjusted		
		Risk estimate value	95% CI	p-value	Risk estimate value	95% CI	p-value
Osteoporosis and Suicide Ideation/Behaviour							
Lutz*	OR	-	-	-	1.19	1.04-1.36	**<0.01**
Kim (Men)	OR	2.13	1.34-3.39	**<0.05**	2.07	1.19-3.59	**<0.05**
Kim (Women)	OR	0.86	0.68-1.07	N/S	1.07	0.81-1.42	N/S
Chan	OR	1.9	1.38-2.62	**Sig**	-	-	-
Osteoporosis and suicide							
Chang 2018	OR	1.28	1.23-1.33	**<0.0001**	0.97	0.93-1.02	0.2582
Erlangsen a (Men)	RR	1.57	1.04-2.37	**<0.05**	1.67	1.1-2.51	**<0.05**
Erlangsen a (Women)	RR	1.56	1.25-1.95	**<0.001**	1.88	1.5-2.35	**<0.001**
Webb	OR	2.33	1.46-3.72	**<0.05**	1.62	0.99-2.63	N/S
Ahmedani	OR	1.22	0.92-1.63	0.171	1.21	0.9-1.62	0.216
Voaklander (phys coded)	OR	1.69	0.62-4.66	N/S	-	-	-
Voaklander (hosp coded)	OR	3.12	1.56-6.21	**Sig**	-	-	-
Fracture & Self-harm							
Erlangsen b¥	IR	1.47	-	-	1.38	1.12-1.71	**<0.05**
Fracture & Suicidal ideation/behaviour							
Tsai	HR	2.37	1.93-2.91	**<0.0001**	2.21	1.80-2.71	**<0.0001**
Lutz*‡	OR	-	-	-	1.3	1.1-1.54	**<0.01**
Any Fractures and Suicide							
Chang 2018 †	OR	1.74	1.52-1.98	**<0.0001**	1.49	1.28-1.73	**<0.0001**
Turvey⁺	OR	3.39	1.16-9.4	**0.02**	-	-	-
Erlangsen b¥	IR	1.16	-	-	1.16	0.76-1.80	N/S

* Adjusted odds ratio (Model 1)

NS- non-significant
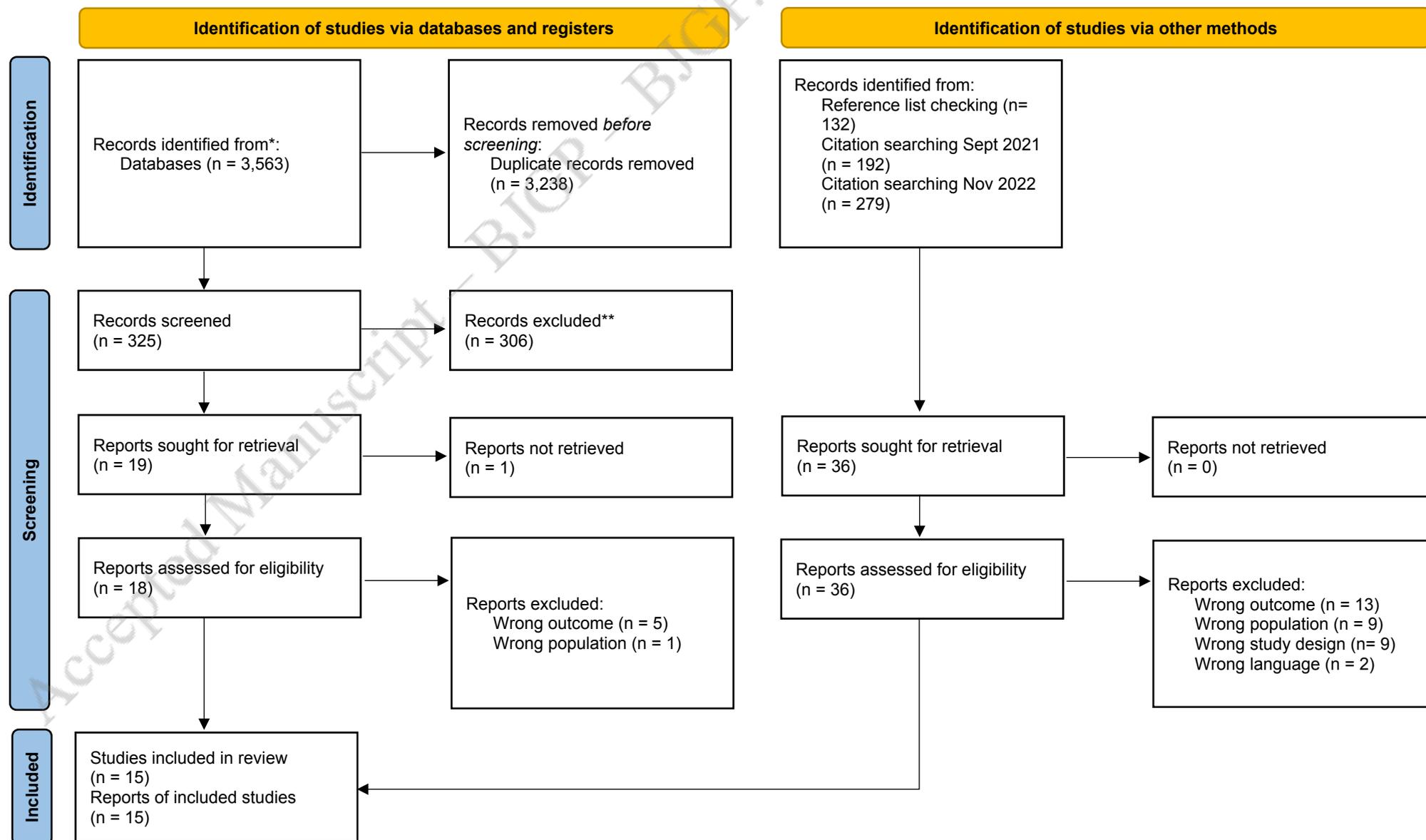
† Pathological Fracture

⁺Fracture >50 years

‡ Other Fracture

¥ Fracture in last 5 years

Table 3. Crude and adjusted risk estimates of fracture and suicide by fracture location

Risk of: Bodily location:		Chang 2018 OR (95% CI)	Erlangsen 2021 (M) RR (95% CI)	Erlangsen 2021 (F) RR (95% CI)	Suicide Jang[a] 2020 HR (95% CI)	Jang[b] 2021 OR (95% CI)	Jang[c] 2022 OR (95% CI)	Turvey 2002 OR (95% CI)
Spine/ vertebrae	Crude	**1.94 (1.83-2.05)**	**1.51 (1.23-1.85)**	**2.06 (1.68-2.53)**		**1.62 (1.25-2.10)**		
	Adj	**1.53 (1.43-1.64)**	**1.51 (1.23-1.85)**	**2.20 (1.79-2.7)**		**1.40 (1.07-1.82)**		
Shoulder/ humerus	Crude	**1.64 (1.47-1.83)**	**1.25 (1.02-1.53)**	0.91 (0.78-1.07)		1.15 (0.48-2.80)		
	Adj	**1.33 (1.17-1.51)**	**1.36 (1.12-1.67)**	-		1.04 (0.42-2.59)		
Forearm	Crude	**1.48 (1.38-1.60)**						
	Adj	**1.25 (1.15-1.36)**						
Wrist	Crude	1.18 (0.93-1.49)						
	Adj	0.99 (0.75-1.31)						
Radius/ulna/ hand	Crude	**1.39 (1.31-1.47)**	1.01 (0.79-1.3)	1.04 (0.82-1.33)		1.02 (0.76-1.37)		
	Adj	**1.15 (1.08-1.23)**	-	-		0.95 (0.7-1.29)		
Hip/femoral neck	Crude	**1.81 (1.62-1.95)**	**1.49 (1.25-1.78)**	1.35 (1.61-1.58)		1.31 (0.96-1.79)		1.45 (0.03-10.40)
	Adj	**1.40 (1.23-1.51)**	**1.28 (1.07-1.53)**	**1.40 (1.19-1.65)**		1.21 (0.87-1.67)		-
Femoral shaft	Crude	**1.93 (1.74-2.08)**			**2.97 (1.32-6.69)**			
	Adj	**1.47 (1.35-1.66)**			2.97 (1.32-6.69)			
Pelvis	Crude	**2.74 (2.33-3.22)**					**1.40 (1.07-0.82)**	
	Adj	**2.04 (1.68-2.47)**					1.55 (0.95-2.54)	
Clavicle	Crude	**1.83 (1.66-2.01)**						
	Adj	**1.42 (1.26-1.59)**						
Patella/tibia/ fibula	Crude	**1.71 (1.59-1.84)**						
	Adj	**1.40 (1.29-1.53)**						
Leg/lower limb	Crude		1.20 (0.99-1.46)	1.09 (0.88-1.35)				
	Adj		**1.29 (1.06-1.57)**	-				
Ankle/foot	Crude	**1.45 (1.35-1.56)**	1.12 (0.81-1.55)	1.09 (0.74-1.61)				
	Adj	**1.19 (1.09-1.29)**	-	-				

Bodily fracture location groupings primarily based on paper reporting. Significant values denoted in bold. Adj- adjusted risk estimates M- Male, F- Female

PRISMA 2020 flow diagram for new systematic reviews which included searches of databases, registers and other sources

Identification of studies via databases and registers

Identification

Records identified from*:
Databases (n = 3,563)

→ Records removed *before screening*:
Duplicate records removed (n = 3,238)

Screening

Records screened (n = 325)

→ Records excluded** (n = 306)

Reports sought for retrieval (n = 19)

→ Reports not retrieved (n = 1)

Reports assessed for eligibility (n = 18)

→ Reports excluded:
Wrong outcome (n = 5)
Wrong population (n = 1)

Identification of studies via other methods

Records identified from:
Reference list checking (n= 132)
Citation searching Sept 2021 (n = 192)
Citation searching Nov 2022 (n = 279)

Reports sought for retrieval (n = 36)

→ Reports not retrieved (n = 0)

Reports assessed for eligibility (n = 36)

→ Reports excluded:
Wrong outcome (n = 13)
Wrong population (n = 9)
Wrong study design (n= 9)
Wrong language (n = 2)

Included

Studies included in review (n = 15)
Reports of included studies (n = 15)

*Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers).
**If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools.

From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/

Figure 2: Pooled adjusted odds ratio estimates from studies examining the association between osteoporosis and suicide.

Article	Year	Country	n		Odds Ratio (95% CI)	% Weight
Webb	2012	UK	22		1.62 (0.99, 2.63)	18.62
Ahmedani	2017	USA	48		1.21 (0.90, 1.62)	31.27
Chang	2018	Taiwan	4053		0.97 (0.93, 1.02)	50.10
Overall, DL (I^2 = 67.9%, p = 0.044)					1.14 (0.88, 1.49)	100.00

.5   1   5