



1-2013

## Polypharmacy and the Elderly: A Case Study and Literature Review

Kristin M. Stevens

[How does access to this work benefit you? Let us know!](#)

Follow this and additional works at: <https://commons.und.edu/theses>

---

### Recommended Citation

Stevens, Kristin M., "Polypharmacy and the Elderly: A Case Study and Literature Review" (2013). *Theses and Dissertations*. 4976.

<https://commons.und.edu/theses/4976>

This Independent Study is brought to you for free and open access by the Theses, Dissertations, and Senior Projects at UND Scholarly Commons. It has been accepted for inclusion in Theses and Dissertations by an authorized administrator of UND Scholarly Commons. For more information, please contact [und.common@library.und.edu](mailto:und.common@library.und.edu).

Polypharmacy and the Elderly: A Case Study and Literature Review

Kristin M. Stevens

University of North Dakota, Grand Forks

*Kristin M. Stevens*

5/29/2015

### Abstract

Polypharmacy is a common issue among the elderly population due to multiple comorbidities that develop as a person ages. With this increase, there is also the increased risk for negative health outcomes such as higher healthcare costs, adverse drug events, drug interactions, and increased mortality rate (Maher, Hanlon, & Hajjar, 2014). The elderly population is increasing worldwide, and it is estimated that 20% of the population will be older than 65 by 2025 (Milos et al., 2013). Patients 65 years old and older are the largest consumer of prescription and nonprescription medications in the United States, which has more than doubled since 1990. Practitioners must appropriately use medications for multiple diseases and attempt to avoid the risks often associated with polypharmacy. Because individuals are living longer and many with chronic disease, practitioners have a responsibility to appropriately prescribe. The following literature review and case study looks at the physical and financial effects of polypharmacy among those 65 years of age and older. This review examines the definition of polypharmacy and provides suggestions for practitioners to decrease polypharmacy among their elderly population.

*Keywords:* polypharmacy, elderly, adverse drug event

## Polypharmacy and the Elderly: A Case Study and Literature Review

“Do no harm is the first rule of medicine, yet it is estimated that 106,000 Americans die each year from properly prescribed and correctly taken medications” (Jesson, 2013, p. 14).

Polypharmacy is a common issue among the elderly population due to the multiple comorbidities that develop as a person ages. With this increase comes the risk for negative health outcomes such as higher healthcare costs, adverse drug events, increased hospitalizations, and increased mortality rate (Maher, Hanlon, & Hajjar, 2014). “There will be approximately 70 million Americans over the age of 65 by the year 2030” (Fulton and Allen, 2005, p. 128). Polypharmacy was identified by Healthy People as medication safety issue a decade ago (Fulton and Allen, 2005). It has been found that elderly Americans spend approximately three billion dollars on prescription medications annually and 61% of individuals older than age 65 take an average of three to five medications, not including over the counter medications or herbal supplements (Oboh, 2013).

The purpose of this literature review is to answer the following questions: 1. What is polypharmacy? 2. What are the effects of polypharmacy on both the aging population and society at large? 3. What can primary care providers do to decrease medication use that is not clinically indicated in the older population and to prevent polypharmacy effects?

### **Background**

Polypharmacy has been a serious problem in the healthcare system and is an expensive practice that is estimated to cost more than 50 billion annually,” (Buschardt, Massey, Simpson, Ariail, & Simpson, 2008). The US General Accounting Office reports significant morbidity and mortality associated with inappropriate polypharmacy (Buschardt et al., 2008). The elderly

population is increasing worldwide, and it is estimated that 20% of the world population will be older than 65 by 2025 (Milos et al., 2013). Patients 65 years old and older are “the largest consumers of prescription and nonprescription medications in the United States, and the use of prescription and non-prescription medications among this group has more than doubled since 1990” (Bushardt et al., 2008, p.386).

Because the elderly population has a higher prevalence of chronic disease states, the use of multiple medications is very common but it is not always considered safe. Chronic medical conditions and age related decline of the organs often times makes it necessary for multiple medications but the issue is that one’s response to medications differ as one ages. Aging increases the risk for drug to drug interactions with multiple medication use. However, other issues can result from polypharmacy including self-medication, vulnerability in the older population, and a poor knowledge base regarding the prescribed medication regimen (Fulton & Allen, 2005).

Medication related problems are common and costly, but are also preventable. One idea is that the problem starts with the primary care providers who write unnecessary prescriptions to feel as though “they did something” and the low follow up rates which for many, ends with an adverse drug effect (Fulton & Allen, 2005). Several studies reviewed by Frazier (2005), have shown that in ambulatory and long term care settings, 27% of adverse drug events in primary care and 42% of adverse drug events in long term care were preventable with most issues happening during the ordering and monitoring stages of care. Avoiding the use of inappropriate and high risk drugs is an important, simple, and effective strategy in reducing medication related problems in older adults.



### Case Study

An 82 year old elderly female was seen for follow up after hospitalization. Patient was in the hospital for three days for a urinary tract infection and fatigue. At time of visit she had also reported feeling dizzy. She has a medical history of diabetes, neuropathy, dementia, hypertension, and anemia. She denied any drug allergies and her medications include: Donepezil 5mg daily, fluticasone propionate and salmeterol 250/50 one puff twice daily, losartan 50mg daily, metoprolol 50mg twice daily, gabapentin 300mg three times daily, paroxetine 20mg daily, Seroquel 200mg twice daily, furosemide 20mg daily, insulin glargline 30 units at bedtime, nitrofurantoin ER 100mg twice daily for seven days and has three days left of the medication, multivitamin daily, and iron sulfate 235mg twice daily. Her only physical complaint was feeling dizzy upon standing, and her review of systems was otherwise negative. Resident reported that the staff at the assisted living facility would check her blood pressure weekly and it ranged between 140-150's systolic and that her blood sugars ranged from 124-180 in the morning, but unsure that this was reliable due to her dementia. She resided in an assisted living facility and had one daughter that would set up her medications in a pill box each week. She reported that she had never smoked, did not drink alcohol and that her immunizations were up to date. Patient was unable to report much of her family history, except that her parents had passed away "many years ago." Patient was widowed. During the physical examination, her blood pressure was 80/40 mmHg, pulse 50 beats per minute, respiratory rate 24/min, and temperature of 98.6. Physical assessment was negative including neurological exam, assessment for carotid bruit, cardiovascular exam, and respiratory exam. Patient was wearing support stockings and did not display peripheral edema. Differential diagnoses included: orthostatic hypotension, vertigo, cardiac arrhythmias, anemia, and inappropriate medication use. Labs included a hemoglobin of

13.4, BMP all within normal limits, Hgb A1C of 8.1, and a TSH within normal limits. EKG findings were normal as well. Her MMSE did indicate moderate signs of dementia, which she currently was on Donezapil daily. During review of medications with patient she was unsure why she was taking several of her medications including gabapentin, paroxetine, quetiapine and furosemide. After review of symptoms, physical exam, lab results, EKG results, and medication review it was determined that patients dizziness was most likely caused by her multiple medications.

As the above case study has indicated, the patient is on several medications that could be causing her dizziness. The main concern at this visit was her markedly low blood pressure (80/40) and pulse (50). Patient had reported random episodes of dizziness, but primarily upon standing from either a lying or sitting position. Patient was taking losartan 50mg daily, metoprolol 50mg twice daily, and furosemide 20mg daily which were most likely contributing to her hypotension and dizziness. Because the patient had no signs of peripheral edema, no recent weight gain, and no history for congestive heart failure the furosemide was discontinued. Secondly, the patient was on metoprolol which was likely contributing to her hypotension and causing her bradycardia, thus was a high priority for tapering with the potential for a complete discontinuation in the future. Common reactions of metoprolol use include fatigue, dizziness, depression, and bradycardia. The metoprolol was tapered to 25mg twice daily with orders to hold if systolic blood pressure less than 120 or heart rate less than 60. Orders also included to check blood pressure and heart rate prior to taking metoprolol and to follow up in clinic in two weeks. Due to the patient's dementia, all orders were faxed to the assisted living facility.

While many of the patient's medications need reviewing, it is important to make changes slowly to allow for effective monitoring. At subsequent visits it will be important to further

review the metoprolol and losartan based on her blood pressure and pulse readings. As the above case study revealed, the patient was unsure as to why she was on gabapentin. Gabapentin has the potential for the following side effects: depression like symptoms, dizziness, fatigue and peripheral edema. This may need to be tapered and eventually discontinued. Another concerning medication is the Seroquel. Antipsychotics are to be used with caution in the elderly and considering she is a community dwelling elderly, is this safe? Seroquel also has adverse reactions of arrhythmias, hypotension, dizziness, and hyperglycemia. In addition to the Seroquel, she is also on Paroxetine. Overall, the patient is on several medications that should be cautioned for use in the elderly because of the side effects. This patient's mixture of medications including multiple cardiac medications, antipsychotics, and antidepressant puts her at high risk for falls, injury, hospitalization, and decrease in functional ability on top of her diagnosis of dementia. Patient is a perfect example of polypharmacy as she is receiving greater than nine medications, with several not being safe considering her age. This is a clear case study of the importance of medication review and reduction that will need to take place over several clinic visits.

### **Literature Review**

A systematic review of the electronic databases CINAHL, Cochran Library and PubMed were completed utilizing the search terms "effects of polypharmacy in the elderly," "polypharmacy in the elderly," "polypharmacy and medication reduction in the elderly," and "multiple medication use in the elderly". Limitations were set for articles in the period of January 2005- January 2015. Articles addressing polypharmacy or multiple medications were searched for by reviewing the titles and abstracts of each article found. The search was also supplemented with online site searches by using "google scholar" which articles were then reviewed for the



possible use in the literature review. All the research articles included had a sample population aged 60 or older and included hospitalized patients, community dwelling elderly, and long term care individuals. Reasons for excluding certain studies was because they did not address polypharmacy in primary care, the sample population was less than 60 years old, and a definition of polypharmacy was not included in the study.

Throughout the literature, numerous articles used the term “polypharmacy” or “inappropriate drug use”. The term polypharmacy is frequently used in the literature; however the definitions of polypharmacy varied between each article reviewed. Definitions of polypharmacy in the literature included “many medications”, “multiple medications”, or “over use of medications” to name a few. In the literature, it was unclear whether the definitions included over the counter medications and/or herbal supplements. In one ambulatory case study by Maher et al. (2014), polypharmacy was defined as a medication count of five or more medications. This study also pointed out that in the current medical guidelines multiple medications were often suggested to treat each chronic disease state which seemed contraindicated. The study by Maher et al. (2014), also looked at community dwelling elders. Among 384 patients studied, it was reported that 41.4% were on at least 5-8 medications, and 37.2% were on nine or more medications. However, overall, 585 of the patients took one or more unnecessary prescribed drugs. Another study was examined and discussed the prevalence of polypharmacy in the hospital setting both at admission and discharge. It was found that on admission 52% of patients were on an average of 4.9 medications and had an average of 5.2 diagnoses. At discharge, this rate increased to 67% with average of six medications and 5.9 diagnoses (Hajjar, Cafiero, & Hanlon, 2007).

The term polypharmacy complicates this issue because it is tagged with a negative connotation in much of the literature, but in other literature the term is used to describe an appropriate combination of multiple medications. The word “polypharmacy” was used both in a negative and positive way which made the inquiry difficult. Through the literature review it was also found that polypharmacy is defined differently among different countries. For example, many of the studies defined polypharmacy according to the number of medications taken, where other studies defined polypharmacy according to whether a medication was clinically indicated or not. In relation to the case study, no matter which definition of polypharmacy was looked at, the patient case clearly indicated that she was on too many medications overall, multiple medications for the same diagnosis without clear indication why, and was also on medications that should be used with caution in the elderly population. Throughout this review it was determined that further research is needed to address a universal definition for the term polypharmacy.

Polypharmacy contributes to health care costs to both the patients and the healthcare system at large. One retrospective cohort study found that polypharmacy was associated with an increased risk of taking inappropriate medications, as well as an increased risk for outpatient visits and hospitalizations. The same study found there was also an approximate 30% increase in medical costs (Zang et al., 2009). In a study by Maher et al., (2014), it was found that individuals who take more than five medications had a 6.2% increase in prescription drug costs and those taking ten or more medications had a 7% increase. With each drug, there is the possibility for increased visits to specialists, emergency care, and primary care visits. The literature also reveals that up to 28% of hospital admissions are secondary to adverse drug events (Fulton & Allen, 2005). Another Swedish randomized controlled study looked at patients’ aged 75 years or

older living in nursing homes and the community. In this study, medication reviews were performed by trained clinical pharmacists based on nursing assessments. There were a total of 339 patients with 182 being in the intervention group and 187 in the control group. The study showed that the number of patients taking ten or more drugs decreased in the intervention group but not in the control group and that medication reviews involving pharmacists reduced the number of medications among the patients. Overall the study showed that inappropriate prescribing is a problem in the Swedish elderly population (Milos et al., 2013). This seemed to be the conclusion among many of the studies reviewed.

An interesting study done by Vyas, Pan, & Sambamoorthi (2012), found an association between greater number of ambulatory care visits and presence of polypharmacy, suggesting that these visits increased the likelihood of polypharmacy and this finding was supported by much of the literature reviewed. In one review on polypharmacy in the elderly, it was reported that five or more visits to a primary care physician increased the risk of polypharmacy by fifteen times. Approximately 75% of all the visits to primary care physicians ended with a written prescription (Frazier, 2005). However, a prospective randomized study at a single urban general practice in Ireland suggested that a ten-minute review of medications by practitioners showed that 70% of the patients had stopped at least one medication after review (Ryan, O'Mahony, Kennedy, Weedle, & Byrne, 2009). This finding suggests that a routine medication review by primary care physicians can be incorporated to reduce the risk of polypharmacy among those with multiple chronic conditions.

In Hajjar et al., population based study (2007), it was found that outpatients taking five or more medications had an 88% increased risk for experiencing an adverse drug event compared to those taking fewer medications. The same study found that nursing home residents who take nine



older living in nursing homes and the community. In this study, medication reviews were performed by trained clinical pharmacists based on nursing assessments. There were a total of 339 patients with 182 being in the intervention group and 187 in the control group. The study showed that the number of patients taking ten or more drugs decreased in the intervention group but not in the control group and that medication reviews involving pharmacists reduced the number of medications among the patients. Overall the study showed that inappropriate prescribing is a problem in the Swedish elderly population (Milos et al., 2013). This seemed to be the conclusion among many of the studies reviewed.

An interesting study done by Vyas, Pan, & Sambamoorthi (2012), found an association between greater number of ambulatory care visits and presence of polypharmacy, suggesting that these visits increased the likelihood of polypharmacy and this finding was supported by much of the literature reviewed. In one review on polypharmacy in the elderly, it was reported that five or more visits to a primary care physician increased the risk of polypharmacy by fifteen times. Approximately 75% of all the visits to primary care physicians ended with a written prescription (Frazier, 2005). However, a prospective randomized study at a single urban general practice in Ireland suggested that a ten-minute review of medications by practitioners showed that 70% of the patients had stopped at least one medication after review (Ryan, O'Mahony, Kennedy, Weedle, & Byrne, 2009). This finding suggests that a routine medication review by primary care physicians can be incorporated to reduce the risk of polypharmacy among those with multiple chronic conditions.

In Hajjar et al., population based study (2007), it was found that outpatients taking five or more medications had an 88% increased risk for experiencing an adverse drug event compared to those taking fewer medications. The same study found that nursing home residents who take nine



or more medications are twice as likely to have adverse drug events compared to those taking less. The previously presented case study indicated that the patient was over medicated with her cardiovascular medications which included metoprolol, losartan, and furosemide. Because of this, she was experiencing hypotension, bradycardia, and dizziness which can lead to complications such as falls, fractures, and hospitalization. She was also on Seroquel and Nitrofurantoin which are cautioned for use in the elderly because of side effects of dizziness, bradycardia, and hypotension to just name a few, which can lead to subsequent provider visits and increased risk for hospitalization.

The literature reveals that polypharmacy also predisposes patients to drug reactions.

Drug- drug interactions are a frequent cause of preventable adverse drug events and medication related hospitalization which emphasizes that practitioners should keep the possibility of a drug- drug interaction in mind when prescribing any new medications. The issue arises when there is a “prescribing cascade” and an adverse reaction to one drug goes unrecognized causing the next provider to inappropriately prescribe a second drug to treat those symptoms. Not only is this potentially dangerous, it is overprescribing (Woodruff, 2010). Considering the above mentioned factors, polypharmacy is more complex than just the number of medications that the patient is taking.

Primary care providers are of utmost importance in minimizing polypharmacy and inappropriate drug use among their patients. Minimizing or controlling polypharmacy requires evaluation of a patient’s drug regimen which is an essential part of medical care in the elderly population. The literature states that medication reviews should consider whether a change in patient status might necessitate dosing adjustment, the potential for drug- drug interaction, whether patient symptoms might reflect a drug side effect, or whether the regimen could be

simplified. In the presented case study the patient was on multiple medications that could have been causing her chief complaint of dizziness. Many of her medications were without clear indication of why she was taking them, and a red flag was that the patient did not know why she was taking them. The case study revealed that a medication review and reduction is a high priority for this patient. The literature suggests that medication reviews should be done in a systematic manner with the patient meeting the provider and/ or pharmacist within a few weeks of starting a new medication (Abdulraheem, 2013).

There are a variety of methods for health care providers to use in assessing for and decreasing the chance of polypharmacy. During the literature review there were several different methods found to help with appropriate medication prescribing and included the utilization of the Beers criteria, or using mnemonics such as SAIL or TIDE. In 1997 Beers and colleagues established criteria to determine inappropriate medications prescribed for the elderly and developed a provider friendly list to use when determining which medication to prescribe for the elderly adult (American Geriatrics Society, 2012). Other research studies suggested the use of the SAIL or TIDE mnemonics. The acronym SAIL represents keeping the prescribed regimen as SIMPLE as possible, be aware of the potential ADVERSE EFFECTS, explore the INDICATION for a prescribed medication and LIST each drug on the chart and provide a copy to the patient. TIDE stands for identifying the importance of scheduling TIME during an office visit to address medications, ensure prescriber awareness of INDIVIDUAL responses to medications, avoidance of potential DRUG TO DRUG INTERACTIONS, and most importantly, EDUCATION for the client (Fulton & Allen, 2005).

Use of safer drugs is also important in preventing polypharmacy. When drug therapy is indicated for the older patient it is important to research the safest treatment (Abdulraheem,

2013). The patient in the case study was on multiple medications that needed review for both its indication, necessity, and if a safer alternative existed. Her medications included medications that are cautioned in the elderly such as Seroquel, Nitrofurantoin, Gabapentin, and Paxil. The decision to discontinue medications is determined in part by the goals of care and the risk for adverse effects. There were limited studies found regarding how best to withdraw medications, but the literature all agreed that it is important to gradually taper off most medications to minimize withdrawal reactions and allow for symptom monitoring (Abdulraheem, 2013).

Many of the research studies discussed the challenges involved with discontinuing medications, including disease exacerbation and risk for hospitalization. It is agreed that drug discontinuation should involve tapering a single drug at time with careful monitoring for symptoms of withdrawal and disease exacerbation. Because the purpose of eliminating non-essential medications includes enhancing quality of life, it is important to pay attention to the discontinuation process and several of the articles suggest that a comprehensive review of a patient's drug regimens should be performed annually or more frequently if indicated (Bushardt et al., 2008). A common factor seen throughout all the literature reviewed was that they all agreed and supported the idea of having open discussions among patient, pharmacist and provider to help decrease the significance of polypharmacy and adverse side effects that occur because of it. Not only will this increase the patients quality of life it will also decrease patient and societal costs and falls in line with an evidenced based practice that all providers should incorporate into their daily model of care.

### **Learning Points**

Through this case study and literature review, the following are learning points that should be considered throughout ones professional practice to maintain safety for all patients.



- The effects of polypharmacy are costly to both the patient and society at large, yet polypharmacy is easily preventable.
- It is best practice to establish routine medication reviews to reduce harmful adverse side effects thus decreasing hospitalizations and unwarranted costs.
- The literature reviewed endorses the importance of follow up visits when starting and discontinuing medications in elderly patients to maintain patient contact while assessing for adverse side effects and overall status.
- It is important that providers are educated about the medications that are cautioned for use in the elderly population and that they know how to use available tools- such as BEERS criteria.
- Collaboration between providers and pharmacists is an important relationship to have to help identify drug related problems.

### **Conclusion**

The population described as elderly and multiple chronic disease states are rising.

Because of this, practitioners must appropriately use medications for multiple diseases and make consciousness attempts to avoid the risks that are often associated with multiple medication use. (Bushardt et al., 2008). Because individuals are living longer, practitioners have a responsibility to prescribe appropriately and complete routine medication reviews for the safety of their patients.

Further research is indicated to address the inconsistencies in the literature related to determining a definition of polypharmacy, the effects of polypharmacy, and the best interventions primary care providers can utilize to decrease medications that are not clinically



indicated. Further study regarding nonprescription medication use in conjunction with prescription medications is also indicated. (Fulton and Allen, 2005).

Research has clearly established a strong relationship between polypharmacy and negative clinical consequences. Collaboration between providers and pharmacists to identify drug related problems has proven to be useful and led to better patient safety, as well as cost savings (Milos et al., 2013). Rational polypharmacy may be necessary and beneficial in those with comorbidities, but inappropriate polypharmacy is associated with increased adverse side effects, hospital admissions, increased costs and non-adherence. Prescribing medications appropriately and completing a patient-focused medication review that applies current evidence, but takes into account individuals' views and situations, is crucial to reducing inappropriate polypharmacy (Kaufman, 2014).

## References

- Abdulraheem, I.S. (2013). Polypharmacy: a risk factor for geriatric syndrome, morbidity and mortality. *Journal of Aging Science 1(2)*. Retrieved from: <http://dx.doi.org/10.4172/2329-8847.1000e103>.
- American Geriatrics Society. (2012). Updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*. Retrieved from: [www.americangeriatrics.org/files/.../beers/2012BeersCriteria\\_JAGS.pdf](http://www.americangeriatrics.org/files/.../beers/2012BeersCriteria_JAGS.pdf)
- Bushardt, R.L, Massey, E.B., Simpson, T.W., Ariail, J.C., & Simpson, K.N (2008). Polypharmacy: misleading, but manageable. *Clinical Interventions in Aging 3(2)*: 383-389.
- Frazier, S.C. (2005). Health outcomes and polypharmacy in elderly individuals: an integrated literature review. *Journal of Gerontological Nursing*.
- Fulton, M.M & Allen, E.R. (2005). Polypharmacy in the elderly: a literature review. *Journal of the American Academy of Nurse Practitioners 17(4)*:123-132.
- Hajjar, E.R., Cafiero, A.C., & Hanlon, J.T. (2007). Polypharmacy in the elderly patients. *The American Journal of Geriatric Pharmacology 5(4)*: 345-351. doi:10.1016/j.amjopharm.2007.12.002
- Jesson, B. (2011). Minimizing the risks of polypharmacy. *Nursing Older People 23(4)*: 14-20.
- Kaufman, G. (2014). Polypharmacy, medicines optimization and concordance. *Nurse Prescribing 12(4)*: 197-201.
- Maher, R.L., Hanlon, J.T., & Hajjar, E.R. (2014). Clinical consequences of polypharmacy in elderly. *Expert Opinion in Drug Safety 13(1)*. Doi: 10.1517/14740338.2013.827660.
- Milos, V., Rekman, E., Bondesson, A., Eriksson, T., Jakobsson, U., Westerlund, T., & Midlov, P. (2013). Improving the quality of pharmacotherapy in elderly primary care patients through medication reviews: a randomized controlled study. *Drugs and Aging 30*: 235-246. Doi: 10.1007/s40266-013-0057-0.
- Oboh, L. (2013). A pill for every ill: the dangers of polypharmacy in older people. *Nursing and Residential Care 15(10)*: 666-669.

- Ryan, C., O'Mahony, D., Kennedy, J., Weedle, P., & Byrne, S. (2009). Potentially inappropriate prescribing in an Irish elderly population in primary care. *British Journal of Clinical Pharmacology* 68(6): 936-947. Doi: 10.1111/j.1365-2125.2009.03531.x
- Vyas, A., Pan, X., & Sambamoorthi, U. (2012). Chronic condition clusters and polypharmacy among adults. *International Journal of Family Medicine*. Retrieved from: <http://www.hindawi.com/journals/ijfm/2012/193168/>
- Woodruff, K. (2010). Preventing polypharmacy in older adults. *American Nurse Today* 5(10): 1-5. Retrieved from: [www.americannursetoday.com/preventing-polypharmacy-in-older-adults/](http://www.americannursetoday.com/preventing-polypharmacy-in-older-adults/)
- Zang, M., Holman, C.D., Price, S.D., Sanfilippo, F.M., Preen, D.B., & Bulsara, M.K. (2009). Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. *BMJ* 338(2752). Doi: 10.1136/bmj.a2752.