
Medication Use and Mental Health Outcome

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Doctor of Philosophy (Gender and Health)



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Maha Alsalami

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Abbreviations

Abbreviation	Descriptor
ADR	Adverse Drug Reaction
WHO	World Health Organisation
MAI	Medication Appropriateness Index
NSW	New South Wales
ALSWH	The Australian Longitudinal Study on Women's Health
ATC	Anatomical Therapeutic Chemical
PBS	Pharmaceutical Benefits Scheme
PIN	Personal Identification Number
Class N	Nervous system medications
Class A	Alimentary tract and metabolism medications
Class M	Musculoskeletal system medications
Class C	Cardiovascular system medications
OR	Odds Ratios
CI	Confidence Intervals
HAM-D	Hamilton rating scale for Depression
GDS	Geriatric Depression Scale
PRISMA	the Preferred Reporting Items for Systematic Reviews and Meta- Analyses
CIDI-SFMD	Composite International Diagnostic Interview Short Form for Major Depression
MCS	Mental Component Scale
ACE inhibitors	angiotensin-converting enzyme inhibitors
NSAIDs	Non-steroidal anti-inflammatory drugs
ICD-9-CM	International Classification of Diseases, Ninth Revision, Clinical Modification
HADS	The Hospital Anxiety and Depression Scale
GEE	Generalized Estimating Equations
S3	Survey 3
S4	Survey 4
S5	Survey 5
S6	Survey 6
MH	Mental Health
NHMRC	the National Health and Medical Research Council
AIHW	the Australian Institute of Health and Welfare
BMI	Body Mass Index
PA	Physical activity
Abbreviation	Descriptor
RPBS	the Repatriation Pharmaceutical Benefits Scheme
PMH	Poor Mental Health
Class B	Blood and blood forming organs medications
N02	Analgesics medications
N03	Antiepileptic medications
N04	Anti-Parkinson medications
N07	Other nervous system medications
COPD	Chronic Obstructive Pulmonary Disorder
CES-D	Centre for Epidemiologic Studies-Depression
ADRs	Adverse Drug Reactions

NSAIDs	Non-Steroidal Anti-Inflammatory Drugs
AE	Adverse Event
RAS	Renin-Angiotensin System
CCBs	Calcium Channel Blockers
ACE inhibitors	Angiotensin-Converting-Enzyme inhibitors
CNS	Central Nervous System
ARBs	angiotensin II receptor blockers
HMG-CoA	3-Hydroxy-3-Methyl-Glutaryl-CoA
MedDRA	Medical Dictionary for Regulatory Activities
COSTART	Coding Symbols for Thesaurus of Adverse Reactions Terms
HAD	Hospital Anxiety and Depression
BBB	blood-brain barrier
PPIs	Proton Pump Inhibitors
Pgp	P-glycoprotein
MDR1	Multiple-Drug Resistance 1
CB1 receptor antagonist	Cannabinoid 1 receptor antagonist
GABA	Gamma-Aminobutyric Acid
SSRIs	Selective Serotonin Reuptake Inhibitors
OCD	Obsessive-Compulsive Disorder
RCTs	Randomised Clinical Trials
DBI	Drug Burden Index

Thesis Publications and Presentations

Published manuscripts

Alsalamy M., Forder P., Milton A., McEvoy M., Byles JE. Associations between medication use and mental health in older women: a cross-sectional analysis of 5,502 women aged 76 to 81. JAGS. 2015. 63 (6): p. 1254-1255.

Conference presentations

Alsalamy M., Byles JE, Milton A., McEvoy M. Medication use and mental health outcome. 11th National Conference of Emerging Researchers in Ageing, held in Brisbane, Australia, November 19-20, 2012.

Alsalamy M., Forder P., Byles JE., Milton A., McEvoy M. Medication use and mental health in women aged 76-81 years. 12th National Conference of Emerging Researchers in Ageing, held in Sydney, Australia, November 25-26, 2013.

Poster presentations

Alsalamy M., Byles JE, Milton A., McEvoy M. Medication use and mental health outcome. 7th Australian Women's Health Conference, held in Sydney, Australia, May 7-10, 2013.

Alsalamy M., Forder P., Byles JE., Milton A., McEvoy M. The Association between classes of different medications and mental health outcome in 5502 women aged 76-81 years old. 15th International Mental Health Conference, held in Gold Coast, Australia, August 25-26, 2014.

Synopsis

Background: Medication use among older people has received increased attention in recent years because the prevalence of multiple medication use in the older population has increased. There is some evidence that some medications can cause mental illness such as depression, anxiety, and mood disorders. However, there is limited evidence of the association between medication use and mental health outcomes, in older women.

Aims: This thesis has six interconnected aims: 1) To describe medications used by women in the ALSWH who were born in 1921-1926 (1921-1926 Cohort). 2) To examine the cross-sectional association between medication use and mental health scores, in women aged 76-81 years, who completed Survey 3 (2002) of the Australian Longitudinal Study on Women's Health. 3) To examine, longitudinally, the association between medication use and poor mental health, in ALSWH participants who completed Survey 3 (2002), Survey 4 (2005), Survey 5 (2008) and Survey 6 (2011). 4) To assess the association between various classes of medication and mental health among ALSWH participants aged 76-81 years, who completed Survey 3 in 2002. 5) To examine, longitudinally, the association between classes of medication used and poor mental health, across surveys 3-6, clarifying, and expanding upon the findings of aim four. 6) To systematically review current literature of studies assessing the association between selected classes of medication and mental health outcomes, in older adults without mental illness.

Methods and Results: To reach these aims, secondary data analyses of ALSWH data and four systematic reviews (in 2014 and 2015) were conducted. Women at greater risk of poor mental health who used medications, had more co-comorbid conditions, more symptoms, were more likely to be obese, and to be a smoker. Two analyses were conducted in order to evaluate aims two and three. First, cross-sectional analyses were undertaken, using a multivariable linear regression, to examine the association between medication use, in terms of two measures, and mental health scores, among women aged 76-81 years, at Survey 3 in 2002. A weak linear association between the number of different medications or number of different therapeutic medication groups used, and mental health scores, was found. A second set of analyses examined longitudinal associations between two measures of medication use and poor mental health, by using Generalized Estimating Equations (GEE) models. From these analyses, it was found that poor mental health was associated with higher medication use (number of different medications and number of different therapeutic medication groups used). However, the association did not persist after adjusting for physical function and bodily pain. Unadjusted univariate analyses, using linear regression to assess the associations between various classes of medication and mental health scores, among similar women who completed Survey 3, showed statistically significant associations between the use of medications for the nervous system (Class N), blood (Class B), alimentary tract and metabolism (Class A), musculoskeletal system (Class M), and cardiovascular system (Class C), and lower mental health scores, among older Australian women, aged 76-81 years. GEE models were then used to explore associations between these four classes of medication (nervous system, alimentary tract and metabolism,

musculoskeletal system, and cardiovascular system medications) and poor mental health, during ten years of follow-up and adjusting for other factors. The evidence from these analyses suggests that there is not a clear association between use of these four classes of medications and poor mental health, in older Australian women. Additional analyses (sensitivity analyses) were also conducted, as part of the fifth aim, excluding women who were using psycholeptics (N05) and psychoanaleptics (N06) medications for anxiety and depression, during 2002-2011. These analyses concluded that using Class A, Class M, and Class C medications were associated with lower risk of having poor mental health, for older women, during 2002-2011. While using Class N medications such as analgesics, antiepileptics, anti-Parkinson and other nervous system medications, was not significantly associated with poor mental health. Following these analyses, four systematic reviews considered whether there is any other published evidence to suggest an association between medications in each of these four classes, and mental health outcomes, in adults aged 65 years and over, without mental illness. These reviews indicated that adverse mental health outcomes such as anxiety or depression, were suspected, for some Class N medications (e.g. tiagabine, topiramate, rasagiline), some Class A medications (e.g. esomeprazole lansoprazole, cimetidine), some Class M medications (e.g. celecoxib, rofecoxib, etoricoxib), and some Class C medications (e.g. indapamide, hydrochlorothiazide/amiloride, metoprolol).

Conclusion and Implications: This thesis has added to the evidence base examining the associations between medication use and mental health, and provided a comprehensive approach to examining these associations by using six different medication measures. The study findings presented in this thesis provides evidence

that the number of different medications or the number of different therapeutic medication groups are not clearly associated with poor mental health after controlling for physical functioning or bodily pain, which themselves are strongly associated with poor mental health. Using Class A, Class M and Class C medications was associated with lower risk of having poor mental health, in older women, after excluding N05 and N06 medications. With a growing proportion of older people in our society, prescribers should be aware of the advantages that these medications have, for improving mental health. Future well designed studies in different population groups are required to confirm and extend these results, and to especially examine the association between using other common classes of medication, and poor mental health, over time. Four reviews provide evidence that some specific medications in Class N, Class A, Class M and Class C, may play a role in the development of mental illness, in older adults. Future research might include well-designed studies, where the aim is to assess the effects of individual medications, and determine their long-term effects on mental health, and whether these effects are different for older women. The results of this thesis contribute insights to the body of existing knowledge and provide justification for on-going research in this area, especially regarding mental health outcomes, for women. The findings enable clinicians and health professionals to be aware of the possible side effects of using various types of prescription medications, so they can better support this population, especially those at risk of poor mental health. It may be informative for other researchers, by providing an understanding of medication use over the life course, and pre-empting the potential long-term hazards of using medications, in terms of compromising mental health.