**Impact of interdisciplinary approaches to deprescribing psychotropics on clinical outcomes in older residents of long-term care facilities**

 *Commentary on: Clinical impact of antipsychotic and benzodiazepine reduction: Findings from a multicomponent psychotropic reduction program within long-term aged care*

Stephanie L Harrisona,b, Janet K Sluggettc,d,e

aCardiovascular and Metabolic Medicine, Institute of Life Course and Medical Sciences, University of Liverpool, Liverpool, United Kingdom

bLiverpool Centre for Cardiovascular Science, University of Liverpool, Liverpool, United Kingdom

cUniversity of South Australia, UniSA Allied Health and Human Performance, Adelaide, South Australia, Australia

dRegistry of Senior Australians (ROSA), Health Ageing Research Consortium, South Australian Health and Medical Research Institute, Adelaide, South Australia, Australia

eCentre for Medicine Use and Safety, Faculty of Pharmacy and Pharmaceutical Sciences, Monash University, Parkville, Victoria, Australia

Concerns about the appropriateness of psychotropic medicines use among residents of long-term care facilities (LTCFs) have been voiced for many years. In 1980, a study of 173 LTCFs in the United States reported a high prevalence of antipsychotic prescribing and called for further research to identify techniques for the management of neuropsychiatric symptoms which rely less upon psychotropics (Ray *et al.*, 1980). More recent studies report that approximately one in five residents of LTCFs in the United States, England and Australia are prescribed antipsychotics (Briesacher *et al.*, 2013; Harrison *et al.*, 2020; Szczepura *et al.*, 2016). Benzodiazepines, which are often used for conditions such as sleep disturbance and anxiety, are dispensed to nearly one in three residents in Australian LTCFs (Harrison *et al.*, 2020). Typical and atypical antipsychotics have been associated with a higher risk of serious adverse drug events (ADEs) including cerebrovascular events and death among older people living with dementia (Maust *et al.*, 2015; Schneider *et al.*, 2006). Benzodiazepines and antipsychotics have also been associated with increased risk of falls in older people. Treatment with these medicines may be appropriate when used in line with guideline recommendations and with concurrent non-pharmacological strategies and monitoring. However, the high prevalence of antipsychotic and benzodiazepine use in LTCFs suggests that not all use is in accordance with guidelines. Antipsychotics are often used in the absence of documented consent from residents or family members and continued for long durations (Westaway *et al.*, 2020). In accord, improving psychotropic use in LTCFs was identified as an urgent priority in the interim report of the ongoing Royal Commission into Aged Care Quality and Safety in Australia (Royal Commission into Aged Care Quality and Safety, 2019).

Widespread concern about psychotropic use among people living with dementia has led to a substantial expansion in the evidence base for non-pharmacological approaches such as functional analysis interventions, which involve exploring the meaning or purpose of a person’s behaviour, and music therapy (Moniz Cook *et al.*, 2012; Tsoi *et al.*, 2018). Although the quality of evidence is not as high as for traditional pharmacological studies, non-pharmacological approaches have shown similar effect sizes to psychotropics for managing neuropsychiatric symptoms, without the risk of serious ADEs (Dyer *et al.*, 2018). Internationally, clinical guidelines for care of people with dementia recommend the use of non-pharmacological interventions as first-line approaches, and to only use antipsychotics when other approaches have failed or when the person is at-risk to themselves or others. Despite recommendations from international guidelines, a well-developed non-pharmacological evidence base, increased awareness of the harms of antipsychotic use in people with dementia and black box warnings, prescribing restrictions and indicator monitoring systems in some countries, psychotropic use is still unacceptably high in LTCFs.

In this issue of *International Psychogeriatrics*, Hoyle and colleagues determine the impact of an interdisciplinary antipsychotic and benzodiazepine reduction intervention in LTCFs on resident outcomes (Hoyle *et al.*, 2020). The study was undertaken within 28 LCTFs participating in the Reducing Use of Sedatives (RedUSe) program that was implemented in 150 Australian LTCFs between 2014 and 2016 (Westbury *et al.*, 2018). The multicomponent RedUSe intervention included auditing and benchmarking of antipsychotic and benzodiazepine prescribing, education to nursing staff, pharmacists and prescribers on evidence-based psychotropic use, and a multidisciplinary review of psychotropic prescribing for residents. At six-month follow-up, a statistically significant reduction in the proportion of residents prescribed antipsychotics (from 21.6% to 18.9%, p<0.001) and benzodiazepines (from 22.2% to 17.6%, p<0.001) in the 150 LTCFs was observed. In 39% of residents in the RedUSe study who were prescribed antipsychotics or benzodiazepines at baseline, these medicines had been stopped or were prescribed at a lower dose at six-month follow-up. In the current paper, Hoyle and colleagues explore the impact of the intervention and subsequent reduction in antipsychotic and benzodiazepine use on resident quality of life, neuropsychiatric symptoms and social withdrawal at four months compared to baseline (Hoyle *et al.*, 2020). At baseline and four-month follow-up, nursing staff in the 28 LTCFs were asked to complete the psychometric assessments for 206 residents included in this study. Neuropsychiatric symptoms were assessed using the Neuropsychiatric Inventory-Nursing Home version (NPI-NH) and the Cohen-Mansfield Agitation Inventory (CMAI), quality of life was assessed using the Assessment of Quality of Life-4D tool (AQoL-4D) and social withdrawal was assessed using the Multidimensional Observation Scale for Elderly Subjects (MOSES)-withdrawal scale. At follow-up, the mean chlorpromazine equivalent dose had decreased by 16.2% in residents taking an antipsychotic at baseline (p=0.005), with a similar reduction in diazepam equivalent doses among those initially receiving a benzodiazepine (15.7% reduction, p=0.002). The authors found no evidence that antipsychotic and benzodiazepine reduction negatively impacted neuropsychiatric symptoms, quality of life or social withdrawal among participants at follow-up.

Findings from Hoyle et al. are an important addition to the growing evidence base that shows reducing psychotropic use in LTCFs is possible with an interdisciplinary, resident-centred approach that addresses barriers and enablers to change among key stakeholders. As noted by the authors, the findings are in keeping with those observed in the Halting Antipsychotic use in Long Term care (HALT) study, which was a single arm interventional study comprising i) education for health professionals and ii) implementation of individualised deprescribing protocols that aimed to reduce inappropriate antipsychotic use in LTCFs (Brodaty *et al.*, 2018). The HALT study, which recruited 139 residents prescribed a long-term antipsychotic from 23 Australian LTCFs, showed an 81.7% reduction in the number of participants taking an antipsychotic regularly. Similarly, no significant changes in the secondary outcomes of neuropsychiatric symptoms (as assessed by the NPI-NH, CMAI) or social withdrawal (as assessed by the MOSES scale) were observed at follow-up after antipsychotic deprescribing. The current paper by Hoyle et al. extends the existing evidence base to include new data on resident outcomes after benzodiazepine reduction.

Medication management problems were described in one third of the written submissions to the Royal Commission into Aged Care Quality and Safety in Australia, and family members and residents have voiced concerns about psychotropic use in LTCFs during public hearings (Royal Commission into Aged Care Quality and Safety, 2019). It is imperative for residents, or their next of kin or significant other to be involved in treatment decisions. However, previous studies have reported that informed consent for antipsychotic use is infrequently documented (Aerts *et al.*, 2019; Westaway *et al.*, 2020). Importantly, the study by Hoyle et al. focuses on assessment of outcomes which are important to residents and family members, such as quality of life, which is a key limitation of existing studies (Hoyle *et al.*, 2018). Monitoring for withdrawal symptoms and possible re-emergence of signs and symptoms of the underlying condition is advised when reducing doses or withdrawing antipsychotics and benzodiazepines among residents. General medical practitioner (GP) concern about withdrawal symptoms or symptoms of the underlying condition is a reported barrier to deprescribing in LTCFs. Encouragingly, the data presented by Hoyle et al. suggest that dose reductions or withdrawal of antipsychotics and benzodiazepines did not negatively impact key resident-centred outcomes. This aligns with findings from a previous systematic review that suggested interventions to reduce exposure to antipsychotics or benzodiazepines in LTCFs were unlikely to have deleterious effects for residents (Hoyle *et al.*, 2018). Together, these results can increase confidence among stakeholders and inform discussions about deprescribing in this population. This is particularly important given a previous LTCF study that reported 79% of residents were willing to have one or more medicines deprescribed if their doctor said it was possible (Kalogianis *et al.*, 2016). In addition, the HALT study identified that LTCF staff and family members are key drivers of antipsychotic dose increases or re-prescribing in residents where antipsychotic withdrawal has been attempted (Aerts *et al.*, 2019).

As noted by Hoyle et al. their conclusions are limited by factors such as the uncontrolled study design and modest sample size. Recruitment for medicines-related interventions in LTCFs is challenging and the overall recruitment rate of 22% (with informed consent from a third party required for 73% of these individuals) achieved by Hoyle and colleagues is in keeping with that observed in previous medicines management intervention studies in Australian LTCFs (Brodaty *et al.*, 2018; Hughes *et al.*, 2019). A recent mixed methods process evaluation of the SImplification of Medications Prescribed to Long-tErm care Residents (SIMPLER) cluster randomised controlled trial of a medication simplification intervention in 8 Australian LTCFs reported that a resident’s decision about trial participation was influenced by existing relationships with their usual GP and LTCF staff (Hughes *et al.*, 2019). Key barriers to participation in the SIMPLER study included resident or family member resistance to change the current medication regimen, concern among family members that participation may cause undue resident distress and perceived lack of resident benefit (Hughes *et al.*, 2019). The complexity of care needs, and high burden of medicines use and medicines-related harm observed among residents highlights that studies to enhance medicines use in LTCFs are imperative. Further research is needed to understand the optimal recruitment strategies for quality use of medicines interventions in LTCFs that ensure participation from a representative sample of residents, while respecting resident choice and other ethical considerations.

Quality use of medicines, a key component of Australia’s National Medicines Policy, involves selecting management options wisely (and recognising that non-pharmacological strategies may be the best approach in some cases), choosing a suitable medicine if this approach is deemed necessary, and using those medicines safely and effectively (Commonwealth Department of Health and Ageing, 2020). Evidence from previous medicines management interventions and behaviour change theory tells us that repetition of key messages to stakeholders is often necessary to achieve sustained improvements in medicines use. In 2019, the Australian Aged Care Quality and Safety Commission received funding to implement a pharmacist outreach service to reduce inappropriate medicines use in LTCFs. Pharmacists employed by the Aged Care Quality and Safety Commission are now facilitating the delivery of the RedUSE intervention in LTCFs throughout rural and remote Australia (Australian Government Aged Care Quality and Safety Commission, 2020). There is also increasing advocacy in Australia and internationally to embed pharmacists within LTCFs to provide clinical services, participate in interdisciplinary discussions with health professionals and residents, provide education and undertake clinical governance activities. Psychotropic stewardship is anticipated to be a key focus of these emerging roles. However, it is clear that system changes and additional resourcing will be paramount to ensuring quality use of medicines interventions, such as those undertaken by Hoyle and colleagues, are translated into routine clinical practice. Innovative strategies to evaluate both impact and cost effectiveness when these types of initiatives are implemented at the population level are also necessary. Greater utilisation of routinely collected health datasets will assist to target interventions to LTCFs or residents with the greatest need, assess changes in utilisation of medicines and health services, and guide provision of targeted feedback.

Previous Australian research has shown that although antipsychotic and benzodiazepine use increases markedly upon admission to a LTCF, the use of these medicines also increases in the months leading up to the admission (Harrison *et al.*, 2020). Further research is necessary to extend the evidence base to people with dementia living in community and hospital settings to limit the increasing use prior to LTCF admission. It would also be of interest to determine whether outcomes reported by interventions such as RedUSe vary by resident or facility-level characteristics e.g. such as whether the residents were living with dementia, staffing levels and mix, and models of GP care at the LTCFs, to inform wider implementation strategies.

In summary, there is mounting evidence that antipsychotics and benzodiazepines can be successfully withdrawn in residents of LTCFs using an interdisciplinary approach, and in many cases, without negative consequences for these individuals. This important contribution from Hoyle and colleagues, along with previous evidence arising from programs such as RedUSe and HALT, should provide health professionals, residents and family members with increased confidence that these medicines can be deprescribed. Yet, there is still more work to be done. System-level changes and additional resources are urgently needed to embed successful initiatives to support quality use of medicines within routine clinical practice in LTCFs.

**References**

**Aerts, L.*, et al.*** (2019). Why deprescribing antipsychotics in older people with dementia in long-term care is not always successful: Insights from the HALT study. *Int J Geriatr*, 34, 1572-1581.

**Australian Government Aged Care Quality and Safety Commission** (2020). Better use of medication in aged care project. Commonwealth of Australia.

**Briesacher, B. A., Tjia, J., Field, T., Peterson, D. and Gurwitz, J. H.** (2013). Antipsychotic use among nursing home residents. *JAMA*, 309, 440-442.

**Brodaty, H.*, et al.*** (2018). Antipsychotic Deprescription for Older Adults in Long-term Care: The HALT Study. *J Am Med Dir Assoc*, 19, 592-600.e597.

**Commonwealth Department of Health and Ageing** (2020). The National Strategy for Quality Use of Medicines. Canberra: Commonwealth of Australia.

**Dyer, S. M., Harrison, S. L., Laver, K., Whitehead, C. and Crotty, M.** (2018). An overview of systematic reviews of pharmacological and non-pharmacological interventions for the treatment of behavioral and psychological symptoms of dementia. *Int Psychogeriatr*, 30, 295-309.

**Harrison, S. L.*, et al.*** (2020). The dispensing of psychotropic medicines to older people before and after they enter residential aged care. *Med J Aust*, 212, 309-313.

**Hoyle, D. J., Bindoff, I. K., Clinnick, L. M., Peterson, G. M. and Westbury, J. L.** (2018). Clinical and Economic Outcomes of Interventions to Reduce Antipsychotic and Benzodiazepine Use Within Nursing Homes: A Systematic Review. *Drugs Aging*, 35, 123-134.

**Hoyle, D. J., Peterson, G. M., Bindoff, I. K., Clinnick, L. M., Bindoff, A. D. and Breen, J. L.** (2020). Clinical impact of antipsychotic and benzodiazepine reduction: findings from a multicomponent psychotropic reduction program within long-term aged care. *Int Psychogeriatr*, online early, 1-13.

**Hughes, G. A.*, et al.*** (2019). Would you like to participate? Factors impacting on participant recruitment for quality use of medicines interventions in residential aged care. *Res Social Adm Pharm*, 15, e12.

**Kalogianis, M. J.*, et al.*** (2016). Are residents of aged care facilities willing to have their medications deprescribed? *Res Social Adm Pharm*, 12, 784-788.

**Maust, D. T.*, et al.*** (2015). Antipsychotics, other psychotropics, and the risk of death in patients with dementia: number needed to harm. *JAMA Psychiat*, 72, 438-445.

**Moniz Cook, E. D., Swift, K., James, I., Malouf, R., De Vugt, M. and Verhey, F.** (2012). Functional analysis-based interventions for challenging behaviour in dementia. *Cochrane Database Syst Rev*, Cd006929.

**Ray, W. A., Federspiel, C. F. and Schaffner, W.** (1980). A study of antipsychotic drug use in nursing homes: epidemiologic evidence suggesting misuse. *Am J Public Health*, 70, 485-491.

**Royal Commission into Aged Care Quality and Safety** (2019). Interim report: Neglect. Volume 1.: Commonwealth of Australia.

**Schneider, L. S., Dagerman, K. and Insel, P. S.** (2006). Efficacy and adverse effects of atypical antipsychotics for dementia: meta-analysis of randomized, placebo-controlled trials. *Am J Geriatr Psychiat*, 14, 191-210.

**Szczepura, A.*, et al.*** (2016). Antipsychotic prescribing in care homes before and after launch of a national dementia strategy: an observational study in English institutions over a 4-year period. *BMJ Open*, 6, e009882.

**Tsoi, K. K. F., Chan, J. Y. C., Ng, Y. M., Lee, M. M. Y., Kwok, T. C. Y. and Wong, S. Y. S.** (2018). Receptive Music Therapy Is More Effective than Interactive Music Therapy to Relieve Behavioral and Psychological Symptoms of Dementia: A Systematic Review and Meta-Analysis. *J Am Med Dir Assoc*, 19, 568-576.e563.

**Westaway, K., Sluggett, J., Alderman, C., Moffat, A., Procter, N. and Roughead, E.** (2020). The extent of antipsychotic use in Australian residential aged care facilities and interventions shown to be effective in reducing antipsychotic use: A literature review. *Dementia*, 19, 1189-1202.

**Westbury, J. L.*, et al.*** (2018). RedUSe: reducing antipsychotic and benzodiazepine prescribing in residential aged care facilities. *Med J Aust*, 208, 398-403.