

2022 Best Research Poster Award



Antipsychotic medication use and fracture: a population-based case-control study

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INTRODUCTION

- Antipsychotic medication is the first line agent in the treatment psychosis¹.
- Antipsychotic use is increasing globally. The number of prescriptions filled for one or more antipsychotics increased from 261,000 in 2005 to 422,000 in 2021 in Australia².
- Common side effects of antipsychotic use include weight gain, diabetes, cognitive impairment, falls and sedation³.
- More recently, antipsychotic use has been associated with an increased risk of osteoporosis⁴.

OBJECTIVE

- We aimed to determine whether antipsychotic use is associated with fracture risk in a population-based sample of men and women.

METHOD

- **Participants:** Cases and controls were recruited from the Barwon Statistical Division (BSD), situated in south - eastern Australia.
 - **Cases:** 1,458 participants (48.2% men) aged 20+ years with a confirmed radiological report of fracture between June 1st 2012 and May 31st 2013⁵.
 - **Controls:** 1,796 participants (53.5% men) were drawn from the Geelong Osteoporosis Study⁶ who had not experienced a fracture between June 1st 2012 to May 31st 2013.
- **Exposures:** Exposure to antipsychotic and other medication use prior to fracture, anthropometry and lifestyle factors were self-reported and area-based socio-economic status was determined
- **Outcome:** Radiologically confirmed fracture
- **Statistical analyses:** Differences between cases and controls were analysed using t-tests for parametric data, Kruskal Wallis for non-parametric data and Chi-Square for categorical data. Binary logistic regression was used to explore the associations between antipsychotic use and fracture following adjustment for possible confounders.

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REFERENCES

1. Hálfðánarson Ó, Zoëga H, Aagaard L, et al. International trends in antipsychotic use: A study in 16 countries, 2005–2014. *Eur Neuropsychopharmacol* 2017; 27: 1064-1076.
2. Health, A.I.o. and Welfare, Mental health services in Australia. 2022. AIHW: Canberra.
3. Stroup TS, Gray N. Management of common adverse effects of antipsychotic medications. *World Psychiatry* 2018; 17: 341-356.
4. Graham SM, Howgate D, Anderson W, Howes C, Heliotis M, Mantalaris A, et al. (2011) Risk of osteoporosis and fracture incidence in patients on antipsychotic medication. *Expert Opin Drug Saf*.
5. Stuart, A.L., et al., Sample selection and reasons for non-participation in the predictors and outcomes of incident FRACTures (PROFRAC) study. *Journal of Public Health Research*, 2019. 8(1): p. 50-55.
6. Pasco, J.A., G.C. Nicholson, and M.A. Kotowicz, Cohort Profile: Geelong Osteoporosis Study. 2012. p. 1565-1575.
7. Crews MP, Howes OD. Is antipsychotic treatment linked to low bone mineral density and osteoporosis? A review of the evidence and the clinical implications. *Hum Psychopharmacol* 2012; 27: 15-23.

ACKNOWLEDGMENT

This work was supported by the National Health and Medical Research Council (NHMRC), Australia (1162867, 628582, 251638, 299831). BAM, DKW were supported by a Deakin University Postgraduate Research Scholarship (DUPRS) and LJW by an NHMRC Emerging Leadership Fellowship (1174060). The authors thank Professor Graham Giles of the Cancer Epidemiology Centre of The Cancer Council Victoria, for permission to use the Dietary Questionnaire for Epidemiological Studies (Version 2), Melbourne: The Cancer Council Victoria 1996. Study data were collected and managed using REDCap electronic data capture tools hosted at Barwon Health.

RESULTS

Table 1. Characteristics of fracture cases and controls for men and women, results displayed as median (interquartile range) or n (%).

	Men			Women		
	Cases n=703	Controls n=961	P	Cases n=755	Controls n=834	P
Age (yrs)	48.5 (31.8-62.7)	59.5 (45.9-73.4)	<0.001	61.7 (49.2-76.7)	56.3 (42.5-69.7)	<0.001
Weight (kg)	82.0 (75.0-92.0)	82.7 (74.6- 92.8)	0.594	68.0 (60.0-78.0)	71.7 (62.3-83.8)	<0.001
Height (cm)	178.0 (172.7-183.0)	174.8 (170.1-179.6)	<0.001	162.0 (157.0-168.0)	161.7 (157.6-166.1)	0.193
Smoking	152 (21.8%)	108 (11.3%)	<0.001	95 (12.8%)	91 (11.1%)	0.295
Mobility (active)	522 (75.3%)	677 (71.0%)	0.050	449 (60.1%)	578 (70.8%)	<0.001
Frequent drinkers	222 (31.6%)	394 (41.0%)	<0.001	180 (23.8%)	186 (22.3%)	0.467
Prior adult fracture	246 (36.5%)	318 (34.2%)	0.340	276 (37.7%)	155 (18.7%)	<0.001
Faller (12 months)	111 (16.0%)	172 (18.1%)	0.274	177 (23.7%)	224 (27.1%)	0.123
Schizophrenia	7 (1.0%)	3 (0.3%)	0.107	2 (0.3%)	1 (0.1%)	0.607
Medication (prior to #)						
Antipsychotics	13 (1.8%)	5 (0.5%)	0.010	20 (2.6%)	10 (1.2%)	0.034
Other psychotropics	106 (15.1%)	87 (9.1%)	<0.001	202 (26.8%)	179 (21.5%)	0.014
Adrenal steroidhormones	15 (2.1%)	10 (1.0%)	0.070	31 (4.1%)	23 (2.8%)	0.139
Gonadal hormones	9 (1.3%)	3 (0.3%)	0.036	37 (4.9%)	32 (3.8%)	0.299
Thyroid hormones	7 (1.0%)	10 (1.0%)	0.928	58 (7.7%)	61 (7.3%)	0.781
Anti-fracture agents	18 (2.6%)	17 (1.8%)	0.266	58 (7.7%)	28 (3.4%)	<0.001
Calcium/ vitamin D	50 (7.1%)	62 (6.5%)	0.595	219 (29.0%)	190 (22.8%)	0.005

- Characteristics of the cases and controls according to sex are in Table 1
- For women, exposure to antipsychotics was documented for 20 of 755 (2.6%) cases and 10 of 834 (1.2%) controls (p=0.034). For men, exposure to antipsychotics was documented for 13 of 703 (1.8%) cases and 5 of 961 (0.5%) controls (p=0.010).
- Following adjustment for age, antipsychotic use was associated with a 2.4-fold increased risk of fracture in women (**OR 2.42, 95%CI 1.11 - 5.24, p=0.025**) and a 3.5-fold increased risk of fracture in men (**OR 3.49, 95%CI 1.20 - 10.14, p=0.021**).
- Following further adjustment for smoking, frequent drinking, other psychotropic medications, and medication that negatively and positively affect bone, activity, fall in the past 12 months, and a history of past fracture did not these patterns persisted.

DISCUSSION & CONCLUSION

- Our results indicate that antipsychotic use is independently associated with increased risk of fracture.
- Antipsychotic-induced hyperprolactinemia and/or side-effects such as hypotension or sedation³ leading to increased falls risk may explain the findings. Furthermore, the use of antipsychotics has been associated with decreased bone mineral density leading to weaker bones⁷ and a higher probability that a fall will result in a fracture.
- While future research exploring underlying mechanisms is needed, regular monitoring of bone health in antipsychotic users should be considered.