SSRI use and risk of fractures among perimenopausal women without mental disorders

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ABSTRACT

Background Selective serotonin reuptake inhibitors (SSRIs) were recently approved by the FDA to treat vasomotor symptoms associated with menopause. No prior study has directly examined whether fracture risk is increased among perimenopausal women who initiate SSRIs or among a population of women without mental disorders more generally.

Methods Female patients without mental illness, aged 40–64 years, who initiated SSRIs were compared with a cohort who initiated H2 antagonists (H2As) or proton-pump inhibitors (PPIs) in 1998–2010, using data from a claims database. Standardised mortality ratio weighting was applied using the propensity score odds of treatment to adapt the distribution of characteristics among patients starting H2A/PPIs to the distribution among SSRI initiators. Poisson regression estimated risk differences and Cox proportional hazards regression the RR of fractures among new users of SSRIs versus H2A/PPIs. Primary analyses allowed for a 6-month lag period (ie, exposure begins 6 months after initiation) to account for a hypothesised delay in the onset of any clinically meaningful effect of SSRIs on bone mineral density.

Results Fracture rates were higher among the 137 031 SSRI initiators compared with the 236 294 H2A/PPI initiators, with HRs (SSRI vs H2A/PPI) over 1, 2 and 5 years of 1.76 (95% CI 1.33 to 2.32), 1.73 (95% CI 1.33 to 2.24) and 1.67 (95% CI 1.30 to 2.14), respectively.

Conclusions SSRIs appear to increase fracture risk among middle-aged women without psychiatric disorders, an effect sustained over time, suggesting that shorter duration of treatment may decrease fracture risk. Future efforts should examine whether this association pertains at lower doses.

INTRODUCTION

Since the introduction of selective serotonin reuptake inhibitors (SSRIs) in the 1990s, SSRIs have become a first-line treatment for depression as well as other mental disorders (eg, anxiety and eating disorders).[1–3] Use of SSRIs for non-psychiatric conditions, such as irritable bowel syndrome, premature ejaculation and perimenopausal symptoms,[4] has also increased, to the point that antidepressant medications are now the third most commonly prescribed class of medications in the USA, with much of this growth attributable to a substantial increase in antidepressant prescriptions by non-psychiatrist providers to patients without a psychiatric diagnosis.[5]

One SSRI, paroxetine, has recently been approved by the US Food and Drug Administration (FDA) for the treatment of vasomotor menopausal symptoms (VMS), including hot flashes and night sweats that occur during the menopausal transition, at about one-third of the dose used to treat most psychiatric disorders.[6] Paroxetine is currently the only FDA-approved, non-hormonal treatment for VMS, although other SSRIs have also shown efficacy for this indication at standard doses used to treat depression.[7–12] For example, escitalopram improves VMS as well as sleep disturbance related to the perimenopausal condition and improves quality of life.[8 9 13] Recent meta-analyses also show that SSRIs as a class are effective in treating menopausal symptoms, decreasing VMS attacks per day by up to 65%.[11 14] Indeed, before the FDA approval of paroxetine, SSRIs as a class had already been suggested as an alternative to hormone replacement therapy (HRT).[15 16]

Although the pharmacovigilance literature has addressed several safety concerns related to the use of antidepressants by patients with psychiatric disorders, including risk of fracture, little is known about related risks among the non-psychiatric population. It has been proposed that psychiatric disorders, such as depression, are associated with increased fracture risk independent of antidepressant treatment.[17 18] The generalisability of this finding to patients without frank psychiatric disorders remains an open empirical question. In fact, whether SSRIs increase fracture risk in the absence of depression and other mental disorders has not been directly examined either in randomised controlled trials or observational studies. To our knowledge, the current study is the first to examine whether SSRI use is related to fracture risks in a population of middle-aged women without known psychiatric disorders, a demographic for which, given the recent FDA approval of paroxetine for the treatment of VMS, SSRI use may increase.

METHODS

Patients and data source

The PharMetrics Claims Database used in this study comes from IMS Health and is comprised of commercial health plan information obtained from managed care plans throughout the USA. The database includes medical and pharmaceutical claims for over 61 million unique patients from over 98 health plans (approximately 16 million covered lives per year). The database includes inpatient and outpatient diagnoses (in ICD-9-CM format) and procedures (in CPT-4 and HCPCS formats) as well as both retail and mail order records of all reimbursed dispensed prescriptions. Available data on prescriptions include the National Drug Code (NDC) as well as the quantity, number of days

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supplied, and the date of dispensing. Additional data elements include demographic variables (age, gender, geographic region), provider specialty, and start and stop dates of health plan enrolment. Only health plans that submit data for all members are included in the database.

The current study involves two cohorts of female patients 40–64 years of age who initiated use of (1) SSRIs; or (2) H2 antagonists (H2A)/proton-pump inhibitors (PPIs) (as a comparator group), between 1 January 1998 and 31 December 2010. Both cohorts exclude patients with diagnoses of any psychiatric disorders (ICD-9 codes 290 to 319). Initiation of SSRIs is defined as filling an SSRI prescription without evidence of having filled a prescription for any kind of antidepressants or anti-ulcer drugs in the preceding 12 months. Initiation of H2A/PPI is defined as filling an H2A/PPI prescription without evidence of having filled a prescription for any kind of antidepressants or anti-ulcer drugs in the preceding 12 months. Such initiators (of SSRIs or H2A/PPIs) are referred to throughout as 'new users' of that specific agent. Subjects were required to be actively enrolled in a health plan with prescription benefits that contributed data to our claims database during the 15 months prior to initiation (ie, 12 months for baseline covariate assessment and an additional 3 months to allow uniform assessment of all patients based on a 60-day grace period and a usual medication supply of 30 days).

Medication exposure

Medications classified as SSRIs included citalopram hydrobromide, escitalopram oxalate, fluoxetine hydrochloride, fluvoxamine maleate, paroxetine hydrochloride and sertraline hydrochloride. Commonly prescribed H2A and PPIs are included for the comparator cohort. The H2As include cimetidine, ranitidine, famotidine nizatidine and roxatidine. The PPIs included esomeprazole, lansoprazole, omeprazole, pantoprazole, dexlansoprazole and rabeprazole. Patients initiating more than one antidepressant or H2A/PPI on the same day were excluded.

Follow-up and study end point

Exposure status was assigned based on the initiated medication and carried forward. For each patient, we created a record of drug coverage by listing consecutive prescription fills, based on dispensing dates and reported days supply. When a dispensing occurred before the previous prescription should have run out, use of the new prescription is assumed to begin the day after the end of the old prescription. Since users of any prescription medicine may experience relatively brief episodes without a supply of medicine or may skip taking the medicine some days, we allowed for up to 60 extra days to elapse beyond the provided days supply before censoring (ie, we use a 60-day grace period, twice the most common days supply).

SSRI initiators were allowed to switch from one SSRI to another SSRI but were censored if they switched to another antidepressant class, or added another antidepressant class to the initiated regimen (ie, treatment augmentation with antidepressants other than SSRIs); SSRI initiators were not censored if they were initiated with an H2A or PPI; H2A/PPI initiators were censored at initiation of any antidepressant during follow-up, but were not censored for either switching to another H2A/PPI or adding another H2A/PPI. There was no censoring for dose changes for either cohort. Patients were also censored at the date of the end of enrolment in their health insurance plan, or the end of the study period, whichever came first. New users were not allowed to become new users again; patients who were prevalent users at the start of their enrolment were allowed to become new users after an appropriate washout period.

The occurrence of hip, humerus, radius and ulna fractures at least 1 day after initiating SSRI or H2A/PPI therapy was our outcome of interest. These fractures were defined as a medical claim with an International Classification of Diseases, Ninth Revision (ICD-9) external cause of injury code (E-code) of hip (733.14 or 820.xx), humerus (733.11 or 812.xx) or radius/ulna (733.12 or 813.xx) fracture diagnosis paired with a medical claim with a corresponding treatment code. Our definition of fractures did not include spine fractures because new vertebral compression fractures cannot be reliably identified in claims data.[19]

Patient characteristics

Patient characteristics included age, sex, and several indicators of past year medical comorbidity based on inpatient, outpatient and pharmacy claims, including the number of acute hospitalisations for any reasons, number of outpatient visits, constituents of the Charlson Comorbidity Index score, number of distinct generic drugs filled, specific drugs that may affect the risk of fractures, previous bone mineral density scans, use of HRT, malignant neoplasms, opiate use, stroke and transient ischaemic attack, Parkinson's disease, perimenopausal symptoms, irritable bowel syndrome, seizure disorders, urinary incontinence, cardiovascular disease and chronic lung disease. Additional risk factors for the outcome of interest included a history of falls and prior hip, humerus and/or radius fracture, based on risk factors identified in the literature.[20]

Statistical analysis

We estimated the propensity score (PS) for initiating SSRIs versus H2A/PPIs using multivariable logistic regression including all of the covariates outlined above. We implemented the PS to balance these measured covariates across treatment groups by assigning a weight of 1 to each person in the SSRI cohort and weighting each person in the comparator (H2A/PPI) cohort by the propensity odds (PS/(1−PS)). This PS weighting proposed by Sato and Matsuyama[21] results in a pseudo-population of H2A/PPI initiators that has the same distribution of measured covariates as that observed in the patients initiating SSRIs (ie, standardised mortality ratio weighting). Weighted Poisson regression was used to calculate fracture rates for patients exposed to SSRIs versus H2A/PPIs allowing for a hypothesised 6-month lag period (ie, starting the clock 6 months after initiation) and informed by examination of Kaplan–Meier (KM) plots of the weighted cohorts. Follow-up continued until the termination of the exposure period. The lag period was chosen to account for a hypothesised delay in the onset of a clinically meaningful effect of SSRIs on bone mineral density. In our main (as-treated) analysis, unless the patient is censored due to death or termination of their insurance programme, exposure periods are extended 6 months beyond the censoring date (the 'induction period'). We used weighted Poisson regression to estimate the risk difference for each defined time period and weighted Cox proportional hazards models to estimate HRs. Robust methods were used to calculate 95% CIs. The following sensitivity analyses were also performed: (1) a first-treatment-carried forward analysis; (2) analyses using different grace periods (30, 45 and 90 days); and (3) an analysis with no lag or induction periods.

RESULTS

Balance of cohorts

Table 1 shows the characteristics of SSRI new users and the un-weighted and weighted H2A/PPI new user comparator cohorts. Patient characteristics were reasonably balanced across

Table 1 Sample characteristics of women, aged 40–64, all mental disorders excluded

Characteristic	SSRI, N=137 031 N=137 031	Per cent	H2A/PPIs, N=236 294 N=236 294	Per cent	H2A/PPIs weighted to SSRI (%)
Age at index date					
40–49	64 227	46.7	91 422	38.6	46.8
50–59	54 297	39.7	101 360	42.9	39.5
60–64	18 507	13.6	43 512	18.4	13.7
ACE inhibitors	11 899	8.7	24 187	10.2	8.8
Antipsychotics	2372	1.7	4661	2.9	1.8
Angiotensin receptor blockers	5116	3.7	11 365	4.8	3.8
Cardiac arrhythmias	4775	3.5	11 472	4.9	3.5
Rheumatoid arthritis	2169	1.6	5517	2.3	1.6
Barbiturate	106	0.1	196	0.1	0.1
β Blockers	14 609	10.7	29 363	12.4	10.8
Benzodiazepine	25 348	18.5	21 372	9.1	18.6
History of falls, syncope or gait abnormality	6623	4.8	14 625	6.2	5.0
Bone mineral density scan	10 864	7.9	23 834	10.1	8.0
Cataracts	4148	3.0	10 086	4.3	3.1
Calcium channel blockers	8468	6.2	19 704	8.3	6.2
Myocardial infarction	719	0.5	2004	0.8	0.5
Paraplegia and hemiplegia	193	0.1	319	0.1	0.1
Moderate or severe liver disease	109	0.1	387	0.2	0.1
AIDS/HIV	110	0.1	288	0.1	0.1
Peripheral vascular disease	1930	1.4	5027	2.1	1.4
Peptic ulcer disease	613	0.4	6234	2.6	0.5
Congestive heart failure	1364	1.0	3786	1.6	1.0
Asthma/COPD	12 514	9.1	29 499	12.5	9.3
Cox-2 inhibitors	7078	5.2	13 348	5.6	5.3
Crohn's disease/gastroenteritis	3274	2.4	9435	4.0	2.4
Diabetes	9806	7.2	21 363	9.0	7.3
Glucocorticosteroids	16 743	12.2	42 231	17.9	12.5
Hip fracture	94	0.1	248	0.1	0.1
Hormone replacement therapy	23 500	17.1	36 663	15.5	17.4
Humerus fracture	208	0.2	381	0.2	0.2
Hyperparathyroidism	304	0.2	776	0.3	0.2
Hyperthyroidism	1750	1.3	3536	1.5	1.3
Irritable bowel syndrome	2867	2.1	4403	1.9	2.2
Kyphosis	670	0.5	1420	0.6	0.5
Liver disease	3328	2.4	8975	3.8	2.5
Malignant neoplasm cancer	8251	6.0	17 071	7.2	6.1
Other NSAIDs	27 493	20.1	60 450	25.6	20.3
Number of drugs					
1 (SSRI/ulcer drug only)	11 811	8.6	13 142	5.6	8.5
2–3	28 683	20.9	40 366	17.1	20.6
4–5	27 022	19.7	46 020	19.5	19.5
6–9	37 066	27.0	73 018	30.9	27.0
10+	32 449	23.7	63 748	27.0	24.4
Number of hospitalisations, 1+	9609	7.0	27 101	11.5	7.2
Number of outpatient visits					
<5	36 219	26.4	37 887	16.0	26.1
5–9	33 513	24.5	50 939	21.6	24.3
10–19	37 209	27.2	77 341	32.7	27.2
20–39	22 108	16.1	52 677	22.3	16.4
40+	7982	5.8	17 450	7.4	6.1
Overweight or obese	4680	3.4	13 240	5.6	3.5
Opioid use	41 066	30.0	79 917	33.8	30.7
Osteoporosis	4663	3.4	11 529	4.9	3.4
Other fracture	2952	2.2	5668	2.4	2.2
Parkinson's disease	1290	0.9	1692	0.7	1.0
Perimenopausal symptoms	13 261	9.7	17 202	7.3	9.7
Radius/ulna fracture	508	0.4	865	0.4	0.4

Continued

Table 1 Continued

Characteristic	SSRI, N=137 031 N=137 031	Per cent	H2A/PPIs, N=236 294 N=236 294	Per cent	H2A/PPIs weighted to SSRI (%)
Renal disease	452	0.3	1373	0.6	0.3
Seizure	545	0.4	934	0.4	0.4
Ischaemic stroke	1010	0.7	1726	0.7	0.8
Thiazides	8355	6.1	17 381	7.4	6.1
Thyroid medication	17 230	12.6	27 909	11.8	12.7
Urinary incontinence	1833	1.3	3484	1.5	1.4
Vertebral fracture	299	0.2	639	0.3	0.2

New users of SSRIs or H2A/PPIs, unweighted and weighted cohorts.
COPD, chronic obstructive pulmonary disease; H2As, H2 antagonists; NSAIDs, non-steroidal anti-inflammatory drugs; PPI, proton-pump inhibitor; SSRI, selective serotonin reuptake inhibitor.

the SSRI and weighted comparator cohorts. For example, age, history of previous fractures, osteoporosis, previous bone mineral density scans, and use of medications that are known to affect risk of fractures were fairly uniformly distributed across our weighted cohorts.

Risk of fractures

A KM survival plot of the two cohorts (figure 1) shows higher fracture rates among initiators of antidepressants than among initiators of H2A/PPIs, with separation of the cohorts apparent by 6 months after initiation. Fracture rates (table 2) were significantly higher among the antidepressant cohort than among the comparator cohort beginning 6 months after initiation. Point estimates remained higher for the SSRI cohort through the fourth year after initial treatment. Five-year average fracture rates were significantly higher for the SSRI cohort (SSRI: 2.1 per 1000 person-years, 95% CI 1.8 to 2.5; H2A/PPI: 1.2 per 1000 person-years, 95% CI 1.0 to 1.5).

HRs (SSRIs vs H2A/PPIs, table 3) over 1, 2 and 5 years were 1.76 (95% CI 1.33 to 2.32), 1.73 (95% CI 1.33 to 2.24) and 1.67 (95% CI 1.30 to 2.14), respectively. First-treatment-carried-forward analyses also showed significantly higher risk among the SSRI cohort (tables 2 and 3). Sensitivity analyses without lag and induction periods yielded similar results after the second year, but the HR between cohorts did not show significance in the first year (table 3). Analyses with different grace periods showed results similar to those from primary analyses (data not shown).

DISCUSSION

Our analyses found that among a population of middle-aged women without psychiatric diagnoses, compared with patients initiating H2A or PPIs, patients who initiated treatment with SSRIs had significantly higher fracture risk over the entire 5-year study period. This finding is consistent with results from studies involving patients with mental health disorders.[22–28] The sustained higher risk among SSRI users is also consistent with the biological hypothesis that fractures associated with SSRI use can be at least partially attributed to antidepressant-related modulation of bone homeostasis in favour of osteoclastic activity, which may result in lower bone mineral density and higher risks of fractures.[29] HRs were significantly different between cohorts only after the second year when we modelled risk without including lag and induction periods, suggesting as well that SSRIs may need several months to produce clinically meaningful cumulative effects on bone mineral density.

Several caveats should be borne in mind when interpreting the results of the current study. First, our study population

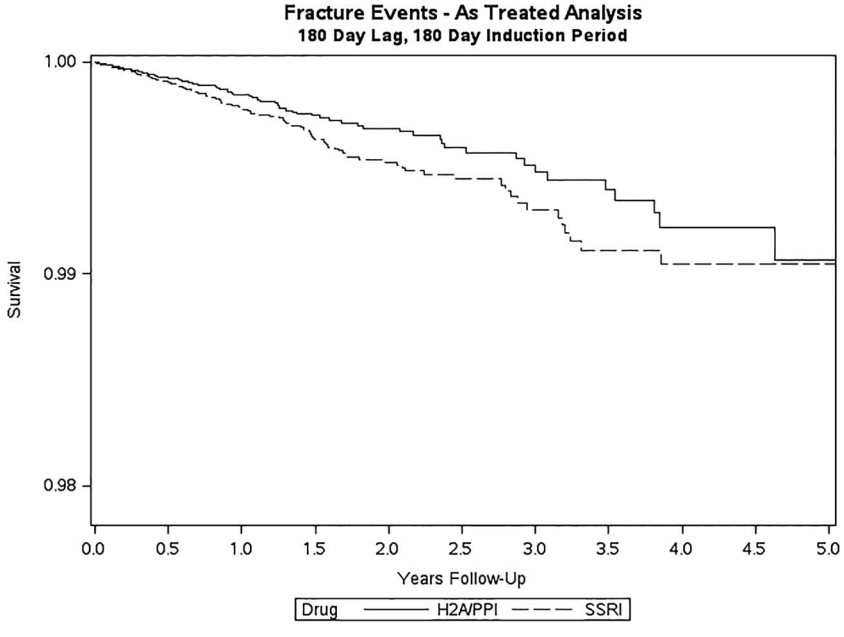

Figure 1 Kaplan-Meier (KM) plot. Selective serotonin reuptake inhibitor (SSRI) versus H2A/proton-pump inhibitor (PPI), as-treated analysis, with 180-day lag period and 180-day induction period. H2As, H2 antagonists; PPI, proton-pump inhibitor; SSRI, selective serotonin reuptake inhibitor.

Table 2 SSRI versus H2A/PPI fracture event rates, stratified by follow-up time

Period	Drug	Number contributing	Number of events	Total person time (years)	Rate per 1000 pr-years	95% CI
Panel A†						
0–180 days	SSRI	110 957	72	39 511.81	1.8	1.4 to 2.3
	H2A/PPI	112 660	39	35 009.82	1.1	0.9 to 1.4
181–360 days	SSRI	45 823	40	16 201.11	2.5	1.8 to 3.4
	H2A/PPI	27 325	10	9008.76	1.1	0.7 to 1.6
0–1 year	SSRI	110 957	112	55 712.93	2.0	1.7 to 2.4
	H2A/PPI	112 660	49	44 018.58	1.1	0.9 to 1.4
1–2 years	SSRI	23 423	37	13 812.44	2.7	1.9 to 3.7
	H2A/PPI	123 712	12	7268.16	1.7	0.9 to 3.0
2–3 years	SSRI	7925	10	4929.88	2.0	1.1 to 3.8
	H2A/PPI	4189	4	2696.20	1.3	0.6 to 2.8
3–4 years	SSRI	3153	6	2184.02	2.8	1.2 to 6.1
	H2A/PPI	1778	3	1227.03	2.3	0.9 to 5.5
4–5 years	SSRI	1385	0	840.60	0	N/A
	H2A/PPI	798	1	483.06	1.8	0.3 to 12.7
0–5 years	SSRI	110 957	165	77 479.87	2.1	1.8 to 2.5
	H2A/PPI	112 660	68	55 693.03	1.2	1.0 to 1.5
Panel B‡						
0–180 days	SSRI	110 957	81	48 805.32	1.7	1.3 to 2.1
	H2A/PPI	112 660	61	49 906.19	1.2	1.0 to 1.5
181–360 days	SSRI	88 126	61	38 663.23	1.6	1.2 to 2.0
	H2A/PPI	90 582	38	39 868.69	1.0	0.7 to 1.2
0–1 year	SSRI	110 957	142	87 468.54	1.6	1.4 to 1.9
	H2A/PPI	112 660	99	89 774.88	1.1	0.9 to 1.3
1–2 years	SSRI	68 960	95	52 368.98	1.8	1.5 to 2.2
	H2A/PPI	71 520	73	55 187.09	1.3	1.1 to 1.6
2–3 years	SSRI	39 704	50	29 756.54	1.7	1.3 to 2.2
	H2A/PPI	42 453	34	32 475.37	1.1	0.8 to 1.4
3–4 years	SSRI	23 135	28	17 633.26	1.6	1.1 to 2.3
	H2A/PPI	25 375	27	19 408.85	1.4	1.0 to 1.9
4–5 years	SSRI	12 996	15	8972.10	1.7	1.0 to 2.8
	H2A/PPI	14 577	23	10 271.05	2.3	1.5 to 3.4
0–5 years	SSRI	110 957	330	196 199.43	1.7	1.5 to 1.9
	H2A/PPI	112 660	257	207 117.24	1.2	1.1 to 1.4

Number contributing and number of events rounded to integers.
†Women, aged 40–64, as-treated analysis, 180-day lag, 180-day induction period.
‡Women, aged 40–64, first-treatment-carried-forward analysis, 180-day lag period.
H2A, H2 antagonist; PPI, proton-pump inhibitor; SSRI, selective serotonin reuptake inhibitor.

Table 3 Fracture HRs and risk differences among women aged 40–64

Analysis	Follow-up Time	Risk difference per 1000 people	95% CI	Numbers needed to harm	HR	95% CI
As treated	1 year	0.9	0.4 to 1.4	1119	1.76	1.33 to 2.32
180-day lag, 180-day induction period	2 year	1.0	0.5 to 1.4	1052	1.73	1.33 to 2.24
	5 year	0.9	0.5 to 1.3	1107	1.67	1.30 to 2.14
First treatment carried forward	1 year	0.5	0.2 to 0.9	1925	1.47	1.17 to 1.85
180-day induction period	2 year	0.5	0.2 to 0.8	1975	1.43	1.19 to 1.71
	5 year	0.5	0.2 to 0.7	2257	1.36	1.17 to 1.58
As treated	1 year	0.4	0.0 to 0.8	2722	1.26	0.97 to 1.65
No lag or induction periods	2 year	0.5	0.1 to 0.9	1840	1.36	1.07 to 1.72
	5 year	0.6	0.2 to 0.9	1767	1.37	1.09 to 1.71
First treatment carried forward,	1 year	0.3	0.0 to 0.6	3400	1.24	1.02 to 1.53
No induction period	2 year	0.4	0.1 to 0.6	2618	1.33	1.13 to 1.56
	5 year	0.4	0.2 to 0.6	2573	1.32	1.16 to 1.51

Numbers needed to harm rounded to integer.

consists of a cohort of middle-aged women who were prescribed SSRIs for several possible and not necessarily well-documented non-psychiatric conditions. Whether our results apply to patients with a specific non-psychiatric condition such as VMS is unknown, although we have no reason to expect otherwise. Second, the relationship between different classes of possible comparator drug classes and fractures is complex and no clear class of agents could be identified that would serve as an ideal analogue of a placebo controlled randomised trial to treat VMS. H2A/PPIs were selected as the comparator agent because studies have shown that H2As have a trivial or no association with risk of fractures,[30–32] while PPIs are associated with a slightly increased risk of fractures.[30 33 34] These considerations would tend to drive the differences in fracture risks between the SSRI and our comparator cohort towards the null, provided SSRIs elevate fracture risk. That we observe fracture risk to be significantly higher in our SSRI cohort than in our comparator cohort suggests that the risk differences we observed likely underestimate the true risk difference. Third, we were not able to analyse the relationship between different doses of SSRIs and the risk of fractures, since there was little variation in the dose prescribed to the vast majority of our patients (and most were prescribed doses similar to those recommended for the treatment of depression). A recent population-based case–control study in Denmark suggests that fracture risk depends on average daily dose, but since average daily dose and cumulative dose were not disentangled, it is not clear whether daily dose is an independent predictor of fracture risk beyond its contribution to cumulative dose.[35] Lastly, although we achieve good balance across known confounders, unmeasured confounding may still exist.

Despite these limitations, the current study is the first to assess the risk of fractures associated with initiation of SSRIs among a population of middle-aged women without psychiatric disorders. We find that SSRIs are associated with higher risks of fractures, an effect that first became evident several months after treatment initiation. Our finding suggests that, if feasible, shorter duration of treatment might mitigate the risk of developing excess fractures. Since the number of SSRI users without psychiatric disorders is expected to increase following the FDA approval of paroxetine for the treatment of VMS, particularly at lower doses, future efforts should be made to examine how SSRI dose (cumulative, daily or both) might modify fracture risk over time.

What is already known on this subject

- Selective serotonin reuptake inhibitors (SSRIs) are an effective substitute for hormonal replacement therapy for the treatment of vasomotor symptoms in perimenopausal women.
- SSRIs have been shown to be associated with increased fracture risks among psychiatric patients.
- Whether SSRIs are associated with increased fracture risks among non-psychiatric patients has not been directly examined.

What this study adds

- A significantly higher fracture risk was observed among patients without frank mental illness who initiated selective serotonin reuptake inhibitors (SSRIs) compared with initiators of common ulcer drugs, with risk apparent after 6 months and sustained over the 5-year study period among patients maintained on SSRI therapy.
- Shorter duration of treatment might mitigate the cumulative risk of developing excess fractures.

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Contributors Y-hS and AL contributed to study design, interpretation of data, drafting and finalising the manuscript. TS contributed to study design, acquisition and interpretation of data, statistical analysis, critical revision of the manuscript, and finalising and supervising the work. VP contributed to study design, statistical analysis, critical revision and finalising the manuscript. DA contributed to study design, interpretation of the data, statistical analysis, critical revision and finalising the manuscript. MM contributed to study design, analysis and interpretation of data, drafting, critical revision, finalising the manuscript, and supervising the work.

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Stunt daredevil dies

Erik Roner, a well-known American stuntman, died in what is referred to as a 'parachuting accident' when, as the newspaper stated, he 'fell victim to a bad landing during a parachute stunt'.. *Editor*: actually, he fell victim to risk taking. An eventual bad landing was predictable. It makes me wonder again what sort of message safety organisations send when they praise stunt pilots or parachutists.

More firearm controversy in Canada

The Prime Minister of Canada argued that guns are needed by rural Canadians '… so they can shoot people who pose a danger' (Mark Kennedy, Ottawa Citizen). However, the Bar Association reminds us that Canadians do not have an automatic right to defend ourselves at home with a gun. Such behaviour could result in criminal charges. Ironically, this issue did not arise during the recent election campaign even though it coincided with the anniversary of the Dawson college shootings (13 September 2006) and the 1989 Montreal Massacre of women engineering students.

Fines for rugby teams failing to follow head injury protocols

A world rugby team that fails to deal with head injuries according to protocol during the Rugby World Cup may be fined. This new rule was prompted in part following several disturbing incidents. As well as fines, video replays may help teams follow players who had a head injury.