

Mental distress and risk of hip fracture. Do broken hearts lead to broken bones?

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Abstract

Objective—Mental distress may entail increased risk of hip fracture, but it is uncertain whether the effect consists solely of an indirect effect through use of medication, or whether it is also mediated through other mechanism. The purpose of this study was to examine the association between mental distress and risk of hip fracture in women, adjusted for medication (that is, use of tranquillisers/sedatives or hypnotics).

Design—A three year follow up of hip fracture was conducted on 18 612 women, consisting of 92.5% of all women aged 50 years or older in a Norwegian county. Three hundred and twenty nine suffered a hip fracture. A mental distress index was based on questions about life dissatisfaction, nervousness, loneliness, sleep disorders, troubled and uneasy feelings, depression and impairment attributable to psychological complaints. Relative risk with 95% confidence intervals (CI) of hip fracture with respect to mental distress were controlled for medication, age, body mass index (BMI), smoking, physical inactivity, and physical illness by means of Cox regression.

Results—The 10% of women with the highest mental distress had more than twofold increased risk of hip fracture compared with the 10% of women with the lowest mental distress, after adjustment for age and medication. The relative risk was 1.95 (95% CI 1.2, 3.3) after additional control for BMI, smoking, physical inactivity, and physical illness. The relative risk of hip fracture for daily users of medication compared with never users was 2.1 (95% CI 1.6, 2.9). After adjusting for mental distress it was 1.5 (95% CI 1.0, 2.2).

Conclusions—Risk of hip fracture was positively related to mental distress, also after adjustment for medication use. The effect of tranquillisers/sedatives or hypnotics on hip fracture risk may be overestimated in studies with no adjustments for mental distress.

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Hip fracture is a leading health problem in the elderly. Increased risk of fracture may be attributable to reduced bone mass, reduced quality of bone, or factors associated with trauma and falling. The use of psychotropic drugs may increase the risk of falling¹⁻³ and

consequently the risk of hip fracture.⁴⁻⁶ An association between the use of long acting benzodiazepines and hip fracture has thus been shown in some,^{7,8} but not all studies.⁹ These studies have, however, not considered the effect of mental distress on use of benzodiazepines, which could produce a spurious association between medication and fracture risk, because mental distress may also act through other mechanisms.

A few studies have suggested a relation between depression and bone mass/fracture risk: in a case-control study¹⁰ performed in 48 women (24 cases, 24 controls), mental depression was associated with low bone density. The authors concluded that the lifetime risk of fracture related to depression could be substantial. Another study on all fractures in 7518 women aged 65 or older (five year follow up) concluded that depression was a risk factor for fractures in older women (MA Wholey *et al.* 19th annual meeting of the American Society of Bone and Mineral Research, Cincinnati, 1997). Depressed women had a 40% increased rate of fractures compared with non-depressed women, after controlling for well known risk factors, such as bone density and use of antidepressant drugs. Further adjustments for falls appeared to explain only a part of the association. An effect of depression on bone mineral density was also found, but only among obese women. A third study with only three men and 15 women meeting the categorical criteria for clinical depression, could not support an association between depressed mood and bone mineral density (D Kritz-Silverstein, *et al.* 19th annual meeting of the American Society of Bone and Mineral Research, 1997).

The purpose of this study was to examine, prospectively, the risk of hip fracture with respect to subjective mental distress adjusted for the use of tranquillisers/sedatives or hypnotics and other confounders.

Methods

STUDY POPULATION

Between January 1984 and 1 March 1986 all residents in a Norwegian county, Nord-Trøndelag, aged 20 years or older were invited to a health screening. In advance, each person received a letter containing information about the screening, and a questionnaire on background factors and personal health. Height, weight, blood pressure, and pulse of each participant were measured at the screening.¹¹⁻¹³ In addition, the participants were asked to return a second questionnaire on lifestyle and quality

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Table 1 Questions from a questionnaire given to 18 612 women aged 50 years or older attending a health screening in a Norwegian county (Nord-Trøndelag) in 1984–86

Questions	Answer alternatives
How often have you taken tranquilisers/sedatives or sleeping pills (hypnotics) in the course of the last month?	"Daily", "Weekly, but not every day", "More rarely than every week", "Never"
When you think about the way your life is going at present, would you say that you are by and large satisfied with life or are you mostly dissatisfied?	"Very satisfied", "Fairly satisfied", "Satisfied", "So so", "Dissatisfied", "Fairly dissatisfied", "Very dissatisfied"
Over the past month, have you suffered from nervousness (felt irritable, anxious, tense or restless)?	"Almost all the time", "Often", "Now and again", "Never"
Do you often feel lonely?	"Very often", "Often", "Now and again", "Very rarely", "Never"
Have you had any problems falling asleep or have you had sleep disorders over the course of the past month?	"Almost every night", "Often", "Now and again", "Never"
Do you by and large feel calm and good about yourself?	"Almost all the time", "Often", "Now and again", "Never"
Would you say you are usually cheerful or dejected?	"Very dejected", "Dejected", "Fairly dejected", "Fifty-fifty", "Fairly happy", "Happy", "Very happy"
Do you suffer from any long term illness, or complaints of physical or psychological nature that impair your functions in your day to day life? (Long term means that it has lasted or will last for at least one year.)	"Yes", "No"
If yes, would you describe your impairment as slight, moderate or considerable?	"Slight", "Moderate", "Considerable"

of life handed out at screening. For the purpose of this study all women aged 50 years or older who attended the screening and who were alive 1 March 1986 (92.5% of 20 130 eligible subjects) were selected. Thus 18 612 women were included in the follow up as the study population. Their age at screening varied from 50 to 101 years (mean=66.0).

FOLLOW UP

In principle, all residents of Nord-Trøndelag with hip fracture are admitted to one of two county hospitals. The follow up lasted from 1 March 1986 to 28 February 1989. The hip fractures were identified using the computed patient registers of the two hospitals. New fractures were verified manually from the medical records of each patient. The patients treated for

late complications of previous fractures or admitted for removal of osteosynthesis materials were thus omitted. Only the first hip fracture during the follow up period among the screened women was used in the analysis (329 hip fractures). The age of the hip fracture patients at the injury varied from 51 to 103 years (mean=78.1). Their mean age at the screening was 75.8.

VARIABLES

Observation time was calculated from 1 March 1986 to date of hip fracture, date of moving, date of death or 28 February 1989. Information concerning BMI, self reported smoking habits, physical inactivity, and mental and physical illness were collected at screening.^{14 15}

Table 2 Age adjusted rates and relative risks of hip fracture by use of tranquilisers/sedatives or hypnotics and by mental health in women attending a health screening in a Norwegian county (Nord-Trøndelag) in 1984–86, followed up for three years on hip fracture

Variables		Number of person/years	Number of fractures	Rate /1000 person/years	Relative risk	95% CI
Use of tranquilisers/sedatives or hypnotics	Never	9381 (65)	113	5.17	1.00	
	Rarely	1877 (13)	25	5.21	1.01	0.65, 1.55
	Weekly	1266 (9)	19	5.36	1.04	0.64, 1.69
	Daily	1837 (13)	70	10.80	2.09	1.55, 2.82
Life satisfaction	Very satisfied	6780 (37)	100	5.35	1.00	
	Fairly satisfied	7616 (42)	137	6.81	1.27	0.98, 1.65
	Yes and no	3335 (18)	68	7.93	1.48	1.09, 2.02
Suffered from nervousness	Dissatisfied	541 (3)	15	11.54	2.16	1.25, 3.71
	Never	6770 (47)	100	5.47	1.00	
	Now and again	6065 (42)	92	6.34	1.16	0.87, 1.54
Suffered from loneliness	Often	968 (7)	15	7.08	1.29	0.75, 2.23
	Almost all of the time	575 (4)	18	12.59	2.30	1.39, 3.80
	Never/rarely	8701 (57)	91	4.65	1.00	
Sleep disorders	Now and again	4943 (32)	101	7.04	1.51	1.14, 2.01
	Often	988 (6)	27	8.70	1.87	1.22, 2.87
	Very often	699 (5)	17	8.62	1.85	1.10, 3.11
Calm and good feelings	Never	6328 (43)	77	5.02	1.00	
	Now and again	6150 (42)	106	6.62	1.31	0.98, 1.76
	Often	1206 (8)	16	5.16	1.03	0.60, 1.76
Cheerful or dejected	Almost every night	978 (7)	33	11.10	2.21	1.47, 3.52
	All the time	7085 (48)	107	5.57	1.00	
	Often	3703 (25)	40	4.76	0.85	0.59, 1.23
Impairment due to psychological complaints	Now and again	3605 (25)	71	7.83	1.41	1.04, 1.90
	Never	345 (2)	12	15.45	2.77	1.53, 5.04
	Very happy	5241 (34)	71	5.49	1.00	
Impairment due to psychological complaints	Fairly happy	4487 (29)	58	5.38	0.98	0.69, 1.39
	Fifty-fifty	5064 (33)	93	6.82	1.24	0.91, 1.69
	Dejected	564 (4)	18	11.41	2.08	1.24, 3.48
Impairment due to psychological complaints	No	16992 (92)	279	6.10	1.00	
	Yes, slight	736 (4)	15	7.92	1.30	0.77, 2.18
	Yes, moderate	444 (2)	13	9.99	1.64	0.94, 2.85
	Yes, heavy	402 (2)	21	18.25	2.99	1.92, 4.66

Table 3 Age adjusted rates and relative risks of hip fracture by a mental distress index in women attending a health screening in a Norwegian county (Nord-Trøndelag) in 1984–86, followed up for three years on hip fracture

The mental distress index	Number of persons (%)	Person/years	Number of fractures	Rate/1000 person/years	Relative risk	95% CI
0–4	1569 (10)	4 603	18	4.82	1.00	
5–9	4354 (28)	12 712	52	4.78	0.99	0.58, 1.69
10–14	5224 (33)	15 115	78	5.65	1.17	0.70, 1.96
15–19	2834 (18)	8 159	55	7.10	1.47	0.87, 2.51
20–29	1468 (9)	4 171	31	8.07	1.67	0.94, 2.99
30–45	269 (2)	743	15	24.04	4.99	2.51, 9.89

Table 1 gives the questions about medication and mental distress.

The questions about tranquillisers/sedatives or hypnotics and at least four of the questions about mental health were answered by 77% of the participants (71% of eligible subjects).

STATISTICAL METHODS

Standardised morbidity ratio (SMR)¹⁶ was applied to make age adjusted rates with 95% confidence intervals for the effect of the mental health variables on the risk of hip fracture. The whole county served as reference population. Principal component analysis¹⁷ was used to justify the construction of a mental distress index based on seven mental health variables (listed in table 1). The index was made only for those women who responded to four or more of the variables on mental health and was computed as a mean of the responses of the actual woman. As the variables had a varying number of categories (table 1) they were standardised before constructing the index. We standardised each variable by subtracting it by its mean among the women and dividing this difference by the corresponding standard deviation. For practical reasons (simpler tabulation and illustration) we multiplied the index with 10 and took the integer value of the resulting figure. In order to scale the index to start on zero, a constant (=12) was added. After the correction the index varied from 0 to 45. Cox regression was used to test the effect of the interaction between mental distress and use of tranquillisers/sedatives or hypnotics on the risk of hip fracture and to adjust for confounders (BMI, physical inactivity, smoking, and impairment because of physical illness). Additional analysis was performed to study how

KEY POINTS

- Our study shows that mental distress is positively related to hip fracture risk.
- This association was still evident after adjustment for use of tranquillisers/sedatives or hypnotics.
- The effect of such medication on hip fracture risk may be overestimated in studies with no adjustments for mental distress.

each term in the mental distress index contributed to the association with fracture risk.

Results

Women who daily used tranquillisers/sedatives or hypnotics had an increased risk of hip fracture compared with never users (table 2). Each of the mental health variables showed an increasing rate of hip fracture with growing mental distress. The relative risk in the worst category versus the best category of mental health was statistically significant in all the mental health variables. A principal component analysis on these seven variables indicated clearly a one dimensional structure, which justified the construction of one mental distress index (eigenvalue factor one = 3.2, factor two = 0.9, Cronbach's alpha = 0.80). This index showed a stronger association with risk of hip fracture (table 3) than each of the single variables in table 2. After controlling for use of tranquillisers/sedatives or hypnotics and other confounders (BMI, physical inactivity, smoking, impairment because of physical illness), the risk of hip fracture still increased by growing mental distress (table 4). The 10% of women with the highest mental distress had a twofold increased risk of hip fracture compared with the 10% of women with the lowest mental distress. Daily users of medication had 50% increased risk of hip fracture compared with never users ($p=0.056$) when adjusted for mental distress and the other confounders (table 4). The association between mental distress and hip fracture risk was strongest among daily users of medicine (data not shown), but the interaction term between use of medicine and mental distress on hip fracture risk was not statistically significant ($p=0.23$).

Table 4 Relative risk (RR) of hip fracture according to a mental distress index and according to use of tranquillisers/sedatives or hypnotics, adjusted for available confounders in women attending a health screening in a Norwegian county (Nord-Trøndelag) in 1984–86 followed up for three years on hip fracture

		Age adjusted only		Adjusted for age, mental distress and use of medication		Adjusted for age, mental distress, use of medication, BMI, smoking, physical inactivity, and impairment because of physical illness	
		RR	95% CI	RR	95% CI	RR	95% CI
Mental* distress	The 10% of women with lowest distress	1.00		1.00		1.00	
	The 10% of women with highest distress	2.79	1.92, 4.06	2.32	1.45, 3.70	1.95	1.15, 3.29
Use of tranquillisers/sedatives or hypnotics	Never	1.00		1.00		1.00	
	Rarely	1.00	0.65, 1.54	0.85	0.54, 1.33	0.92	0.58, 1.48
	Weekly	1.00	0.62, 1.63	0.77	0.46, 1.28	0.75	0.43, 1.31
	Daily	2.11	1.55, 2.86	1.49	1.03, 2.16	1.48	0.99, 2.21

*The mental distress index is included as a continuous variable in the Cox regression model. We have chosen to give the RR for the 10% of women with the highest mental distress (mean=24.7) compared with the 10% of women with the lowest mental distress (mean=3.2)—that is, the RR for a difference of 21.5 in the mental distress index.

Stratified analyses for women above and below 75 years of age, respectively, gave the same estimates concerning mental distress as in the total analysis, but for women below 75 the association between medication and hip fracture risk was not statistically significant.

An additional, separate Cox regression analysis for each term in the index showed that each term contributed to the increasing risk of hip fracture for increasing mental distress, but only the variables "life dissatisfaction" and "loneliness" were statistically significant alone after adjustment for the confounders.

Discussion

Our prospective population-based study of a county in Norway, showed an association between mental distress and the risk of hip fracture. The risk was positively related to mental distress, also after adjustment to use of tranquillisers/sedatives or hypnotics and other confounders.

METHODOLOGICAL CONSIDERATIONS

The mental distress index was based on seven questions about self reported mental health and did not correspond to one of the established instruments.¹⁸ However, a previous cross validation study¹⁹ revealed a high degree of empirical overlap between an outcome measure²⁰ based on questions in table 1 and HSCL (Hopkins Symptom Check List²¹).

As several studies have shown an association between use of psychotropics and risk of hip fracture,^{4-6,8} we wanted to examine whether the mental problems that probably had led to the medication could have a direct effect on risk of hip fracture independent of the medication. Previously only clinical depression has shown association with low bone mineral density and fracture—Michelson *et al*,¹⁰ and M A Wholey, *et al* (19th annual meeting of the American Society of Bone and Mineral Research, 1997). We were able to study women with varying mental distress in the whole population of women, and not only clinically depressed patients, who represent only a small proportion.

It is a limitation that we only have information about use of tranquillisers/sedatives or hypnotics—and not antidepressant drugs. In addition, in the control for medication it was impossible to distinguish between use of tranquillisers/sedatives and pure hypnotics. Besides, we had no information about dose. Obviously, higher distress could imply greater dose than lower distress. It is therefore possible that part of the association between mental distress and fracture among users of medicine can be explained by greater dose among the women with highest distress, especially among daily users of medicine. For a given value of the mental distress index there might also have been a difference in level of problems between the daily users and those using medication less frequently. However, we did not find any statistically significant interaction between mental distress and medication.

Seventy seven per cent of the women who attended the screening (14 254 of 18 612) had

a non-missing value on the mental distress index and use of tranquillisers (71% of eligible subjects). In an earlier study of non-attendance¹²⁻¹³ the largest non-attendance rates were seen among the oldest with poor self reported health. However, the association between mental distress and hip fracture risk in this study showed no interaction with age.

POSSIBLE MECHANISM

The adverse effect of mental distress on risk of hip fracture may act through several mechanisms. Medication may induce dizziness and increase risk of falling¹⁻³ and consequently risk of fracture.⁴⁻⁶ It is also possible that mental distress acts through health neglecting behaviour such as bad nutrition and smoking, and consequently increases fracture risk.^{14-15, 22} Our adjustment for BMI and smoking might not be thorough enough for health neglecting behaviour. Another possible mechanism may be an increased level of cortisol for mentally distressed persons.²³ Corticosteroid induced osteoporosis is well known.²⁴ Cortisol inhibits the osteoblastic activity²³⁻²⁶ and may also increase the osteoclasts²⁴ contributing to an imbalance in the bone remodelling process, resulting in bone loss and increased fracture risk. Further investigation is warranted regarding the possible pathways between mental distress and risk of hip fracture.

In conclusion, our finding of a direct effect of mental distress on hip fracture risk, after adjustment for medication use, needs to be verified in other studies that both include information about mental distress and the dose of medicine. Watchful care with respect to prevention of hip fracture should be given women with high mental distress, especially those who use medicine daily.

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