3.2 Literature Review

3.2.1 POLYPHARMACY

3.2.1.1 Polypharmacy

Polypharmacy is the use of multiple drugs by a patient, although there is not a universally accepted definition (1). Various authors stipulate a specific number of medications a patient takes as representing polypharmacy, ranging from 3 up to 10 or more (2).

Polypharmacy presents challenges for residents and aged care providers (3, 4) and is certainly a much maligned issue for nursing staff 'on the floor'. According to one systematic review, the reported prevalence of polypharmacy, defined as 9 or more medications in RACFs ranges from 12.8% to 74.4% (5). Australian data suggest that over 90% of residents use five or more medicines (6). These figures are in-line with levels evident from Choice Aged Care's clinical database. International literature suggests that the use of multiple medications is increasing, with one study reporting a rise from 3.1 to 6.6 medicines per resident between 1992 to 2002 (7). More recently in 2016, data indicates a mean number of 8.9 medications per resident (8). Confirming this profound upward trend, preliminary polypharmacy data as at April 2017 from Choice Aged Care's client base indicates an average of 9.1 medications per resident (9). Reasons for the increase in polypharmacy are multifactorial and understanding those factors may help to develop interventions to manage polypharmacy in residential aged care facilities (RACFs) (10).

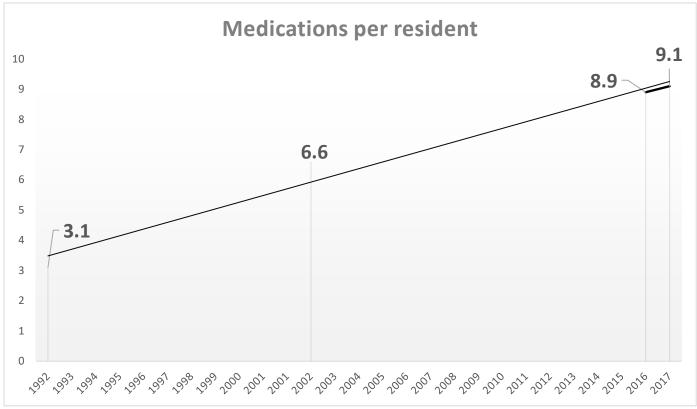


Fig 1: A concerning trend of unabated increasing levels of polypharmacy in aged care facilities.

3.2.1.2 Polypharmacy and adverse health outcomes

The elderly have a relatively high risk of medication misadventure and associated complications, which often results in lower quality of life and represents a burden to the health system. Polypharmacy has been associated with adverse drug reactions, drug-drug interactions, drug-disease interactions, non-adherence, functional decline, cognitive impairment, falls, hospitalisation and mortality (11 - 19). Falls are the most common cause of accidents among the older population, leading to both fatal and non-fatal injuries (20, 21). Falls studies have determined that taking ≥ 4 drugs is associated with an increased incidence of falls, recurrent falls, and injurious falls (22). Furthermore, the use of ≥ 5 drugs is associated with an 88% increased risk of an ADR-related visit to an outpatient clinic or emergency department (23). A direct positive correlation has been found between ageing, polypharmacy and an increased risk of drug related problems and negative clinical outcomes related to medicines (24) with associated economic burden (25). The aging population and increasing rates of polypharmacy represents a significant and increasing cost to the health budget. In addition, increased medicine utilisation further contributes to rising costs to patients and the health care system (26). Therein lies a key reason for this research in providing policy makers with useful data on the actual impact of the RMMR service.

Measurable adverse health outcomes which will be analysed in this research project will target falls, hospitalisations and mortality. As a practicality of the research, these 'outcomes' reflect the most important and feasibly trackable parameters using a RACF's clinical care software which is required to accurately document such events.

3.2.1.3 The impact of medication reviews on polypharmacy

An RMMR is undertaken by an accredited pharmacist in collaboration with the resident's GP and involves a comprehensive assessment to identify, resolve and prevent medication related problems (27). RMMRs are an independent source of medication and QUM information directed to the GP (and also nurses). This is important as Doctors in general receive a great deal of information about the indication for starting medicines but very little guidance on when and how to stop them (28). Possible triggers (e.g. ineffective or unnecessary treatment or a possible adverse effect) that may prompt consideration of ceasing a drug can only be identified by medication review (29). Indeed, independent clinical pharmacists often bear the burden, and do so proudly, of proactively targeting medications that may no longer be indicated. A retrospective analysis demonstrated that RMMRs can reduce prescribing of drugs in older people, resulting in a significant decrease in the Drug Burden Index score (30). A number of studies have also demonstrated that RMMRs identify clinically important medication related problems and improve medicine use in residents of RACFs (31-34). Specific to polypharmacy, a randomised control study completed by Roberts et al (40) found that clinical pharmacy services reduced medication use in the intervention group by 11 - 15%. A finding further supported by a Study (35) that found clinical medication reviews routinely conducted by pharmacists contribute to a reduction of drug related problems in the medication of older patients with polypharmacy. The term 'routinely' may be of interest to policy makers who in early 2014 sought to contain pharmacy costs by reducing the RMMR service from annual to biennial. Evidence would suggest that reducing the frequency of medication review may only serve to increase the costs to other areas of the health budget (i.e. the PBS via increased polypharmacy or the hospital system via increased admissions). Indeed, evidence suggests that deprescribing is not occurring as often as it should be: between 21 and 79 percent of older adults are taking a potentially inappropriate medication (36).

3.2.2 PSYCHOTROPICS

3.2.2.1 Psychotropic medications

Psychotropic medication is a broad term, usually referring to medications that affect mental function, behaviour and experience (37). The psychotropic medications specifically studied in this research project are limited to antipsychotics, benzodiazepines and antidepressants.

The use of psychotropics in older adults remains controversial given the risk of adverse effects, in contrast to the limited effectiveness (38). Supported by usage rates in CAC's clinical database, high rates of psychotropic medications use have been reported in Australian nursing homes, particularly antipsychotics (24-29%) and benzodiazepines (15-37%) (39, 40). Also corroborated by CAC's data, other studies in Australia point to a combined rate of psychotropic drug use in long term care facilities that varies from 39% to 78% (41). Up to 80% of residents with dementia receive psychotropic medications and there is evidence to suggest that in some cases these medications have been prescribed inappropriately (42). Hence the use of psychotropic medications in the aged care setting reflects a somewhat emotive and politically charged issue.

3.2.2.2 Psychotropic medications and adverse health outcomes

The use of psychotropic medications in long term care facilities is associated with significant adverse effects and morbidity (43) and the incidence of side effects in the older population is especially high, such as psychomotor and cognitive impairment, falls and fractures (44-46). As a result, there have been increasing concerns regarding the efficacy, tolerability and safety of antipsychotic agents in older adults (38). Serious adverse events have been reported (increased mortality rate and stroke) along with other risks (arrhythmias, pneumonia, falls, fractures, metabolic disorders and extrapyramidal effects) (47). The next psychotropic, benzodiazepines, also has high utilisation in older adults, which is especially worrying since age-related pharmacokinetic and pharmacodynamic alterations may lead to an increased risk of confusion, sedation, hangover effects and subsequent risk of falling (38). The final psychotropic for this research are antidepressants. Depression is often reported to be under-recognised and undertreated in older adults (48). An item for investigation in this research project will be

recognised and undertreated in older adults (48). An item for investigation in this research project will be whether there is any correlation or trends between utilisation of the different psychotropics (e.g. do RACFs with high utilisation of antidepressants achieve lower usage rates of benzodiazepines or antipsychotics?). In any case, the use of antidepressants in the nursing home population has increased over the last decade (38) and because these medications are associated with a range of adverse effects (e.g. sedation, hyponatraemia, GIT effects) the potential benefit must be weighed against the risks (49).

3.2.2.3 The impact of medication reviews on psychotropic drug usage

Medication reviews performed by an accredited pharmacist are seen as one avenue that can be employed by the health team to minimise the use of high risk medications. Several strategies to ensure the appropriate use of psychotropic drugs in long term care facilities have been implemented and most of these interventions have focused on the delivery of medication review services (41). A literature review of 26 publications (41) concluded that medication reviews are effective at reducing psychotropic prescribing in long term facilities. Anecdotally, nursing staff often seek the support of the RACF's clinical pharmacist to target prescribing of psychotropics (particularly antipsychotics). The combined strategies of a clinical pharmacist medication review and education for nursing staff led to a decrease in both antipsychotic and benzodiazepine use (40). Strategies that reduce the psychoactive medicines burden are likely to translate into significant health benefits (50). This research will attempt to identify whether a reduced psychotropic burden does indeed translate in health benefits.

3.2.3 ANTICHOLINERGICS

3.2.3.1 Anticholinergic medications

Anticholinergic use is a less 'visible' issue for RACF nurses and certainly it does not garner the same level of contempt as polypharmacy or psychotropic use. However, increased exposure to anticholinergic medication is problematic, particularly in those aged 80 years and older (51). Older people are commonly subjected to a high anticholinergic load or burden due to the widespread use of anticholinergic / antimuscarinic medications and the wide range of medications possessing anticholinergic side effects (such as antihistamines, antidepressants, anti-Parkinson agents, antipsychotics, antispasmodics, and skeletal muscle relaxants) (52). Similar to psychotropics, studies have also demonstrated a high anticholinergic load among people with dementia with reports of between 40 – 60% of dementia patients using at least one anticholinergic medication, and 10 - 25% using higher potency anticholinergic drugs or medications with clinically significant anticholinergic activity (53). The lack of genuine awareness from nursing staff is likely due to simply not being aware of which drugs exert an anticholinergic effect. Instruments have been devised to measure the cumulative effect of exposure to medications with anticholinergic effects, such as the Anticholinergic Cognitive Burden (ACB) Scale (54) which reflects the chosen tool used in this research project and CAC's clinical software. CAC RMMR reports highlight the ACB score for the resident, benchmarked against the average ACB score for that site, affiliated organisation/company, and also CAC's client's base.

3.2.3.2 Anticholinergic medications and adverse health outcomes

Anticholinergics exhibit a wide spectrum of adverse effects, particularly in the elderly (51). There is a growing body of evidence that medicines with anticholinergic properties have adverse effects on a range of cognitive capacities, from mild cognitive impairment and memory loss to acute confusion and delirium (54). Taking more anticholinergic medications is associated with greater risk of hospitalisation for confusion or dementia (54). This should warrant considerable concern given the aforementioned high-usage rate of anticholinergic medications in the elderly. Furthermore, increased exposure to anticholinergic medication is associated with physical impairment and an increased frequency of falls (51).

3.2.3.3 The impact of medication reviews on anticholinergic drug use

Strategies to reduce anticholinergic medication burden are likely to translate into significant health benefits (54). A retrospective analysis (30) demonstrated that pharmacist recommended dose regimen changes for anticholinergic medications were accepted by the GP, which resulted in a statistically significant change in the drug burden index score. However, one study from Norway (55) showed that while pharmacist initiated drug changes significantly reduced the anticholinergic drug scale score, this did not reflect in improved cognitive function in nursing home residents. Similarly, another study from the UK (56) found that taking a low dose anticholinergic medication (ABS score of 1) in persons with Alzheimer's did not predict more impaired cognition or more rapid cognitive decline over an 18 month period. There is however evidence that cognitive dysfunction has improved 1-4 years after withdrawal of anticholinergic drugs (57, 58), a consideration that will need to be accommodated when analysing the results from this particular research project.

5. Reference List

- 1. Cherubini, Antonio, Andrea Corsonello, and Fabrizia Lattanzio. "Polypharmacy in Nursing Home Residents: What Is the Way Forward?" Journal of the American Medical Directors Association. Elsevier Inc., 19 Mar. 2016. Web. 30 Apr. 2017. 2.
 - Hajjar E.R., Cafiero A.C., and Hanlon J.T.: Polypharmacy in elderly patients. Am J Geriatr Pharmacother 2007; 5: pp. 345-351
- Thomson, M. S., Gruneir, A., Lee, M., Baril, J., Field, T. S., Gurwitz, J. H. & Rochon, P. A. (2009) Nursing time devoted to medication 3. administration in long-term care: clinical, safety, and resource implications. Journal of the American Geriatrics Society, 57 (2), 266-272.
- Lee, W. C. & Sumaya, C. V. (2013) Geriatric workforce capacity: a pending crisis for nursing home residents. Frontiers in Public Health, 4. 1.24.
- Jokanovic, N., Tan, E. C. K., Dooley, M. J., Kirkpatrick, C. M. & Bell, J. S. (2015) Prevalence and factors associated with polypharmacy in 5. long term care facilities: a systematic review. Journal of the American Medical Directors Association, 16 (6), 535.e1–535.e12.
- Poudel, A., Peel, N. M., Mitchell, C. A., Gray, L. C., Nissen, L. M. & Hubbard, R. E. (2015) Geriatrician interventions on medication 6. prescribing for frail older people in residential aged care facilities. Clinical Interventions in Aging, 10, 1043–1051.
- 7. Haider, S. I., Johnell, K., Thorslund, M. & Fastborn, J. (2007) Trends in polypharmacy and potential drug-drug interactions across educational groups in elderly patients in Sweden for the period 1992–2002. International Journal of Clinical Pharmacology and Therapeutics, 45 (12), 643-653.
- Soulsby, Natalie. An age old problem: caring for the frail elderly in aged care facilities. Journal of pharmacy practice and research 8. (1445-937X), 46 (3), p. 265.
- 9. iChoice Advisor: Clinical Decision Support Software, database. Accessed 26/04/2017.
- 10. Jokanovic, Natali, Edwin C. K. Tan, Michael J. Dooley, Carl M. Kirkpatrick, Rohan A. Elliott, and J. Simon Bell. "Why Is Polypharmacy Increasing in Aged Care Facilities? The Views of Australian Health Care Professionals." Journal of Evaluation in Clinical Practice 22.5 (2016): 677-82.
- 11. Maher, R. L., Hanlon, J. & Hajjar, E. R. (2014) Clinical consequences of polypharmacy in elderly. Expert Opinion on Drug Safety, 13 (1), 57-65.
- 12. Shah, B. M. & Hajjar, E. R. (2012) Polypharmacy, adverse drug reactions, and geriatric syndromes. Clinics in Geriatric Medicine, 28 (2), 173-186.
- 13. Tamura B.K., Bell C.L., Inaba M., and Masaki K.H.: Outcomes of polypharmacy in nursing home residents. Clin Geriatr Med 2012; 28: pp. 217-236
- 14. . Landi F., Dell'Aquila G., Collamati A., et al: Anticholinergic drug use and negative outcomes among the frail elderly population living in a nursing home. J Am Med Dir Assoc 2014; 15: pp. 825-829
- 15. . Field T.S., Gurwitz J.H., Avorn J., et al: Risk factors for adverse drug events among nursing home residents. Arch Intern Med 2001; 161: pp. 1629-1634
- 16. . Nguyen J.K., Fouts M.M., Kotabe S.E., and Lo E.: Polypharmacy as a risk factor for adverse drug reactions in geriatric nursing home residents. Am J Geriatr Pharmacother 2006; 4: pp. 36-41
- 17. Ruggiero C., Dell'Aquila G., Gasperini B., et al: Potentially inappropriate drug prescriptions and risk of hospitalization among Italian older nursing home residents: The U.L.I.S.S.E. project on behalf of the Ulisse study group. Drugs Aging 2010; 27: pp. 747-758
- 18. Cherubini A., Eusebi P., Dell'aquila G., et al: Predictors of hospitalization in Italian nursing home residents: the U.L.I.S.S.E. Project. J Am Med Dir Assoc 2012; 13: pp. 84.e5-84.e10
- 19. Loganathan M., Singh S., Franklin B.D., et al: Interventions to optimise prescribing in care homes: Systematic review. Age Ageing 2011; 40: pp. 150-162
- 20. Kwok T, Liddle J, Hastie IR. Postural hypotension and falls. Postgrad Med J 1995;71:278-80
- 21. Centers for Disease Control and Prevention. Falls among older adults: an overview. 2013.
- http://www.cdc.gov.ezp01.library.qut.edu.au/HomeandRecreationalSafety/Falls/adultfalls.html. Accessed 10 July 2014
- 22. Zia, Anam, Shahrul Bahyah Kamaruzzaman, and Maw Pin Tan. "Polypharmacy and Falls in Older People: Balancing Evidence-based Medicine against Falls Risk." Postgraduate Medicine 127.3 (2014): 330-37.
- 23. Bourgeois, F. T., Shannon, M. W., Valim, C. & Mandl, K. D. (2010) Adverse drug events in the outpatient setting: an 11-year national analysis. Pharmacoepidemiology and Drug Safety, 19 (9), 901–910.
- 24. Malet-Larrea, Amaia, EstAbaliz Goyenechea, Miguel A. Gastelurrutia, BegoA±a Calvo, Victoria GarcAa-CAjrdenas, Juan M. Cabases, ArÃj nzazu Noain, Fernando MartÃnez-MartÃnez, Daniel Sabater-HernÃj ndez, and Shalom I. Benrimoj. "Cost Analysis and Costbenefit Analysis of a Medication Review with Follow-up Service in Aged Polypharmacy Patients." The European Journal of Health Economics (2016)
- 25. Chiatti, C., Bustacchini, S., Furneri, G., Mantovani, L., Cristian, M., Misuraca, C., et al.: The economic burden of inappropriate drug prescribing, lack of adherence and compliance, adverse drug events in older people: a systematic review. Drug Saf. 35(Suppl 1), 73-87 (2012)
- 26. Hovstadius, B. & Petersson, G. (2013) The impact of increasing polypharmacy on prescribed drug expenditure-a register-based study in Sweden 2005–2009. Health Policy, 109 (2), 166–174.
- 27. 6cpa.com.au. (2017). Residential Medication Management Review and QUM The 6CPA. [online] Available at: http://6cpa.com.au/medication-management-programmes/residential-medication-management-review/ [Accessed 30 Apr. 2017].
- 28. Potter, Kathleen, Leon Flicker, Amy Page, and Christopher Etherton-Beer. "Deprescribing in Frail Older People: A Randomised Controlled Trial." Plos One 11.3 (2016):
- 29. Jansen, Jesse, Vasi Naganathan, Stacy M. Carter, Andrew J. McLachlan, Brooke Nickel, Les Irwig, Carissa Bonner, Jenny Doust, Jim Colvin, Aine Heaney, Robin Turner, and Kirsten McCaffery. "Too Much Medicine in Older People? Deprescribing through Shared Decision Making." BMJ. British Medical Journal Publishing Group, 03 June 2016.
- 30. Nishtala, P. S., Hilmer, S. N., McLachlan, A. J., Hannan, P. J., & Chen, T. F. (2009). Impact of residential medication management reviews on drug burden index in aged-care homes. Drugs & Aging, 26(8), 677-86.
- 31. Khalil H . A review of pharmacist recommendations in an aged care facility. Aust J Prim Health 2011; 17: 35–9.
- 32. Nishtala PS, McLachlan AJ, Bell JS, Chen TF. A retrospective study of drug-related problems in Australian aged care homes: medication reviews involving pharmacists and general practitioners. J Eval Clin Pract 2011; 17: 97–103.

- 33. Castelino RL, Bajorek BV, Chen TF. Are interventions recommended by pharmacists during Home Medicines Review evidence-based? J Eval Clin Pract 2011; 17: 104–10.
- 34. Elliott RA , Thomson WA . Assessment of a nursing home medication review service provided by hospital-based clinical pharmacists. Aust J Hosp Pharm 1999; 29: 255–60.
- 35. Chau, S. H., Jansen, A. P., D., van de Ven, P.,M., Hoogland, P., Elders, P. J., . . . Hugtenburg, J. G. (2016). Clinical medication reviews in elderly patients with polypharmacy: A cross-sectional study on drug-related problems in the netherlands. *International Journal of Clinical Pharmacy*, *38*(1), 46-53.
- Hill-Taylor, B., I. Sketris, J. Hayden, S. Byrne, D. O'Sullivan, and R. Christie. 2013. Application of the STOPP/START criteria: A systematic review of the prevalence of potentially inappropriate prescribing in older adults, and evidence of clinical, humanistic and economic impact. *Journal of Clinical Pharmacy and Therapeutics* 38(5): 360–372.
- 37. NSW Department of Health. *Psychotropic Medication Use in Nursing Homes: Report of the NSW Ministerial Taskforce.* Department of Health, New South Wales, Australia (1997).
- 38. Azermai, Majda, et al. "Inappropriate use of psychotropic drugs in older individuals: implications for practice." *Aging Health*, vol. 9, no. 3, 2013, p. 255-264
- 39. B. Draper et al. (2001). Use of psychotropics in Sydney nursing homes: associations with depression, psychosis, and behavioral disturbances. International Psychogeriatrics, 13, 107–120.
- 40. M. Roberts et al. (2001). Outcomes of a randomised controlled trial of a clinical pharmacy intervention in 52 nursing homes. British Journal of Clinical Pharmacology, 51, 257–265.
- 41. Nishtala, P. S., M.Pharm, McLachlan, A. J., PhD., Bell, J. S., & Chen, T. F., PhD. (2008). Psychotropic prescribing in long-term care facilities: Impact of medication reviews and educational interventions. *The American Journal of Geriatric Psychiatry*, *16*(8), 621-32.
- 42. Hosia-Randell, H. and Pitkälä, K. (2005). Use of psychotropic drugs in elderly nursing home residents with and without dementia in Helsinki, Finland. *Drugs and Aging*, 22, 793–800.
- 43. Yip YB, Gumming RG: The association between medications and falls in Australian nursing-home residents. Med J Aust 1994; 160:14-18
- 44. Fraser LA, Liu K, Naylor KL, Hwang YJ, Dixon SN, Shariff SZ, Garg AX (2015) Falls and fractures with atypical antipsychotic medication use: a population-based cohort study. JAMA Intern Med 175:450–452
- 45. Payne RA, Abel GA, Simpson CR, Maxwell SR (2013) Association between prescribing of cardiovascular and psychotropic medications and hospital admission for falls or fractures. Drugs Aging 30:247–254
- 46. Pratt NL, Ramsay EN, Kalisch Ellett LM, Nguyen TA, Barratt JD, Roughead EE (2014) Association between use of multiple psychoactive medicines and hospitalization for falls: retrospective analysis of a large healthcare claim database. Drug Saf 37:529–535
- 47. Trifiro G, Spina E, Gambassi G. Use of antipsychotics in elderly patients with dementia: do atypical and conventional agents have a similar safety profile? *Pharmacol. Res.* 59(1), 1-12 (2009).
- 48. Beekman AT, Copeland JR, Prince MJ. Review of community prevalence of depression in later life. *Br. J. Psychiatry* 174, 307-311 (1999).
- 49. Peisah C, Skladzien E. The Use of Restraints and Psychotropic Medications in People with Dementia: A report for Alzherimer's Australia. Paper 38, March 2014.
- 50. Pratt, N. L., Ramsay, E. N., Ellett, L. M. K., Nguyen, T. A., Barratt, J. D., & Roughead, E. E. (2014). Association between use of multiple psychoactive medicines and hospitalization for falls: Retrospective analysis of a large healthcare claim database. *Drug Safety, 37*(7), 529-35.
- 51. Cardwell, K., Hughes, C. M., & Ryan, C. (2015). The association between anticholinergic medication burden and health related outcomes in the 'oldest old': A systematic review of the literature. *Drugs & Aging*, *32*(10), 835-848.
- 52. Mate K., Kerr K., Pond D., Williams E., Marley J., Disler P., . (2015) Impact of multiple low-level anticholinergic medications on anticholinergic load of community-dwelling elderly with and without dementia. Drugs Aging 32: 159–67.
- 53. Parsons, Carole. "Polypharmacy and Inappropriate Medication Use in Patients with Dementia: An Underresearched Problem." *Therapeutic Advances in Drug Safety* 8.1 (2017): 31-46.
- Ellett, Lisa M. Kalisch, Nicole L. Pratt, Emmae N. Ramsay, John D. Barratt, and Elizabeth E. Roughead. "Multiple Anticholinergic Medication Use and Risk of Hospital Admission for Confusion or Dementia." *Journal of the American Geriatrics Society* 62.10 (2014): 1916-922
- 55. Hege Kersten, Espen Molden, Inga Kristin Tolo, Eva Skovlund, Knut Engedal, Torgeir Bruun Wyller; Cognitive Effects of Reducing Anticholinergic Drug Burden in a Frail Elderly Population: A Randomized Controlled Trial. *J Gerontol A Biol Sci Med Sci* 2013; 68 (3): 271-278.
- 56. Chris Fox, Gill Livingston, Ian D. Maidment, Simon Coulton, David G. Smithard, Malaz Boustani, Cornelius Katona; The impact of anticholinergic burden in Alzheimer's Dementia-the Laser-AD study. *Age Ageing* 2011; 40 (6): 730-735
- 57. Han L Agostini JV Allore HG. Cumulative anticholinergic exposure is associated with poor memory and executive function in older men. J Am Geriatr Soc . 2008 56 2203 2210
- 58. Carrière I Fourrier-Reglat A Dartigues JF et al . Drugs with anticholinergic properties, cognitive decline, and dementia in an elderly general population: the 3-city study. Arch Intern Med . 2009 169 1317–1324.
- 59. Vinks, T. H. A. M., Egberts, T. C. G., de Lange, T., M., & de Koning, F., H.P. (2009). Pharmacist-based medication review reduces potential drug-related problems in the elderly: The SMOG controlled trial. *Drugs & Aging, 26*(2), 123-33.
- Heppenstall, Claire Patricia, Joanna B. Broad, Michal Boyd, Joanna Hikaka, Xian Zhang, Julia Kennedy, and Martin J. Connolly. "Medication Use and Potentially Inappropriate Medications in Those with Limited Prognosis Living in Residential Aged Care." *Australasian Journal on Ageing* 35.2 (2015)
- 61. He, Z., & Ball, P. A. (2013). Can medication management review reduce anticholinergic burden (ACB) in the elderly: encouraging results from a theoretical model. *International Psychogeriatrics*, *25*(9), 1425-31.