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De-prescribing, a Solution to the Issue of Polypharmacy:

Case Report and Review

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Abstract

The physiological process of aging is undeniable complex. Changes in metabolism (i.e., increased fat and decreased water content, decreased liver function secondary to loss of hepatocytes leading to decreased metabolism, etc.) lead to an alteration in the pharmacokinetics and pharmacodynamics of medications in the body. A drug may accumulate in the serum of the body for a prolonged time secondary to diminished distribution. Disruption in the mechanism of drug metabolism may result in the elder individual experiencing adverse effects from the medication. The addition of morbidities into the mix enhances complexity whereby creating new challenges as the result is generally polypharmacy. Individuals with multiple chronic conditions are more likely to be on more medications. The more medications an individual is on increases their risk for drug to drug interactions and subsequent adverse effects. Providing care for an older individual (i.e., 60 or older), or an individual whose chronic conditions include dementia, requires additional care. This work will analyze a patient case involving multi-morbidities, dementia and polypharmacy. Through this patient situation, the need for interventions, such as de-prescribing will be clearly demonstrated.

Keywords: deprescribing, inappropriate prescribing, polypharmacy, dementia, elderly

De-prescribing, a Solution to the Issue of Polypharmacy:

Case Report and Review

Advancements in technology and ongoing discovery of new research findings in medicine have led to individuals having a longer life expectancy. According to the National Institute on Aging (2015), over half of the causation for the increase in life expectancy for females of developed countries between 1850 and 1900 can be attributed to these individuals living past 15 years of age. Prior to vaccinations, the culprits known for shortening the life expectancy included infectious and parasitic diseases. However, vaccinations are now widely available to counteract what used to be the "childhood killers." Individuals are living longer and with that comes new challenges. Development and progression of chronic disease, in addition to non-communicable diseases are among those challenges. Small strides have been made in the medical management of chronic conditions, however the percentage of the population affected is growing. Chronic disease was at one time, thought to be a death sentence. Learning how to effectively manage all the associated factors of chronic disease is challenging. The extent of this challenge is enhanced with the presence of co-morbid conditions. We continue to research these diseases and improve prevention and management methods.

Chronic disease is further challenged by the normal physiological process of aging. The complications of aging with chronic disease requires polypharmacy, which brings with it additional risks. It is important to routinely review a patient's medications to evaluate for necessity. According to the National Institute of Health (NIH, 2016), roughly fifteen percent of the population is 65 years or older. This age group contributes to thirty percent of outpatient prescription costs. Evidence shows that over half of community dwelling elderly individuals (ages 65 and older) in the USA and Australia have five or more daily medications. It

demonstrates a directly proportional relationship between aging and the number of routine medications.

Potentially inappropriate medications (PIMs) can be described as the medications suggested to avoid prescribing to the elderly based on a clinical tool such as the AGS Beers Criteria, STOPP/START, or Medication Appropriateness Index (Cooper et al., 2015). Various studies have demonstrated the association between PIMs and adverse drug outcomes, hospitalizations, diminished quality of life as well as mortality. Utilizing interventions to prevent PIM and associated outcomes is longstanding. However, de-prescribing is a relatively new concept, which can be explained as cutting down or discontinuing medications with the intended outcomes of appropriate prescribing and elimination of the increased potential for adverse effects (Page, Clifford, Potter, Schwartz, & Etherton-Beer, 2016). The challenges of PMIs that necessitate an intervention such as de-prescribing, are clearly demonstrated in an unexpected case study involving an elderly patient with polypharmacy. The issue of polypharmacy is one that affects all age groups, in a variety of environments. The elderly population is vulnerable and as such, are at a higher risk for the detrimental effects of polypharmacy.

Case Report

A 59-year-old Caucasian, overweight woman with multiple active health problems presented to the clinic for follow-up on a recent hospitalization for UTI and fatigue. She had been discharged from the hospital four days earlier on nitrofurantoin, and had three days left. UTI symptoms were reportedly resolved. Endorsed ongoing fatigue for two months and noted a new complaint of intermittent dizziness, often positional. Otherwise, reported she felt well. Past medical history is significant for anemia, dementia, diabetes, COPD, hypertension, depression and neuropathy. At that time, she was taking 12 different scheduled medications including, daily

doses of losartan 50mg, furosemide 20mg and paroxetine 20mg, as well as twice daily doses of metoprolol 50mg and quetiapine 200mg. Also, 300mg of gabapentin was scheduled three times daily. As a resident at an assisted living apartment, she has staff to administer her medications.

The patient presented hypotensive with bradycardia, blood pressure 88/40 and heart rate 50. The remainder of her physical examination was fairly unremarkable. No apparent goiter, edema, abdominal tenderness or mass. Laboratory results included: thyroid stimulating hormone 3.41 mIU/L, hemoglobin 12 g/dL, hematocrit 37%, platelets 400,000/mL, glucose 96 mg/dL, blood urea nitrogen 9 mg/dL, creatinine 0.8 mg/dL, sodium 140 mmol/L, potassium 3.9 mmol/L, aspartate aminotransferase 25 IU/L, alanine aminotransferase 11 IU/L, and albumin 4.1 gm/dL. ECG interpretation revealed sinus bradycardia, HR 48 bpm. Assessment dictated the following differential diagnoses: hypotension, hypothyroidism and anemia. Treatment for her hypotension included the following interventions: push fluids, decrease metoprolol to 25mg two times per day, discontinue furosemide, reduce dose of quetiapine to 150mg two times per day and return for follow up appointment in one week.

Discussion

The case study discussed demonstrates the strong impact of polypharmacy in the aging population. It denotes the importance of having the best interventions available. This leads to many questions: how does de-prescribing polypharmacy compared with other available interventions affect patient outcomes? How is this different in older patients? Or patients with dementia?

Evidence Search

The intention of this work is to further explore the practice of de-prescribing, specifically in the older adult population. In the midst of this search, the author aimed to learn how de-prescribing could be a solution to polypharmacy in aging individuals struggling with chronic multiple morbidities or comorbid conditions. A thorough review of the literature was accomplished by means of CINAHL, Cochrane, PubMed, and ScienceDirect electronic databases. McKeever, Nguyen, Peterson, Gomez-Perez, and Braunschweig (2016) recommended that a search of Mesh terms be conducted and, afterwards the Mesh terms should be listed with not "Medline [sb]". Separating the searches of Medline and not-Medline allow for the approximately 10% lost the by Medline search to be discovered through the second, not-Medline search. This method allows the researcher to conduct a gold-standard search that is both, proficient and clearly exhaustive to the reader.

Through the use the PubMed database, the achievement of an exhaustive search is quite evident. The initial results were in the thousands. Limits were strategically placed to reduce the number of results. English was selected as a limit, with the focus on the human species and the full free text filter on to allow analysis of the documents entirety if selected. The 5-year limit was placed to ensure current research findings in the database. The Mesh terms, "Deprescriptions" or "Inappropriate Prescribing/prevention and control" or "Drug-Related Side Effects and Adverse Reactions/prevention and control" and "Humans" were searched in the sequence displayed. The related articles function was applied to limit the search. As previously noted, the not-Medline search was conducted with the same 4 phrase sequence, however with not "Medline [sb]" after "Humans". The not-Medline search yielded 31 findings, of which 10 met the criteria.

Mateo and Foreman (2014) stressed that a researcher should use multiple databases throughout their research to ensure that important findings are not missed. Keywords "deprescription" and "elderly" were terms searched utilizing the ScienceDirect database. Limits were not necessary. The search yielded 14 results, with only 2 being applicable to this works. The CINAHL database was employed through the Boolean/Phrase search mode. The following terms were utilized: "deprescribing" or "inappropriate prescribing" and "elderly". In an effort to decrease the number of findings the limits placed include: publication date between 2014 and 2017 for current results, and the English language. Results produced in the search were over 100. Terms searched for on the Cochrane database include: "deprescribe" or "polypharmacy" or "inappropriate prescribing or medical overuse". A total of 21 results were yielded in this search.

The results of the PubMed, CINAHL, ScienceDirect and Cochrane databases were sifted through to determine the relevant findings. This proved to be a challenging task as the majority of the research findings in the listed databases were considered irrelevant to the author. In light of this, additional studies were discovered through utilizing the "snowball" approach. Analysis was completed on 11 of the articles discovered during these searches.

Grading the Evidence

Classification of evidence via a level grading system allows for the promotion of confidence in the researcher's findings. The evidence found throughout this research was graded based on the AACN's New Evidence-Leveling System. This system ranges from levels A-E and M with the highest level starting at level A and the lowest level M.

Level A is classified as meta-analysis of controlled studies or meta-synthesis of qualitative studies (Armola et. al, 2009). Randomized and non-randomized controlled studies are level B evidence. Descriptive, correlational and quantitative studies as well as randomized

controlled and systematic or integrative reviews with findings that are inconsistent would be classified as level C evidence. Level D evidence includes clinical guidelines by professional organizations that have been peer-reviewed. Case studies or expert opinions based on theory are classified as level E evidence. The recommendations provided by a manufacturer is graded as level M (Armola et. al, 2009).

The mission of the American Association of Critical Care Nurses (AACN) focuses on the development of interventions that will lead to a better understanding of the resources in question to allow members of the nursing profession to determine the best possible evidence for clinical practice (Armola et. al, 2009). As a member of the nursing professional and a goal to yield strong evidence for clinical practice, the AACN's hierarchy of evidence is indubitably appropriate. The levels of evidence for the 11 studies analyzed are as follows: 2 randomized control studies (RCTs) fit the criteria for level B, and the remaining 9 fit the criteria for level C. All of the 7 level C studies are systematic review and/or meta-analysis that revealed inconsistent, heterogeneous findings.

Synthesis of Findings

Cooper et al. (2015) demonstrated how validated screening tools (i.e., Medication Appropriateness Index(MAI), Beers' Criteria, Mcleod criteria, STOPP/START criteria, Assessment of Underutilization of Medication and ACOVE) effectively reduce potentially inappropriate prescribing (PIMs) in individuals ages 65 and older. It was noted that some of the studies in the review did not consider the reverse effect of under-prescribing, which is another major issue (especially in the older population). Utilization of MAI revealed a statistically significant decrease in PIM. In addition, the other tools previously mentioned divulged a

reduction as well though not significant. Unfortunately, the results of this review were inconsistent which decreases its validity.

Another systemic review demonstrated similar findings regarding reductions in MAI in a study population ages 65 and older, however there was additional focus on the presence of dementia (Walsh, O’Riordan, Kearney, Timmons, & Byrne, 2016). The importance of reducing PIM in individuals with dementia is amplified. This disease enhances the likelihood of the individual experiencing an adverse effect as a result of polypharmacy, specifically anticholinergics, antipsychotics, and benzodiazepines (Walsh, O’Riordan, Kearney, Timmons, & Byrne, 2016). Our case patient came into the clinic on a high dose of quetiapine which is often used in addition to an anti-depressant. This is likely why the patient in the case study has both paroxetine and quetiapine on her active medication list. It is known that many of the mental health medications carry a black box warning. Quetiapine is an anti-psychotic that holds a blackbox warning. Its use in patients who are elderly with psychosis secondary to dementia heightens their mortality risk. Antipsychotics increase the risk that the patient with dementia will experience a cerebrovascular accident (American Geriatrics Society, 2015).

According to the Beers criteria (2015), paroxetine and quetiapine should be avoided in ages 65 and older. The criteria states that quetiapine should not be administered to individuals with dementia. Our case patient is younger than 65, however with her diagnosis of dementia and multi-morbidities quetiapine is inappropriate. Her current medication list includes three CNS-active medications. This medication regimen places her at risk for adverse CNS effects, and likely are at least partially to blame for her complaints of dizziness and persistent fatigue. The furosemide and metoprolol are likely contributors to this as well.

Interventions to improve patient adherence to medication regimens revealed statistically significant increases in secondary outcomes including knowledge, physical functioning, overall quality of life and general mood, cardiac and respiratory symptoms (Conn, Ruppap, Enriquez, & Cooper, 2016). This demonstrates the importance of patient-centered interventions to achieve patient-centered outcomes. Fried et al. (2014) found evidence indicating de-prescribing can reverse symptoms. The evidence also showed that in addition to improvement of physical functioning, de-prescribing enhances cognitive function. Interestingly, Scott, Anderson, Freeman, and Stowasser (2014) demonstrated common themes related to barriers as well as facilitators influencing the ruction of PIM. The themes discovered include awareness, inertia (i.e. fear of the unknown), and self-efficacy (i.e., knowledge). Perhaps the educational interventions for improving patient adherence to medication regimens mentioned earlier in this paragraph would be effective interventions to the themes. Patients are much more likely to agree with a plan for de-prescribing if they are cued in as to why. Reeve et al. (2013) identified barriers and facilitators influencing patient agreement to de-prescribing. Understanding the “appropriateness” of de-prescribing is one of the themes, which again indicates the need for education.

According to Page, Clifford, Potter, Schwartz, and Etherton-Ber (2016), de-prescribing exhibited a statistically significant decrease in mortality in two non-randomized control trials. A systematic review including 19 studies implemented by Johansson et al. (2016) demonstrated a downward trend in mortality associated with ongoing follow-ups post-hospitalization. Physician-led medication review verified statistically significant outcomes through reduction of PIM use in the elderly (Tjia, Velten, Parsons, Valluri, & Briesache, 2013). Johansson et al. (2016) found minimal evidence supporting reductions in hospital admissions secondary to reductions in PIM

through a multi-disciplinary approach to medication review. One study showed a non-statistically significant decrease in hospital admission. Whereas, Dreischulte et al. (2016) demonstrated statistically significant reductions in hospital admissions for gastrointestinal bleeds and heart failure. The results were non-statistically significant for acute kidney injury. Perhaps the difference is related to the kidneys role in metabolism. Clyne (2015) verified the efficiency of the pharmacist-led medication review in reducing PIM. This involved the utilization of OPTI-SCRIPT, which led to statistically significant reductions in proton pump inhibitors. Results for all studies discussed are in Table 1.

De-prescribing involves a great deal more than the term implies. Multiple factors must be taken into consideration including, a collaborative agreement between the patient and their provider. Evidence supports the recommendation of de-prescribing, however this is often not performed by providers secondary to challenges including time constraints and lack of patient centered guidelines. More than a quarter of medications de-prescribed are re-initiated in less than a year's time. Re-initiation of previously de-prescribed medications has resulted in adverse patient outcomes (Scott, Anderson, Freeman, & Stowasser, 2014). It is clear that de-prescribing has shown beneficial outcomes. However, in order for this to be a successful intervention there must be a patient-provider relationship built on trust.

When a provider is faced with the decision of whether or not to discontinue a medication, the most important aspect that must be considered is the risks verses the benefits. This should include the preferences of the patient and their family in addition to the availability of non-pharmacological treatment alternatives. The second step involves collaboration with the patient and their family regarding the discontinuation process. Planning the strategy is the final step,

which should include a discussion with the patient regarding if and when the medication should be re-initiated (Ferral, 2017).

The issue of polypharmacy is one that affects all age groups, in a variety of environments. The elderly population is vulnerable and as such, are at a higher risk for the detrimental effects of polypharmacy. Of the promising interventions known to combat this problem, deprescribing is a more recent development with the potential to minimize the effects of multiple medications use. Polypharmacy in older adults has been shown to yield many negative results. This age group often carries with it a collection of multiple health problems, leading to multiple medications and ultimately, polypharmacy. As a complication, the utilization of multiple medications in the same elderly individual may end up in harm through adverse effects, altered cognition, falls, as well as hospitalization or death.

De-prescribing is not merely a method of reducing medications; it should be utilized in an effort to eliminate inappropriate medications. Polypharmacy in older adults has been shown to yield many negative results. This age group often carries with it a collection of multiple health problems, leading to multiple medications and ultimately, polypharmacy. As a complication, the utilization of multiple medications in the same elderly individual may end up in harm through adverse effects, altered cognition, falls, as well as hospitalization or death. Farrell et al. (2016) developed guidelines for the de-prescribing process for patients 18 and older. The intention was to construct a set of guidelines specific to the elderly population, however a decision was made to broaden the age span based on the literature revealing insufficient evidence for this age group.

There is a plethora of research indicating the severity of the issue regarding polypharmacy in the elderly population, however there is a lack of consistent evidence supporting de-prescribing and other interventions to reduce polypharmacy. Concrete evidence is

necessary for change. As outlined in this works, the age group with the greatest propensity of harm as a result of polypharmacy is the elderly. For this reason, as well as the obvious differences that are a consequence of aging (physiological vs. pathological), there should be a separate set of guidelines for individuals ages 65 and older. This necessitates the attention of the members in the health care community. It has been made abundantly clear that the elderly population, ages 65 and older, is vulnerable. Additional research needs to be conducted to determine how to further define the criteria for specific guidelines for this population.

Learning Points

- 1) When making a decision about whether or not to discontinue a medication, the emphasis should be placed on the benefits versus risks.
- 2) The art of de-prescribing should be a patient-centered approach. This means considering the preferences of the patient and their family and collaborating throughout the entire process.
- 3) It is clear that de-prescribing has shown beneficial outcomes. However, in order for this to be a successful intervention there must be a patient- provider relationship built on trust.
- 4) Deprescribing should place a greater emphasis on the technique of prescribing rather than simply focusing on a decrease in medications prescribed.

References

- American Geriatrics Society. (2015). American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of American Geriatrics Society*, 63, 2227-2246. doi: 10.1111/jgs.13702
- Armola, R. R., Bourgault, A. M., Halm, M. A., Board, R. M., Bucher, L., Harrington, L., . . . Medina, J. (2009). AACN levels of evidence: What's new? *Critical Care Nurse*, 29(24), 70-73. doi: 10.4037/ccn2009969
- Clyne, B., Smith, S. M., Hughes, C. M., Boland, F., Bradley, M. C., Cooper, J. A., & Fahey, T. (2015). Effectiveness of a multifaceted intervention for potentially inappropriate prescribing in older patients in primary care: A cluster-randomized controlled trial. *Annals of Family Medicine*, 13(6), 545-53. doi: 10.1370/afm.1838
- Conn, V. S., Ruppar, T. M., Enriquez, M., & Cooper, P. S. (2016). Patient-centered outcomes of medication adherence interventions: Systematic review and meta-analysis. *Value Health*, 19(2), 277-285. doi:10.1016/j.jval.2015.12.001
- Cooper, J. A., Cadogan, C. A., Patterson, S. M., Kerse, N., Bradley, M. C., Ryan, C., & Hughes, C. M. (2015) Interventions to improve the appropriate use of polypharmacy in older people: a cochrane systematic review. *BMJ Open*, 5(12). doi: 10.1136/bmjopen-2015-009235
- Dreischulte, T., Donnan, P., Grant, A., Hapca, A., McCowan, C., & Guthrie, B. (2016). Safe Prescribing- A trial of education, informatics, and financial incentives. *New England Journal of Medicine*, 374, 1053-64. doi: 10.1056/NEJMsa1508955
- Farrell, B., Pottie, K., Rojas-Fernandez, C. H., Bjerre, L. M., Thompson, W., & Welch, V. (2016). Methodology for developing deprescribing guidelines: using evidence and

- GRADE to guide recommendations for deprescribing. *PLoS One*, 11(8). doi: 10.1371/journal.pone.0161248.
- Fried, T. R., O'Leary, J., Towle, V., Goldstein, M. K., Trentalange, M., & Martin, D. K. (2014). Health outcomes associated with polypharmacy in community-dwelling older adults: a systematic review. *Journal of the American Geriatrics Society*, 62(12), 2261-2272. doi: 10.1111/jgs.13153
- Johansson, T., Abuzahra, M. E., Keller, S., Mann, E., Faller, B., Sommerauer, C., . . . Sönnichsen, A. (2016). Impact of strategies to reduce polypharmacy on clinically relevant endpoints: a systematic review and meta-analysis. *British Journal of Clinical Pharmacology*, 82, 532-548. doi:10.1111/bcp.12959
- Mateo, M., & Foreman, M. (2013). *Research for advanced practice nurses: From evidence to practice (2nd ed)*. New York: Springer Publishing.
- McKeever, L., Nguyen, V., Peterson, S., Gomez-Perez, S., & Braunschweig, C. (2016). Demystifying the search button: A comprehensive pubmed search strategy for performing an exhaustive literature review. *Journal of Parenteral & Enteral Nutrition*, 39(6), 622-635. doi: <http://dx.doi.org.ezproxy.undmedlibrary.org/10.1177/0148607115593791>
- National Institute on Aging. (2015). Living longer. Retrieved from <https://www.nia.nih.gov/research/publication/global-health-and-aging/living-longer>
- National Institute on drug abuse. (2016). Misuse of prescription drugs older adults. Retrieved from <https://www.drugabuse.gov/publications/research-reports/prescription-drugs/trends-in-prescription-drug-abuse/older-adults>
- Page, A. T., Clifford, R. M., Potter, K., Schwartz, D., & Etherton-Bear, C. D. (2016). The feasibility and effect of deprescribing in older adults on mortality and health: a systematic

- review and meta-analysis. *British Journal of Clinical Pharmacology*, 82, 583–623. doi: 10.1111/bcp.12975
- Reeve, E., To, J., Hendrix, I., Shakib, S., Roberts, M. S., & Weise. (2013). Patient barriers to and enablers of deprescribing: a systematic review. *Drugs Aging*, 30(10),793-807. doi: 10.1007/s40266-013-0106-8
- Scott, I. A., Anderson, K., Freeman, C. R., & Stowasser, D. A. (2014). First do no harm: a real need to deprescribe in older patients. *Medical Journal of Australia*, 201(7), 390-2. doi:10.5694/mja14.00146
- Tjia, J., Velten, S. J., Parsons, C., Valluri, S., & Briesache, B. A. (2013). Studies to reduce unnecessary medication use in frail older adults: A systematic review. *Drugs Aging*, 30, 285–307. doi: 10.1007/s40266-013-0064-1
- U.S. Preventive Services Task Force. 2014. Grade definitions. Retrieved from <http://www.uspreventiveservicestaskforce.org/Page/Name/grade-definitions>
- Walsh, K. A., O’Riordan, D., Kearney, P. M., Timmons, S., & Byrne, S. (2016). Improving the appropriateness of prescribing in older patients: a systematic review and meta-analysis of pharmacists' interventions in secondary care. *Age Ageing*, 45(2), 201-9. doi: 10.1093/ageing/afv190

Authors/ Publication Year	Purpose and Design	Sample	Data Collection, Measurement Findings	Strengths and Limitations	AACN's New Evidence- Leveling System
<p>Cooper, Cadogan, Patterson, Kerse, Bradley, Ryan, Hughes/ 2015</p>	<p>Update the current literature on the effectiveness of interventions in reducing PIMs</p> <p>Cochrane systematic review and meta-analysis</p>	<p>N= 12</p> <p>Participants 22,438</p>	<p>11 studies on pharmaceutical care based intervention using a validated assessment tool</p> <p>4 studies on patient education and tools to schedule medications to improve compliance</p> <p>5 studies on education to health care providers and team members</p> <p>A single unificated study on computerized decision support</p> <p>7 validated screening tools were utilized in the 12 studies (i.e, Medication Appropriateness Index, Beers' Criteria, Mcleod criteria, STOPP/START criteria, Assessment of Underutilization of Medication and ACOVE)</p> <p>Some studies focused on the reduction of polypharmacy without considering the</p>	<p>Evaluation of quality of evidence utilizing a GRADE approach</p> <p>Randomization utilized in all studies</p> <p>No language restrictions</p> <p>Studies with small sample size and low quality based on GRADE approach, resultant increased risk of bias</p> <p>Lack of allocation concealment and protection against contamination</p> <p>Studies lacking a validated assessment of under-prescribing</p> <p>Effect estimate inaccuracy</p>	<p>C</p>

			<p>occurrence of the opposite effect (i.e., under-prescribing)</p> <p>Significant reduction in inappropriate prescribing using MAI</p> <p>Reduction using the other tools compared to no using a tool</p> <p>Interventions not effective against ADEs and hospitalizations</p>		
<p>Conn, Ruppap, Enriquez, Cooper/ 2016</p>	<p>Analyze effectiveness of interventions implemented for medication adherence through patient outcomes</p> <p>Synthesis review and meta-analysis</p>	<p>n= 141</p> <p>23,318 participants</p>	<p>Data collection via coding frame</p> <p>Statistically significant results were revealed in knowledge of medication, function, specified symptoms (i.e., depression, pain, energy, cardiac and respiratory and overall quality of life.</p> <p>The most significant increase was found in knowledge</p> <p>Patient centered outcomes were moderately increased post-interventions</p>	<p>Most studies utilized random assignment</p> <p>Use of allocation concealment</p> <p>Presence of heterogeneous results</p> <p>Significant risk of bias analysis</p>	<p>C</p>

Tjia, Velten, Parsons, Valluri, Briesache/ 2013	Analyze current interventions used to reduce inappropriate medication use in the elderly Systematic review	n= 36 13,906 subjects	Studies: 15 RCT, 4 non-RCT, 6 pre-post studies, and 11 case series. Pharmacy-led medication review: 6 of 12 demonstrated statistical analysis with 4 of the 6 noting results that were statistically significant. The other 6 indicated variable results. Multi-disciplinary approach: 10 of 13 revealed statistical analysis with 8 indicating statistically significant results. Statistically significant medication reductions occurred in 4 of 4 studies on academic detailing, 5 of 5 studies of medication reviews by physicians and in audit/feedback Direct relationship noted between presence of cohort group and strength of study	Multiple studies with moderate to high risk of bias secondary to failing to adjust for potential confounding variables as well as non-blinded assessment of outcomes Heterogeneity of results, unable to complete meta-analysis	C
Walsh, O’riordan, Kearney, Timmons, Byrne, 2016	Update the current literature on the effectiveness of interventions in reducing PIMs	n= 1,164 4 trials: 2 non-RTCs and 2 RTCs	comprehensive review utilizing 12 electronic databases reductions in MAI were statistically significant in 3 RTCs utilizing tools	All studies were at moderate risk for bias	A

	Cochrane systematic review and meta-analysis				
Page, Clifford, Potter, Schwartz, Etherton-Beer/ 2016	Discover the level of safety, effectiveness as well as practicability of de-prescribing Systematic review and meta-analysis	N= 116 studies for analysis	Evidence shows that de-prescribing is practical, may not influence mortality Evidence is available to guide a provider when the situation fits a classic presentation meaning there is a lack of applicability in the guidelines Statistically significant reduction in mortality with de-prescribing revealed in non-RTCs, not significant in RTCs	Potential for language bias, limit placed for English Broad inclusion criteria Potential for bias based on methodology Small size of RCT and low quality Non-randomized studies	C
Fried, O’Leary, Towle, Goldstein, Trentalange, Martin/ 2014	Discover the clinical outcomes that result from the polypharmacy management of chronic conditions in community	N= 58	Data elements included: design, population, measure of polypharmacy and main findings. All observational studies, most cross sectional or longitudinal cohort studies, few were case control	Adjustments were made for confounding variables (i.e., chronic conditions) Large and population based cohort studies Studies analyzed are observational studies, confounding is a greater issue	C

	<p>members ages 65 and older</p> <p>Systematic review of MEDLINE</p>	<p>23 studies analyzed falls as the health outcome of polypharmacy.</p> <ul style="list-style-type: none"> - 14 of 23 studies were rated good. - 12 of 14 found positive association between polypharmacy and the outcome. Greater polypharmacy showed association to outcomes, whereas 1-3 medications did not show association. <p>14 studies analyzed ADEs as the health outcome of polypharmacy.</p> <ul style="list-style-type: none"> - 8 of 14 studies were rated good. - 5 of 8 found association. - 1 of the 5 showed association only at use of 14 medications. - 6 of 14 studies were rated fair or poor and 4 of the 6 found an association <p>10 studies analyzed hospitalization or mortality as the health outcome of polypharmacy.</p> <ul style="list-style-type: none"> - 4 of the 10 were rated good and found associations with the outcome. - 6 of 10 were rated fair or poor and 3 of 6 found association 		
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			<p>15 studies analyzed multiple health outcomes of polypharmacy including symptoms, function and cognition. - 11 of 15 studies were rated good and all 11 found association with one or more outcomes.</p> <p>A single study analyzed the potential development of Parkinson’s disease as the health outcome of polypharmacy</p>		
<p>Dreischulte, Donnan, Grant, Hapca, McCowan, Guthrie, 2016</p>	<p>Determine how the implementation of “Data-Driven Quality Improvement in Primary Care (DQIP)” affects the hospitalization course of specified conditions</p> <p>RCT</p>	<p>N= 34 practices 33,334</p>	<p>Outcome measured was patient exposure to 1 of 9 anti-coagulating drugs defined as high risk</p> <p>Intervention implementation revealed statistically significant results found include decreased admission to the hospital for gastrointestinal bleed and heart failure</p> <p>Results were not significant regarding hospital admission for acute kidney injury</p>	<p>RCT design</p> <p>Evaluation completed in primary care</p> <p>Continued positive outcomes through analysis post-financial incentive</p> <p>Stepped-wedge design Small study size</p>	<p>B</p>

<p>Johansson, Abuzahra, Keller, Mann, Faller, Sommerauer, Höck, Löffler, Köchling, Schuler, Flamm, Sönnichsen 2016</p>	<p>Analyze available interventions for polypharmacy to determine their level of efficiency</p> <p>systematic review and meta-analysis</p>	<p>N= 25</p> <p>21 RCTs and 4 non-RCTS</p>	<p>Study focus: ages 65 and older with polypharmacy (4 or more medications)</p> <p>Interventions included electronic based and non-electronic based (i.e., Beers' criteria)</p> <p>- pharmacist, physician or multiple discipline-led medication review- inconsistent results</p> <p>Interventions analyzed:</p> <p>Hospitalization- 11 studies, 2 showed significant results, others were inconsistent</p> <p>Mortality- 19 studies, revealed a downward trend with longer follow up period inconsistent results</p>	<p>Approach to assess quality involved utilization of the Grade Pro Tool</p> <p>Included studies were heterogeneous</p>	<p>C</p>
<p>Clyne, Smith, Hughes, Boland, Bradley, Cooper, Fahey/ 2015</p>	<p>Analyze the efficiency of OPTI-SCRIPT (multi-intervention) against PIMs</p> <p>RCT</p>	<p>n= 21 practices, 190 patients</p>	<p>Statistically significant results found in the reduction of inappropriate prescribing of proton pump inhibitors utilizing the OPTI-SCRIPT intervention.</p> <p>OPTI-SCRIPT incorporates the review of medications, pharmacy visit to discuss potentially inappropriate medications and the pharmaceutical based treatments guides on the web</p>	<p>Relevance to clinical practice</p> <p>Retention of study participants</p> <p>Potential selection bias reduced via data collection by independent third party prior to minimization.</p> <p>Blindness to allocation</p> <p>Setting in primary care with available resources</p>	<p>B</p>

				Possible limitation in external validity	
<p>Scott, Anderson, Freeman, Stowasser /2014</p>	<p>To determine what the barriers and facilitators to reducing the prescription of inappropriate medications</p> <p>Systematic review</p>	<p>N= 21</p>	<p>Analysis of study design and aims, location and setting, participants and enrollment process, viewpoints of provider/prescriber, PIMs</p> <p>Methods included descriptive survey, SSIs, interviews, group discussions, focus groups</p> <p>Utilization of focus groups and partly structured interviews</p> <p>Development of descriptive and analytical themes utilizing subthemes discovered</p> <p>Collection through thematic synthesis yielded 42 subthemes, 12 descriptive themes and 4 analytical themes</p> <p>Intrinsic themes: 1) Awareness (i.e., poor insight, discrepant beliefs and practice), 2) Inertia (i.e., fear of unknown/negative outcome, medication effect greater benefit than risk, prescribing is desired by patient, challenge of cessation and low priority)</p>	<p>Assessment of quality utilizing COREQ -Ave score 17 (range 8—22) -Better assessment of credibility, dependability and transferability of findings</p> <p>Consistency with raw data</p> <p>Interpretations were peer reviewed, (aside for 1)</p> <p>Obedience with reporting requirements of ENTREQ</p> <p>COREQ: researcher bias could not be excluded</p> <p>Ethics approval indeterminable in 5 studies</p> <p>Terminology inconsistency and poor indexing of search terms interference with study findings</p> <p>Only 4 studies on polypharmacy, other studies on similar single medication/drug classes</p>	<p>C</p>

			<p>3) Self-efficacy (i.e., skills, knowledge)</p> <p>Extrinsic theme: 1) Feasibility (i.e., patient resistance to change, limited alternatives, time/effort needed to de-prescribe)</p> <p>More facilitating factors than barriers</p>		
<p>Reeve, To, Hendrix, Shakib, Roberts, wise/2013</p>	<p>Identification of potential barriers and facilitators leading to a patient decision to agree to de-prescribe</p> <p>Systematic review</p>	<p>N= 21</p>	<p>Content analysis with coding</p> <p>Data extracted via two reviewers through standardized data extraction</p> <p>Method included principles of systematic review of quantitative and qualitative research</p> <p>Categories determined at time of review Data was extracted and categorized then divided into themes and subthemes</p> <p>Quality assessment based on the COREQ criteria</p> <p>Themes identified:</p>	<p>Variability in completeness of reporting</p> <p>Utilization of quantitative and qualitative studies</p> <p>Uncertainty of true inappropriateness of a medication in question for de-prescription.</p> <p>Studies included all age groups, the variation between adolescence and elderly must be considered. Themes were found to be similar.</p> <p>Only able to use published data, which equates to an inability to support the idea that the only factors relevant to prescribing are the factors discussed in this article</p>	<p>C</p>

			<p>1) Viewpoint regarding “appropriateness” of de-prescription 2) Availability of a process for de-prescribing 3) Influences 4) Fright or dislike</p> <p>Most common was “appropriateness of de-prescribing- 18 studies found it to be a facilitator, 15 found it to be a barrier</p> <p>20 studies on single medication class or therapeutic group, a single study on any chronic med</p> <p>De-prescribing should be patient centered</p> <p>Patients need to be educated on why the medication is inappropriate (i.e., side effects can occur at any time)</p>	<p>Studies focused only on commonly utilized medications</p> <p>Quality assessment was not formal. Results were poor as most studies had mixed methodology</p> <p>Potential for personal and publication bias as these are qualitative studies</p>	

Table 1

Abbreviations.

Randomized Control Trial (RCT)

Consolidated Criteria for Reporting Qualitative Research (COREQ)

Potentially inappropriate medications (PIMs)

Grades of Recommendation Assessment, Development and Evaluation (GRADE)

Optimizing Prescribing for Older People in Primary Care, a cluster-randomized controlled trial (OPTI-SCRIPT study)