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# Reducing Polypharmacy in Older Adults at End of Life: The Outcome on Quality of Life

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## Abstract

**Background:** Older adults at the end of life are commonly prescribed multiple medications which can lead to polypharmacy. Research has shown that optimizing medications through targeted deprescribing reduces inappropriate medications, reduces adverse effects and improves select outcomes. However, the impact of deprescribing remains uncertain--specifically whether this intervention improves quality of life (QOL). **Objective**: Explore polypharmacy in older adults at the end of life examining outcomes of deprescribing on the QOL. **Methods**: A systematic literature search using Academic Search Premier, CINAHL, Medline, JSTOR and Nursing and Allied Health Database was conducted between October 2020 to November 2020. Select articles published between 2010-2020 were included in the review. Articles using any design or setting were included in the analysis as long as they addressed interventions to reduce polypharmacy among older adults at the end of life and the outcome of the study addressed QOL. One reviewer independently reviewed articles for eligibility, evaluated article quality and extracted key data within the subset of articles retained for analysis. **Results**: The findings were inconsistent with regard to the effect of deprescribing on QOL in older adults at end of life. **Conclusion**: Further randomized controlled studies investigating the effects of reducing polypharmacy on QOL in older adults at the end of life are needed to determine the impact of reducing polypharmacy.


*Keywords*: older adults, end of life, quality of life, deprescribing, inappropriate medications, outcomes

**Reducing Polypharmacy in Older Adults at the End of Life:**

**The Outcome on Quality of Life**

The term polypharmacy is defined by the World Health Organization as "the administration of many drugs at the same time or the administration of an excessive number of drugs" and is a common occurrence in older adults (Schenker et al., 2019; Leblanc et al., 2015). There is not an exact number of medications that has been specified to define the term polypharmacy, however, numerous publications have defined polypharmacy as the use of more than four to five medications at one time (Kierner et al., 2016). At the end of life, polypharmacy is particularly burdensome as patients accumulate medications and experience an increasing risk for being prescribed inappropriate medications (Schenker et al., 2019). Patients tend to be prescribed medications to treat symptoms at the end of life in addition to the medications used to prevent age related diseases and control comorbidities that may not be life threatening (Schenker et al., 2019). These medications may carry harmful adverse effects, drug to drug interactions, pill burden, and are costly (Schenker et al., 2019). A higher symptom burden has been associated with poor health outcomes such as reduced quality of life (QOL), adverse drug reactions, falls, hospitalization and mortality (Shrestha et al., 2020). There is evidence that suggests that with a diagnosis of a limited life disease (LLD) or limited life expectancy (LLE), a reduction of unnecessary or inappropriate medications is favored (Shrestha et al., 2020). At this point, the primary focus should be on enhancing QOL including symptom control (Curtin et al., 2020; Gardner, 2019; Lindsay et al., 2014). This literature review will explore polypharmacy, the impact that deprescribing has on QOL in older adults at end of life, and provide

recommendations for primary care providers on education, policy, research, and best practices for deprescribing in older adults at end of life.

## Background

Polypharmacy is a widespread phenomenon at the end-of-life care in settings such as palliative care and hospice (Kierner et al., 2016). In a study conducted in the United States that examined over 4000 patients in hospice, if was found that patients had been prescribed an average of 15 medications at any one time (LeBlanc et al., 2015). Over 350 of these patients had been prescribed 30 or more medications (LeBlanc et al., 2015). An average of 7.9 medications were prescribed "as needed" and 8.3 medications were regularly scheduled (LeBlanc et al., 2015). This study reveals the troubling occurrence of polypharmacy at end of life. Many medications that are prescribed are to prevent disease where in these circumstances, the life expectancy is limited (Schenker et al., 2019). Many of these patients at end of life have co-morbidities that can increase risk of medication side effects and medications that are administered at the end of life for symptom management carry significant side effects (Schenker et al., 2019).

According to Gardner (2019), deprescribing is a recommended intervention to decrease potentially inappropriate or unnecessary medications and reduce the harms of these medications. Deprescribing is defined as a process of screening, identifying, and discontinuing medications when the harm outweighs the benefits within the parameters of goals of care, treatment targets, and patient's remaining life expectancy (Lindsay et al., 2013). Screening for polypharmacy and determining which medications are potentially no longer appropriate pose challenges for providers (LeBlanc et al., 2015). Using evidence-based guidelines can help guide the clinician with deprescribing decisions (Schenker et al., 2019). Deprescribing interventions have been

shown to improve medication appropriateness and has the potential for mortality reduction and cost savings (Shrestha et al., 2020). Unfortunately, the evidence associated with the benefits of deprescribing has not been directly correlated with an improvement in QOL (Shrestha et al., 2020). This literature review aims to answer the clinical question, *Can reducing polypharmacy for older adults at end of life improve QOL?* The purpose is to advance understanding of the impact of reducing polypharmacy at end of life and further guide evidence-based interventions for primary care providers to address the phenomenon of polypharmacy and to achieve a better QOL for patients at the end of life.

Answering this practice question is of clinical significance for advanced practice providers and patients alike. Research on this topic suggests that primary care providers are open to deprescribing but are reluctant to do so (Curtin et al., 2020). If consistent, rigorous evidence exists regarding the benefits of deprescribing outweighing the risks associated with polypharmacy, this will provide further support for the primary care provider to engage in conversations with patients promptly at the end of life to reduce inappropriate or non-beneficial medications.

## Methods

An extensive literature search was completed on 11/13/20 with the assistance of a librarian from Minnesota State University, Mankato. The following databases were searched including Academic Search Premier, CINAHL, Medline, JSTOR and Nursing and Allied Health Database. Terms used in the search include deprescribe, polypharmacy, reducing medication, quality of life, end of life, palliative, hospice, and life limiting disease. Limits applied to the database searches included studies published between 2010-2020, full text availability, scholarly peer-reviewed journals, and English language. Within each database, the number of article ‘hits’

received for every keyword search were recorded (see Table 2 of the appendix). The articles that were relevant to the clinical question were marked for full review. After eliminating duplicate articles, the review of article titles and abstracts yielded 31 studies to further determine inclusion or exclusion based on select criteria. Nine articles met the inclusion criteria. All unique hits after scanning and eliminating titles and bibliographic review are indicated in bold in Table 2 of the appendix. These hits are subsequently included in Table 3 of the appendix for specific inclusion or exclusion.

**Inclusion and Exclusion Criteria**

The nine articles that met inclusion criteria directly address: (a) older adults (aged > 65 years), (b) participant needed to be considered at end of life, receiving palliative care or hospice, limited life illness, or limited life expectancy, (c) deprescribing intervention, (d) QOL and health related outcomes of deprescribing. The articles were excluded if they (a) age < 65 years of age, (b) did not fall under the criteria of end of life, (c) did not involve the intervention of deprescribing, (d) QOL and health related outcomes of deprescribing were not addressed. Refer to the appendix in Table 3 for the articles that were reviewed and the rationale for inclusion and exclusion are provided for each reference.

A total of 863 articles were identified through electronic search databases. After removing duplicates and searching keywords used within abstracts, 31 articles were reviewed from which nine articles were included within this literature review (Table 4). Data from the articles included were extracted independently by one author and inserted into a pre-designed template for interpretation and synthesis of the literature review (Table 4). Data abstracted included: authors, year of publication, study purpose, population, sample size, setting, type of

design and level of evidence, variable/instruments, and intervention. Outcome data were summarized for each study.

## Summary of the Findings

Within the review of literature, the highest level of evidence within the nine articles in this review was level I (LeBlanc et al., 2015; Lindsay et al., 2014; Shrestha et al., 2020); other evidence was level II, IV and V (Curtin et al., 2020; Gardner, 2019; Kierner et al., 2016; Kutner et al., 2015; Parker et al., 2019; Schenker et al., 2019). Two of the three systematic reviews addressed polypharmacy in advanced cancer and the outcomes of deprescribing (LeBlanc et al., 2015; Lindsay et al., 2014). The other systematic review investigated the evidence surrounding the outcome of deprescribing in patients with limited life expectancy and life limiting illness (Shrestha et al., 2020). The level II articles encompassed three randomized control studies that examined the outcomes from deprescribing (Curtin et al., 2020; Kutner et al., 2015; Parker et al., 2019). The other articles include a retrospective study examining polypharmacy at the end of life and a secondary analysis of the association of polypharmacy, symptom burden, and QOL (Kierner et al., 2016; Schenker et al., 2019). An expert opinion was included that addressed deprescribing at the end of life (Gardner, 2019).

### Polypharmacy

Polypharmacy has been defined as the use of several medications, the underuse of medications when the indicated medication is not used, or when there is a duplication of medications (Kierner et al., 2016). Although the number of medications has not been identified for polypharmacy, there is evidence that negative outcomes are associated with polypharmacy even when taking as few as four medications at a given time (LeBlanc et al., 2015). The prevalence of polypharmacy is a well-recognized problem in older patients and is associated with

comorbid conditions as well as cancer (LeBlanc et al., 2015). According to LeBlanc et al. (2017), older patients with cancer received more polypharmacy than younger patients (2015). For example, nursing home residents are prescribed an abundance of medications and are at an increased risk of adverse drug events (Curtin et al., 2020). Many of the residents in nursing homes have limited life expectancy (average of time until death is five months) therefore many do not live long enough to reap the benefits of their prescribed medications (Curtin et al., 2020).

Palliative care patients experience polypharmacy and when they suffer worsening symptoms, they are prescribed additional medications to treat these symptoms (Kierner et al., 2016; LeBlanc et al., 2015; Schenker et al., 2019;). This is referred as the "prescribing cascade" where medication related adverse effects leads to additional medications prescribed (Schenker et al., 2019). Schenker et al. (2019) examined the associations between polypharmacy, symptom burden, and QOL in patients with a life limiting illness. They discovered that the results are bidirectional; polypharmacy was associated with higher symptom burden and lower QOL (Schenker et al., 2019). In contrast, a different way to view the data is patients with poorer QOL are more ill, have more symptoms, which increases the number of medications they require, attributing to polypharmacy (Schenker et al., 2020). The authors suggested areas for future research to include a focus on developing and evaluating deprescribing strategies to reduce inappropriate medications in patients at the end of life (Schenker et al., 2020).

Polypharmacy is shown to occur even days before death in advanced cancer patients (Kierner et al., 2016). Kierner et al. (2016) completed a retrospective study, reviewing charts of 100 patients that had died due to advanced cancer. The study revealed that nine days before death, patients were prescribed 11 medications (Kierner et al., 2016). Although this number decreased significantly towards the day of death, patients were still prescribed a median of 6.5

drugs on their last day (Kierner et al., 2016). Due to an increase in anticholinergic and serotonergic loads, polypharmacy can be extremely dangerous in patients at the end of life (LeBlanc et al., 2015). For example, research conducted in hospice settings demonstrated that dying patients experience an anticholinergic burden that is associated with adverse effects such as poor mental concentration, reduced QOL, and worsening physical function (LeBlanc et al., 2015).

**Potentially Inappropriate Medications**

Published studies have reported harm with even one unnecessary or inappropriate medication (LeBlanc et al., 2015). Furthermore, there has been an association with PIM and health outcomes including reduced QOL, falls, hospitalization and even mortality. Despite these known risks, patients continue to receive preventative medications including statins, antihypertensives, antiplatelets, antidiabetics, antiulcer, vitamins and mineral supplements (Shrestha et al., 2020). LeBlanc et al. (2015) reported that in a study of 87 patients with advanced cancer in an ambulatory setting, 21 (24%) patients were taking at least one unnecessary drug. This was often noted when a provider did not reconcile their medication list (LeBlanc et al., 2015). This helps support the need for interventions, such as a full medication reconciliation in order to discontinue unnecessary medications (LeBlanc et al., 2015).

**Interventions to Reduce Polypharmacy**

Schenker et al. (2019) and Gardner (2019) suggest that clinicians who work with advanced, life limited illnesses should learn targeted strategies for deprescribing, and this should be completed routinely (Schenker et al., 2019). A collaboration between provider and patient preference should assist with making deprescribing decisions, especially if the risk and benefits of the medication is unknown (Schenker et al., 2019; Gardner, 2019). Deprescribing is

considered an intervention that is completed by cautiously tapering and withdrawing medications utilizing approved tools or algorithms with a multidisciplinary approach led by a clinician or pharmacist (Shrestha et al., 2020).

Within the literature, there were several guidelines recommended for use when considering a deprescribing initiative. Lindsay et al (2014) reported that most of the guidelines to identify PIMs in the older adult medicine were mostly based on Beers Criteria or Screening Tool of Older Person's Prescriptions (STOPP)/Screening Tool to Alert doctors to Right Treatment (START). The Beers Criteria provides a concise list of medications, dosages, and duration of therapy that should be avoided in patients over the age of 65 years and older (Lindsay et al., 2014). The STOPP Criteria consists of 65 indicators that are associated with drug-to-drug interactions, drug to disease interactions, and duplication of therapy (Lindsay et al., 2014). A benefit of these guidelines is that PIM can be identified effectively by novice or experienced clinician or pharmacists (Lindsay et al., 2014). Unfortunately, there are limitations for using these guidelines in palliative care. Patients in palliative care often suffer from distressing symptoms and receive appropriate medications to treat those symptoms which are deemed inappropriate according to these deprescribing guidelines (Lindsay et al., 2014). In addition, there is the complexity factor to consider with patients receiving palliative care (Lindsay et al., 2014; Curtin et al., 2020). Within this population at the end of life, physiology changes such as body mass, metabolism, and elimination can affect the pharmacokinetics and pharmacodynamics of any medication administered (Shrestha et al., 2020) and cause a potential for drug related toxicity, drug interactions and the patient response to the medication (Gardner, 2019).

There are practice guidelines that are being explored for use in palliative care such as the Good Palliative Geriatric Practice guideline (GP-GP) and 5-point algorithm (Lindsay et al.,

2014). The GP-GP has targeted statements that question if the medication is appropriate (Lindsay et al., 2014). The 5-point algorithm considers medications that provide a limited benefit for patients at end of life (Lindsay et al., 2014). However, there are limitations to these guidelines, as it requires skilled clinicians to use the algorithm (Lindsay et al., 2014). Some of the criteria within these guidelines are broad and rely heavily on an experienced clinician's assessment (Lindsay et al., 2014). For example, the GP-GP algorithm has two criteria for discontinuing a medication are "Indication seems valid and relevant in this patient's age group and disability level" and "Do the known possible adverse reactions of the drug outweigh possible benefit in old, disabled patients" (Lindsey et al., 2014, p. 1116). Lindsey et al. (2014) recommended for future studies are warranted to establish clear guidelines for identifying PIMs in palliative cancer patients and outcomes of discontinuing PIMs for these patients.

The balance of discontinuing medications during end of life can be challenging (Gardner, 2019). Deprescribing medication too soon can be viewed as negligent or causing harm but if too late, this may result in inappropriate treatment and cause additional stress on the patient (Gardner, 2019). Another consideration at the end of life is that the patient is no longer benefiting from the medication to preserve life (Gardner, 2019). Curtin et al. (2020) reported that there is a functional decline in patients transferred to the nursing home from the hospital setting and this provides an opportune time to conduct a medication review with a focus on QOL rather than focusing on long term prevention strategies on chronic disease management (Curtin et al., 2020).

LeBlanc et al. (2015) reported in a systematic review that in an ambulatory study, an interdisciplinary team approach to a comprehensive review was conducted and patients were noted to be resistant to accepting the recommendations for reductions in their drug regimens.

This suggests that there are concerns from patients and families for accepting these deprescribing strategies (LeBlanc et al., 2015). The study also mentioned concerns about providers accepting these strategies. In fact, Curtin et al. (2020) highlighted evidence that hospital physicians do not take the opportunity to deprescribe in frail multimorbid older people due to "fear of negative consequences such as that symptoms would return, clinical deterioration, litigation, or increased workload" (Curtin et al., 2020, p. 739). Further investigation is warranted on successful ways to communicate the goals of these interventions to reduce polypharmacy for patients, family members and prescribers (LeBlanc et al., 2015).

Despite clear guidelines for polypharmacy in patients with advanced cancer or end of life, LeBlanc et al., (2015) recommend that clinicians be aware of the issue and complete an informal screening for polypharmacy, specifically in elderly frail patients that are at high-risk to develop an adverse drug reaction. Greater attention to polypharmacy in patients with advanced cancer and end of life would ultimately lead to reductions in adverse drug events, cost, and even improvements in QOL (LeBlanc et al., 2015; Gardner, 2019). Lindsay et al. (2014) and LeBlanc et al. (2015) suggest that further research is necessary to establish guidelines for identification of PIMs in end of life and palliative care.

**Non-Essential and Essential Medications**

Gardner (2019) provided an expert opinion including recommendations that conversations surrounding deprescribing at the end of life should be patient-centered and initiated early (Gardner, 2019). The author reported that within end of life medication management, prescriptions need to be classified into non-essential and essential groups (Gardner, 2019). Non-essential medications would be considered those medications prescribed to manage underlying conditions where there is no chance to recover, and the administration of the

medication would prolong the dying process as well as serve no therapeutic purpose (Gardner, 2019). Essential medications manage symptoms such as breathlessness, pain, and nausea (Gardner, 2019). When a patient is no longer able to swallow, alternative routes of administration should be considered (Gardner, 2019). Gardner (2019) also suggests that at end of life, each medication should be evaluated for the route, time of administration and risk versus symptom management.

## Outcomes of Deprescribing

### *Reduction of Polypharmacy*

Gardner (2019) reports that deprescribing enhances the patient's QOL by ultimately reducing the drug burden without compromising patient safety or well-being (Curtin et al., 2020). Each study approached deprescribing differently, but data supports that deprescribing interventions can reduce inappropriate medications. Shrestha et al. (2019), in their systematic review revealed a reduction in the number of medications after deprescribing intervention in six of the nine studies, despite the use of varying deprescribing tools. Whereas in a randomized controlled study by Curtin et al. (2020), a protocol referred to as "STOPPFrail" guided the deprescribing plan and was used in older people approaching end of life. A significant reduction in polypharmacy was reported (Curtin et al., 2020). The results wer that almost one in four medications in polypharmacy patients were discontinued (Curtin et al., 2020). The primary indication for deprescribing a medication included not having a valid clinical indication for the patient to take the medication (Curtin et al., 2020). This supports routinely reviewing whether a medication is linked to a diagnosis or a symptom that is active or reoccurring during formal medication reviews in older patients at end of life (Curtin et al., 2020).

In a systematic review of 21 articles, LeBlanc et al. (2015) found the data reflects the effectiveness to reduce polypharmacy by using interventions to identify potential inappropriate medications. For example, the Beers criteria was applied to an oncology acute unit of elders, which showed that 32% of patients were prescribed nine or more medications and 42 of the 51 recommendations were implemented (LeBlanc et al., 2015). A drug error was corrected in one of every eight patients that could have or did result in an adverse drug event (LeBlanc et al., 2015). The only study that did not demonstrate a decrease in polypharmacy was an intervention study with older adults diagnosed with chronic kidney disease. A medication review using the STOPP/START criteria revealed there was no improvement in reduction of PIMs although the low impact of this study may be due to the judgement left to the attending physician, differences in populations, and the length of time period (Parker et al., 2019).

***Mortality***

The US Palliative Care Research Cooperative Group conducted a randomized control study to assess the safety and clinical impact of discontinuing statin medications for patients in a palliative care setting (Kutner et al., 2015). Participants that were eligible to participate included those with a life expectancy between a month and a year and were taking a statin for at least three months for primary and secondary prevention of cardiovascular events (Kutner et al., 2015). The study reported that survival 60-days after the intervention did not differ significantly between the groups and suggested that there is no immediate or short-term harm (Kutner et al., 2015). With these results, it appears that it is safe to stop statin therapy when there is high risk for death with the next six to 12 months (Kutner et al., 2015). Kutner et al. (2015) reported that it is possible that when discontinuing statins, this will decrease adverse effects and ultimately decrease medications that may have been needed to treat the possible adverse effects.

A study that was conducted by Curtin et al. (2020) found that there was no statistically significant difference between the intervention and control groups on mortality. The intervention consisted of applying STOPPFrail protocol to the medication regimens of older adults with limited life expectancy within two hospitals in Ireland (Curtin et al., 2020). Measurement of the intervention effect on patient health outcomes such as mortality was difficult to determine due to the small sample size (Curtin et al., 2020). A study by LeBlanc et al (2015) reported that using a GP-GP algorithm resulted in medication reduction and a global improvement in health. Mortality rate was reduced after one year follow up with a 21% death rate in the intervention group compared to 45% death rate in the control group (LeBlanc et al., 2015). It is important to note that this study's participants were community dwelling adults with a mean age over 80 years old and those with LLE were excluded (LeBlanc et al., 2015). In a systematic review completed by Shestha et al. (2020), two random controlled trials (RCTs) and a quasi-experimental study reported on mortality and/or survival. Shrestha et al. (2020) discussed that the evidence within the literature on the effects of deprescribing on mortality is conflicting. The overall reduction in the percentage of mortality was found in the residential aged care facility and hospitals but there was no significant difference between intervention group and control group assessed at 6 and 12 months after the intervention (Shrestha et al., 2020). Shrestha et al. (2020) suggested that deprescribing is safe and does not quicken death in patients at the end of life care (Shrestha et al., 2020).

***Cost***

Many studies have analyzed costs and shown that reducing polypharmacy lessens the burden on healthcare costs (Lindsay et al., 2014; Shrestha et al., 2020). In a study conducted by Kutner et al. (2015), a cost savings with the discontinuation of the statin was found to be $3.37

per day per patient and $716 per patient during the course of the study. In another study, the mean change of monthly medication costs at the 3-month follow up after deprescribing was $74.97 in the intervention group compared to $13.22 in the control group (Curtin et al., 2020). Within a systematic review of outcomes after deprescribing at the end of life, Shrestha et al. (2020) reported in a pre-experimental pre-post study where there was an overall cost reduction and predicted healthcare costs could be reduced by $4,2827.27 per person.

***Clinical Outcomes***

The primary outcome measure of this review was to examine the effect of deprescribing on quality of life. However, many of the studies included in this review measured other clinical outcomes. Three randomized controlled trials and a systematic review reported on other health outcomes besides quality of life, mortality, and costs. Most studies found no differences in clinical outcomes. The clinical outcomes that were measured after deprescribing intervention included unscheduled hospital presentations, number of falls, medication adherence, performance status, symptoms, sleep quality, bowel function, cognitive function, physical function, and general health, performance between the intervention and control groups. Only the systematic review by Shrestha et al. (2020) identified two studies that reported an impact on clinical outcomes. A randomized controlled study reported a reduction in the number of falls at 12 months in the intervention group but not in the control group (Shrestha et al., 2020). In another randomized controlled study that examined clinical outcomes after deprescribing as the intervention reported no significant difference in the sleep quality, bowel function, cognitive function, physical function, and general health, performance between the intervention and control groups however although not the results were not significant there was an improvement in sleep quality and bowel function noted (Shrestha et al., 2020).

All three randomized controlled studies measured clinical outcomes as secondary outcomes. Curtin et al., (2020) applied the STOPPFrail protocol to medication regimens in older adults with frailty and examined outcomes including unscheduled hospital presentations and falls. The study detected no impact on these secondary outcomes (Curtin et al., 2020). The limitations of the study were that the trial was most likely underpowered to detect the differences of outcomes (Curtin et al., 2020). Parker et al. (2019) examined medication adherence as a clinical outcome and also found no detectable impact of the intervention on medication adherence. It should be noted that the adherence was high at baseline which supports previous studies results reporting that in older adults, medication adherence is high (Parker et al., 2019). Curtin et al. (2020) and Shrestha et al (2020) recommended a larger trial be conducted with greater statistical capabilities to determine clinical outcomes of deprescribing interventions within patients at end of life

**Quality of Life.** Many of the articles reviewed hypothesized that by reducing the burden of polypharmacy at end of life, it would lead to reductions in adverse drug events, cost and potentially improve QOL (LeBlanc et al., 2015). Within the literature reviewed, there were varying results of deprescribing on QOL and a variety of tools used to measure QOL. For example, in the US Palliative Care Research Cooperative Group that promoted the unnecessary statin use in the last year of life assessed QOL using the McGill QOL. The McGill QOL instrument is a questionnaire that reflects a single-item overall QOL score and subscale scores (Kutner et al., 2015). Higher scores indicate better QOL and range from 0 to 10 (Kutner et al., 2015). The total McGill QOL was higher in the statin discontinuation group, however the single question addressing overall QOL showed no significant difference between the intervention group discontinuing stating therapy and control group (Kutner et al., 2015). Kutner et al. (2015)

concluded that for patients seeking to reduce pill burden and comfort goals, physicians may promote the discontinuation of statins without affecting survival or QOL. In a study conducted by Curtin et al. (2020), QOL was measured using two different assessment tools: Quality of Life in Alzheimer's dementia (QUALIDEM), an instrument completed by the healthcare team and assesses QOL across all domains for patients at all stages of dementia and the Index of Capability for Older Adults (ICECAP-O), a questionnaire that is a broad measure of QOL covering five capabilities (attachment, security, role, enjoyment, and control). The study found that QOL deteriorated significantly in the intervention group that received a deprescribing method using the STOPPFrail criteria and control group at both the baseline and 3-monthfollow up but the difference was not statistically significant within scores (Curtin et al., 2020). A randomized controlled trial published by Parker et al. (2019) used the STOPP/START criteria for deprescribing medications in elderly patients with chronic kidney disease (CKD) to detect inappropriate medications after 6 months follow-up and used the 12 item Short-Form Health Survey to assess health-related quality of life (HRQoL). The 12-item Short-Form Health Survey is self-administered and is validated for use in multiple patient groups including CKD patients to assess the physical and mental health status of patients (Parker et al., 2019). The findings revealed that there was no significant impact on HRQoL scores between the intervention and control groups (Parker et al., 2019). The findings of HRQoL scores within this study were low and is consistent with those found in other patients with CKD (Parker et al., 2019).

In a systematic review completed by Shrestha et al. (2020), the findings revealed that deprescribing had the potential for mortality reduction and cost savings but the impact on QOL and falls were not consistent. A measure that matters most to older patients with LLI and LLE and to their family members is QOL. This systematic review included two RCTs. In one study

using the Quality of Life in Alzheimer's Disease (QOLAD) tool with a high percentage of participants with dementia, the QOL was shown to be reduced. In the other study with a higher number of participants with cancer, the results of the McGill QOL questionnaire found that QOL improved.

## Strengths and Limitations of This Review

This literature review identified numerous articles on the incidence of polypharmacy, the effectiveness of deprescribing to lower drug burden, along with the secondary outcomes of deprescribing medications, however there were limited interventional studies that investigated QOL as the primary outcome when deprescribing medications at the end of life. This author searched numerous databases to include all different types of studies including systematic reviews which have higher level of evidence. The research included within this article has considerable heterogeneity in regard to the participant population and setting, deprescribing measurement tools utilized, and QOL measurement tools used within the studies.

This review was not without limitations. A limitation of this review was the inclusion/exclusion criteria. Due to the lack of interventional studies completed on assessing QOL, systematic reviews and an expert opinion were included. There is an abundance of research addressing deprescribing and the impact on QOL in older adults however terminal ill is an exclusion criterion in the majority of articles. There are few retrospective studies that are included within this review that may have allowed for overestimated quantities of medications because the patients that were experiencing a variety of unexpected complications and need additional treatment were included within those studies. Although it should be mentioned that if the study was completed in real time, there might have been an influence on the prescribing behaviors (Kierner et al., 2016).

## Gaps in Literature

The review of the literature included three interventional studies addressing clinical impact including QOL when deprescribing at end of life. There are systematic reviews that address clinical outcomes that either directly address patients with cancer or clinical outcomes within a variation of limiting life illnesses. The systematic reviews that were included encompassing a cancer diagnosis highlight the vulnerability of this population and the lack of descriptive studies on the impact of deprescribing at end of life including older adults but also for younger adults.

There are previous studies that have been conducted to evaluate the clinical impact of deprescribing (including QOL) of older adults, but patients with limited life expectancy are generally excluded. Hypothetically, these findings in older adults could be transferrable to patients at end of life, however this would be an untested and unvalidated assumption. Within these three interventional studies, the primary focus was not on the clinical outcomes; rather they were investigating the impact of deprescribing on polypharmacy or on potential inappropriate medications. More evidence is needed on the clinical impact of deprescribing and the effect on other areas including physical, cognitive, and psychosocial health status (Shrestha et al., 2020). In addition, the studies included for review within this manuscript contain a variety of instruments to measure QOL. It would be important to be consistent with the review to evaluate the validity, reliability and impact of one measurement tool or compare measurement tools for validity of data retrieved.

## Discussion

This literature search sought to explore polypharmacy and the impact that deprescribing has on QOL in older patients at the end of life. It was evident that polypharmacy exists in

patients nearing end of life and as death nears, the number of medications typically increase (LeBlanc et al., 2015; Lindsay et al., 2014; Kierner et al., 2016; Schenker et al., 2019; Shrestha et al., 2020). In randomized controlled settings, deprescribing interventions were carried out and there were significant reductions in potentially inappropriate prescriptions (Curtin et al., 2020; Shrestha et al., 2020). Additionally, the findings regarding the impact of deprescribing on QOL were inconsistent. There were limited studies addressing the topic and the studies that were identified did not have the clinical question as the primary outcome of the study. This made it challenging to answer the clinical question posed. Based on the three randomized control studies that were identified within the literature search, only one of them found that deprescribing was associated with a significant improvement of QOL whereas the other two studies found no significant change between groups. Within the systematic review by Shrestha et al. (2020), one of the studies found no significant improvement in QOL and the other study found a significant improvement on QOL. It should be noted that the study that found a significant improvement on QOL within the systematic review by Shrestha et al. (2020) was the study conducted by Kutner et al. (2015) which was a randomized controlled study that was included within this current review.

This is the first review of literature examining the effect of deprescribing on QOL at the end of life. A prior review of 12 studies conducted by Pruskowski et al (2019) investigated the impact of deprescribing on QOL and secondary outcomes including satisfaction with care and emergency department visits and hospitalizations on older adults and older persons with life limiting conditions were included. The results were similar in that there was a reduction on at least one medication deprescribed in ten of the studies and found no difference in QOL of two studies that measured this outcome (Pruskowski et al., 2019). The focus of this review is on

patients at the end of life because they experience a high medication burden with a limited life expectancy; medications administered should be given only if it improves QOL and symptom control (Lindsay et al., 2014).

There are possible explanations for the inconsistency observed in the studies with the effect of deprescribing on QOL. There were different QOL measurement tools that were used within the studies that may affected results as mentioned by Shrestha et al. (2020). Within each of the studies, participants were reported to be at the end of life, but they varied in medical conditions. Another consideration for a variation in results is the length of the study. The time length of the studies varied from three months to six months. The study that had a three-month follow up reported that the QOL dropped but it was not statistically significant (Curtin et al., 2020) whereas in a different with a six month follow up reported an increase in QOL. One could ponder that the reason for a drop may be due to withdrawal symptoms or the progression in the end of life. It is also uncertain if a patient's QOL would improve in a short time or if a longer duration is needed to see improvements. In the statin discontinuation trial where an increase in QOL was reported, the difference with this study compared to the others is that it was a specific medication that was discontinued (Kutner et al., 2015). The patient had agreed to have this medication removed and was there an increase in QOL reported based on their own decision. Lastly, another way to view the results that showed no significant change in QOL is that the removal of the medication did not harm the patient.

In addition to investigating polypharmacy and the impact of deprescribing on QOL, there were several other clinical outcomes investigated within the studies such as medication adherence, unscheduled hospital presentations, falls, monthly medication costs, and mortality. Although the findings associated with clinical outcomes varied, cost savings were reported. In

addition to clinical outcomes being investigated, a study included within this review examined the associations between polypharmacy, symptom burden, and QOL (Schenker et al., 2019). This study provides a link between polypharmacy and association with higher symptom burden and worse QOL for patients at the end of life (Schenker et al., 2019). This builds upon the growing body of research related to deprescribing and using this association when developing and evaluating deprescribing strategies could improve patient's outcomes (Schenker et al., 2019).

## Implications for future

### Clinical practice recommendations

Primary care providers working with patients at end of life should take personal responsibility to educate themselves on the targeted strategies to deprescribing and should include this intervention routinely with patients at end of life (Schenker et al., 2019). All discussions should be patient centered and include advance care planning in the process to avoid any misinterpretation of actions (Gardner, 2019). Although there is not a standard guideline for deprescribing at the end of life, there are many evidence-based guidelines available to assist with making these decisions for deprescribing (Schenker et al., 2019). Each medication should be reviewed and evaluated for the route, time of administration, adverse effects, drug-drug interactions, benefit to continuing medication, risk of deprescribing, and symptom management (Gardner, 2019). It is important for clinicians to have discussions on medication management promptly and repeatedly throughout the dying process making sure that the patient's preferences are included (Gardner, 2019).

### Recommendations for research

This literature review identified many opportunities for future research. Although polypharmacy is well reported in older adult patients, the outcomes and effects are less clear for

patients at end of life (LeBlanc et al., 2015). In addition, a standardized measure and definition of polypharmacy that are appropriate in this unique population, for example patients with advanced cancer (LeBlanc et al., 2015) require further exploration. There were limited interventional studies that examined the impact of deprescribing on QOL and the studies that were completed investigated QOL as a secondary outcome rather than the primary outcome. Further studies could focus on examining the impact on QOL when using a deprescribing tool (Parker et al., 2019). Curtin et al. (2020) suggested that a larger scale multicenter trial with higher statistical power is necessary to provide evidence for clinicians that deprescribing medications can be achieved without jeopardizing health outcomes. The study of the discontinuation of a statin by Kutner et al. (2015) suggested that QOL could be improved. Additional research is needed in identifying other medications in this population that they would benefit from discontinuation (Kutner et al., 2015). A consensus in many of the articles was the need for tested and implementable strategies to reduce polypharmacy for individual medications and cumulative effects of medications prescribed (LeBlanc et al., 2015; Schenker et al., 2019; Kierner et al., 2016). Another area of research identified was effective ways to communicate the goals of reducing polypharmacy to patients, families, and even providers (LeBlanc et al., 2015). Providing education to the patient on reasons for medications that should be discontinued will increase their understanding and increase the patient's participation in making decisions (LeBlanc et al., 2015).

**Education recommendations**

Provider's experience with addressing end of life care can vary and some avoid engaging in these conversations surrounding discontinuing medications (Gardner, 2019). Each provider may vary in their assessment of the importance and inappropriateness of medications (Curtin et

al., 2020). In addition, there is fear for negative consequences of deprescribing such as "symptom relapse, clinical deterioration, litigation, or increased workload" (Curtin et al., 2020, p. 763). Many providers advocate to reduce drug burden at end of life but are unsure of the medications to discontinue, when to discontinue, and uncertain if it is safe to discontinue (Kutner et al., 2015). There is a great deal of research on when to start medication but there is a lack of effort towards when to discontinue especially at end of life (LeBlanc et al., 2015). Education and training programs can incorporate deprescribing into their curriculum standards for providers and continuing education should be provided on an ongoing basis. As highlighted in the literature, guidelines and evidence on the benefits to deprescribing would motivate primary care providers and patients to routinely make those shared decisions surrounding the discontinuation of medications.

**Recommendations for policy**

Many clinicians are hesitant to deprescribe for various reasons. Clinicians may be reluctant to discontinue a medication if the patient is seeing a specialist that they believe are overseeing the patient's medications (Curtin et al., 2020). Curtin et al. (2020) highlighted a barrier to deprescribing is time constraints. Providers may also be hesitant to discontinue medications because their actions may be misinterpreted from the patient or family feeling that they are giving up on the patient (Gardner, 2019). A systems approach to deprescribing could address many of these reasons that prescribers may forgo deprescribing at end of life until it is immediate when the patient is no longer able to swallow. There is a culture within our society that considers medications to be valuable. There is also an ideation that if a patient has been on a medication for a long time, they question why they would stop now. Deprescribing plans should be discussed with a patient when prescribing the medication. A multidisciplinary approach to

deprescribing interventions will lessen the burden on the primary care provider and also provide a collaboration between healthcare professionals. These professionals include nurses, pharmacists, primary care providers, and specialists. Another incentive to deprescribing is to add reimbursement, therefore the primary care provider could schedule a visit to complete deprescribing interventions.

## Conclusion

Overall, there is a lack of research on examining the direct impact of deprescribing on quality of life in older adults at the end of life. Although the deprescribing interventions resulted in improvement of medication reduction, the impact on improving quality of life was not clear. This was consistent with other clinical outcomes not found to be statistically significant; with the exception of cost savings. These results do not undermine the need for discontinuing inappropriate medications at the end of life. Primary care providers are involved with patient's advanced care planning at end of life and require evidence based deprescribing interventions that consider preventative and symptom control to identify potentially inappropriate medications. In addition, continued progress in education, practice, policy, and research on deprescribing at the end of life will ultimately impact the QOL for this population.

## References

Curtin, D., Jennings, E., Daunt, R., Curtin, S., Randles, M., Gallagher, P., & O'Mahony, D. (2020). Deprescribing in older people approaching end of life: A randomized controlled trial using STOPPFrail criteria. *Journal of the American Geriatrics Society*, *68*(4), 762–769. https://doi-org.ezproxy.mnsu.edu/10.1111/jgs.16278.

Gardner, E. (2019). Deprescribing in end-of-life care. *British Journal of Community Nursing, 24(*10), 474–477. https://doi-org.ezproxy.mnsu.edu/10.12968/bjcn.2019.24.10.474.

LeBlanc, T. W., McNeil, M. J., Kamal, A. H., Currow, D. C., & Abernethy, A. P. (2015). Polypharmacy in patients with advanced cancer and the role of medication discontinuation. *Lancet Oncology, 16*(7), e333-e341. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1016/S1470-2045(15)00080-7.

Kierner, K., Weixler, D., Masel, E., Gartner, V., Watzke, H., Kierner, K. A., Masel, E. K., & Watzke, H. H. (2016). Polypharmacy in the terminal stage of cancer. *Supportive Care in Cancer, 24*(5), 2067–2074. https://doi-org.ezproxy.mnsu.edu/10.1007/s00520-015-3007-z.

Kutner, J., Blatchford, P., Taylor, D., Ritchie, C., Bull, J., Fairclough, D., Hanson, L., LeBlanc, T., Samsa, G., Wolf, S., Aziz, N., Currow, D., Ferrell, B., Wagner-Johnston, N., Zafar, S., Cleary, J., Dev, S., Goode, P., Kamal, A., … Abernethy, A. (2015). Safety and benefit of discontinuing statin therapy in the setting of advanced, life-limiting illness: A randomized clinical trial. *JAMA Internal Medicine, 175*(5), 691–700. https://doi.org/10.1001/jamainternmed.2015.0289.

Lindsay, J., Dooley, M., Martin, J., Fay, M., Kearney, A., & Barras, M. (2014). Reducing potentially inappropriate medications in palliative cancer patients: Evidence to support deprescribing approaches. *Supportive Care in Cancer, 22*(4), 1113-9. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1007/s00520-013-2098-7.

Parker, K., Bull-Engelstad, I., Benth, J., Aasebø, W., von der Lippe, N., Reier-Nilsen, M., Os, I., & Stavem, K. (2019). Effectiveness of using STOPP/START criteria to identify potentially inappropriate medication in people aged ≥ 65 years with chronic kidney disease: a randomized clinical trial. *European Journal of Clinical Pharmacology, 75*(11), 1503–1511. https://doi.org/10.1007/s00228-019-02727-9.

Pruskowski, J., Springer, S., Thorpe, C., Klein-Fedyshin, M., & Handler, S. (2019). Does deprescribing improve quality of life? A systematic review of the literature. *Drugs & Aging, 36*(12), 1097–1110. https://doi.org/10.1007/s40266-019-00717-1.

Schenker, Y., Kavalieratos, D., Resick, J., Park, S. Y., Jeong, K., Pruskowski, J., Abernethy, A., & Kutner, J. S. (2019). Associations between polypharmacy, symptom burden, and quality of life in patients with advanced, life-limiting illness. *JGIM: Journal of General Internal Medicine, 34*(4), 559–566. https://doi-org.ezproxy.mnsu.edu/10.1007/s11606-019-04837-7.

Shrestha, S., Poudel, A., Steadman, K., & Nissen, L. (2020). Outcomes of deprescribing interventions in older patients with life-limiting illness and limited life expectancy: A systematic review. *British Journal of Clinical Pharmacology, 86*(10), 1931–1945. https://doi-org.ezproxy.mnsu.edu/10.1111/bcp.14113.

# Appendix

## Table 1

*Database Search Description*

| Database (or Search Engine) | Restrictions Added to Search | Dates Included in Database | General Subjects Covered by Database |
|---|---|---|---|
| Academic Search Premier | Full Text; Scholarly (Peer Reviewed); English Language | 2010-2020 | The database offers information in nearly every area of academic study, including arts, biology, chemistry, computer sciences, ethnic studies, engineering, language and linguistics, literature, medical sciences, philosophy, physics, psychology, religion, social sciences, and more. |
| CINAHL | Full Text; English Language; Abstract Available; Peer Reviewed | 2010-2020 | Provides full text with comprehensive indexing of nursing and allied health journals including publications in nursing and allied health, consumer health, alternative/complementary medicine, biomedicine, and health sciences librarianship |
| MEDLINE | Full Text; English Language | 2010-2020 | Produced by the U.S. National Library of Medicine and is widely recognized as the premier source for citations, indexing, and abstracts of biomedical literature. MEDLINE provides information relevant to the fields of medicine, nursing, and dentistry, and it also covers areas of life sciences, behavioral sciences, chemical sciences, and bioengineering that are related to health and biomedicine. |
| JSTOR | Full Text | 2010-2020 | Journals in the social sciences, arts and humanities and life sciences. Listed under philosophy database |
| Nursing and Allied Health Database | Full Text; Peer Reviewed; English Language | 2010-2020 | Provides users with reliable healthcare information covering nursing, nutrition, oncology, pediatric care, pharmacology, public health, allied health, alternative and complementary medicine, and much more. |

**Table 2**

*Data Abstraction Process*

| **Date of Search** | **Key Words** | **Results in Academic Search Premier** | **Results in CINAHL** | **Results in JSTOR** | **Results in Medline** | **Results in Nursing Allied and Health** |
|---|---|---|---|---|---|---|
| 11/13/20 | "deprescrib*" or "polypharmacy" or "reducing medication" AND “quality of life” or “QOL" AND "end of life" or "palliative" or "hospice" or “life limiting disease” | **14** | **10** | **4** | 10 | 809 |
| | "deprescrib*" or "polypharmacy" or "reducing medication" AND “quality of life” or “QOL" AND "end of life" or "palliative" or "hospice" or “life limiting disease” -Abstract | - | - | - | - | **11** |
| | "deprescrib*" or "polypharmacy" or "reducing medication" AND “quality of life” or “QOL" AND "end of life" or "palliative" or "hospice" or “life limiting disease” -Subject | - | - | **-** | **3** | - |
| | Bibliography | **2** | - | **-** | **-** | - |

***BOLD** = articles reviewed for match with systematic review inclusion criteria

**Table 3**

*Characteristics of Literature Included and Excluded*

| **Reference** (Include the full reference here) | **Included or Excluded and Document** | **Rationale** |
|---|---|---|
| Alexa, I. D., & Pîslaru, A. I. (2017). When is time to consider palliation in the general therapeutic plan in senior patients? Paliatia: Journal of Palliative Care, 10(3), 8. | Excluded | Case study on when to consider palliative care |
| Briscoe, J., & Casarett, D. (2018). Medical Marijuana Use in Older Adults. Journal of the American Geriatrics Society, 66(5), 859–863. https://doi-org.ezproxy.mnsu.edu/10.1111/jgs.15346 | Excluded | Not pertaining to subject, instead discusses medical marijuana |
| Chadwick, S. (2019). P-135 Evaluation of tolerability and deprescribing of anti-fibrotics in pulmonary fibrosis (IPF) patients. BMJ Supportive & Palliative Care, 9 doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1136/bmjspcare-2019-HUKNC.158 | Excluded | The aim of study was to collect data on proportion of patients in hospice with cystic fibrosis taking antifibrotics and the side effects that would be described and obstacles to deprescribing |
| Cortis, L. J. (2017). A qualitative study to describe patient-specific factors that relate to clinical need for and potential to benefit from a medication management service in palliative care. Journal of Pharmacy Practice & Research, 47(1), 34–40. https://doi-org.ezproxy.mnsu.edu/10.1002/jppr.1147 | Excluded | Discusses types of palliative care patients benefit from medication management services |
| Curtin, D., Jennings, E., Daunt, R., Curtin, S., Randles, M., Gallagher, P., & O'Mahony, D. (2020). Deprescribing in Older People Approaching End of Life: A Randomized Controlled Trial Using STOPPFrail Criteria. Journal of the American Geriatrics Society, 68(4), 762–769. https://doi-org.ezproxy.mnsu.edu/10.1111/jgs.16278 | Included | Examined the effect of using a deprescribing tool to medication regimen for older adults |
| Development of a health-system palliative care clinical pharmacist. (2017). American Journal of Health-System Pharmacy, 74(1), e6–e8. https://doi-org.ezproxy.mnsu.edu/10.2146/ajhp160055 | Excluded | Discusses the pharmacists role in improving patient outcomes with medication use deprescribing |
| Economos, G., Lovell, N., Johnston, A., & Higginson, I. J. (2020). What is the evidence for mirtazapine in treating cancer-related symptomatology? A systematic review. Supportive Care in Cancer, 28(4), 1597–1606. https://doi-org.ezproxy.mnsu.edu/10.1007/s00520-019-05229-7 | Excluded | Article revolves around mirtazapine's safety and effectiveness of treating cancer symptoms |
| Frechen, S., Zoeller, A., Ruberg, K., Voltz, R., & Gaertner, J. (2012). Drug interactions in dying patients: An international journal of medical toxicology and drug experience. Drug Safety, 35(9), 745-758. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.2165/11631280-000000000-00000 | Excluded | Focused on assessing drug interactions at end of life without addressing health related outcomes or quality of life |
| Gardner, E. (2019). Deprescribing in end-of-life care. British Journal of Community Nursing, 24(10), 474–477. https://doi-org.ezproxy.mnsu.edu/10.12968/bjcn.2019.24.10.474 | Included | Reviews medications that should be stopped at the end of life |
| Garfinkel, D. (2018). Poly-de-prescribing to treat polypharmacy: Efficacy and safety. Therapeutic Advances in Drug Safety, 9(1), 25-43. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1177/2042098617736192 | Excluded | Describes the efficacy and safety of deprescribing in older adults and excluded patients with limited life expectancy |

| **Reference**<br>(Include the full reference here) | **Included or Excluded and Document** | **Rationale** |
|---|---|---|
| Garfinkel, D. (2019). Poly-de-prescribing vs polypharmacy - the weapon to fight an iatrogenic epidemic: An overview. European Journal of Geriatrics and Gerontology, 1(1), 1-10. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.4274/ejgg.galenos.2019.14 | Excluded | Review on deprescribing, discussing factors of barriers and enabling its implementation, attitudes of patients and providers and recommendations from the international group for deprescribing and polypharmacy |
| Kierner, K., Weixler, D., Masel, E., Gartner, V., Watzke, H., Kierner, K. A., Masel, E. K., & Watzke, H. H. (2016). Polypharmacy in the terminal stage of cancer. Supportive Care in Cancer, 24(5), 2067–2074. https://doi-org.ezproxy.mnsu.edu/10.1007/s00520-015-3007-z | Included | Analyzes the number of patients receiving polypharmacy at the end of life and analyzes the difference between the medications |
| Kolovetsios, M., & Yones, H. (2018). P-206 The role and impact of pharmacists within a hospice's care home support team. BMJ Supportive & Palliative Care, 8 doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1136/bmjspcare-2018-hospiceabs.231 | Excluded | Aims at pharmacists completing medication reviews using specific guidelines |
| Kutner, J., Blatchford, P., Taylor, D., Ritchie, C., Bull, J., Fairclough, D., Hanson, L., LeBlanc, T., Samsa, G., Wolf, S., Aziz, N., Currow, D., Ferrell, B., Wagner-Johnston, N., Zafar, S., Cleary, J., Dev, S., Goode, P., Kamal, A., … Abernethy, A. (2015). Safety and Benefit of Discontinuing Statin Therapy in the Setting of Advanced, Life-Limiting Illness: A Randomized Clinical Trial. JAMA Internal Medicine, 175(5), 691–700. https://doi.org/10.1001/jamainternmed.2015.0289 | Included | Evaluates the safety, clinical and cost impact of discontinuing statin medications for patients in the palliative care setting |
| LeBlanc, T. W., McNeil, M. J., Kamal, A. H., Currow, D. C., & Abernethy, A. P. (2015). Polypharmacy in patients with advanced cancer and the role of medication discontinuation. Lancet Oncology, 16(7), e333-e341. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1016/S1470-2045(15)00080-7 | Included | Reviews existing literature on polypharmacy on the end of life with cancer of approaches to deprescribing and the benefits of deprescribing |
| Lindsay, J., Dooley, M., Martin, J., Fay, M., Kearney, A., & Barras, M. (2014). Reducing potentially inappropriate medications in palliative cancer patients: Evidence to support deprescribing approaches. Supportive Care in Cancer, 22(4), 1113-9. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1007/s00520-013-2098-7 | Included | Analyzes the most current evidence on outcomes of PID and methods used to identifying and deprescribing PIDs |
| Marin, H., Mayo, P., Thai, V., Dersch-Mills, D., Ling, S., Folkman, F., & Chambers, C. (2020). The impact of palliative care consults on deprescribing in palliative cancer patients. Supportive Care in Cancer, 28(9), 4107–4113. https://doi-org.ezproxy.mnsu.edu/10.1007/s00520-019-05234-w | Excluded | Compares inappropriate medications prior to the palliative care consult vs after the PCC; Examines association of inappropriate medications and goals of care |
| McNulty, J. P., & Muller, G. (2014). Compounded drugs of value in outpatient hospice and palliative care practice. International Journal of Pharmaceutical Compounding, 18(3), 190-200. Retrieved from http://ezproxy.mnsu.edu/login?url=https://www-proquest-com.ezproxy.mnsu.edu/docview/1611612423?accountid=12259 | Excluded | Discusses common compounds used in outpatient hospice and palliative care to treat common conditions |
| Parekh, N., Good, C. B., Neilson, L., Shrank, W. H., & Schenker, Y. (2019). Deprescribing in Advanced Illness: | Excluded | Addresses barrier for deprescribing and proposes action steps |

| **Reference**<br>(Include the full reference here) | **Included or Excluded and Document** | **Rationale** |
|---|---|---|
| Aligning Patient, Clinician, and Health Plan Goals. JGIM: Journal of General Internal Medicine, 34(4), 631–633. https://doi-org.ezproxy.mnsu.edu/10.1007/s11606-019-04845-7 | | |
| Parker, K., Bull-Engelstad, I., Benth, J., Aasebø, W., von der Lippe, N., Reier-Nilsen, M., Os, I., & Stavem, K. (2019). Effectiveness of using STOPP/START criteria to identify potentially inappropriate medication in people aged ≥ 65 years with chronic kidney disease: a randomized clinical trial. European Journal of Clinical Pharmacology, 75(11), 1503–1511. https://doi.org/10.1007/s00228-019-02727-9 | Included | Identified potentially inappropriate prescriptions and potential prescribing omissions using a deprescribing tool and determined the effect on medication adherence and qol |
| Paque, K., Elseviers, M., Vander Stichele, R., Pardon, K., Vinkeroye, C., Deliens, L., Christiaens, T., & Dilles, T. (2019). Balancing medication use in nursing home residents with life-limiting disease. European Journal of Clinical Pharmacology, 75(7), 969–977. https://doi-org.ezproxy.mnsu.edu/10.1007/s00228-019-02649-6 | Excluded | Study that examines deprescription and prevalence in a nursing home |
| Parsons C, Hughes CM, Passmore AP, & Lapane KL. (2010). Withholding, discontinuing and withdrawing medications in dementia patients at the end of life: a neglected problem in the disadvantaged dying? Drugs & Aging, 27(6), 435–449. https://doi-org.ezproxy.mnsu.edu/10.2165/11536760-000000000-00000 | Excluded | Addresses research surrounding end of life patient care of patients and the discontinuation of medications by physicians |
| Prabhu, A., Sutherland, A., Bradley, V., & Pegrum, H. (2017). P-99 the use of an oncological palliative deprescribing guideline to aid rationalising medications in patients in the last six months of life. BMJ Supportive & Palliative Care, 7 doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1136/bmjspcare-2017-00133.98 | Excluded | Study aimed at reviewing the use of a deprescribing tool available in the EHR |
| Schenker, Y., Kavalieratos, D., Resick, J., Park, S. Y., Jeong, K., Pruskowski, J., Abernethy, A., & Kutner, J. S. (2019). Associations Between Polypharmacy, Symptom Burden, and Quality of Life in Patients with Advanced, Life-Limiting Illness. JGIM: Journal of General Internal Medicine, 34(4), 559–566. https://doi-org.ezproxy.mnsu.edu/10.1007/s11606-019-04837-7 | Included | Synthesis of evidence in adults with advanced illness and the impact that more medications has on symptom burden and quality of life |
| Shrestha, S., Poudel, A., Steadman, K., & Nissen, L. (2020). Outcomes of deprescribing interventions in older patients with life-limiting illness and limited life expectancy: A systematic review. British Journal of Clinical Pharmacology, 86(10), 1931–1945. https://doi-org.ezproxy.mnsu.edu/10.1111/bcp.14113 | Included | Investigates the outcomes of deprescribing in the older patients with limited life expectancy |
| Takahashi, M., Maeda, K., & Wakabayashi, H. (2018). Prevalence of sarcopenia and association with oral health-related quality of life and oral health status in older dental clinic outpatients. Geriatrics & Gerontology International, 18(6), 915–921. https://doi-org.ezproxy.mnsu.edu/10.1111/ggi.13279 | Exclude | Discussion of oral health related quality of life and sarcopenia |
| Thillainadesan J, Gnjidic D, Green S, Hilmer SN. Impact of Deprescribing Interventions in Older Hospitalised Patients on Prescribing and Clinical Outcomes: A Systematic Review of | Excluded | Examine the efficacy of deprescribing intervention in reducing PIMs and clinical |

| **Reference**<br>(Include the full reference here) | **Included or Excluded and Document** | **Rationale** |
|---|---|---|
| Randomised Trials. Drugs Aging. 2018 Apr;35(4):303-319. doi: 10.1007/s40266-018-0536-4. PMID: 29541966. | | health outcomes; Participants did not fit in the categories of end of life |
| Todd, A., Holmes, H., Pearson, S., Hughes, C., Andrew, I., Baker, L., & Husband, A. (2016). 'I don't think I'd be frightened if the statins went': A phenomenological qualitative study exploring medicines use in palliative care patients, carers and healthcare professionals. BMC Palliative Care, 15, 13. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1186/s12904-016-0086-7 | Excluded | Patient, caregiver, and healthcare provider's experience with medication use with life limiting illness |
| Walsh, S., Sills, E., & Free, A. (2018). 86 the burden of polypharmacy in the hospice in-patient setting. BMJ Supportive & Palliative Care, 8 doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1136/bmjspcare-2018-ASPabstracts.113 | Excluded | Article aims at quantifying number of patients with polypharmacy in hospice setting and consider adding a describing tool |
| Wilcock, A., & Charlesworth, S. (2018). Palliativedrugs.com. BMJ Supportive & Palliative Care, 8(1), 21. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1136/bmjspcare-2018-001501 | Excluded | Article provides direct reference on guidelines on prescribing antiepileptic drugs in palliative care |
| Zueger, P. M., Holmes, H. M., Calip, G. S., Qato, D. M., Pickard, A. S., & Lee, T. A. (2019). Older Medicare Beneficiaries Frequently Continue Medications with Limited Benefit Following Hospice Admission. JGIM: Journal of General Internal Medicine, 34(10), 2029–2037. https://doi-org.ezproxy.mnsu.edu/10.1007/s11606-019-05152-x | Excluded | Evaluating the frequency and factors for continuation of medications that have limited benefit after being admitted to hospice |

## Table 4

*Literature Review Table of All Studies Included*

| **Citation** (Include the citation of all studies that met inclusion criteria from Table 3 above) | **Study Purpose** | **Pop (N)/ Sample Size (n) /Setting(s)** | **Design/ Level of Evidence** (Melnyk & Fineout-Overholt, 2015) | **Variables/ Instruments** | **Intervention** | **Findings** | **Implications** |
|---|---|---|---|---|---|---|---|
| Curtin, D., Jennings, E., Daunt, R., Curtin, S., Randles, M., Gallagher, P., & O'Mahony, D. (2020). Deprescribing in Older People Approaching End of Life: A Randomized Controlled Trial Using STOPPFrail Criteria. Journal of the American Geriatrics Society, 68(4), 762–769. https://doi-org.ezproxy.mnsu.edu/10.1111/jgs.16278 | Examine the effect of the application of a deprescribing tool to medication regimens of older adults with limited life expectancy | N=130, adults 75+yo with and limited life expectancy polypharmacy /Two hospitals in Ireland | Randomized Control Trial/Level 2 | Intervention group-65; Control group=65/STOPP Frail-guided deprescribing tool | Measure of the primary outcome including the change in number of medications at 3 months and secondary outcomes including unscheduled hospital presentations, falls, quality of life, monthly medication costs, and mortality | -Application of STOPPFrail criteria resulted in significant reduction in polypharmacy and monthly medication costs<br><br>-No significant differences were noted in the health-related outcomes including quality of life although as noted that the study was underpowered to detect significant changes in these outcomes | -Strength of the study included patients with dementia which this population group is typically excluded<br>-Larger scale trial with greater statistical abilities is required to provide evidence for clinicians that using the STOPPFrail to deprescribe medications can be achieved without compromising clinical outcomes |
| Gardner, E. (2019). Deprescribing in end-of-life care. British Journal of Community Nursing, 24(10), 474–477. https://doi-org.ezproxy.mnsu.edu/10.12968/bjcn.2019.24.10.474 | The aim is to address polypharmacy within end-of-life care | N/a | Expert Opinion/Level 5 | N/a | N/a | - Within end-of-life medication management, each drug needs to be divided into nonessential and essential groups<br><br>-Initiation of medicines is guideline-driven, but guidance regarding when it may be safe or appropriate to discontinue treatment is less prevalent | - Nurse medical prescribers need to carefully consider the therapeutic benefits of continuing medication as well as the risks of deprescribing at the end of life.<br><br>- The aim would be to improve patients' quality of life by reducing their drug burden<br><br>-It is imperative that discussions about medication management occur promptly and throughout the dying process, involving the patient at all times |
| Kierner, K., Weixler, D., Masel, E., Gartner, V., Watzke, H., Kierner, K. A., Masel, E. K., & Watzke, H. H. (2016). Polypharmacy in the terminal stage of cancer. Supportive Care in Cancer, 24(5), 2067–2074. | Determine number of patients receiving polypharmacy at the end of life with | Patients that had passed away with advanced cancer between January 2011- | Retrospective, longitudinal, single cohort study/Level 4 | -Sociodemographic, disease-related, and medical variables were retrieved | -Sociodemographic and medications were collected at each predefined time period<br><br>-Medication prescriptions were | -9 days prior to death, polypharmacy was registered in 95% of patients<br><br>-Prescriptions for 11 different medications/day | -First detailed analysis of the quantity composition and course of medical therapy in terminal ill patients<br>-Further projects should be focused on drug-drug interactions and impact |

| **Citation** (Include the citation of all studies that met inclusion criteria from Table 3 above) | **Study Purpose** | **Pop (N)/ Sample Size (n) /Setting(s)** | **Design/ Level of Evidence** (Melnyk & Fineout-Overholt, 2015) | **Variables/ Instruments** | **Intervention** | **Findings** | **Implications** |
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| https://doi-org.ezproxy.mnsu.edu/10.1007/s00520-015-3007-z | advanced cancer and look at the difference of medications between hospice and palliative care wards | March 2013/N=100 patient charts/Two specialized wards, hospice and palliative care at University Hospital of Vienna | | -Drugs were categorized into classes<br><br>-Drugs that were prescribed for the day of assessment along were considered acute medication whereas drugs prescribed earlier than 1 day before or after were considered chronic medications<br><br>-Polypharmacy was defined as 5 or more drugs/day | determined at four predefined time points 9, 6, 3, 0 days before death | -The number dropped significantly on the last day as many 61% of patients were still taking more than 4 drugs<br><br>-No difference was noted between the oncology and palliative ward<br><br>-polypharmacy was dependent on the patients' ECOG performance status, type of ward, number of day before death and age | of polypharmacy on the patient's quality of life<br>-Recommended for more controlled trials with structured programs will be needed to reduce quantity of medications and generate scientific evidence on discontinuation of medication in terminally ill cancer patients |
| Kutner, J., Blatchford, P., Taylor, D., Ritchie, C., Bull, J., Fairclough, D., Hanson, L., LeBlanc, T., Samsa, G., Wolf, S., Aziz, N., Currow, D., Ferrell, B., Wagner-Johnston, N., Zafar, S., Cleary, J., Dev, S., Goode, P., Kamal, A., … Abernethy, A. (2015). Safety and Benefit of Discontinuing Statin Therapy in the Setting of Advanced, Life-Limiting Illness: A Randomized Clinical Trial. JAMA Internal Medicine, 175(5), 691–700. https://doi.org/10.1001/jamainternmed.2015.0289 | Evaluate safety, clinical, and cost impact of discontinuing statin medications in palliative care setting | Limited life expectancy in adults older than 18 years of age/N=381/Palliative care | Randomized control trial/Level 2 | -n=189 intervention; n=192 control<br><br>-Primary outcome: Death within 60 days<br><br>Secondary outcomes: survival, cardiovascular events, performance status, qol, symptoms, number of nonstatin | -Up to 12 months<br><br>-Discontinuation of stain on the basis of randomization in coordination of clinical research coordinator with physician or primary care provider | -Proportion of patients that died within 60 days did not have a significant difference between the groups<br><br>-QOL was better in the interventional group<br><br>-13 participants in intervention group and 11 participants in the control group experienced cardiovascular event<br><br>-Cost savings $3.37 per day and $716 per patient | -Evidence that deprescribing statins do not affect survival when prescribed for primary or secondary prevention of cardiovascular disease<br>-Cost savings<br>-May improve QOL<br>-Merits patient and provider discussion to continue or stop therapy with statin medications<br>-Future research to explore use of other medications in populations with limited life expectamcy |

| **Citation** (Include the citation of all studies that met inclusion criteria from Table 3 above) | **Study Purpose** | **Pop (N)/ Sample Size (n) /Setting(s)** | **Design/ Level of Evidence** (Melnyk & Fineout-Overholt, 2015) | **Variables/ Instruments** | **Intervention** | **Findings** | **Implications** |
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| | | | | medications, and cost savings<br><br>-McGill to measure QOL<br><br>-Edmonton Symptom Assessment System Scale to measure symptom | | | |
| LeBlanc, T. W., McNeil, M. J., Kamal, A. H., Currow, D. C., & Abernethy, A. P. (2015). Polypharmacy in patients with advanced cancer and the role of medication discontinuation. Lancet Oncology, 16(7), e333-e341. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1016/S1470-2045(15)00080-7 | Examines the existing literature on polypharmacy in advanced cancer and end-of-life settings by reviewing evidence-based approaches to reduce polypharmacy, and outlining the potential benefits of decreasing the number of drugs | N=22 articles addressing polypharmacy frequency, the amount of inappropriate medications and symptom burden, and interventions to reduce polypharmacy | Systematic Review/Level I | n/a | n/a | -Polypharmacy is prevalent in the advanced cancer population with mean of 3-9.1 prescribed drugs and older patients often had more prescribed drugs<br><br>-Much of the drugs prescribed were for long term chronic care management<br><br>-End of life approaches, increase in prescribed drugs<br><br>-Anticholinergic drugs are often increased at end of life and is associated with adverse effects<br><br>-When inappropriate medications were discontinued, a reduction of mortality existed | -Need a balance of medication usefulness and burden of adverse effects<br>--Adverse effects include poor concentration, reduced quality of life and worsening physical functioning<br><br>-Inadequate attention given to drugs that are prescribed for comorbidities and long term complications<br><br>-Define and screen for polypharmacy in advanced cancer populations |
| Lindsay, J., Dooley, M., Martin, J., Fay, M., Kearney, A., & Barras, M. (2014). Reducing potentially inappropriate medications in palliative cancer patients: Evidence to support deprescribing approaches. | Evaluates the evidence to assess the outcomes and potential methods used for identifying | N=51 articles assessed initially | Systematic Review/Level 1 | N/a | N/a | -Evidence of incidences of polypharmacy and PIMs in geriatric<br><br>- No interventional, follow-up or randomized controlled trials have been performed in | -Arguably in the article, it is stated that "all medications are assumed inappropriate until they improve symptom control or quality of life"<br><br>-Prior to designing and implementing programs for deprescription, |

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| Supportive Care in Cancer, 22(4), 1113-9. doi:http://dx.doi.org.ezproxy.mnsu.edu/10.1007/s00520-013-2098-7 | and ceasing potentially inappropriate medications (PIMs) in palliative cancer patients | | | | | palliative cancer patients, demonstrating that while PIMs exist in this population, there is no evidence of benefits of ceasing medications<br><br>- Ceasing PIMs in geriatric patients lead to an improvement in health with no major adverse effects reported<br><br>-Cost analysis have shown that the incidence of PIMs contributes a significant burden to the healthcare system | quantitative data on health outcomes should be obtained |
| Parker, K., Bull-Engelstad, I., Benth, J., Aasebø, W., von der Lippe, N., Reier-Nilsen, M., Os, I., & Stavem, K. (2019). Effectiveness of using STOPP/START criteria to identify potentially inappropriate medication in people aged ≥ 65 years with chronic kidney disease: a randomized clinical trial. European Journal of Clinical Pharmacology, 75(11), 1503–1511. https://doi.org/10.1007/s00228-019-02727-9 | Identifies potentially inappropriate prescriptions and potential prescribing omissions using a deprescribing tool and determined effect on medication adherence and qol | Older adults over the age of 65 years with CKD end stage 5/N=180/Nephrology centers | Randomized control trial/Level 2 | -STOPP/START criteria for medication review<br><br>-Morisky Medication Adherence Saale to assess medication adherence<br><br>-Short Form Health Survey to assess HRQOL | -Interventions completed at baseline and at 6 month follow up | -Patients with one or more PIPs decreased in the intervention group whereas in the control group, it remained the same<br><br>-Probability of PIPs didn't differ between the groups but the PPOs were lower in the intervention group<br><br>-At 6 months, no difference between the groups of medication adherence<br><br>-No significant different in average number of medications or HRQol at followup<br><br>-PIMs identified were preventative medications or medications that had no therapeutic effects in advanced CKD | -Limitation of study was criteria in patients with advanced CKD is not known<br>-Screening tool for medication review can initiate dialog between those involved with medications and with the patient<br>-Further research on finding ways to evaluate impact on medication adherence and the HRQoL |

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| | | | | | | -ACE inhibitor was the most common medication ommitted | |
| Schenker, Y., Kavalieratos, D., Resick, J., Park, S. Y., Jeong, K., Pruskowski, J., Abernethy, A., & Kutner, J. S. (2019). Associations Between Polypharmacy, Symptom Burden, and Quality of Life in Patients with Advanced, Life-Limiting Illness. JGIM: Journal of General Internal Medicine, 34(4), 559–566. https://doi-org.ezproxy.mnsu.edu/10.1007/s11606-019-04837-7 | Evaluate associations between polypharmacy , symptom burden, and quality of life (QOL) in patients with advanced, life-limiting illness | N=372 participants that are adults with advanced, life limiting illness enrolled in palliative care from 15 sites in U.S.A | Secondary analysis of data from a large, multi-center randomized clinical trial/Level 4 | Measures collected at baseline<br><br>Medications were assessed by documenting the number of prescriptions and OTC<br><br>Symptom burden was assessed by administering the Edmonton Symptom Assessment Scale<br><br>Quality of Life was measured using the McGill Quality of Life Questionnaire<br><br>Participant characteristics included demographics, primary diagnosis, Charlson Comorbidity Index score, performance status, and enrollment in hospice. | Polypharmacy groups were defined as low (0–8 medications), medium (9–13 medications), and high (≥14 medications)<br><br>Statistical analysis with descriptive statistics using STATA | -Polypharmacy in adults with life limited illness is associated with higher burden of symptoms and lower quality of life<br><br>-Suggests worsening quality of life is attributed to the worsening symptoms associated with medications<br><br>-Significant medication burden placed on patients near the end of life warrants careful consideration | -Significant medication burden placed on patients at the end of life warrants careful consideration<br><br>-Future research for deprescribing strategies to reduce the use of inappropriate medications and implementing and evaluating these strategies |

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|---|---|---|---|---|---|---|---|
| Shrestha, S., Poudel, A., Steadman, K., & Nissen, L. (2020). Outcomes of deprescribing interventions in older patients with life-limiting illness and limited life expectancy: A systematic review. British Journal of Clinical Pharmacology, 86(10), 1931–1945. https://doi-org.ezproxy.mnsu.edu/10.1111/bcp.14113 | Investigate the evidence for outcomes of deprescribing interventions in older patients with limited life expectancy or illness | N=9 articles (n=1375 participants) | Systematic Review/Level I | n/a | -Primary outcome is medication appropriateness<br><br>-Secondary outcome is clinical outcomes and cost | -One review stated that deprescribing intervention reduced the symptoms and side effects related to polypharmacy<br><br>-With deprescribing interventions, medicine related harms were reduced<br><br>-Deprescribing may not accelerate death in patient with palliative care<br><br>-QOL is high priority with patient and caregivers. Effect of deprescribing on QOL was found to be inconsistent.<br><br>-Additional outcomes including cost savings associated with deprescribing and sleep quality, bowel function, cognitive function, physical function, general health, performance and symptoms were also reported but changes in the intervention group were not significantly | -When studying clinical outcomes, it is important to consider the illness progression and patient characteristics such as age, their disease patterns and settings during deprescribing.<br>More evidence is needed on the clinical impact of deprescribing and the effect on other areas including physical, cognitive and psychosocial |