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Predictors of falls and fractures leading to hospitalization in 36,101 people with affective disorders: A large representative cohort study

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3 **1 Predictors of falls and fractures leading to hospitalization in 36,101 people with**
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5 **2 affective disorders: A large representative cohort study**
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8 Running title: Predictors of falls and fractures in people with affective disorders
9

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2
3 **23 Abstract (257/300)**
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6 **24 Objectives:** To investigate predictors of falls and fractures leading to hospitalisation in people
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8 **25** with affective disorders.
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11 **26 Design:** Cohort study
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14 **27 Setting:** the South London and Maudsley NHS Foundation Trust (SLaM) Biomedical Research
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16 **28** Centre (BRC) Case Register
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19 **29 Participants:** A large cohort of people with affective disorders (ICD10 codes F30-F34)
20
21 diagnosed between January 2008 and March 2016 was assembled using data from the SLaM
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23 **31** BRC Case Register
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27 **32 Primary and secondary outcome measures:** Falls and fractures leading to hospitalisation
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29 were ascertained from linked national hospitalization data. Multivariable Cox proportional
30
31 hazards analyses were administered to identify predictors of first falls and fractures.
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34
35 **35 Results:** Of 36,101 people with affective disorders (mean age 44.4 years, 60.2% female), 816
36
37 (incidence rate 9.91 per 1000 person years) and 1,117 (incidence rate 11.92 per 1000 person
38
39 years) experienced either a fall or fracture respectively. In multivariable analyses, older age,
40
41 analgesics use, increased physical illness burden, previous hospital admission due to certain
42
43 co-morbid physical illnesses and increase in attendances to accident and emergency services
44
45 following diagnosis were significant risk factors for both falls and fractures. Having a history
46
47 of falls was a strong risk factor for recurrent falls, and a previous fracture was also associated
48
49 with future fractures.
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53 **43 Conclusions:** Over a mean 5 years' follow-up, approximately 8% of people with affective
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55 disorders were hospitalised with a fall or fracture. Several similar factors were found to
56
57 predict risk of falls and fracture, for example, older age, comorbid physical disorders and
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3 46 analgesic use. Routine screening for bone mineral density and falls prevention programmes
4
5 47 should be considered for this clinical group.
6
7

8 48 **Key words:** osteoporosis, affective disorders, falls, fractures, hospital admission
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14 50 **Strength and limitation of the study:**
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- 16
17 51 • Predictors of falls and fractures leading to hospitalization in people with affective
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19 52 disorders were investigated with a large representative cohort
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22 53 • Data of the study were derived directly from the electronic health record
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24 54 • Falls and fractures leading to hospitalisation were ascertained from linked national
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26 55 hospitalization data
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28 56 • We did not stratify according to different affective disorder subtypes and psychotropic
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30 57 medication categories
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32 58 • We had no information on lifestyle factors and type of fractures recorded at admission
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3 60 **Word count: 3636/4000**
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6 61 **Introduction**
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9 62 Falls and fractures are strongly related with increased morbidity, mortality, disability, and
10 63 healthcare expenditure in the general population [1, 2], and they are a frequent issue in older
11 64 adults [3]. Their causes are multifactorial, such as muscle weakness [4] and use of antiepileptic
12 65 drugs [5]. Several government strategies have been implemented to prevent and assess falls in
13 66 the general population [3, 6]. Fractures, for example, hip and spine fractures increase the risk
14 67 of future falls and fractures [7]. Over 3 million people in the UK are at a high risk for fractures
15 68 [8], and prevention has been acknowledged as a worldwide priority [9].

16 69 Despite some progress in the general population, there is poor evidence on risk factors for falls
17 70 and fractures for patients with affective disorders. People with mental health problems like
18 71 depression and schizophrenia report higher risks of falls and fractures compared to the general
19 72 population [10, 11], and despite poor evidence in people with bipolar disorders, a few studies
20 73 suggest this population may also be at increased risk [12, 13].

21 74 Several studies have investigated the association between bone loss and depression, but there
22 75 is a lack of large-scale cohort studies focussing on falls and fractures and related predictors.
23 76 Another major limitation is that the majority of studies have relied on self-reported affective
24 77 symptoms rather than clinical diagnosis [14, 15].

25 78 Given these limitations and the increased concerns about the adverse events of falls and
26 79 fractures, this representative cohort study investigates predictors of falls and fractures leading
27 80 to hospitalisation among people with clinically diagnosed affective disorders.
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30 82 **Methods**
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3 83 A retrospective observational study was carried out using data from the South London and
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5 84 Maudsley NHS Foundation Trust (SLaM) Biomedical Research Centre (BRC) Case Register.
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7 85 SLaM is one of the largest mental health and dementia care providers in Europe, serving a
8
9 86 geographic catchment of four South London Boroughs (including Lambeth, Lewisham,
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11 87 Southwark, and Croydon) with a population in excess of 1.3 million. Data for this study were
12
13 88 retrieved using the Clinical Record Interactive Search (CRIS) platform, which enables a de-
14
15 89 identified version of SLaM's electronic health record to be accessible for research projects
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17 90 within a robust and patient-led government framework [16]. The SLaM BRC Case Register
18
19 91 has been described in detail elsewhere [17] and has supported a wide range of studies [18,
20
21 92 19], including longitudinal cohort studies investigating falls and fractures in other populations
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23 93 [20, 21]. Data are currently archived in CRIS on more than 450,000 cases with a wide variety
24
25 94 of mental disorders. CRIS has full approval for secondary analysis (Oxford Research Ethnic
26
27 95 Committee C, reference 18/SC/0372). Data from source structured fields have been
28
29 96 extensively supplemented through natural language process (NLP) applications using
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31 97 Generalised Architecture for Text Engineering software, applying information extraction
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33 98 techniques to derive structured information from the extensive text fields held in the mental
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35 99 health record [17].
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101 **Participants, study period and additional data sources**

102 All SLaM patients with mood [affective] disorders (ICD10 codes F30-F34), diagnosed
103 between 1st of January 2008 and 31st March 2016, were included. SLaM patient records have
104 been linked with national Hospital Episode Statistics (HES) which are compiled from all NHS
105 Trusts in England (both acute and mental health services), including statistical abstracts of
106 records of all inpatient episodes, as well as outpatient and emergency care [17]. In addition,

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3 107 CRIS data have been linked to the Office for National Statistics (ONS) mortality records over
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5 108 the same period.
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110 **Patient and public involvement (PPI)**

111 The entire research program was developed after extensive patient, public and carer input, who
112 helped develop the study, and contributed to the funding applicable. They co-developed the
113 research questions, outcomes and contributed to factors included in the models. Moreover, they
114 reinforced this research as a neglected topic of utmost importance to them. The PPI group
115 designed the study with the senior researcher of the paper (Dr BS), they were involved in the
116 conception of the idea, the planning of the study during bimonthly meetings to discuss study
117 design, hypotheses, outcomes and what matters to patients of interest. They were also involved
118 in helping interpret the data outputs and publication. Results will be summarised and made
119 available to the PPI group through local newsletters and inform clinical services and local co-
120 developed Recovery College Courses.
121
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123 **Co-primary outcome: falls and any fractures**

124 The co-primary outcomes were hospital admissions relating to a fall or any fracture extracted
125 from linked HES data and all discharge diagnoses (primary or any secondary diagnosis codes)
126 recorded between January 2008 to March 2016, and based on the following ICD 10 codes: i)
127 falls (W00-W19); ii) fractures (M80-M84, M907, S02, S12, S32, S42, S52, S62, S72, S82,
128 S92, S22, T02, T08, T10, T12X, T902, T911, T912, T921). In addition, linked mortality
129 records from the ONS linkage were examined for any instance of fall or fracture ICD codes in
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3 130 any cause of death field on the death certificate to identify the date of death attributed to a fall
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5 131 or fracture.
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10 11 133 **Measurements**

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14 134 Several additional measurements were obtained from CRIS. All independent variables
15
16 135 (covariates) were defined according to the value closest to the date of the first recorded mood
17
18 136 [affective] disorder diagnosis. Demographic covariates comprised: age at diagnosis, gender,
19
20 137 and ethnicity [multiple codes categorised into 1) White, consists of White British, White Irish
21
22 138 and other White; and 2) Non-White]. Index of Multiple Deprivation (IMD 2015) for the
23
24 139 neighbourhood of residence (i.e. Lower Super Output Area, which consists of approximately
25
26 140 650 households) at the time of diagnosis was divided into quintiles according to deprivation
27
28 141 scores with equal size allocated to each group. The IMD has previously been used in CRIS [22]
29
30 142 and combines Census-derived data at area level across several domains including income,
31
32 143 employment, health, education, barriers to housing and services, living environment, and crime
33
34 144 [23]. Information on cohabiting status (Cohabiting: married/civil partner, married, cohabiting;
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36 145 Non-cohabiting: single, divorced, civil partnership dissolved, widowed, separated) was also
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38 146 ascertained at the index diagnosis.
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48 148 ***Illness burden***

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50 149 The Health of the Nation Outcome Scales (HoNOS) [24] are routinely administered measures
51
52 150 of illness burden in UK mental health services and are recorded in structured fields on the
53
54 151 electronic health record. Individual HoNOS item scores (agitated behaviour, self-injury,
55
56 152 problem drinking & drugs, cognitive problems, physical illness, hallucinations, depressed
57
58 153 mood, relationship problems, daily living problems, living conditions problems, occupational
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3 154 problems) and dates were obtained within 6 months before or after the date of the index
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5 155 diagnosis, and the closest scores in time to this date were included in analyses. Each HoNOS
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8 156 item is rated on a Likert Scale, ranging from 0 (i.e. no problem) to 4 (i.e. severe or very severe
9
10 157 problem). A detailed glossary for HoNOS is reported elsewhere [25]. Scores 2 or over in the
11
12 158 individual HoNOS scales were classified as having a problem on each item, generating binary
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15 159 covariates.

160

161 ***Mental disorder comorbidity***

162 Diagnoses of F00-F03 (dementia); F20-F29 (schizophrenia spectrum disorder); F40-F48
163 (neurotic, stress-related and somatoform disorders); F50 (eating disorders); F60-F69 (disorders
164 of adult personality and behaviour) were ascertained within one year before or after the index
165 diagnosis of mood [affective] disorder.

166 ***Medication***

167 Medications received were extracted from structured medication fields in the record,
168 supplemented by an NLP application applied to text fields ascertaining mentions of current
169 medication [17]. Presence or not of the following medication groups was ascertained on the
170 basis of information within six months before or after the index diagnosis: anticholinergics,
171 antihypertensives, antidepressants, antipsychotics, anxiolytics and hypnotics, and analgesics.
172 The total number of medications prescribed for any condition was calculated for each
173 participant and used as a continuous variable.

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3 175 ***Physical comorbidity***
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6 176 Information on physical comorbidities was ascertained utilising the data linkage between CRIS
7
8 177 and national HES records. Information on all ICD-10 diagnoses at discharge (primary or any
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10 178 secondary diagnosis codes) was ascertained from any hospitalisations within 6 months before
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13 179 or after the index diagnosis date and the following binary variables generated: i) Ischaemic
14
15 180 heart disease (IHD; I20, I21, I22, including coronary heart disease (CHD; I25); ii) Arrhythmia
16
17 181 (I44-I49, including atrial fibrillation (AF; I48); iii) Heart failure (I50); iv) Diabetes (E08, E09,
18
19 182 E10, E11, E12, E13; v) Hypotension (I95-99); vi) Hypercholesterolemia (E78); vii)
20
21 183 Hypertension (I10-15); viii) Urinary tract infections (UTI) (N39); ix) Osteoporosis (M80-85);
22
23 184 x) Visual disturbance and blindness (H53-54); xi) Hearing loss (H90-95); xii) Syncope or
24
25 185 collapse (R50-R69); xiii) Parkinson's disease (G20). Furthermore, occurrence of falls and/or
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27 186 fractures before the index diagnosis was also collected. Finally, the number of attendances to
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29 187 accident and emergency services (A&E) following the index diagnosis was also recorded.
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37 189 **Statistical analysis**
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40 190 The study sample was described initially in terms of demographic and clinical variables,
41
42 191 followed by unadjusted Cox proportional hazard models to predict the first fall and first fracture
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44 192 separately after the index diagnosis of mood [affective] disorder. The predictor variables at
45
46 193 baseline used in the first univariate models included sociodemographic information (year of
47
48 194 index diagnosis, mean age, gender, ethnicity, marital status), medications (antipsychotics,
49
50 195 anxiolytics & hypnotics, antidepressants, analgesics, anticholinergics, antihypertensives),
51
52 196 comorbid psychiatric diagnosis (F20-29 schizophrenia spectrum disorder, F40-48
53
54 197 neurotic/stress disorders, F00-F03 dementia, F50 eating disorders, F60 disorders of adult
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56 198 personality and behaviour), HONOS scores (mean total and each individual item) and physical
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3 199 health comorbidities (as indicated above). Factors that yielded a p-value < 0.10 in the univariate
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5 200 model for fall or fracture outcome were subsequently entered into the multivariable model. A
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8 201 final multivariable Cox proportional hazards model, using stepwise backward elimination
9
10 202 technique where those variables not significant (p-value > 0.05) were eliminated, with hazard
11
12 203 ratios and 95% confidence intervals (CI) displayed. Having checked a correlation matrix of
13
14 204 coefficients in the Cox model, total number of medications received was substantially collinear
15
16 205 with individual types of medication received; therefore, this total number was removed as a
17
18 206 covariate. All analyses were conducted utilising STATA, version 13.
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208 **Results**

209 The sample comprised 36,101 people with a diagnosis of mood [affective] disorder (F30* -
210 F34*) (mean age at first diagnosis 44.4, SD: 17.8, 60.2% female). Over a mean 5 years' follow-
211 up, 2,948 patients had a fall and/or a fracture recorded: 816 only a fall, 1,117 only a fracture,
212 and 1,015 both; 1,831 with any fall and 2,193 with any fracture. The incidence rate of falls was
213 9.91 per 1,000 person years and that for fractures 11.92 per 1,000 person years. Table 1
214 summarises characteristics of those who had a recorded fall or fracture compared to those who
215 did not.
216

217

218 [Table 1]

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219 **Length of hospital stay**

220 The mean length of hospitalisation following a fall (n = 1,831) was 7.9 days (range 0-374), for
221 a total of 20,767 full days in hospital. The mean length of stay in hospital following a fracture

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3 222 (n=2,193) was 13.2 days (range 0-374), for a total of 40,548 days. This equates to 18.51 years
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5 223 of inpatient hospital stay for 1,000-person years of follow-up due to a fall and 36.15 years of
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7 224 inpatient hospital stay for 1,000-person years of follow-up due to a fracture. For the 1,831
8
9 225 patients reporting a fall, the mean hospital admissions due to a fall was 1.5 (range 1- 15); for
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11 226 the 2,193 patients reporting a fracture, the mean number of hospital admissions due to a fracture
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13 227 was 2.3 (range 1-42).
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21 229 **Factors associated with falls and fractures**

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23 230 Cox proportional hazard models analysing unadjusted predictors of falls and fractures (95%
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25 231 CI) are reported in Table 2.
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32 233 [Table 2]
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35 234 **Multivariable predictors of falls**

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37 235 Multivariable models of factors associated with first fall hospital admission are presented in
38
39 236 Table 3. In Model 2, older age was strongly associated with higher risk, and Non-European
40
41 237 ethnicity with lower risk, but neighbourhood deprivation reported no association. Analgesics
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43 238 had a significant association (with increased risk), and of co-morbid psychiatric conditions,
44
45 239 only the ICD-10 F40-F48 group had a significant association (with reduced risk). Of the
46
47 240 HoNOS items, cognitive problems and physical illness were associated with higher risk, and
48
49 241 depressed mood problems with lower risk. Higher risk of falls was associated with several
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51 242 hospitalisation discharge diagnoses, namely heart failure, diabetes, hypotension, UTI,
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53 243 osteoporosis, and syncope or collapse. Hospitalised fall was associated with having a previous
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3 244 history of falls reported before the index diagnosis and with increased A&E attendance after
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5 245 the index diagnosis.
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11 247 [Table 3]
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17 249 **Multivariable predictors of fractures**

20 250 Table 4 presents multivariable models of factors associated with first fracture hospitalisation.

22 251 Fracture risk was increased in older patients and women and was decreased in those of Non-

24 252 European. Fracture risk was lower in patients receiving antihypertensives and higher in those

26 253 receiving analgesics. It was also lower in those with neurotic, stress-related and somatoform

28 254 disorders (i.e. F40-F48), as well as bipolar affective disorder and manic episodes (i.e. F30-

30 255 F31). An elevated fracture risk was associated with physical illness on the HoNOS. Fracture

32 256 risk was independently predicted by previous hospitalisations for heart failure, diabetes, UTI,

34 257 osteoporosis, hearing loss and preceding fracture-related (but not fall-related) hospitalisations.

36 258 Fracture risk was also associated with higher levels of post-diagnostic A&E attendance.
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44 260 [Table 4]
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263 Discussion

264 To our knowledge, the current study is the first using representative data to investigate the
265 predictors of hospitalised falls and fractures in people with clinically diagnosed affective
266 disorders. Our data suggest that out of 36,101 people with affective disorders, 816 (i.e. 2.26%)
267 and 1,117 (i.e. 3.09%) of patients experienced a fall and fracture, respectively. Length of
268 hospital stay was considerable, equating to 18.51 and 36.15 years of inpatient hospital stay for
269 1,000-person years of follow-up due to a fall and a fracture, respectively. The key factors
270 increasing the risk of a hospitalised fall were older age, analgesic use, increased illness burden
271 due to cognitive problems and physical illness, a history of general hospital admission due to
272 co-morbid physical illnesses (in particular syncope or collapse), increase in one attendance to
273 A & E following affective disorder diagnosis, and falls before the diagnosis. Similar risk factors
274 for fractures were noted.

275
276 Approximately 8.2% of our sample experienced a hospital admission due to either a fall or
277 fracture. Studies on healthy populations have suggested several mechanisms which may
278 explain these elevated risks in our sample, such as vitamin D deficiency [26, 27] and use of
279 antidepressants [28]. Several studies also proposed a negative effect of leptin on bone mass and
280 bone formation through a hypothalamic relay [29]. Some lifestyle factors seem to also be
281 associated with a poor bone health, including physical inactivity [30] and alcohol consumption
282 [31]. Previous studies have hypothesised other risk factors contributing to falls and fractures in
283 people with depressive disorders [32], but no large-scale study has yet focused on patients with
284 clinically diagnosed affective disorders. Our data advance the current literature by providing
285 detailed evidence on how a multitude of demographic, medical, and psychological factors can
286 differently affect risks of falls and fractures in people with affective disorder.

287

288 The association between older age and incidence of fall may be due to age-related physical
289 conditions, as well as physiologic (e.g. loss of BMD) [33] and pathologic changes (e.g.
290 decreased cardiovascular functions) [34]. Female gender is also a well-established risk factor
291 for osteoporosis [35], consistent with our finding. Surprisingly, we found no relationship
292 between deprivation and falls and fractures, although previous evidence has associated
293 deprivation with fractures across different age groups [36, 37]. We might suppose that while
294 deprivation is associated with poor nutrition and physical inactivity, people with affective
295 disorders have a poorer lifestyle, compared to the general population [38], regardless of their
296 financial status or living condition. Finally, the protective role of a non-European ethnic
297 background is comparable with previous evidence supporting a higher fracture rate in
298 Caucasian women compared to women from other ethnic groups [39], and a lower fall rate in
299 older immigrants than those with an English-speaking background [40].

300

301 Our results provide new evidence on how hospitalisation due to falls or fractures can be an
302 important burden for the NHS resources and for people with affective disorders, who are
303 already at risk for a prolonged hospitalisation [41]. Given the long hospital stay among our
304 sample, its burden on NHS costs is unsurprising. The total cost of fracture is estimated to reach
305 £4.4 billion per year in the UK alone [8]. Several items from the HoNOS were also associated
306 with increased hazard of hospitalisation due to falls or fractures (e.g. cognitive problems).
307 Evidence on the role of these factors on hospital stay among this population is warranted for
308 future research.

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3 310 Our study reports stress-related and somatoform disorders to be associated with a decreased
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5 311 risk of falls and fractures, which could be due to increased fear avoidance and reduced activities
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7 312 due to stress-related disorders, leading to fewer falls [42]. We also found the presence of bipolar
8
9 313 affective disorder and manic episodes to be protective factors against increased fracture risk.
10
11 314 Although there has been little evidence investigating the role of bipolar affective disorder or
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13 315 its characteristics (including manic symptoms) in the risk of fracture, preliminary evidence has
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15 316 suggested an association between the use of lithium (i.e. a primary treatment for bipolar
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17 317 disorder) and decreased fracture risk [43], the preservation and enhancement of bone mass [44].
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25 319 Surprisingly, neither antidepressants nor antipsychotics were associated with risks of falls or
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27 320 fracture, despite documented associations between antipsychotic medications and reduced
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29 321 bone metabolism [45] and BMD [46]. Evidence on the association between antidepressants and
30
31 322 BMD is ambiguous: while some authors reported that some antidepressants, especially SSRIs,
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33 323 have a negative impact on bone strength [47, 48], other findings have been null [49]. However,
34
35 324 we did not attempt to account for specific types of antidepressants in the analysis, and previous
36
37 325 studies indicate that tricyclic antidepressants have no adverse effect on bone health [28]. On
38
39 326 the other hand, analgesics use was associated with increased risks for falls and fractures,
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41 327 consistently with previous findings [50], and possibly mediated by central nervous system
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43 328 effects, such as dizziness [51]. Antihypertensive drugs use was associated with a decreased
44
45 329 fracture risk, confirming previous results [52], potentially due to their improving effect on
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47 330 calcium absorption [53].
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56 332 Finally, extensive evidence has indicated several physical conditions as risk factors for falls or
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58 333 fractures in the general population [54, 55], including UTI [56] and diabetes [57]. It is known
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3 334 that mental health disorders (e.g. depression) increase the chance of major physical co-
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5 335 morbidities [58]. However, few studies have established the impact of comorbid physical
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8 336 conditions on risks of falls and fractures among people with affective disorders. Our study
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10 337 indicates heart failure, diabetes, UTI and osteoporosis to be associated with hospitalisation due
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12 338 to falls or fractures. Hypotension and syncope or collapse were additionally associated with an
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14 339 increased risk of falls, and hearing loss was associated with an elevated fracture risk.
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16
17 340 Unsurprisingly, osteoporosis was strongly associated with falls and fractures, as it has been
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19 341 acknowledged as the most important yet potentially treatable factor for falls [54] and fractures
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21 342 [59] due to its effect on BMD. Moreover, osteoporosis tends to occur simultaneously with heart
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23 343 failure [60] due to shared risk factors such as diabetes. Unsurprisingly, syncope or collapse was
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25 344 also strongly associated with an increased risk of falls, as syncope is frequently mistaken for
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27 345 falls, to the point that the European Society of Cardiology has emphasised the need to explore
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29 346 syncope as an independent factor leading to falls [61]. Diabetes was another risk factor for both
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31 347 falls and fracture, confirming the association found in the general population [62]. Hearing loss
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33 348 was the only factor associated with an elevated risk of fracture in our study, an association
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35 349 previously confirmed in the general population [63]. This finding may be explained by the
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37 350 damaging impact of hearing loss on orientation skills and physical activity [64]. Finally, our
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39 351 study confirmed the association between history of falls and increased risk of future falls,
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41 352 previously reported in the general population [34, 65] and in people with depression [66].
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43 353 Moreover, our data confirmed how a prior fracture represents a 50-100% higher risk for
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45 354 experiencing future fracture, as reported in the general population [67].
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55 356 The main strengths of our study are: i) analyses controlling for various confounders; and ii) a
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57 357 large sample including people with clinically diagnosed affective disorders. However, there are
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59 358 important limitations. Firstly, we did not stratify according to different affective disorder

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3 359 subtypes which could report different risk factors; similarly, we analysed psychotropic
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5 360 medication categories but did not investigate specific agents or sub-categories. Second, we had
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8 361 no information on the types of fractures reported at admission and on factors (e.g. balance) that
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10 362 are influenced by neuropathological lesions in people with depression [68]. Third, lifestyle
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12 363 factors, such as alcohol consumption [31, 38], could not be explored. Fourth, our study only
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14 364 ascertained information on physical co-morbidities from hospitalisation records and could have
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16 365 overlooked patients with mild osteoporosis. Additionally, physical co-morbidities were
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18 366 ascertained within six months of diagnosis, and patients who were hospitalised for a fall or
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20 367 fracture within these six months would be more likely to have their osteoporosis ascertained.
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22 368 Finally, since medication records were ascertained within one year of diagnosis, we cannot
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24 369 assess whether medications were prescribed as a result or as a cause of falls for those who had
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26 370 a fall or fracture within six months of their diagnosis.
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372 **Conclusion**

373 Our study reports that over a mean 5 years' follow-up, approximately 8% of a large cohort with
374 affective disorders was hospitalised due to either a fall or fracture. Factors such as older age,
375 certain medications and having a history of fall or fracture are significant predictors, broadly
376 comparable to risk factors established in the general population. Heavy hospital burden
377 following a fall or fracture was also described.
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379 Our current study provides important implications for future research and clinical practice.
380 BMD checks and osteoporosis screenings should be a routine for people with affective
381 disorders, especially if older and with established co-morbid chronic illnesses. However,
382 evidence suggests a lack of osteoporosis screening and fracture prevention for people with

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3 383 mental health problems [69]. Fall assessments (e.g. the Fracture Risk Assessment Tool) should
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5 384 be considered for people with affective disorders, since approximately 70% of low-energy
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7 385 fractures are due to falls [70]. However, there is a lack of fall prevention programmes for this
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9 386 population, despite research indicating an average 14% reduction in falls risk in the general
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11 387 population [71]. Fall/fracture prevention programmes should therefore be offered; for example,
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13 388 the combination of cognitive behavioural therapy and exercise for improving depressive
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15 389 symptoms [72] and self-efficacy [73].
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393 Author's contributions

394 BS acquired funding for the study. GP conducted the analysis with support from all co-authors.
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399

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6 408 Ethics approval
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9 409 This study has full approval for secondary analysis of CRIS (Oxford Research Ethnic
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11 410 Committee C, reference 18/SC/0372).
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17 412 Conflicts of interest
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19 413 All authors declare no conflicts of interest.
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24 415 Data availability statement
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27 416 Data are available on reasonable request. For questions regarding the study, please contact RM
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29 417 at ruimin.l.ma@kcl.ac.uk
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Table 1: Characteristics of those Mood [affective] disorders patients who were admitted to hospital with a fall/fracture after a diagnosis of Mood [affective] disorders (F30* to F34*).

Characteristics of sample	Presence of falls		Presence of fractures	
	No (n=34,270)	Yes (n=1,831)	No (n=33,908)	Yes (n=2,193)
Age at the time of Mood [affective] disorders diagnosis				
18- 34	12685 (37.0)	205 (11.2)	12572 (37.1)	318 (14.5)
35- 49	11409 (33.3)	336 (18.4)	11346 (33.5)	399 (18.2)
50- 64	5829 (17.0)	362 (19.8)	5751 (17.0)	440 (20.1)
65- 79	2797 (8.2)	485 (26.5)	2728 (8.0)	554 (25.3)
80 & over	1550 (4.5)	443 (24.2)	1511 (4.5)	482 (22.0)
Gender				
Female	20627 (60.2)	1107 (60.5)	20348 (60.0)	1386 (63.2)
Male	13638 (39.8)	724 (39.5)	13555 (40.0)	807 (36.8)
Ethnicity				
White	20772 (60.6)	1519 (83.0)	20536 (60.6)	1755 (80.0)
Non-white	12450 (36.3)	288 (15.7)	12333 (36.4)	405 (18.5)
Marital status				
Cohabiting	7957 (23.2)	416 (22.7)	7867 (23.2)	506 (23.1)
Non-cohabiting	23028 (67.2)	1345 (73.5)	22776 (67.2)	1597 (72.8)
Index of multiple deprivation: IMD 2015 (SD)				
Least deprived quintile	27.97 (11.31)	27.90 (11.53)	27.97 (11.30)	27.97 (11.52)
2nd most deprived quintile	6657 (19.4)	388 (21.2)	6593 (19.4)	452 (20.6)
3rd most deprived quintile	6682 (19.5)	378 (20.6)	6643 (19.6)	417 (19.0)
Most deprived quintile	6706 (19.6)	354 (19.3)	6637 (19.6)	423 (19.3)
	6708 (19.6)	346 (18.9)	6612 (19.5)	442 (20.2)

Medication prescription (within 6 months before or after Mood [affective] disorders diagnosis)

Anticholinergics	17714 (51.7)	1089 (59.5)	17489 (51.6)	1314 (59.9)
Antihypertensives	2561 (7.5)	386 (21.1)	2553 (7.5)	394 (18.0)
Antidepressants	19351 (56.5)	1168 (63.8)	19113 (56.4)	1406 (64.1)
Antipsychotics	8777 (25.6)	469 (25.6)	8694 (25.6)	552 (25.2)
Anxiolytics and Hypnotics	9443 (27.6)	558 (30.5)	9349 (27.6)	652 (29.7)
Analgesics	3083 (9.0)	405 (22.1)	3059 (9.0)	429 (19.6)

Number of medications received (within 6 months before or after Mood [affective] disorders diagnosis)

0	10207 (29.8)	394 (21.5)	10126 (29.9)	475 (21.7)
1	5330 (15.6)	259 (14.1)	5275 (15.6)	314 (14.3)
2	7062 (20.6)	360 (19.7)	6961 (20.5)	461 (21.0)
3	6599 (19.3)	361 (19.7)	6503 (19.2)	457 (20.8)
4	3858 (11.3)	304 (16.6)	3839 (11.3)	323 (14.7)
5	1038 (3.0)	121 (6.6)	1029 (3.0)	130 (5.9)
6	176 (0.5)	32 (1.7)	175 (0.5)	33 (1.5)

Other psychiatric conditions (within six months before or after Mood [affective] disorders diagnosis)

F00- F03 (Dementia)	754 (2.2)	207 (11.3)	749 (2.2)	212 (9.7)
F 20- F29 (Schizophrenia spectrum disorder)	2701 (7.9)	119 (6.5)	2676 (7.9)	144 (6.6)
F30- F31 (Bipolar affective disorder)	5489 (16.0)	222 (12.1)	5475 (16.1)	236 (10.8)
F50 (Eating Disorders)	447 (1.3)	13 (0.7)	441 (1.3)	19 (0.9)
F40- F48 (Neurotic, stress-related and somatoform disorders)	3652 (10.7)	147 (8.0)	3601 (10.6)	198 (9.0)
F 60 (Disorders of adult personality and behaviour)	1436 (4.2)	77 (4.2)	1428 (4.2)	85 (3.9)

Problem HoNOS (score 2 or over) (within six months before or after Mood [affective] disorders diagnosis)

Agitated Behaviour	3571 (10.4)	234 (12.8)	3547 (10.5)	258 (11.8)
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3	Self-Injury	3586 (10.5)	186 (10.2)	3545 (10.5)	227 (10.4)
4	Problem Drinking Drugs	2957 (8.6)	204 (11.1)	2932 (8.6)	229 (10.4)
5	Cognitive Problems	2821 (8.2)	349 (19.1)	2792 (8.2)	378 (17.2)
6	Physical Illness	6514 (19.0)	770 (42.1)	6355 (18.7)	929 (42.4)
7	Hallucinations	3198 (9.3)	175 (9.6)	3176 (9.4)	197 (9.0)
8	Depressed Mood	14582 (42.6)	766 (41.8)	14390 (42.4)	958 (43.7)
9	Relationship Problems	7644 (22.3)	342 (18.7)	7560 (22.3)	426 (19.4)
10	Daily Living Problems	5854 (17.1)	576 (31.5)	5723 (16.9)	707 (32.2)
11	Living Conditions Problems Score	3431 (10)	190 (10.4)	3404 (10.0)	217 (9.9)
12	Occupational Problems	5574 (16.3)	392 (21.4)	5513 (16.3)	453 (20.7)
13	Mean overall HoNoS score (SD)	10.67 (5.63)	11.64 (5.53)	10.64 (5.63)	11.91 (5.46)
14	Number with missing HoNoS	12545 (36.6)	523 (28.6)	12411 (36.6)	657 (30.0)

Hospital admissions (within six months before or after Mood [affective] disorders diagnosis)

15	Ischaemia +CHD+ IHD	1128 (3.3)	210 (11.5)	1089 (3.2)	249 (11.4)
16	Arrhythmia + AF	1003 (2.9)	197 (10.8)	967 (2.9)	233 (10.6)
17	Heart failure	437 (1.3)	88 (4.8)	417 (1.2)	108 (4.9)
18	Diabetes	1516 (4.4)	264 (14.4)	1488 (4.4)	292 (13.3)
19	Hypotension	435 (1.3)	104 (5.7)	424 (1.3)	115 (5.2)
20	Hypercholesterolemia	1097 (3.2)	221 (12.1)	1090 (3.2)	228 (10.4)
21	Hypertension	2837 (8.3)	546 (29.8)	2752 (8.1)	631 (28.8)
22	Urinary tract infections (UTI)	1366 (4.0)	324 (17.7)	1297 (3.8)	393 (17.9)
23	Osteoporosis	409 (1.2)	121 (6.6)	183 (0.5)	347 (15.8)
24	Visual Disturbance and Blindness	241 (0.7)	53 (2.9)	246 (0.8)	48 (2.2)
25	Hearing Loss	189 (0.6)	41 (2.2)	174 (0.5)	56 (2.6)
26	Syncope or Collapse	1990 (5.8)	444 (24.2)	2022 (6.0)	412 (18.8)
27	Parkinson's Disease	116 (0.3)	45 (2.5)	128 (0.4)	33 (1.5)
28	Falls before diagnosis	750 (2.2)	267 (14.6)	749 (2.2)	268 (12.2)

Fractures before diagnosis	1075 (3.1)	231 (12.6)	860 (20.7)	446 (20.3)
mean number of attendances to A&E following Mood [affective] disorders diagnosis (SD)	3.94 (9.98)	16.64 (28.88)	4.00 (9.62)	13.67 (29.35)

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Table 2: Univariate Cox proportional hazard model (95% CI) showing factors affecting time to first fall/fracture hospital admission since diagnosis of Mood [affective] disorders

Characteristics	Outcome falls		Outcome fractures	
	HR (95% CI)	P value	HR (95% CI)	P value
Age at the time of Mood [affective] disorders diagnosis				
18- 34	Ref.		Ref.	
35- 49	1.74 (1.46, 2.07)	<0.001	1.33 (1.15, 1.54)	<0.001
50- 64	3.88 (3.27, 4.61)	<0.001	3.03 (2.62, 3.50)	<0.001
65- 79	12.41 (10.54, 14.62)	<0.001	9.11 (7.94, 10.46)	<0.001
80 & over	26.94 (22.8, 31.83)	<0.001	18.46 (16.00, 21.29)	<0.001
Female gender	0.99 (0.90, 1.09)	0.87	1.12 (1.03, 1.22)	0.01
Non-European ethnicity	0.32 (0.28, 0.37)	<0.001	0.39 (0.35, 0.44)	<0.001
Non-cohabiting marital status	1.08 (0.97, 1.21)	0.17	1.05 (0.95, 1.16)	0.31
Deprivation quintile (IMD 2015)				
Least deprived quintile	Ref.		Ref.	
2nd least deprived quintile	0.83 (0.71, 0.96)	0.01	0.89 (0.78, 0.99)	0.04
3rd most deprived quintile	0.88 (0.76, 1.02)	0.09	0.90 (0.79, 1.03)	0.13
2nd most deprived quintile	0.94 (0.82, 1.09)	0.43	0.89 (0.78, 1.00)	0.05
Most deprived quintile	0.86 (0.74, 0.99)	0.04	0.94 (0.82, 1.07)	0.35
Medication prescribed (within one year before or after Mood [affective] disorders diagnosis)				
Anticholinergics received	1.42 (1.3, 1.56)	<0.001	1.45 (1.33, 1.57)	<0.001
Antihypertensive received	3.69 (3.3, 4.13)	<0.001	2.98 (2.67, 3.33)	<0.001
Antidepressants received	1.41 (1.29, 1.56)	<0.001	1.43 (1.31, 1.56)	<0.001

Antipsychotics received	0.95 (0.86, 1.06)	0.35	0.93 (0.84, 1.02)	0.12
Anxiolytics and Hypnotics received	1.11 (1.00, 1.22)	0.05	1.06 (0.97, 1.17)	0.18
Analgesics received	2.97 (2.66, 3.32)	<0.001	2.52 (2.27, 2.80)	<0.001
Increase in one type of polypharmacy	1.21 (1.18, 1.25)	<0.001	1.18 (1.15, 1.21)	<0.001
Presence of other psychiatric conditions (within one year before or after Mood [affective] disorders diagnosis)				
F00- F03 (Dementia)	6.90 (5.97, 7.98)	<0.001	5.65 (4.90, 6.51)	<0.001
F20- F29 (Schizophrenia spectrum disorder)	0.75 (0.62, 0.91)	<0.001	0.76 (0.64, 0.90)	0.01
F30- F31 (Bipolar affective disorder)	0.71 (0.62, 0.82)	<0.001	0.61 (0.54, 0.71)	<0.001
F40- F48 (Neurotic, stress-related and somatoform disorders)	0.76 (0.64, 0.90)	<0.001	0.86 (0.75, 0.99)	0.05
F50 (Eating Disorders)	0.53 (0.31, 0.91)	0.02	0.64 (0.41, 1.01)	0.06
F 60 (Disorders of adult personality and behaviour)	0.95 (0.76, 1.20)	0.68	0.87 (0.7, 1.09)	0.22
Problem in HoNoS (scored 2 or more)				
Agitated Behaviour	1.11 (0.97, 1.28)	0.14	1.03 (0.90, 1.17)	0.71
Self-Injury	0.84 (0.72, 0.98)	0.02	0.87 (0.76, 1.01)	0.06
Problem Drinking Drugs	1.11 (0.96, 1.29)	0.17	1.05 (0.91, 1.21)	0.48
Cognitive Problems	2.66 (2.35, 3.00)	<0.001	2.37 (2.11, 2.66)	<0.001
Physical Illness	3.88 (3.48, 4.34)	<0.001	4.17 (3.77, 4.63)	<0.001
Hallucinations	0.87 (0.74, 1.02)	0.08	0.82 (0.71, 0.96)	0.01
Depressed Mood	0.75 (0.67, 0.83)	<0.001	0.88 (0.80, 0.98)	0.02
Relationship Problems	0.65 (0.58, 0.74)	<0.001	0.71 (0.63, 0.79)	<0.001
Daily Living Problems	2.41 (2.16, 2.69)	<0.001	2.61 (2.36, 2.89)	<0.001
Living Conditions Problems	0.93 (0.80, 1.08)	0.34	0.89 (0.77, 1.02)	0.10
Occupational Problems	1.30 (1.15, 1.47)	<0.001	1.30 (1.16, 1.45)	<0.001
Overall increase in one unit of HoNoS	1.04 (1.03, 1.05)	<0.001	1.04 (1.04, 1.05)	<0.001
Admitted to general hospital (within one year before or after Mood [affective] disorders diagnosis)				

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3	Ischaemia +CHD+ IHD	5.25 (4.54, 6.06)	<0.001	5.17 (4.53, 5.90)	<0.001
4	Arrhythmia + AF	6.30 (5.43, 7.31)	<0.001	6.10 (5.32, 6.99)	<0.001
5	Heart failure	7.81 (6.29, 9.68)	<0.001	7.89 (6.49, 9.59)	<0.001
6	Diabetes	4.66 (4.09, 5.31)	<0.001	4.18 (3.69, 4.73)	<0.001
7	Hypotension	7.29 (5.98, 8.90)	<0.001	6.51 (5.39, 7.86)	<0.001
8	Hypercholesterolemia	5.14 (4.47, 5.92)	<0.001	4.24 (3.70, 4.87)	<0.001
9	Hypertension	6.08 (5.50, 6.72)	<0.001	5.78 (5.26, 6.34)	<0.001
10	Urinary tract infections (UTI)	7.24 (6.42, 8.17)	<0.001	7.36 (6.59, 8.21)	<0.001
11	Osteoporosis	7.75 (6.44, 9.32)	<0.001	36.39 (32.35, 40.94)	<0.001
12	Visual Disturbance and Blindness	5.25 (3.99, 6.90)	<0.001	3.78 (2.84, 5.03)	<0.001
13	Hearing Loss	5.57 (4.09, 7.60)	<0.001	6.45 (4.95, 8.41)	<0.001
14	Syncope or Collapse	6.17 (5.54, 6.86)	<0.001	4.27 (3.84, 4.76)	<0.001
15	Parkinson's Disease	9.83 (7.31, 13.23)	<0.001	5.60 (3.97, 7.89)	<0.001
16					
17	Falls before Mood [affective] disorders diagnosis	8.88 (7.8, 10.12)	<0.001	7.03 (6.18, 7.99)	<0.001
18	Fractures before Mood [affective] disorders diagnosis	5.31 (4.62, 6.10)	<0.001	10.67 (9.61, 11.85)	<0.001
19	Increase in one attendance to A&E following Mood [affective] disorders diagnosis	1.01 (1.01, 1.01)	<0.001	1.01 (1.01, 1.01)	<0.001
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Table 3: Two models showing predictors of first fall hospital admission among Mood [affective] disorders. (used stepwise removal of factors that were not significant at 0.05 P value).

Characteristics	Falls			
	Model 1 (n=20,938)	P value	Model 2 (n=22,414)	P value
Age at the time of Mood [affective] disorders diagnosis				
18- 34	Ref.		Ref.	
35- 49	1.59 (1.23, 2.06)	<0.001	1.58 (1.24, 2.02)	<0.001
50- 64	3.11 (2.40, 4.01)	<0.001	2.98 (2.33, 3.81)	<0.001
65- 79	8.07 (6.31, 10.33)	<0.001	7.65 (6.07, 9.64)	<0.001
80 & over	12.40 (9.51, 16.17)	<0.001	11.80 (9.25, 15.05)	<0.001
Non-European ethnicity	0.43 (0.36, 0.51)	<0.001	0.45 (0.38, 0.52)	<0.001
Deprivation quintile (IMD 2015)				
Least deprived quintile	Ref.			
2nd least deprived quintile	0.99 (0.83, 1.19)	0.92		
3rd most deprived quintile	1.14 (0.95, 1.36)	0.17		
2nd most deprived quintile	1.15 (0.96, 1.38)	0.13		
Most deprived quintile	1.00 (0.84, 1.20)	0.85		
Medication prescribed (within one year before or after diagnosis of Mood [affective] disorders)				
Anticholinergics received	0.95 (0.74, 1.22)	0.68		
Antihypertensive received	0.98 (0.79, 1.21)	0.82		
Antidepressants received	0.91 (0.74, 1.11)	0.36		
Anxiolytics and Hypnotics received	1.00 (0.80, 1.24)	0.97		
Analgesics received	1.36 (1.10, 1.68)	0.01	1.39 (1.22, 1.58)	<0.001

Increase in one type of polypharmacy	1.02 (0.87, 1.19)	0.80		
Presence of other psychiatric conditions (within one year before or after diagnosis of Mood [affective] disorders)				
F00- F03 (Dementia)	1.05 (0.86, 1.27)	0.64		
F20- F29 (Schizophrenia spectrum disorder)	1.07 (0.85, 1.34)	0.57		
F30-F31 (Bipolar affective disorder)	0.87 (0.72, 1.06)	0.16		
F40- F48 (Neurotic, stress-related and somatoform disorders)	0.74 (0.60, 0.91)	0.01	0.75 (0.61, 0.91)	0.01
F50 (Eating Disorders)	0.86 (0.36, 2.09)	0.74		
One unit increase in HoNoS				
Self-Injury	1.10 (0.92, 1.32)	0.30		
Cognitive Problems	1.25 (1.06, 1.46)	0.01	1.28 (1.12, 1.46)	<0.001
Physical Illness	1.23 (1.07, 1.42)	<0.001	1.25 (1.10, 1.42)	<0.001
Depressed Mood	0.80 (0.70, 0.92)	<0.001	0.83 (0.74, 0.93)	<0.001
Relationship Problems	0.98 (0.84, 1.14)	0.77		
Daily Living Problems	1.01 (0.87, 1.17)	0.94		
Occupational Problems	0.90 (0.78, 1.03)	0.13		
Admitted to general hospital (within one year before or after diagnosis of Mood [affective] disorders)				
Ischaemia +CHD+ IHD	0.95 (0.78, 1.15)	0.59		
Arrhythmia + AF	0.88 (0.73, 1.07)	0.20		
Heart failure	1.37 (1.05, 1.78)	0.02	1.27 (1.00, 1.63)	0.05
Diabetes	1.37 (1.16, 1.63)	<0.001	1.36 (1.16, 1.59)	<0.001
Hypotension	1.38 (1.09, 1.75)	0.01	1.34 (1.07, 1.68)	0.01
Hypercholesterolemia	1.16 (0.96, 1.39)	0.13		
Hypertension	1.05 (0.88, 1.23)	0.63		
Urinary tract infections (UTI)	1.33 (1.13, 1.56)	<0.001	1.33 (1.14, 1.54)	<0.001

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3	Osteoporosis	1.41 (1.08, 1.83)	0.01	1.37 (1.11, 1.70)	<0.001
4	Visual Disturbance and Blindness	1.22 (0.86, 1.71)	0.26		
5	Hearing Loss	0.91 (0.64, 1.30)	0.61		
6	Syncope or Collapse	1.94 (1.71, 2.26)	<0.001	2.05 (1.79, 2.36)	<0.001
7	Parkinson's Disease	1.25 (0.89, 1.77)	0.20		
8					
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11	Falls before Mood [affective] disorders diagnosis	1.81 (1.51, 2.18)	<0.001	1.81 (1.54, 2.13)	<0.001
12	Fractures before Mood [affective] disorders diagnosis	0.98 (0.78, 1.22)	0.86		
13	Increase in one attendance to A&E following Mood				
14	[affective] disorders * diagnosis	1.01 (1.01, 1.01)	<0.001	1.01 (1.01, 1.01)	<0.001
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Table 4: Two models showing predictors of first fracture hospital admission among Mood [affective] disorders patients.

Characteristics	Model 1 (n=20,936)		Model 2 (n=22,322)	
	HR (95% CI)	P value	HR (95% CI)	P value
Age at the time of Mood [affective] disorders diagnosis				
18- 34	Ref.		Ref.	
35- 49	1.27 (1.02, 1.57)	0.03	1.27 (1.03, 1.55)	0.02
50- 64	2.31 (1.85, 2.88)	<0.001	2.28 (1.85, 2.81)	<0.001
65- 79	5.75 (4.65, 7.11)	<0.001	5.55 (4.54, 6.77)	<0.001
80 & over	7.46 (5.90, 9.45)	<0.001	7.37 (5.93, 9.16)	<0.001
Female gender	1.21 (1.08, 1.36)	<0.001	1.15 (1.03, 1.29)	0.01
Non-European ethnicity	0.59 (0.51, 0.68)	<0.001	0.59 (0.51, 0.67)	<0.001
Deprivation quintile (IMD 2015)				
Least deprived quintile	Ref.			
2nd least deprived quintile	1.07 (0.91, 1.28)	0.41		
3rd most deprived quintile	1.11 (0.94, 1.32)	0.23		
2nd most deprived quintile	1.17 (0.99, 1.39)	0.07		
Most deprived quintile	1.00 (0.85, 1.19)	0.96		
Medication prescribed (within one year before or after diagnosis of Mood [affective] disorders)				
Anticholinergics received	1.08 (0.85, 1.26)	0.76		
Antihypertensive received	0.76 (0.65, 0.91)	<0.001	0.80 (0.70, 0.92)	<0.001
Antidepressants received	1.08 (0.91, 1.28)	0.37		
Analgesics received	1.28 (1.08, 1.52)	<0.001	1.33 (1.17, 1.51)	<0.001

Increase in one type of polypharmacy	1.01 (0.93, 1.11)	0.75		
Presence of other psychiatric conditions (within one year before or after diagnosis of Mood [affective] disorders)				
F00- F03 (Dementia)	1.14 (0.96, 1.41)	0.12		
F20- F29 (Schizophrenia spectrum disorder)	1.11 (0.91, 1.38)	0.30		
F30- F31 (Bipolar affective disorder)	0.81 (0.67, 0.98)	0.03	0.80 (0.68, 0.95)	0.01
F40- F48 (Neurotic, stress-related and somatoform disorders)	0.82 (0.68, 0.99)	0.04	0.83 (0.70, 0.99)	0.04
One unit increase in HoNoS				
Cognitive Problems	1.02 (0.87, 1.19)	0.83		
Physical Illness	1.36 (1.19, 1.56)	<0.001	1.48 (1.31, 1.67)	<0.001
Hallucinations	0.91 (0.76, 1.10)	0.34		
Depressed Mood	0.83 (0.72, 0.94)	0.01	0.91 (0.82, 1.00)	0.05
Relationship Problems	0.89 (0.77, 1.02)	0.10		
Daily Living Problems	1.12 (0.98, 1.29)	0.11		
Occupational Problems	0.91 (0.79, 1.04)	0.15		
Admitted to general hospital (within one year before or after diagnosis of Mood [affective] disorder)				
Ischaemia +CHD+ IHD	1.01 (0.85, 1.22)	0.88		
Arrhythmia + AF	1.03 (0.86, 1.23)	0.78		
Heart failure	1.44 (1.12, 1.86)	0.01	1.43 (1.14, 1.80)	<0.001
Diabetes	1.22 (1.04, 1.44)	0.02	1.23 (1.06, 1.44)	<0.001
Hypotension	1.18 (0.93, 1.48)	0.17		
Hypercholesterolemia	0.85 (0.71, 1.03)	0.10		
Hypertension	1.05 (0.90, 1.23)	0.53		
Urinary tract infections (UTI)	1.49 (1.28, 1.74)	<0.001	1.52 (1.32, 1.75)	<0.001
Osteoporosis	7.31 (5.82, 9.18)	<0.001	7.00 (5.65, 8.70)	<0.001
Visual Disturbance and Blindness	1.06 (0.74, 1.53)	0.74		

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3	Hearing Loss	1.40 (1.03, 1.92)	0.03	1.46 (1.09, 1.96)	0.01
4	Syncope or Collapse	1.18 (1.02, 1.36)	0.03		
5	Parkinson's Disease	0.85 (0.58, 1.25)	0.41		
6					
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8	Falls before Mood [affective] disorders diagnosis	1.02 (0.85, 1.22)	0.83		
9	Fractures before Mood [affective] disorders diagnosis	1.26 (1.01, 1.57)	0.04	1.33 (1.10, 1.63)	<0.001
10	Increase in one attendances to A&E following Mood				
11	[affective] disorders diagnosis	1.01 (1.01, 1.01)	<0.001	1.01 (1.01, 1.01)	<0.001
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The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 1 and 2	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Page 2
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4		
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4		
Methods					
Study Design	4	Present key elements of study design early in the paper	Page 5		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5		
Participants	6	(a) Cohort study - Give the eligibility criteria, and the sources and methods of selection of participants. Describe	Page 5	RECORD 6.1: The methods of study population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not	Page 5

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Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Page 6-8	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Page 6-8
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	Page 6-8		
Bias	9	Describe any efforts to address potential sources of bias	Page 9		
Study size	10	Explain how the study size was arrived at	Page 5		
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Page 6-8		

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<p>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23</p> <p>Statistical methods</p>	<p>12</p>	<p>(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (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 (e) Describe any sensitivity analyses</p>	<p>Page 9</p>		
<p>24 25 26 27 28 29 30 31 32 33 34</p> <p>Data access and cleaning methods</p>		<p>..</p>		<p>RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population.</p> <p>RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.</p>	<p>Page 5</p>
<p>35 36</p> <p>Linkage</p>		<p>..</p>		<p>RECORD 12.3: State whether the</p>	<p>Page 6</p>
				<p>study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.</p>	

Results

Participants	13	<p>(a) Report the numbers of individuals at each stage of the study (<i>e.g.</i>, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed)</p> <p>(b) Give reasons for non-participation at each stage.</p> <p>(c) Consider use of a flow diagram</p>	Page 9	<p>RECORD 13.1: Describe in detail the selection of the persons included in the study (<i>i.e.</i>, study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.</p>	Page 9
Descriptive data	14	<p>(a) Give characteristics of study participants (<i>e.g.</i>, demographic, clinical, social) and information on exposures and potential confounders</p> <p>(b) Indicate the number of participants with missing data for each variable of interest</p> <p>(c) <i>Cohort study</i> - summarise follow-up time (<i>e.g.</i>, average and total amount)</p>	Table 1 and page 9		
Outcome data	15	<p><i>Cohort study</i> - Report numbers of outcome events or summary measures over time</p> <p><i>Case-control study</i> - Report numbers in each exposure category, or summary measures of exposure</p> <p><i>Cross-sectional study</i> - Report numbers of outcome events or</p>	Page 10		
		summary measures			

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16 17 18 19 20	Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Not applicable		
21	Discussion					
22 23 24	Key results	18	Summarise key results with reference to study objectives	Page 13-16		
25 26 27 28 29 30 31 32 33 34	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	Page 16-17	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Page 16-17
35 36 37 38 39 40 41 42	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 17-18		
43 44 45 46 47	Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17		

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	Page 18		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, and programming code.	Page 19

*Reference: Benchimol EI, Smeeth L, Guttman A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langen SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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BMJ Open

Predictors of falls and fractures leading to hospitalisation in 36,101 people with affective disorders: A large representative cohort study

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1 **Predictors of falls and fractures leading to hospitalisation in 36,101 people with**
2 **affective disorders: A large representative cohort study**

3 Running title: Predictors of falls and fractures in people with affective disorders

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3 **23 Abstract (257/300)**
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6 **24 Objectives:** To investigate predictors of falls and fractures leading to hospitalisation in people
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8 **25** with affective disorders.
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11 **26 Design:** Cohort study
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13 **27 Setting:** the South London and Maudsley NHS Foundation Trust (SLaM) Biomedical Research
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15 **28** Centre (BRC) Case Register
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17 **29 Participants:** A large cohort of people with affective disorders (ICD10 codes F30-F34)
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20 **30** diagnosed between January 2008 and March 2016 was assembled using data from the SLaM
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22 **31** BRC Case Register
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24 **32 Primary and secondary outcome measures:** Falls and fractures leading to hospitalisation
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27 **33** were ascertained from linked national hospitalisation data. Multivariable Cox proportional
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29 **34** hazards analyses were administered to identify predictors of first falls and fractures.
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31 **35 Results:** Of 36,101 people with affective disorders (mean age 44.4 years, 60.2% female), 816
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33 **36** (incidence rate 9.91 per 1000 person years) and 1,117 (incidence rate 11.92 per 1000 person
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36 **37** years) experienced either a fall or fracture respectively. In multivariable analyses, older age,
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38 **38** analgesics use, increased physical illness burden, previous hospital admission due to certain
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40 **39** co-morbid physical illnesses and increase in attendances to accident and emergency services
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42 **40** following diagnosis were significant risk factors for both falls and fractures. Having a history
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44 **41** of falls was a strong risk factor for recurrent falls, and a previous fracture was also associated
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46 **42** with future fractures.
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49 **43 Conclusions:** Over a mean 5 years' follow-up, approximately 8% of people with affective
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51 **44** disorders were hospitalised with a fall or fracture. Several similar factors were found to
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53 **45** predict risk of falls and fracture, for example, older age, comorbid physical disorders and
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55 **46** analgesic use. Routine screening for bone mineral density and falls prevention programmes
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57 **47** should be considered for this clinical group.
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3 48 **Key words:** osteoporosis, affective disorders, falls, fractures, hospital admission
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8 50 **Strength and limitation of the study:**
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- 10 51 • Predictors of falls and fractures leading to hospitalisation in people with affective
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12 52 disorders were investigated with a large representative cohort
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14 53 • Data of the study were derived directly from the electronic health record
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16 54 • Falls and fractures leading to hospitalisation were ascertained from linked national
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18 55 hospitalisation data
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20 56 • We did not stratify according to different affective disorder subtypes and psychotropic
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22 57 medication categories
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24 58 • We had no information on lifestyle factors and type of fractures recorded at admission
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6 61 **Introduction**
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9 62 Falls and fractures are strongly related with increased morbidity, mortality, disability, and
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11 63 healthcare expenditure in the general population [1], and they are a frequent issue in older
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13 64 adults [2]. They often overlap, with more than 90% of hip fractures caused by falls [3] and
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15 65 share similar and multifactorial causes, such as muscle weakness [4] and use of antiepileptic
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17 66 drugs [5]. Several government strategies have been implemented to prevent and assess falls in
18
19 67 the general population [6]. Fractures, for example, hip and spine fractures increase the risk of
20
21 68 future falls and fractures [7]. Over 3 million people in the UK are at a high risk for fractures
22
23 69 [8], and prevention has been acknowledged as a worldwide priority [9]. However, management
24
25 70 is difficult, as causes for falls and fractures can be both intrinsic and extrinsic, and prevention
26
27 71 requires both pharmacologic and nonpharmacologic interventions [3].
28
29

30
31
32 72 Despite some progress in the general population, there is poor evidence on risk factors for falls
33
34 73 and fractures for patients with affective disorders. People with mental health problems like
35
36 74 depression and schizophrenia report higher risks of falls and fractures compared to the general
37
38 75 population [10, 11], and despite poor evidence in people with bipolar disorders, a few studies
39
40 76 suggest this population may also be at increased risk [12, 13].
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44 77 Several studies have investigated the association between bone loss and depression, but there
45
46 78 is a lack of large-scale cohort studies focussing on falls and fractures and related predictors.
47
48 79 Another major limitation is that the majority of studies have relied on self-reported affective
49
50 80 symptoms rather than clinical diagnosis [14, 15].
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52
53 81 Given the increased concerns about the multifactorial causes of falls and fractures [3, 4, 5], and
54
55 82 as an answer to the lack of large-scale studies on the matter, this study examines a large
56
57 83 representative cohort study to investigate predictors of falls and fractures leading to
58
59 84 hospitalisation among people with clinically diagnosed affective disorders. In this way, we aim
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3 85 to provide results based on clinical diagnosis rather than self-reported data [14, 15], presenting
4
5 86 a solid overview on potential risk factors for falls and fractures in the high-risk population of
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7
8 87 people with affective disorders.
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10 88

12 89 **Methods**

13 90 A retrospective observational study was carried out using data from the South London and
14
15 91 Maudsley NHS Foundation Trust (SLaM) Biomedical Research Centre (BRC) Case Register.
16
17 92 SLaM is one of the largest mental health and dementia care providers in Europe, serving a
18
19 93 geographic catchment of four South London Boroughs (including Lambeth, Lewisham,
20
21 94 Southwark, and Croydon) with a population in excess of 1.3 million. Data for this study were
22
23 95 retrieved using the Clinical Record Interactive Search (CRIS) platform, which enables a de-
24
25 96 identified version of SLaM's electronic health record to be accessible for research projects
26
27 97 within a robust and patient-led government framework [16]. The SLaM BRC Case Register
28
29 98 has been described in detail elsewhere [17] and has supported a wide range of studies [18,
30
31 99 19], including longitudinal cohort studies investigating falls and fractures in other populations
32
33 100 [20, 21]. Data are currently archived in CRIS on more than 450,000 cases with a wide variety
34
35 101 of mental disorders. CRIS has full approval for secondary analysis (Oxford Research Ethnic
36
37 102 Committee C, reference 18/SC/0372). Data from source structured fields have been
38
39 103 extensively supplemented through natural language process (NLP) applications using
40
41 104 Generalised Architecture for Text Engineering software, applying information extraction
42
43 105 techniques to derive structured information from the extensive text fields held in the mental
44
45 106 health record [17].
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55 108 **Participants, study period and additional data sources**

56
57 109 All SLaM patients with mood [affective] disorders (ICD10 codes F30-F34), diagnosed
58
59 110 between 1st of January 2008 and 31st March 2016, were included. Those patients with an age
60

1
2
3 111 under 18 at the time of mood disorders were excluded. SLaM patient records have been linked
4
5 112 with national Hospital Episode Statistics (HES) which are compiled from all NHS Trusts in
6
7 113 England (both acute and mental health services), including statistical abstracts of records of all
8
9 114 inpatient episodes, as well as outpatient and emergency care [17]. In addition, CRIS data have
10
11 115 been linked to the Office for National Statistics (ONS) mortality records over the same period.
12
13
14
15 116

17 117 **Patient and public involvement (PPI)**

18
19 118 The entire research program was developed after extensive patient, public and carer input, who
20
21 119 helped develop the study, and contributed to the funding applicable. They co-developed the
22
23 120 research questions, outcomes and contributed to factors included in the models. Moreover, they
24
25 121 reinforced this research as a neglected topic of utmost importance to them. The PPI group
26
27 122 designed the study with the senior researcher of the paper (Dr BS), they were involved in the
28
29 123 conception of the idea, the planning of the study during bimonthly meetings to discuss study
30
31 124 design, hypotheses, outcomes and what matters to patients of interest. They were also involved
32
33 125 in helping interpret the data outputs and publication. Results will be summarised and made
34
35 126 available to the PPI group through local newsletters and inform clinical services and local co-
36
37 127 developed Recovery College Courses.
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45 130 **Co-primary outcome: falls and any fractures**

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48 131 The co-primary outcomes were hospital admissions relating to a fall or any fracture extracted
49
50 132 from linked HES data and all discharge diagnoses (primary or any secondary diagnosis codes)
51
52 133 recorded between January 2008 to March 2016, and based on the following ICD 10 codes: i)
53
54 134 falls (W00-W19); ii) fractures (M80-M84, M907, S02, S12, S32, S42, S52, S62, S72, S82,
55
56 135 S92, S22, T02, T08, T10, T12X, T902, T911, T912, T921). In addition, linked mortality
57
58 136 records from the ONS linkage were examined for any instance of fall or fracture ICD codes in
59
60

1
2
3 137 any cause of death field on the death certificate to identify the date of death attributed to a fall
4
5 138 or fracture.
6
7

8 139

9
10 140 **Measurements**

11
12
13 141 Several additional measurements were obtained from CRIS. All independent variables
14
15 142 (covariates) were defined according to the value closest to the date of the first recorded mood
16
17 143 [affective] disorder diagnosis. Demographic covariates comprised: age at diagnosis, gender,
18
19 144 and ethnicity [multiple codes categorised into 1) White, consists of White British, White Irish
20
21 and other White; and 2) Non-White]. Index of Multiple Deprivation (IMD 2015) for the
22
23 145 neighbourhood of residence (i.e. Lower Super Output Area, which consists of approximately
24
25 146 650 households) at the time of diagnosis was divided into quintiles according to deprivation
26
27 147 scores with equal size allocated to each group. The IMD has previously been used in CRIS [22]
28
29 148 and combines Census-derived data at area level across several domains including income,
30
31 149 employment, health, education, barriers to housing and services, living environment, and crime
32
33 150 [23]. Information on cohabiting status (Cohabiting: married/civil partner, married, cohabiting;
34
35 151 Non-cohabiting: single, divorced, civil partnership dissolved, widowed, separated) was also
36
37 152 ascertained at the index diagnosis.
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45 155 ***Illness burden***

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48 156 The Health of the Nation Outcome Scales (HoNOS) [24] are routinely administered measures
49
50 157 of illness burden in UK mental health services and are recorded in structured fields on the
51
52 158 electronic health record. Individual HoNOS item scores (agitated behaviour, self-injury,
53
54 159 problem drinking & drugs, cognitive problems, physical illness, hallucinations, depressed
55
56 160 mood, relationship problems, daily living problems, living conditions problems, occupational
57
58 161 problems) and dates were obtained within 6 months before or after the date of the index
59
60

1
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3 162 diagnosis, and the closest scores in time to this date were included in analyses. Each HoNOS
4
5 163 item is rated on a Likert Scale, ranging from 0 (i.e. no problem) to 4 (i.e. severe or very severe
6
7
8 164 problem). A detailed glossary for HoNOS is reported elsewhere [25]. Scores 2 or over in the
9
10 165 individual HoNOS scales were classified as having a problem on each item, generating binary
11
12 166 covariates.

13
14
15 167

168 ***Mental disorder comorbidity***

19
20 169 Diagnoses of F00-F03 (dementia); F20-F29 (schizophrenia spectrum disorder); F40-F48
21
22 170 (neurotic, stress-related and somatoform disorders); F50 (eating disorders); F60-F69 (disorders
23
24 171 of adult personality and behaviour) were ascertained within one year before or after the index
25
26 172 diagnosis of mood [affective] disorder.

27 173 ***Medication***

28
29
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31 174 Medications received were extracted from structured medication fields in the record,
32
33 175 supplemented by an NLP application applied to text fields ascertaining mentions of current
34
35 176 medication [17]. Presence or not of the following medication groups was ascertained on the
36
37 177 basis of information within six months before or after the index diagnosis: anticholinergics,
38
39 178 antihypertensives, antidepressants, antipsychotics, anxiolytics and hypnotics, and analgesics.
40
41 179 The total number of medications prescribed for any condition was calculated for each
42
43 180 participant and used as a continuous variable.
44
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48 181

49 182 ***Physical comorbidity***

50
51
52 183 Information on physical comorbidities was ascertained utilising the data linkage between CRIS
53
54 184 and national HES records. Information on all ICD-10 diagnoses at discharge (primary or any
55
56 185 secondary diagnosis codes) was ascertained from any hospitalisations within 6 months before
57
58 186 or after the index diagnosis date and the following binary variables generated: i) Ischaemic

1
2
3 187 heart disease (IHD; I20, I21, I22, including coronary heart disease (CHD; I25); ii) Arrhythmia
4
5 188 (I44-I49, including atrial fibrillation (AF; I48); iii) Heart failure (I50); iv) Diabetes (E08, E09,
6
7
8 189 E10, E11, E12, E13; v) Hypotension (I95-99); vi) Hypercholesterolemia (E78); vii)
9
10 190 Hypertension (I10-15); viii) Urinary tract infections (UTI) (N39); ix) Osteoporosis (M80-85);
11
12 191 x) Visual disturbance and blindness (H53-54); xi) Hearing loss (H90-95); xii) Syncope or
13
14 192 collapse (R50-R69); xiii) Parkinson's disease (G20). Furthermore, occurrence of falls and/or
15
16 193 fractures before the index diagnosis was also collected. Finally, the number of attendances to
17
18 194 accident and emergency services (A&E) following the index diagnosis was also recorded.
19
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23 24 196 **Statistical analysis**

25
26 197 The study sample was described initially in terms of demographic and clinical variables,
27
28 198 followed by unadjusted Cox proportional hazard models to predict the first fall and first fracture
29
30 199 separately after the index diagnosis of mood [affective] disorder. The predictor variables at
31
32 200 baseline used in the first univariate models included sociodemographic information (year of
33
34 201 index diagnosis, mean age, gender, ethnicity, marital status), medications (antipsychotics,
35
36 202 anxiolytics & hypnotics, antidepressants, analgesics, anticholinergics, antihypertensives),
37
38 203 comorbid psychiatric diagnosis (F20-29 schizophrenia spectrum disorder, F40-48
39
40 204 neurotic/stress disorders, F00-F03 dementia, F50 eating disorders, F60 disorders of adult
41
42 205 personality and behaviour), HONOS scores (mean total and each individual item) and physical
43
44 206 health comorbidities (as indicated above). Factors that yielded a p-value < 0.10 in the univariate
45
46 207 model for fall or fracture outcome were subsequently entered into the multivariable model. A
47
48 208 final multivariable Cox proportional hazards model, using stepwise backward elimination
49
50 209 technique where those variables not significant (p-value > 0.05) were eliminated, with hazard
51
52 210 ratios and 95% confidence intervals (CI) displayed. Having checked a correlation matrix of
53
54 211 coefficients in the Cox model, total number of medications received was substantially collinear
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212 with individual types of medication received; therefore, this total number was removed as a
213 covariate. All analyses were conducted utilising STATA, version 13.

214

215 **Results**

216 The sample comprised 36,101 people with a diagnosis of mood [affective] disorder (F30* -
217 F34*) (mean age at first diagnosis 44.4, SD: 17.8, 60.2% female). Over a mean 5 years' follow-
218 up, 2,948 patients had a fall and/or a fracture recorded: 816 only a fall, 1,117 only a fracture,
219 and 1,015 both; 1,831 with any fall and 2,193 with any fracture (mean age at first fall 64.2, SD:
220 24.8; mean age at first fracture 62.5, SD: 22.8 (Supplementary material Table 1). The incidence
221 rate of falls was 9.91 per 1,000 person years and that for fractures 11.92 per 1,000 person years.
222 Table 1 summarises characteristics of those who had a recorded fall or fracture compared to
223 those who did not.

224

225 [Table 1]

226

227 **Length of hospital stay**

228 The mean length of hospitalisation following a fall (n = 1,831) was 7.9 days (range 0-374), for
229 a total of 20,767 full days in hospital. The mean length of stay in hospital following a fracture
230 (n=2,193) was 13.2 days (range 0-374), for a total of 40,548 days. This equates to 18.51 years
231 of inpatient hospital stay for 1,000-person years of follow-up due to a fall and 36.15 years of
232 inpatient hospital stay for 1,000-person years of follow-up due to a fracture. For the 1,831
233 patients reporting a fall, the mean hospital admissions due to a fall was 1.5 (range 1- 15); for
234 the 2,193 patients reporting a fracture, the mean number of hospital admissions due to a fracture
235 was 2.3 (range 1-42).

236

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3 237 **Factors associated with falls and fractures**
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5 238 Cox proportional hazard models analysing unadjusted predictors of falls and fractures (95%
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7
8 239 CI) are reported in Table 2.
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10 240

11
12 241 [Table 2]
13

14 242 **Multivariable predictors of falls**
15

16
17 243 Multivariable models of factors associated with first fall hospital admission are presented in
18
19 244 Table 3. In Model 2, older age was strongly associated with higher risk, and Non-European
20
21 245 ethnicity with lower risk, but neighbourhood deprivation reported no association. Analgesics
22
23 246 had a significant association (with increased risk), and of co-morbid psychiatric conditions,
24
25 247 only the ICD-10 F40-F48 group had a significant association (with reduced risk). Of the
26
27 248 HoNOS items, cognitive problems and physical illness were associated with higher risk, and
28
29 249 depressed mood problems with lower risk. Higher risk of falls was associated with several
30
31 250 hospitalisation discharge diagnoses, namely heart failure, diabetes, hypotension, UTI,
32
33 251 osteoporosis, and syncope or collapse. Hospitalised fall was associated with having a previous
34
35 252 history of falls reported before the index diagnosis and with increased A&E attendance after
36
37 253 the index diagnosis.
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44 255 [Table 3]
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49 257 **Multivariable predictors of fractures**
50

51 258 Table 4 presents multivariable models of factors associated with first fracture hospitalisation.
52
53 259 Fracture risk was increased in older patients and women and was decreased in those of Non-
54
55 260 European. Fracture risk was lower in patients receiving antihypertensives and higher in those
56
57 261 receiving analgesics. It was also lower in those with neurotic, stress-related and somatoform
58
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3 262 disorders (i.e. F40-F48), as well as bipolar affective disorder and manic episodes (i.e. F30-
4
5 263 F31). An elevated fracture risk was associated with physical illness on the HoNOS. Fracture
6
7
8 264 risk was independently predicted by previous hospitalisations for heart failure, diabetes, UTI,
9
10 265 osteoporosis, hearing loss and preceding fracture-related (but not fall-related) hospitalisations.
11
12 266 Fracture risk was also associated with higher levels of post-diagnostic A&E attendance.
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17 268 [Table 4]
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271 Discussion

272 To our knowledge, the current study is the first using representative data to investigate the
273 predictors of hospitalised falls and fractures in people with clinically diagnosed affective
274 disorders. Our data suggest that out of 36,101 people with affective disorders, 816 (i.e. 2.26%)
275 and 1,117 (i.e. 3.09%) of patients experienced a fall and fracture, respectively. Length of
276 hospital stay was considerable, equating to 18.51 and 36.15 years of inpatient hospital stay for
277 1,000-person years of follow-up due to a fall and a fracture, respectively. The key factors
278 increasing the risk of a hospitalised fall were older age, analgesic use, increased illness burden
279 due to cognitive problems and physical illness, a history of general hospital admission due to
280 co-morbid physical illnesses (in particular syncope or collapse), increase in one attendance to
281 A & E following affective disorder diagnosis, and falls before the diagnosis. Similar risk factors
282 for fractures were noted.

283
284 Approximately 8.2% of our sample experienced a hospital admission due to either a fall or
285 fracture. Studies on healthy populations have suggested several mechanisms which may
286 explain these elevated risks in our sample, such as vitamin D deficiency [26, 27] and use of
287 antidepressants [28]. Several studies also proposed a negative effect of leptin on bone mass and
288 bone formation through a hypothalamic relay [29]. Some lifestyle factors seem to also be
289 associated with a poor bone health, including physical inactivity [30] and alcohol consumption
290 [31]. Previous studies have hypothesised other risk factors contributing to falls and fractures in
291 people with depressive disorders [32], but no large-scale study has yet focused on patients with
292 clinically diagnosed affective disorders. Our data advance the current literature by providing
293 detailed evidence on how a multitude of demographic, medical, and psychological factors can
294 differently affect risks of falls and fractures in people with affective disorder.

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3 296 The association between older age and incidence of fall may be due to age-related physical
4
5 297 conditions, as well as physiologic (e.g. loss of BMD) [33] and pathologic changes (e.g.
6
7 298 decreased cardiovascular functions) [34]. Female gender is also a well-established risk factor
8
9
10 299 for osteoporosis [35], consistent with our finding. Surprisingly, we found no relationship
11
12 300 between deprivation and falls and fractures, although previous evidence has associated
13
14 301 deprivation with fractures across different age groups [36, 37]. We might suppose that while
15
16 302 deprivation is associated with poor nutrition and physical inactivity, people with affective
17
18 303 disorders have a poorer lifestyle, compared to the general population [38], regardless of their
19
20 304 financial status or living condition. Finally, the protective role of a non-European ethnic
21
22 305 background is comparable with previous evidence supporting a higher fracture rate in
23
24 306 Caucasian women compared to women from other ethnic groups [39], and a lower fall rate in
25
26 307 older immigrants than those with an English-speaking background [40].
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33 309 Our results provide new evidence on how hospitalisation due to falls or fractures can be an
34
35 310 important burden for the NHS resources and for people with affective disorders, who are
36
37 311 already at risk for a prolonged hospitalisation [41]. Given the long hospital stay among our
38
39 312 sample, its burden on NHS costs is unsurprising. The total cost of fracture is estimated to reach
40
41 313 £4.4 billion per year in the UK alone [8]. Several items from the HoNOS were also associated
42
43 314 with increased hazard of hospitalisation due to falls or fractures (e.g. cognitive problems).
44
45 315 Evidence on the role of these factors on hospital stay among this population is warranted for
46
47 316 future research.
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51 317
52
53 318 Our study reports stress-related and somatoform disorders to be associated with a decreased
54
55 319 risk of falls and fractures, which could be due to increased fear avoidance and reduced activities
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57 320 due to stress-related disorders, leading to fewer falls [42]. We also found the presence of bipolar
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3 321 affective disorder and manic episodes to be protective factors against increased fracture risk.
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5 322 Although there has been little evidence investigating the role of bipolar affective disorder or
6
7 323 its characteristics (including manic symptoms) in the risk of fracture, preliminary evidence has
8
9 324 suggested an association between the use of lithium (i.e. a primary treatment for bipolar
10
11 325 disorder) and decreased fracture risk [43], the preservation and enhancement of bone mass [44].
12
13 326
14
15 327 Surprisingly, neither antidepressants nor antipsychotics were associated with risks of falls or
16
17 328 fracture, despite documented associations between antipsychotic medications and reduced
18
19 329 bone metabolism [45] and BMD [46]. Evidence on the association between antidepressants and
20
21 330 BMD is ambiguous: while some authors reported that some antidepressants, especially SSRIs,
22
23 331 have a negative impact on bone strength [47, 48], other findings have been null [49]. However,
24
25 332 we did not attempt to account for specific types of antidepressants in the analysis, and previous
26
27 333 studies indicate that tricyclic antidepressants have no adverse effect on bone health [28]. On
28
29 334 the other hand, analgesics use was associated with increased risks for falls and fractures,
30
31 335 consistently with previous findings [50], and possibly mediated by central nervous system
32
33 336 effects, such as dizziness [51]. Antihypertensive drugs use was associated with a decreased
34
35 337 fracture risk, confirming previous results [52], potentially due to their improving effect on
36
37 338 calcium absorption [53].
38
39 339
40
41 340 Finally, extensive evidence has indicated several physical conditions as risk factors for falls or
42
43 341 fractures in the general population [54, 55], including UTI [56] and diabetes [57]. It is known
44
45 342 that mental health disorders (e.g. depression) increase the chance of major physical co-
46
47 343 morbidities [58]. However, few studies have established the impact of comorbid physical
48
49 344 conditions on risks of falls and fractures among people with affective disorders. Our study
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51 345 indicates heart failure, diabetes, UTI and osteoporosis to be associated with hospitalisation due
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3 346 to falls or fractures. Hypotension and syncope or collapse were additionally associated with an
4
5 347 increased risk of falls, and hearing loss was associated with an elevated fracture risk.
6
7
8 348 Unsurprisingly, osteoporosis was strongly associated with falls and fractures, as it has been
9
10 349 acknowledged as the most important yet potentially treatable factor for falls [54] and fractures
11
12 350 [59] due to its effect on BMD. Moreover, osteoporosis tends to occur simultaneously with heart
13
14 351 failure [60] due to shared risk factors such as diabetes. Unsurprisingly, syncope or collapse was
15
16 352 also strongly associated with an increased risk of falls, as syncope is frequently mistaken for
17
18 353 falls, to the point that the European Society of Cardiology has emphasised the need to explore
19
20 354 syncope as an independent factor leading to falls [61]. Diabetes was another risk factor for both
21
22 355 falls and fracture, confirming the association found in the general population [62]. Hearing loss
23
24 356 was the only factor associated with an elevated risk of fracture in our study, an association
25
26 357 previously confirmed in the general population [63]. This finding may be explained by the
27
28 358 damaging impact of hearing loss on orientation skills and physical activity [64]. Finally, our
29
30 359 study confirmed the association between history of falls and increased risk of future falls,
31
32 360 previously reported in the general population [34, 65] and in people with depression [66].
33
34 361 Moreover, our data confirmed how a prior fracture represents a 50-100% higher risk for
35
36 362 experiencing future fracture, as reported in the general population [67].
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44 364 The main strengths of our study are: i) analyses controlling for various confounders; and ii) a
45
46 365 large sample including people with clinically diagnosed affective disorders. However, there are
47
48 366 important limitations. Firstly, we did not stratify according to different affective disorder
49
50 367 subtypes which could report different risk factors; similarly, we analysed psychotropic
51
52 368 medication categories but did not investigate specific agents or sub-categories. Second, we had
53
54 369 no information on the types of fractures reported at admission and on factors (e.g. balance) that
55
56 370 are influenced by neuropathological lesions in people with depression [68]. Additionally, the
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3 371 majority of studies investigating falls and fractures rely upon self-report data whilst our study
4
5 372 relied on ICD hospitalisation codes increasing reliability. However, the causes of fractures and
6
7 373 the types of falls could not be explored in the current study, although we investigate factors
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9
10 374 associated with falls across the whole sample from the rich mental health record database.
11
12 375 Future research should attempt to disentangle of the potential risk factors/causes of falls and
13
14 376 fractures research in affective disorders. A limitation of health administrative data is some
15
16 377 inconsistency or limited data on the granular detail. Third, lifestyle factors, such as alcohol
17
18 378 consumption [31, 38], could not be explored. Fourth, our study only ascertained information
19
20 379 on physical co-morbidities from hospitalisation records and could have overlooked patients
21
22 380 with mild osteoporosis. Additionally, physical co-morbidities were ascertained within six
23
24 381 months of diagnosis, and patients who were hospitalised for a fall or fracture within these six
25
26 382 months would be more likely to have their osteoporosis ascertained. Fifth, falls and fractures
27
28 383 are closely related and often co-occur [69]. In this study, although falls and fractures were
29
30 384 identified from ICD hospitalisation codes, falls and fractures categories were not mutually
31
32 385 exclusive, as a patient could be counted in both the fall and fracture cohort if he/she had a fall
33
34 386 and a fracture in the same event. Moreover, factors such as inaccurate recording and fine
35
36 387 distinction between ICD hospitalisation codes for falls and fractures, could also potentially
37
38 388 hinder our attempt to differentiate the two concepts. Thus, further work is needed to elucidate
39
40 389 the potential overlap and distinct relationship among falls and fractures in people with affective
41
42 390 disorders. Finally, since medication records were ascertained within one year of diagnosis, we
43
44 391 cannot assess whether medications were prescribed as a result or as a cause of falls for those
45
46 392 who had a fall or fracture within six months of their diagnosis.
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394 **Conclusion**

395 Our study reports that over a mean 5 years' follow-up, approximately 8% of a large cohort with
396 affective disorders was hospitalised due to either a fall or fracture. Factors such as older age,
397 certain medications and having a history of fall or fracture are significant predictors, broadly
398 comparable to risk factors established in the general population. Heavy hospital burden
399 following a fall or fracture was also described.

400 Our current study provides important implications for future research and clinical practice.
401 Future research should take into account the limitations listed above and potentially explore
402 the mechanisms through which the factors identified in this study (e.g., physical conditions
403 such as UTI, or medication use) may impact risks for falls and fractures in people with affective
404 disorders. The associations between certain factors (e.g., psychotropic medication use) and risk
405 for falls and fractures were not confirmed in the current study, future studies are encouraged to
406 replicate our findings and explore these factors further.

407 In terms of implications for future clinical practice, given the lack of osteoporosis screening
408 for people with mental health problems in current clinical settings [70], BMD checks and
409 osteoporosis screenings should be a routine for people with affective disorders, especially if
410 older and with established co-morbid chronic illnesses. Fall assessments (e.g., the Fracture Risk
411 Assessment Tool) should be routinely conducted for people with affective disorders, since
412 approximately 70% of low-energy fractures are due to falls [71]. Fall/fracture prevention
413 programmes should also be offered due to an average 14% reduction in falls risk in the general
414 population following fall prevention programmes [72]. For example, the combination of
415 cognitive behavioural therapy and exercise have been previously found to be effective in
416 improving depressive symptoms [73] and self-efficacy [74] in the general population. The
417 effectiveness of these prevention programmes should also be examined in people with affective
418 disorders and subsequently provided if their benefits are confirmed.

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3 4194
5 4206 421 **Acknowledgments**7
8
9 422 Author's contributions10
11 423 BS acquired funding for the study. GP conducted the analysis with support from all co-authors.12
13 424 RM drafted introduction and discussion sections, ER drafted results section and all authors14
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58 44359
60 444 Data availability statement

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446 at ruimin.1.ma@kcl.ac.uk
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Table 1: Characteristics of those Mood [affective] disorders patients who were admitted to hospital with a fall/fracture after a diagnosis of Mood [affective] disorders (F30* to F34*).

Characteristics of sample	Presence of falls		Presence of fractures	
	No (n=34,270)	Yes (n=1,831)	No (n=33,908)	Yes (n=2,193)
Age at the time of Mood [affective] disorders diagnosis				
18- 34	12685 (37.0)	205 (11.2)	12572 (37.1)	318 (14.5)
35- 49	11409 (33.3)	336 (18.4)	11346 (33.5)	399 (18.2)
50- 64	5829 (17.0)	362 (19.8)	5751 (17.0)	440 (20.1)
65- 79	2797 (8.2)	485 (26.5)	2728 (8.0)	554 (25.3)
80 & over	1550 (4.5)	443 (24.2)	1511 (4.5)	482 (22.0)
Gender				
Female	20627 (60.2)	1107 (60.5)	20348 (60.0)	1386 (63.2)
Male	13638 (39.8)	724 (39.5)	13555 (40.0)	807 (36.8)
Ethnicity				
White	20772 (60.6)	1519 (83.0)	20536 (60.6)	1755 (80.0)
Non-white	12450 (36.3)	288 (15.7)	12333 (36.4)	405 (18.5)
Marital status				
Cohabiting	7957 (23.2)	416 (22.7)	7867 (23.2)	506 (23.1)
Non-cohabiting	23028 (67.2)	1345 (73.5)	22776 (67.2)	1597 (72.8)
Index of multiple deprivation: IMD 2015 (SD)				
Least deprived quintile	6657 (19.4)	388 (21.2)	6593 (19.4)	452 (20.6)
2nd most deprived quintile	6682 (19.5)	378 (20.6)	6643 (19.6)	417 (19.0)
3rd most deprived quintile	6706 (19.6)	354 (19.3)	6637 (19.6)	423 (19.3)
Most deprived quintile	6708 (19.6)	346 (18.9)	6612 (19.5)	442 (20.2)
Medication prescription (within 6 months before or after Mood [affective] disorders diagnosis)				

Anticholinergics	17714 (51.7)	1089 (59.5)	17489 (51.6)	1314 (59.9)
Antihypertensives	2561 (7.5)	386 (21.1)	2553 (7.5)	394 (18.0)
Antidepressants	19351 (56.5)	1168 (63.8)	19113 (56.4)	1406 (64.1)
Antipsychotics	8777 (25.6)	469 (25.6)	8694 (25.6)	552 (25.2)
Anxiolytics and Hypnotics	9443 (27.6)	558 (30.5)	9349 (27.6)	652 (29.7)
Analgesics	3083 (9.0)	405 (22.1)	3059 (9.0)	429 (19.6)

Number of medications received (within 6 months before or after Mood [affective] disorders diagnosis)

0	10207 (29.8)	394 (21.5)	10126 (29.9)	475 (21.7)
1	5330 (15.6)	259 (14.1)	5275 (15.6)	314 (14.3)
2	7062 (20.6)	360 (19.7)	6961 (20.5)	461 (21.0)
3	6599 (19.3)	361 (19.7)	6503 (19.2)	457 (20.8)
4	3858 (11.3)	304 (16.6)	3839 (11.3)	323 (14.7)
5	1038 (3.0)	121 (6.6)	1029 (3.0)	130 (5.9)
6	176 (0.5)	32 (1.7)	175 (0.5)	33 (1.5)

Other psychiatric conditions (within six months before or after Mood [affective] disorders diagnosis)

F00- F03 (Dementia)	754 (2.2)	207 (11.3)	749 (2.2)	212 (9.7)
F 20- F29 (Schizophrenia spectrum disorder)	2701 (7.9)	119 (6.5)	2676 (7.9)	144 (6.6)
F30- F31 (Bipolar affective disorder)	5489 (16.0)	222 (12.1)	5475 (16.1)	236 (10.8)
F50 (Eating Disorders)	447 (1.3)	13 (0.7)	441 (1.3)	19 (0.9)
F40- F48 (Neurotic, stress-related and somatoform disorders)	3652 (10.7)	147 (8.0)	3601 (10.6)	198 (9.0)
F 60 (Disorders of adult personality and behaviour)	1436 (4.2)	77 (4.2)	1428 (4.2)	85 (3.9)

Problem HoNOS (score 2 or over) (within six months before or after Mood [affective] disorders diagnosis)

Agitated Behaviour	3571 (10.4)	234 (12.8)	3547 (10.5)	258 (11.8)
Self-Injury	3586 (10.5)	186 (10.2)	3545 (10.5)	227 (10.4)
Problem Drinking Drugs	2957 (8.6)	204 (11.1)	2932 (8.6)	229 (10.4)

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3	Cognitive Problems	2821 (8.2)	349 (19.1)	2792 (8.2)	378 (17.2)
4	Physical Illness	6514 (19.0)	770 (42.1)	6355 (18.7)	929 (42.4)
5	Hallucinations	3198 (9.3)	175 (9.6)	3176 (9.4)	197 (9.0)
6	Depressed Mood	14582 (42.6)	766 (41.8)	14390 (42.4)	958 (43.7)
7	Relationship Problems	7644 (22.3)	342 (18.7)	7560 (22.3)	426 (19.4)
8	Daily Living Problems	5854 (17.1)	576 (31.5)	5723 (16.9)	707 (32.2)
9	Living Conditions Problems Score	3431 (10)	190 (10.4)	3404 (10.0)	217 (9.9)
10	Occupational Problems	5574 (16.3)	392 (21.4)	5513 (16.3)	453 (20.7)
11	Mean overall HoNoS score (SD)	10.67 (5.63)	11.64 (5.53)	10.64 (5.63)	11.91 (5.46)
12	Number with missing HoNoS	12545 (36.6)	523 (28.6)	12411 (36.6)	657 (30.0)
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18	Hospital admissions (within six months before or after Mood [affective] disorders diagnosis)				
19	Ischaemia +CHD+ IHD	1128 (3.3)	210 (11.5)	1089 (3.2)	249 (11.4)
20	Arrhythmia + AF	1003 (2.9)	197 (10.8)	967 (2.9)	233 (10.6)
21	Heart failure	437 (1.3)	88 (4.8)	417 (1.2)	108 (4.9)
22	Diabetes	1516 (4.4)	264 (14.4)	1488 (4.4)	292 (13.3)
23	Hypotension	435 (1.3)	104 (5.7)	424 (1.3)	115 (5.2)
24	Hypercholesterolemia	1097 (3.2)	221 (12.1)	1090 (3.2)	228 (10.4)
25	Hypertension	2837 (8.3)	546 (29.8)	2752 (8.1)	631 (28.8)
26	Urinary tract infections (UTI)	1366 (4.0)	324 (17.7)	1297 (3.8)	393 (17.9)
27	Osteoporosis	409 (1.2)	121 (6.6)	183 (0.5)	347 (15.8)
28	Visual Disturbance and Blindness	241 (0.7)	53 (2.9)	246 (0.7)	48 (2.2)
29	Hearing Loss	189 (0.6)	41 (2.2)	174 (0.5)	56 (2.6)
30	Syncope or Collapse	1990 (5.8)	444 (24.2)	2022 (6.0)	412 (18.8)
31	Parkinson's Disease	116 (0.3)	45 (2.5)	128 (0.4)	33 (1.5)
32	Falls before diagnosis	750 (2.2)	267 (14.6)	749 (2.2)	268 (12.2)
33	Fractures before diagnosis	1075 (3.1)	231 (12.6)	860 (2.5)	446 (20.3)
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mean number of attendances to A&E following Mood [affective] disorders diagnosis (SD)	3.94 (9.98)	16.64 (28.88)	4.00 (9.62)	13.67 (29.35)
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Table 2: Univariate Cox proportional hazard model (95% CI) showing factors affecting time to first fall/fracture hospital admission since diagnosis of Mood [affective] disorders

Characteristics	Outcome falls		Outcome fractures	
	HR (95% CI)	P value	HR (95% CI)	P value
Age at the time of Mood [affective] disorders diagnosis				
18- 34	Ref.		Ref.	
35- 49	1.74 (1.46, 2.07)	<0.001	1.33 (1.15, 1.54)	<0.001
50- 64	3.88 (3.27, 4.61)	<0.001	3.03 (2.62, 3.50)	<0.001
65- 79	12.41 (10.54, 14.62)	<0.001	9.11 (7.94, 10.46)	<0.001
80 & over	26.94 (22.8, 31.83)	<0.001	18.46 (16.00, 21.29)	<0.001
Female gender	0.99 (0.90, 1.09)	0.87	1.12 (1.03, 1.22)	0.01
Non-European ethnicity	0.32 (0.28, 0.37)	<0.001	0.39 (0.35, 0.44)	<0.001
Non-cohabiting marital status	1.08 (0.97, 1.21)	0.17	1.05 (0.95, 1.16)	0.31
Deprivation quintile (IMD 2015)				
Least deprived quintile	Ref.		Ref.	
2nd least deprived quintile	0.83 (0.71, 0.96)	0.01	0.89 (0.78, 0.99)	0.04
3rd most deprived quintile	0.88 (0.76, 1.02)	0.09	0.90 (0.79, 1.03)	0.13
2nd most deprived quintile	0.94 (0.82, 1.09)	0.43	0.89 (0.78, 1.00)	0.05
Most deprived quintile	0.86 (0.74, 0.99)	0.04	0.94 (0.82, 1.07)	0.35
Medication prescribed (within one year before or after Mood [affective] disorders diagnosis)				
Anticholinergics received	1.42 (1.3, 1.56)	<0.001	1.45 (1.33, 1.57)	<0.001
Antihypertensive received	3.69 (3.3, 4.13)	<0.001	2.98 (2.67, 3.33)	<0.001
Antidepressants received	1.41 (1.29, 1.56)	<0.001	1.43 (1.31, 1.56)	<0.001

Antipsychotics received	0.95 (0.86, 1.06)	0.35	0.93 (0.84, 1.02)	0.12
Anxiolytics and Hypnotics received	1.11 (1.00, 1.22)	0.05	1.06 (0.97, 1.17)	0.18
Analgesics received	2.97 (2.66, 3.32)	<0.001	2.52 (2.27, 2.80)	<0.001
Increase in one type of polypharmacy	1.21 (1.18, 1.25)	<0.001	1.18 (1.15, 1.21)	<0.001
Presence of other psychiatric conditions (within one year before or after Mood [affective] disorders diagnosis)				
F00- F03 (Dementia)	6.90 (5.97, 7.98)	<0.001	5.65 (4.90, 6.51)	<0.001
F20- F29 (Schizophrenia spectrum disorder)	0.75 (0.62, 0.91)	<0.001	0.76 (0.64, 0.90)	0.01
F30- F31 (Bipolar affective disorder)	0.71 (0.62, 0.82)	<0.001	0.61 (0.54, 0.71)	<0.001
F40- F48 (Neurotic, stress-related and somatoform disorders)	0.76 (0.64, 0.90)	<0.001	0.86 (0.75, 0.99)	0.05
F50 (Eating Disorders)	0.53 (0.31, 0.91)	0.02	0.64 (0.41, 1.01)	0.06
F 60 (Disorders of adult personality and behaviour)	0.95 (0.76, 1.20)	0.68	0.87 (0.7, 1.09)	0.22
Problem in HoNoS (scored 2 or more)				
Agitated Behaviour	1.11 (0.97, 1.28)	0.14	1.03 (0.90, 1.17)	0.71
Self-Injury	0.84 (0.72, 0.98)	0.02	0.87 (0.76, 1.01)	0.06
Problem Drinking Drugs	1.11 (0.96, 1.29)	0.17	1.05 (0.91, 1.21)	0.48
Cognitive Problems	2.66 (2.35, 3.00)	<0.001	2.37 (2.11, 2.66)	<0.001
Physical Illness	3.88 (3.48, 4.34)	<0.001	4.17 (3.77, 4.63)	<0.001
Hallucinations	0.87 (0.74, 1.02)	0.08	0.82 (0.71, 0.96)	0.01
Depressed Mood	0.75 (0.67, 0.83)	<0.001	0.88 (0.80, 0.98)	0.02
Relationship Problems	0.65 (0.58, 0.74)	<0.001	0.71 (0.63, 0.79)	<0.001
Daily Living Problems	2.41 (2.16, 2.69)	<0.001	2.61 (2.36, 2.89)	<0.001
Living Conditions Problems	0.93 (0.80, 1.08)	0.34	0.89 (0.77, 1.02)	0.10
Occupational Problems	1.30 (1.15, 1.47)	<0.001	1.30 (1.16, 1.45)	<0.001
Overall increase in one unit of HoNoS	1.04 (1.03, 1.05)	<0.001	1.04 (1.04, 1.05)	<0.001
Admitted to general hospital (within one year before or after Mood [affective] disorders diagnosis)				

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3	Ischaemia +CHD+ IHD	5.25 (4.54, 6.06)	<0.001	5.17 (4.53, 5.90)	<0.001
4	Arrhythmia + AF	6.30 (5.43, 7.31)	<0.001	6.10 (5.32, 6.99)	<0.001
5	Heart failure	7.81 (6.29, 9.68)	<0.001	7.89 (6.49, 9.59)	<0.001
6	Diabetes	4.66 (4.09, 5.31)	<0.001	4.18 (3.69, 4.73)	<0.001
7	Hypotension	7.29 (5.98, 8.90)	<0.001	6.51 (5.39, 7.86)	<0.001
8	Hypercholesterolemia	5.14 (4.47, 5.92)	<0.001	4.24 (3.70, 4.87)	<0.001
9	Hypertension	6.08 (5.50, 6.72)	<0.001	5.78 (5.26, 6.34)	<0.001
10	Urinary tract infections (UTI)	7.24 (6.42, 8.17)	<0.001	7.36 (6.59, 8.21)	<0.001
11	Osteoporosis	7.75 (6.44, 9.32)	<0.001	36.39 (32.35, 40.94)	<0.001
12	Visual Disturbance and Blindness	5.25 (3.99, 6.90)	<0.001	3.78 (2.84, 5.03)	<0.001
13	Hearing Loss	5.57 (4.09, 7.60)	<0.001	6.45 (4.95, 8.41)	<0.001
14	Syncope or Collapse	6.17 (5.54, 6.86)	<0.001	4.27 (3.84, 4.76)	<0.001
15	Parkinson's Disease	9.83 (7.31, 13.23)	<0.001	5.60 (3.97, 7.89)	<0.001
16					
17	Falls before Mood [affective] disorders diagnosis	8.88 (7.8, 10.12)	<0.001	7.03 (6.18, 7.99)	<0.001
18	Fractures before Mood [affective] disorders diagnosis	5.31 (4.62, 6.10)	<0.001	10.67 (9.61, 11.85)	<0.001
19	Increase in one attendance to A&E following Mood [affective] disorders diagnosis	1.01 (1.01, 1.01)	<0.001	1.01 (1.01, 1.01)	<0.001
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Table 3: Two models showing predictors of first fall hospital admission among Mood [affective] disorders. (used stepwise removal of factors that were not significant at 0.05 P value).

Characteristics	Falls			
	Model 1 (n=20,938)		Model 2 (n=22,414)	
	HR (95% CI)	P value	HR (95% CI)	P value
Age at the time of Mood [affective] disorders diagnosis				
18- 34	Ref.		Ref.	
35- 49	1.59 (1.23, 2.06)	<0.001	1.58 (1.24, 2.02)	<0.001
50- 64	3.11 (2.40, 4.01)	<0.001	2.98 (2.33, 3.81)	<0.001
65- 79	8.07 (6.31, 10.33)	<0.001	7.65 (6.07, 9.64)	<0.001
80 & over	12.40 (9.51, 16.17)	<0.001	11.80 (9.25, 15.05)	<0.001
Non-European ethnicity	0.43 (0.36, 0.51)	<0.001	0.45 (0.38, 0.52)	<0.001
Deprivation quintile (IMD 2015)				
Least deprived quintile	Ref.			
2nd least deprived quintile	0.99 (0.83, 1.19)	0.92		
3rd most deprived quintile	1.14 (0.95, 1.36)	0.17		
2nd most deprived quintile	1.15 (0.96, 1.38)	0.13		
Most deprived quintile	1.00 (0.84, 1.20)	0.85		
Medication prescribed (within one year before or after diagnosis of Mood [affective] disorders)				
Anticholinergics received	0.95 (0.74, 1.22)	0.68		
Antihypertensive received	0.98 (0.79, 1.21)	0.82		
Antidepressants received	0.91 (0.74, 1.11)	0.36		
Anxiolytics and Hypnotics received	1.00 (0.80, 1.24)	0.97		
Analgesics received	1.36 (1.10, 1.68)	0.01	1.39 (1.22, 1.58)	<0.001

Increase in one type of polypharmacy	1.02 (0.87, 1.19)	0.80		
Presence of other psychiatric conditions (within one year before or after diagnosis of Mood [affective] disorders)				
F00- F03 (Dementia)	1.05 (0.86, 1.27)	0.64		
F20- F29 (Schizophrenia spectrum disorder)	1.07 (0.85, 1.34)	0.57		
F30-F31 (Bipolar affective disorder)	0.87 (0.72, 1.06)	0.16		
F40- F48 (Neurotic, stress-related and somatoform disorders)	0.74 (0.60, 0.91)	0.01	0.75 (0.61, 0.91)	0.01
F50 (Eating Disorders)	0.86 (0.36, 2.09)	0.74		
One unit increase in HoNoS				
Self-Injury	1.10 (0.92, 1.32)	0.30		
Cognitive Problems	1.25 (1.06, 1.46)	0.01	1.28 (1.12, 1.46)	<0.001
Physical Illness	1.23 (1.07, 1.42)	<0.001	1.25 (1.10, 1.42)	<0.001
Depressed Mood	0.80 (0.70, 0.92)	<0.001	0.83 (0.74, 0.93)	<0.001
Relationship Problems	0.98 (0.84, 1.14)	0.77		
Daily Living Problems	1.01 (0.87, 1.17)	0.94		
Occupational Problems	0.90 (0.78, 1.03)	0.13		
Admitted to general hospital (within one year before or after diagnosis of Mood [affective] disorders)				
Ischaemia +CHD+ IHD	0.95 (0.78, 1.15)	0.59		
Arrhythmia + AF	0.88 (0.73, 1.07)	0.20		
Heart failure	1.37 (1.05, 1.78)	0.02	1.27 (1.00, 1.63)	0.05
Diabetes	1.37 (1.16, 1.63)	<0.001	1.36 (1.16, 1.59)	<0.001
Hypotension	1.38 (1.09, 1.75)	0.01	1.34 (1.07, 1.68)	0.01
Hypercholesterolemia	1.16 (0.96, 1.39)	0.13		
Hypertension	1.05 (0.88, 1.23)	0.63		
Urinary tract infections (UTI)	1.33 (1.13, 1.56)	<0.001	1.33 (1.14, 1.54)	<0.001

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3	Osteoporosis	1.41 (1.08, 1.83)	0.01	1.37 (1.11, 1.70)	<0.001
4	Visual Disturbance and Blindness	1.22 (0.86, 1.71)	0.26		
5	Hearing Loss	0.91 (0.64, 1.30)	0.61		
6	Syncope or Collapse	1.94 (1.71, 2.26)	<0.001	2.05 (1.79, 2.36)	<0.001
7	Parkinson's Disease	1.25 (0.89, 1.77)	0.20		
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11	Falls before Mood [affective] disorders diagnosis	1.81 (1.51, 2.18)	<0.001	1.81 (1.54, 2.13)	<0.001
12	Fractures before Mood [affective] disorders diagnosis	0.98 (0.78, 1.22)	0.86		
13	Increase in one attendance to A&E following Mood				
14	[affective] disorders * diagnosis	1.01 (1.01, 1.01)	<0.001	1.01 (1.01, 1.01)	<0.001
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Table 4: Two models showing predictors of first fracture hospital admission among Mood [affective] disorders patients.

Characteristics	Model 1 (n=20,936)		Model 2 (n=22,322)	
	HR (95% CI)	P value	HR (95% CI)	P value
Age at the time of Mood [affective] disorders diagnosis				
18- 34	Ref.		Ref.	
35- 49	1.27 (1.02, 1.57)	0.03	1.27 (1.03, 1.55)	0.02
50- 64	2.31 (1.85, 2.88)	<0.001	2.28 (1.85, 2.81)	<0.001
65- 79	5.75 (4.65, 7.11)	<0.001	5.55 (4.54, 6.77)	<0.001
80 & over	7.46 (5.90, 9.45)	<0.001	7.37 (5.93, 9.16)	<0.001
Female gender	1.21 (1.08, 1.36)	<0.001	1.15 (1.03, 1.29)	0.01
Non-European ethnicity	0.59 (0.51, 0.68)	<0.001	0.59 (0.51, 0.67)	<0.001
Deprivation quintile (IMD 2015)				
Least deprived quintile	Ref.			
2nd least deprived quintile	1.07 (0.91, 1.28)	0.41		
3rd most deprived quintile	1.11 (0.94, 1.32)	0.23		
2nd most deprived quintile	1.17 (0.99, 1.39)	0.07		
Most deprived quintile	1.00 (0.85, 1.19)	0.96		
Medication prescribed (within one year before or after diagnosis of Mood [affective] disorders)				
Anticholinergics received	1.08 (0.85, 1.26)	0.76		
Antihypertensive received	0.76 (0.65, 0.91)	<0.001	0.80 (0.70, 0.92)	<0.001
Antidepressants received	1.08 (0.91, 1.28)	0.37		
Analgesics received	1.28 (1.08, 1.52)	<0.001	1.33 (1.17, 1.51)	<0.001
Increase in one type of polypharmacy	1.01 (0.93, 1.11)	0.75		

Presence of other psychiatric conditions (within one year before or after diagnosis of Mood [affective] disorders)

F00- F03 (Dementia)	1.14 (0.96, 1.41)	0.12		
F20- F29 (Schizophrenia spectrum disorder)	1.11 (0.91, 1.38)	0.30		
F30- F31 (Bipolar affective disorder)	0.81 (0.67, 0.98)	0.03	0.80 (0.68, 0.95)	0.01
F40- F48 (Neurotic, stress-related and somatoform disorders)	0.82 (0.68, 0.99)	0.04	0.83 (0.70, 0.99)	0.04

One unit increase in HoNoS

Cognitive Problems	1.02 (0.87, 1.19)	0.83		
Physical Illness	1.36 (1.19, 1.56)	<0.001	1.48 (1.31, 1.67)	<0.001
Hallucinations	0.91 (0.76, 1.10)	0.34		
Depressed Mood	0.83 (0.72, 0.94)	0.01	0.91 (0.82, 1.00)	0.05
Relationship Problems	0.89 (0.77, 1.02)	0.10		
Daily Living Problems	1.12 (0.98, 1.29)	0.11		
Occupational Problems	0.91 (0.79, 1.04)	0.15		

Admitted to general hospital (within one year before or after diagnosis of Mood [affective] disorder)

Ischaemia +CHD+ IHD	1.01 (0.85, 1.22)	0.88		
Arrhythmia + AF	1.03 (0.86, 1.23)	0.78		
Heart failure	1.44 (1.12, 1.86)	0.01	1.43 (1.14, 1.80)	<0.001
Diabetes	1.22 (1.04, 1.44)	0.02	1.23 (1.06, 1.44)	<0.001
Hypotension	1.18 (0.93, 1.48)	0.17		
Hypercholesterolemia	0.85 (0.71, 1.03)	0.10		
Hypertension	1.05 (0.90, 1.23)	0.53		
Urinary tract infections (UTI)	1.49 (1.28, 1.74)	<0.001	1.52 (1.32, 1.75)	<0.001
Osteoporosis	7.31 (5.82, 9.18)	<0.001	7.00 (5.65, 8.70)	<0.001
Visual Disturbance and Blindness	1.06 (0.74, 1.53)	0.74		
Hearing Loss	1.40 (1.03, 1.92)	0.03	1.46 (1.09, 1.96)	0.01

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3	Syncope or Collapse	1.18 (1.02, 1.36)	0.03	
4	Parkinson's Disease	0.85 (0.58, 1.25)	0.41	
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7	Falls before Mood [affective] disorders diagnosis	1.02 (0.85, 1.22)	0.83	
8	Fractures before Mood [affective] disorders diagnosis	1.26 (1.01, 1.57)	0.04	1.33 (1.10, 1.63) <0.001
9	Increase in one attendances to A&E following Mood			
10	[affective] disorders diagnosis	1.01 (1.01, 1.01)	<0.001	1.01 (1.01, 1.01) <0.001
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The RECORD statement – checklist of items, extended from the STROBE statement, that should be reported in observational studies using routinely collected health data.

	Item No.	STROBE items	Location in manuscript where items are reported	RECORD items	Location in manuscript where items are reported
Title and abstract					
	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract (b) Provide in the abstract an informative and balanced summary of what was done and what was found	Page 1 and 2	RECORD 1.1: The type of data used should be specified in the title or abstract. When possible, the name of the databases used should be included. RECORD 1.2: If applicable, the geographic region and timeframe within which the study took place should be reported in the title or abstract. RECORD 1.3: If linkage between databases was conducted for the study, this should be clearly stated in the title or abstract.	Page 2
Introduction					
Background rationale	2	Explain the scientific background and rationale for the investigation being reported	Page 4		
Objectives	3	State specific objectives, including any prespecified hypotheses	Page 4		
Methods					
Study Design	4	Present key elements of study design early in the paper	Page 5		
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Page 5		
Participants	6	(a) <i>Cohort study</i> - Give the eligibility criteria, and the sources and methods of selection of participants. Describe	Page 5	RECORD 6.1: The methods of study	Page 5
		eligibility criteria, and the sources and methods of selection of participants. Describe		population selection (such as codes or algorithms used to identify subjects) should be listed in detail. If this is not	

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1 2 3 4 5 6	Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable.	Page 6-8	RECORD 7.1: A complete list of codes and algorithms used to classify exposures, outcomes, confounders, and effect modifiers should be provided. If these cannot be reported, an explanation should be provided.	Page 6-8
7 8 9 10 11 12 13 14	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	Page 6-8		
15 16 17	Bias	9	Describe any efforts to address potential sources of bias	Page 9		
18 19	Study size	10	Explain how the study size was arrived at	Page 5		
20 21 22 23 24 25	Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen, and why	Page 6-8		

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<p>1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23</p> <p>Statistical methods</p>	<p>12</p>	<p>(a) Describe all statistical methods, including those used to control for confounding (b) Describe any methods used to examine subgroups and interactions (c) Explain how missing data were addressed (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 (e) Describe any sensitivity analyses</p>	<p>Page 9</p>		
<p>24 25 26 27 28 29 30 31 32 33 34</p> <p>Data access and cleaning methods</p>	<p>..</p>	<p>..</p>		<p>RECORD 12.1: Authors should describe the extent to which the investigators had access to the database population used to create the study population. RECORD 12.2: Authors should provide information on the data cleaning methods used in the study.</p>	<p>Page 5</p>
<p>35 36</p> <p>Linkage</p>	<p>..</p>	<p>..</p>		<p>RECORD 12.3: State whether the</p>	<p>Page 6</p>
				<p>study included person-level, institutional-level, or other data linkage across two or more databases. The methods of linkage and methods of linkage quality evaluation should be provided.</p>	

Results

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Participants	13	<p>(a) Report the numbers of individuals at each stage of the study (<i>e.g.</i>, numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed)</p> <p>(b) Give reasons for non-participation at each stage.</p> <p>(c) Consider use of a flow diagram</p>	Page 9	<p>RECORD 13.1: Describe in detail the selection of the persons included in the study (<i>i.e.</i>, study population selection) including filtering based on data quality, data availability and linkage. The selection of included persons can be described in the text and/or by means of the study flow diagram.</p>	Page 9
Descriptive data	14	<p>(a) Give characteristics of study participants (<i>e.g.</i>, demographic, clinical, social) and information on exposures and potential confounders</p> <p>(b) Indicate the number of participants with missing data for each variable of interest</p> <p>(c) <i>Cohort study</i> - summarise follow-up time (<i>e.g.</i>, average and total amount)</p>	Table 1 and page 9		
Outcome data	15	<p><i>Cohort study</i> - Report numbers of outcome events or summary measures over time</p> <p><i>Case-control study</i> - Report numbers in each exposure category, or summary measures of exposure</p> <p><i>Cross-sectional study</i> - Report numbers of outcome events or</p>	Page 10		
		summary measures			

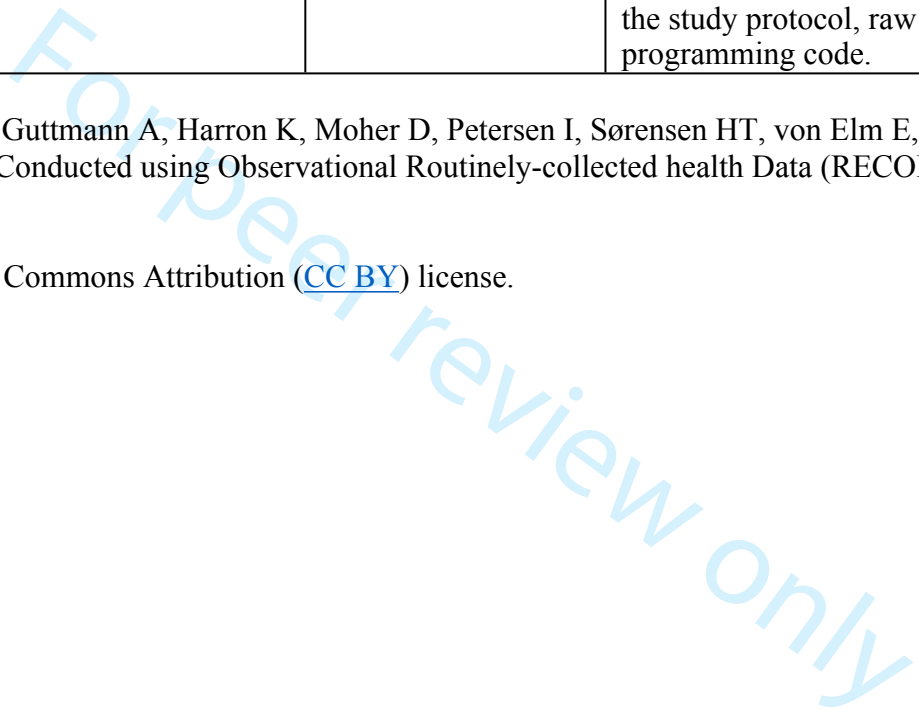
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16 17 18 19 20	Other analyses	17	Report other analyses done—e.g., analyses of subgroups and interactions, and sensitivity analyses	Not applicable		
21	Discussion					
22 23 24	Key results	18	Summarise key results with reference to study objectives	Page 13-16		
25 26 27 28 29 30 31 32 33 34	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	Page 16-17	RECORD 19.1: Discuss the implications of using data that were not created or collected to answer the specific research question(s). Include discussion of misclassification bias, unmeasured confounding, missing data, and changing eligibility over time, as they pertain to the study being reported.	Page 16-17
35 36 37 38 39 40 41 42	Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Page 17-18		
43 44 45 46 47	Generalisability	21	Discuss the generalisability (external validity) of the study results	Page 17		

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	Page 18		
Accessibility of protocol, raw data, and programming code		..		RECORD 22.1: Authors should provide information on how to access any supplemental information such as the study protocol, raw data, and programming code.	Page 19

*Reference: Benchimol EI, Smeeth L, Guttman A, Harron K, Moher D, Petersen I, Sørensen HT, von Elm E, Langhin SM, the RECORD Working Committee. The REporting of studies Conducted using Observational Routinely-collected health Data (RECORD) Statement. *PLoS Medicine* 2015; in press.

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Supplementary material Table 1. Mean age at the time of fall/ fracture and mood disorder diagnosis among patients with Mood [affective] disorders

Age	Presence of falls		Presence of fractures	
	No (n= 34,270)	Yes (n= 1,831)	No (n= 33,908)	Yes (n= 2,193)
Mean age at diagnosis (SD)	43.4 (17.1)	62.4 (19.9)	43.3 (17.1)	60.6 (20.6)
Mean age at fall/ fracture/ (SD)		64.2 (20.8)		62.5 (22.8)

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