Consumer attitudes towards deprescribing: a systematic review and meta-analysis

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Abstract

Background

Harmful and/or unnecessary medications use in older adults is common. This indicates deprescribing (supervised withdrawal of inappropriate medicines) is not happening as often as it should. This study aimed to synthesise the results of the Patients’ Attitudes Towards Deprescribing (PATD) questionnaire (and revised versions).

Methods

Databases were searched from January 2013 to March 2020. Google Scholar was used for citation searching of the development and validation manuscripts to identify original research using the validated PATD, revised PATD (older adult and caregiver versions) and the version for people with cognitive impairment (rPATDcog).

Two authors extracted data independently.

A meta-analysis of proportions (random-effects model) was conducted with sub-group meta-analyses for setting and population.

The primary outcome was the question: “If my doctor said it was possible, I would be willing to stop one or more of my medicines”. Secondary outcomes were associations between participant characteristics and primary outcome and other (r)PATD results.
Results

We included 46 articles describing 40 studies (n = 10,816 participants). The meta-analysis found the proportion of participants who agreed or strongly agreed with this statement was 84% (95% CI 81% - 88%) and 80% (95% CI 74% - 86%) in patients and caregivers respectively, with significant heterogeneity (I² = 95% and 77%).

Conclusion

Consumers reported willingness to have a medication deprescribed although results should be interpreted with caution due to heterogeneity. The findings from this study moves towards understanding attitudes towards deprescribing, which could increase the discussion and uptake of deprescribing recommendations in clinical practice.

Key words

Polypharmacy, medications, caregivers, older adults, inappropriate prescribing
Introduction

Internationally, there has been focus on the increasing prevalence and harms of multiple medication use in the older population. As people age, there may be changes in medical conditions and other medications, as well as a change in their preferences and treatment goals, which can shift medications towards an unfavourable benefit to risk ratio. A medication is considered inappropriate when potential harms outweigh potential benefits in the individual. An American study of older veterans (n = 462,405) found that 50% were dispensed one or more potentially inappropriate medications. The use of potentially inappropriate medications in older adults increases the risk of adverse drug reactions, functional impairment, hospitalization and mortality. This places a high burden on older adults and healthcare systems due to associated costs. This highlights the need for deprescribing which has been defined as the process of withdrawal of an inappropriate medication, supervised by a health care professional with the goal of managing polypharmacy and improving outcomes.

Systematic reviews of randomised controlled trials assessing the effectiveness of deprescribing interventions showed that deprescribing is feasible and safe to implement in a research setting. In order to implement deprescribing in ‘real life’ clinical practice, it is essential to understand the barriers and enablers for deprescribing. Clinicians commonly report consumers (patients and their caregivers) as being resistant to deprescribing and patients can have internally contradictory beliefs in that they perceive all their medications are necessary but also want to take fewer.
The most frequently used patient questionnaires for the assessment of self-reported attitudes towards deprescribing is the Patients’ Attitudes Towards Deprescribing (PATD) questionnaire.\(^\text{17}\) It was developed in 2013 as an exploratory research tool and revised with versions for older adults, caregivers and people with cognitive impairment (rPATD\(^\text{18}\) and rPATDcog).\(^\text{19}\) This manuscript uses ‘(r)PATD’ to denote all versions of the questionnaire. The original PATD underwent face, content, criterion, internal validity, and sensitivity and reliability testing. The questionnaire was then revised due to limitations of the original PATD (designed to be exploratory, no scoring ability, limited scope of potential barriers and enablers) and to simultaneously develop a version for informal caregivers. The rPATD underwent face, construct, content and criterion-related validity testing and internal consistency (Chronbach’s alpha >0.65 for all factors), and test-retest consistency (gamma values between 0.57-0.89, p<0.00 for factor scores). The rPATDcog was adapted from the older adult’s version of the rPATD, including shortening the questionnaire and simplifying the wording and response options, making it researcher/clinician administered (rather than self-administered) and conducting face validity. The retained questions were those with the greatest item-to-total correlation to the overall factor score. (r)PATD has been used internationally in multiple research studies with variable findings. Substantial differences exist between the published studies using the (r)PATD in terms of population, method of measurement and associations with participant characteristics. No systematic review has previously been conducted to synthesise the findings of these studies.
The aims of this systematic review were: (1) to determine the willingness of adults, caregivers and people living with cognitive impairment to have a medication deprescribed; (2) to describe the participant characteristics associated with willingness to have a medication deprescribed; and (3) to report the attitudes and beliefs of adults and caregivers about their medications and deprescribing as reported through use of the (r)PATD.

Methods

We followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA). The protocol was preregistered in PROSPERO (CRD42020150007).

Inclusion and exclusion criteria

Studies were eligible if they were original studies that enrolled adults (>18 years) with any medical condition taking at least one medication or caregivers of such adults. All study types and settings were included if one or more of the questionnaires of interest were administered and quantitative results captured. No language or other limits were applied.

Search

Medline via Ovid, EMBASE, Scopus, International Pharmaceutical Abstracts, and Web of Science core collections for conference abstracts were searched from the date of first publication of the original PATD manuscript, January 2013, to March 2020. Google Scholar was used for citation searching of the development and validation manuscripts of the (r)PATD questionnaires. We emailed anyone who had contacted the primary author of the (r)PATD (ER) for permission to use the questionnaires to identify grey literature.
Title/abstract and full text screening was conducted independently by two researchers. Disagreements were resolved by discussion.

Data extraction

Data extracted independently by two authors using a standardised form included author, year of publication, study setting, design, participant characteristics, self-reported attitudes towards deprescribing ((r)PATD), and associations between willingness to deprescribe and participants’ characteristics. Modifications to any (r)PATD questions and details regarding translations were captured. Studies written in a language other than English were translated using a professional translation service. Corresponding authors were contacted when the primary outcome was not clearly reported.

Two authors independently assessed the quality of reporting using the SURvey Reporting GuidelinE (SURGE)\textsuperscript{20} (modified slightly for the purposes of this review).

Outcomes

The primary outcome of interest was self-reported willingness to have a medication deprescribed, defined as the proportion of participants who responded ‘agree’ or ‘strongly agree’ to: ‘Would you be willing to have one or more of your medicines stopped if your doctor said it was possible?’. A version of this question is present in all versions of the (r)PATD. Secondary outcomes were associations between the primary outcome and participant characteristics and other (r)PATD results.
Analysis

For the primary outcome, a random effects meta-analysis of proportions using the restricted maximum likelihood method was performed in R v3.5.1 using the ‘meta’ package. The proportion was re-calculated from the relevant numerator (number who responded agree or strongly agree) and denominator (number who responded to the questionnaire). Proportions were transformed for meta-analysis via the Freeman-Tukey double arsine function to normalise distributions. Funnel plots were used to identify publication bias by plotting the proportion against the standard error and sample size.

To investigate heterogeneity, we performed analyses of predefined sub-groups based on study setting, population, survey administration, and peer-reviewed status.

Secondary outcomes were synthesised and presented narratively. Caregiver and rPATDcog results are presented separately.
Results

Study characteristics

We identified and included 40 eligible studies reported in 46 articles (eFigure 1).

Sample sizes ranged from 18 to 1981 participants with a total of 10,816 participants (Table 1). The studies were conducted in Australia (n = 12), Malaysia (n = 4), the United States (n = 4), Canada (n = 3), the Netherlands (n = 3), Denmark (n = 2), Singapore (n = 2) and Jordan, Belgium, Ethiopia, India, Italy, Spain, Japan, Pakistan, Ireland, and the United Kingdom (one each). Twenty-two studies used the original PATD, 17,21-24,26,27,29,30,32,33,38,43-45,48,49,51,53-57,61 17 used the older adults version of the rPATD 18,25,28,31,34-37,39-42,46,47,50,52,54-56,62,63 and one used the rPATDcog. 19 Six studies that used the rPATD/rPATDcog also used the caregiver version of the rPATD. 19,31,34,35,52,55,63 Most studies used the (r)PATD questionnaires specifically for measuring attitudes in a cross-sectional study. However, some studies (n = 4) 21,22,41,44,62 used the questionnaires as a baseline and/or outcome measure in a deprescribing intervention study. More than half of the 40 studies (n = 24, 60%) 18,19,21,22,24-27,29,31,33,39,40,43-45,48-52,55-58,62,63 focused on older adults. The median age of participants included in the studies ranged from 51 – 87 years old. Seventeen (43%) studies 18,21,22,24,30,31,33-35,38,41-44,46,47,49,52,53,61,62 were conducted in the community or primary care setting, 9 (23%) in the hospital setting 17,25,29,32,45,52,54,61,63 and 8 (20%) 19,23,39,40,53,54,56,59,60 in the outpatient setting. Six studies translated the PATD 43,48,49,51,58,59 and seven studies translated the rPATD 34,35,37,46,47,50,54-56; thirteen studies in total (eTable 2). Four studies used medication-specific questions in adapted (r)PATD questionnaires on statins, 29 alpha-blockers, 46,47 benzodiazepines 25 and proton pump inhibitors (eTable 3). 39,40
Regarding the quality of reporting, all studies described or partially described the questionnaire used (100%, 38/38) and most referenced the original work (95%, 36/38). (See eTables 4 and 5). Assessment of quality reporting was unable to be performed on two of the studies.38,59 Most studies gave a description of the desired population (89%, 34/38), 79% (30/38) reported how the survey was administered and 74% (28/38) at least partially reported the psychometric properties of the (r)PATD. However, 26 studies (68%) did not report the format of the survey (paper, online or both) and half (19/38) did not present a sample size calculation or justification of sample size.

**Willingness to have a medication deprescribed**

Overall, 49-98% (n= 36 studies) of patients in the included studies were willing to stop one or more of their medications if their doctor said it was possible (Table 2 and Table 3). Three studies did not report the results to this question as a proportion. From the rPATDcog (n = 1), 82% of patients (with cognitive impairment) were willing to have a medication deprescribed if their doctor said it was possible.19 Our meta-analysis showed the pooled proportion was 84% (95% CI 81% - 88%, I² = 95%) of patients who responded ‘agree’ or ‘strongly agree’ to the question: ‘Would you be willing to have one or more of your medicines stopped if your doctor said it was possible?’ (Figure 1). There was significant heterogeneity overall and the sub-group analyses (eFigure 2) were not able to explain the heterogeneity. We found limited evidence of publication bias based on visual inspection of the funnel plots (eFigure 3).
The majority of caregivers (65-87%, n = 5 studies) reported they would be willing for one or more of their care recipient's medications to be stopped if their care recipient's doctor said it was possible (eTable 6). The pooled effect estimate was 80% (95% CI 74% - 86%, $I^2 = 77%$).

**Responses to the (r)PATD questionnaires**

The questions from the PATD which had the smallest ranges of responses (i.e. least variation in findings across studies) were “I feel that I may be taking one or more medications that I no longer need” (studies found between 8-38% agreement in 32/39 studies (as this question is in both the PATD and rPATD questionnaires), “I believe one or more of my medications is giving me side effects” (11-44% over 19/22 studies), and “I believe that all my medications are necessary” (56-92% in 18/22 studies). While the questions with the greatest variation across studies were “I would like to reduce the number of medications that I am taking” (17-89% over 18/22 studies) and “I would accept taking more medications for my health conditions” (10-84% in 17/22 studies). (See Table 2)

Studies that used the rPATD questionnaire (Table 3) found that 27-52% of participants would be reluctant to stop a medicine they had taken for a long time (12/17 studies). Most participants (67 – 93%) reported they were satisfied with their current medicines (12/17 studies) while 24-100% of participants felt they knew exactly which medicines they take and/or have an up-to-date list (12/17 studies) and 7-90% of participants felt that one or more of their medicines may not be working (11/17 studies). In response to the statement: “I would like to try stopping one of my medicines to see how I feel without it”, 9-44% of participants agreed (14/17). (See table 3)
Findings of the caregivers’ version of the rPATD are presented in eTable 6.

**Associations between participant characteristics and willingness to have a medication deprescribed**

Fourteen studies examined relationships between participant characteristics and the primary outcome willingness to have a medication deprescribed (Table 4 and eTable 7). The most common patient characteristics examined were age (n = 12), gender (n = 6), education level (n = 6), number of medications (n = 11) and chronic health conditions (n = 4). Five out of twelve studies reported a significant association between age and willingness to have a medication deprescribed, although the direction of this association varied (e.g. older age compared to younger age were both found to be associated with greater willingness to have a medication deprescribed). Three studies examined relationships between caregiver characteristics and the primary outcome willingness to have a medication deprescribed (eTable 8).

**Discussion**

**Main findings**

We synthesised results of 40 studies that used the (r)PATD questionnaires. The included studies were diverse in study design, intended purpose, and characteristics examined. Overall, many participants were willing to have a medication deprescribed if their doctor said it was possible (84%, 95% CI 81% - 88). Caregiver data provided a similar result, 80% (95% CI 74% - 86%). However, there was significant heterogeneity ($I^2 = 95\%$ patients, 77% for
carers) and no explanation for this was identified through the sub-group analyses.

Approximately one third of the studies examined associations between participant characteristics and the primary outcome. However, there was inconsistency in whether there was statistical significance between characteristics and the primary outcome. In the studies where there was an association found, there was inconsistency in the direction of the association (i.e. if the characteristic was associated with higher or lower willingness). As such, it is still unclear whether individual characteristics (such as age or number of medications) could predict participant willingness to have their medications deprescribed.

**Strengths and limitations**

A strength of this review is that we included articles published in any language, conference abstracts and grey literature. We identified unpublished (or locally published) articles/reports through contacting those who had requested permission to use the (r)PATD. Our multi-pronged search strategy which included methods outside of traditional database searching led to additional studies being included. Studies within the review were diverse in terms of setting, country and design. Most studies in this review were from high income countries which may reflect missing studies, or that studies have not been done in these lower income countries. Few studies examined caregivers’ attitudes, and only a single study used the rPATDcog.

Many of the included studies were cross-sectional and as such do not allow conclusions on causality (when examining the associations between participant characteristics and willingness to deprescribe). The (r)PATD, as a self-reported measure, is susceptible to social desirability bias. Although, no difference was found in the sub-analysis looking at method of
administration (self-report, researcher administered) and several studies collected responses anonymously. Convenience samples were used in several studies; representativeness of the sample was described as one of the limitations in many of the included articles, and how non-respondents differed from participants was rarely described. Overall, participants may have been healthier or more involved in managing their medications, particularly in studies of self-selected participants. One US study was conducted in a representative population and several studies targeted disadvantaged populations without any obvious differences in (r)PATD responses in these studies.

A checklist to assess the quality of reporting was used in place of a risk of bias tool. Such reporting checklists do not technically assess a study’s quality, however, no quality assessment tool was identified for surveys. The sections that were generally well reported included background, discussion and ethics whereas methods and results were less well reported. The studies within this review were somewhat heterogeneous, including how the (r)PATD was used. While a number of translations have been published, it is unclear if they are all semantically equivalent to the English version. There was variation in the use of items and response scales, and few of the studies that modified the (r)PATD reported validation for their local context. However, most translated versions of the (r)PATD involved some piloting (5 to 28 patients) and modified questions were often reviewed by the research team. It is possible that cultural, or country specific differences exist in relation to patients’ attitudes towards deprescribing that may affect responses to the (r)PATD.
Comparison with other studies

There is an increasing understanding that medication optimisation can be achieved by engaging older adults and their caregivers in deprescribing decisions and prioritising patient-centred care. The synthesised results from this review can be interpreted in the context of findings using complementary surveys. The Patient Perceptions of Discontinuation survey (PPoD)\textsuperscript{64,65} found that one third of participants (34\%, \(n = 803\)) had experience stopping a medication. Significant factors associated with past deprescribing experience included being told by a doctor or the patient asking to stop a medication, interest in deprescribing, shared decision-making, and higher education. Alternatively, factors associated with decreased likelihood to deprescribe included polypharmacy and participants having higher trust in their doctor.

Qualitative findings of patient-related barriers to deprescribing\textsuperscript{66,67} recognise the often co-existing positive and negative attitudes towards deprescribing that patients have, as well as the complex interplay that exists between attitudes, beliefs and decision-making. The (r)PATD results reflect these seemingly contradictory attitudes in that individuals may say they are open to deprescribing but also report high satisfaction with their medications.

Indeed, qualitative findings show clinicians perceive their patients are reluctant to deprescribe medications.\textsuperscript{68,69} Additionally, in previous studies, 30-40\% of participants have refused to participate in a deprescribing intervention study,\textsuperscript{70-72} irrespective of taking potentially inappropriate medications.\textsuperscript{73} Presently, the predictive ability of the (r)PATD has not been
established and it may be difficult to discriminate patient behaviour from hypothetical willingness to deprescribe. Additionally, even though participants in the included studies overwhelmingly report agreement with deprescribing if their doctor said it was possible, the factors influencing acceptance of deprescribing in clinical practice at a single point in time are complex and multi-faceted.\textsuperscript{74}

**Research, Clinical and Policy Implications**

We found inconsistency in the participant characteristics that were associated with willingness to deprescribe. Understanding predictors of positive attitudes towards deprescribing more generally could enable tailored deprescribing practices as singular, external or measurable factors might not consistently predict attitudes to deprescribing. There were some participant characteristics, such as frailty and dementia, that were only captured in a few studies or were measured in different ways. This highlights the need to consistently measure characteristics to add to the evidence base, particularly for these patients that stand to benefit the most from deprescribing.\textsuperscript{75} Deprescribing is a process that should involve the patient,\textsuperscript{76} therefore, an ongoing conversation with the patient and caregiver, and consideration of the complex internal and external factors that affect the implementation of deprescribing is required.\textsuperscript{77}

Although mostly used in the research setting, the (r)PATD is increasingly used as part of a deprescribing intervention strategy, such as the Australian G-MEDSS (Goal-directed Medication Review Electronic Decision Support System) study \textsuperscript{78,79} and the US OPTIMISE study.\textsuperscript{80,81} This highlights a shift toward implementation of self-assessment surveys in clinical
practice to promote ‘real-time’ support for deprescribing conversations. Further work is required to determine how and when the (r)PATD can be best utilised in clinical practice.

Different public health and policy initiatives may be implemented to increase deprescribing activities. For instance, raising public awareness and acceptance of deprescribing as a normal and positive part of patient care may alleviate concerns patients may have to trial stopping a medication (this review found between 27 and 52% of participants were reluctant to stop a long term medication). Additionally, it is important to prioritise shared decision-making with a focus on patients’ goals and preferences, to navigate the seemingly contradictory beliefs of willingness to deprescribe yet feeling that their medications are appropriate. Remuneration and dedicated clinical consultations for these discussions may be needed to increase widespread deprescribing in practice.

Conclusions

Overall, clinicians should be reassured of their patients’ and caregivers’ willingness to have medications deprescribed. As such, this could encourage clinicians to initiate a conversation about deprescribing with those they care for. The findings from this study moves towards understanding attitudes towards deprescribing, which could, in turn, increase the discussion and uptake of deprescribing recommendations in clinical practice.
Contributors: All authors were involved in designing the study. KRW and NJA were involved in searching the database. KRW and NJA screened citations for inclusion. KRW, ER and NJA, were involved in extracting data and interpretation. KRW and ER synthesised the data and CS conducted the meta-analysis. KRW drafted the manuscript and ER and NJA contributed to the drafting of the review. SH and CS revised the manuscript critically for important intellectual content. All authors reviewed the final manuscript and agreed to be accountable for all aspects of the work and approved the final manuscript for submission.

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Tables and figures

Table 1. Study and participant characteristics

Table 2: PATD questionnaire results

Table 3. Older adults’ results from the rPATD questionnaire

Table 4. Associations with the primary outcome question “If my doctor said it was possible, I would be willing to stop one or more of my regular medicines”

Figure 1: Forest plots of proportion of participants who agreed or strongly agreed with the question “If my doctor said it was possible, I would be willing to stop one or more of my medicines”
Table 1. Study and participant characteristics

| Source, year, country | Sample size, study design | Study population | Age, years (median) | Female % | Number of medications (median) | Translated, language | Questionnaire modified, how |
|----------------------|---------------------------|------------------|--------------------|----------|-------------------------------|----------------------|--------------------------|
| **PATD questionnaire** |                           |                  |                    |          |                               |                      |                          |
| Anderson et al, 2020, Australia | 78, pragmatic controlled, pre-post, mixed methods study | Community setting, aged 65+ years, taking ≥5 medications | 74 | 59 | 8 | N | Y, only first 10 questions reported |
| Aoki et al, 2019, Japan | 1483, cross-sectional survey | Outpatient, adults aged 18+ years, taking ≥1 medication | NR | 49 | NR | N | N |
| Candela et al, 2019 (thesis), Spain | 210, cross-sectional survey | Outpatient, adults aged 18+ years, HIV-positive patients on antiretroviral therapy | 51 | 23 | 5 | Y, Spanish | Y, translated |
| Study                        | Country | Design                        | Setting                                                                 | Sample Size | Number | Gender | Medications | Language | Findings                                                                 |
|------------------------------|---------|-------------------------------|-------------------------------------------------------------------------|-------------|--------|---------|-------------|----------|--------------------------------------------------------------------------|
| Cross et al, 2020<sup>23</sup> | Australia | 50, feasibility study, pre-post intervention study | Outpatient, patients at risk of a medication-related problem          | 81          | 36     | N       | N           | Y<sup>a</sup> | only first 10 questions reported                                          |
| Frankowski et al, 2019<sup>48</sup> | Netherlands | 47, observational descriptive study | Geriatric psychiatry residential ward, taking ≥5 medications | 67          | 51     | 11      | Y<sup>a</sup>, Dutch | Y | deleted Q8, Q14 and Q15                                                  |
| Galazzi et al, 2016<sup>58</sup> | Italy    | 100, cross-sectional survey    | Hospital setting, aged 65+ years                                       | 79          | 47     | 6       | Y, Italian | Y | translated and deleted Q14                                               |
| Gillespie et al, 2019<sup>24</sup> | Australia | 137, cross-sectional survey    | Community setting, aged 65+ years, taking ≥5 medications               | 76          | 61     | 7       | N           | Y | deleted Q14 and Q15                                                     |
| Goulding unpublished<sup>38</sup> | USA      | 75, pre-post intervention study | Community setting, patients with serious mental illness enrolled in a medication adherence | 60<sup>c</sup> | 56     | NR      | N           | N |                                                                          |
| Study                  | Sample Size | Setting                      | Age Range          | Medications | Statin Use | Comments |
|-----------------------|-------------|------------------------------|--------------------|-------------|------------|----------|
| **Hao et al, 2018**   | 222         | Community setting, aged 65+ years, taking ≥5 medications | 70/58/6 | NR          | Y, Q11 modified |
| **Malaysia**          |             |                              |                    |             |            |          |
| **Hendrix et al, 2019** | 383        | Residential aged care facility, aged 65+ years | 88<sup>c</sup> | 76/10 | N | N |
| **Australia**         |             |                              |                    |             |            |          |
| **Kalogianis et al, 2016** | 232       | Residential aged care facility, aged 65+ years | 87<sup>c</sup> | 76/15<sup>b,c</sup> | N | Y, minor wording changes to allow for interviewer administered |
| **Australia**         |             |                              |                    |             |            |          |
| **Ng et al, 2017**    | 136         | Outpatient healthcare centres, adults aged 45+ years, taking ≥5 medications | 68/41/6 | N | NR |
| **Singapore**         |             |                              |                    |             |            |          |
| **Qi et al, 2015**    | 180         | Hospital setting, aged 65+ years, taking a statin medication | 78/47/8/10<sup>d</sup> | N | Y, 5 statin specific questions added |
| **Australia**         |             |                              |                    |             |            |          |
| Authors | Sample Size | Setting | Participants | Country | Design | Results |
|---------|-------------|---------|--------------|---------|--------|---------|
| Reeves et al, 2014 | 77 | Cross-sectional survey in community pharmacies | Adults aged 18+ years, taking ≥1 medication | Australia | N | Y, Q11 was not used |
| Reeves et al, 2013 | 100 | Development of a questionnaire, cross-sectional survey of outpatients | Adults aged 18+ years, taking ≥1 medication | Australia | N | N |
| Saraswathy et al, 2018 | 257 | Observational study in residential aged care facility | NR | India | NR | NR |
| Schiøtz et al, 2018 | 100 | Cross-sectional survey in outpatient clinics | Aged 65+ years, taking ≥10 medications | Denmark | Y, Danish | Y, translated and Q9 modified |
| Siros et al, 2017 | 129 | Cross-sectional survey in community setting | Aged 65+ years, taking ≥1 | Canada | Y, French | Y, translated. 2 questions added about |
| Study                  | Participants                                                                 | Setting and Design                                                                 | Nurse Involvement | Follow-up for Deprescribing |
|-----------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|-------------------|-----------------------------|
| Turner et al, 2018, 44 Canada | 489, secondary analysis of a randomised controlled trial, Community setting, aged 65+ years, taking ≥1 medication, taking specific medication | 75<sup>c</sup>, 66, 9<sup>c</sup>, N                                           | Y, only first 10 questions reported |
| ul Haq et al, 2016, 61 Pakistan | 207, cross-sectional survey, Hospitals and community pharmacies | NR, NR, NR, NR, NR, NR                                                              |                   |
| Van Marum et al, 2016, 49 Netherlands | 40, interview and cross-sectional survey, Community setting, older adults aged 70+ years, taking ≥7 medications | 79, 55, 11<sup>c</sup>, Y, Dutch                                                  | Y, translated. Deleted Q8, Q14 and Q15 |
| Whitty et al, 2018, 45 Canada | 53, pilot study, Hospital setting, seriously ill or frail older patients | 80<sup>c</sup>, 43, 13<sup>c</sup>, NR                                              | Y, Q11 response items changed to 2-point scale (Yes and No), |
| Study                  | Country      | Setting                          | Target Population                  | Questionnaires | Modified Questions |
|-----------------------|--------------|----------------------------------|------------------------------------|----------------|--------------------|
| Cardwell et al, 2020   | Ireland      | Community setting, aged 65+ years, taking ≥10 medications | 70 65 10 | N | N               |
| Edelman et al, 2019    | Netherlands  | Community setting, men aged 30+ years, taking an alpha-blocker, diagnosed with lower urinary tract symptoms | 69 0 4 | Y, Dutch | Y, translated. Modified questions to create alpha-blocker-specific rPATD factors |
| Gnjidic et al, 2019    | Australia    | Hospital setting, aged 65+ years, taking a benzodiazepine | 72 55 10 | N | Y, 5 benzodiazepine-specific questions were added |
| Ikeji et al, 2019      | USA          | Outpatient, aged 65+, years, taking a Proton Pump Inhibitor | NR 60 NR | N | Y, the questionnaire was modified to focus on proton pump inhibitors |

deleted Q12 and Q13
| Study          | Sample Size | Setting                                    | Participants                              | Caregivers | Language | Translation |
|---------------|-------------|--------------------------------------------|-------------------------------------------|------------|----------|-------------|
| Kua C-H et al., 2020, Singapore | 615 | Cross-sectional survey | Hospitals, community pharmacies and primary care clinics, aged 65+ years, taking ≥1 medication. Caregivers | 73<sup>c</sup> | 44 | 5<sup>c</sup> | N | N |
| Kua K et al., 2019, Malaysia | 502 | Cross-sectional survey | Community pharmacies and primary care clinics, aged 60+ years, taking ≥1 medication. Caregivers | 67 | 50 | 3 | Y, Mandarin | Y, translated and Malay |
| Lundby et al., 2019, Denmark | 159 | Validation study and cross-sectional survey | Residential aged care facility | 82 | 61 | NR | Y, Danish | Y, translated |
| Major et al., 2019, Australia | 66 | Intervention study and survey | Community setting | NR | NR | 12<sup>c</sup> | N | Y, Q7 (primary outcome) was not asked |
| Martinez et al., | 30 | Pre-post | Community setting, | 56<sup>c</sup> | 100 | 4<sup>c</sup> | N | NR |
| Year, Location | Study Type | Setting | Population Characteristics | Sample Size | Follow-up | 
|---------------|------------|---------|-----------------------------|-------------|-----------| 
| 2020, USA     | Intervention study | Community setting, adults aged 18+ years, diagnosed with Parkinson’s Disease | 64 | 44 | 5 | NR | 
| 2020, Malaysia | Cross-sectional survey | Outpatient, adults aged 18+ years, taking ≥5 medications | 60 | 52 | 7 | Y, Arabic | 
| 2020, Jordan  | Validation study and survey | Primary care clinics, aged 65+ years, taking ≥1 medication | 72 | 52 | 6 | Y, Malay | 
| 2019, Belgium | Cross-sectional survey | Residential aged care facility, aged 65+ years, limited life expectancy. Caregivers | 86 | 74 | 7 | Y, Dutch | 

*Ng et al., 2019, Malaysia
*Nusair et al., 2020, Jordan
*Omar et al., 2020, Malaysia
*Paque et al., 2019, Belgium
| Study                        | Sample Size | Setting                          | Participants | Caregivers | Outcome |
|------------------------------|-------------|----------------------------------|--------------|------------|---------|
| Reeve et al, 2019 (rPATD)    | 386         | Community setting, aged 65+ years, taking ≥1 medication. Caregivers | 74           | 57         | NR      | N       | N       |
| Australia                    |             |                                  |              |            |         |         |         |
| Reeve et al, 2018 USA        | 1981        | Community setting, aged 65+ years | NR           | 55         | NR      | N       | Y, combined 10 questions from the PATD and rPATD (older adults’ version), modified to a 4-point Likert scale (deleted unsure) |
| USA                          |             |                                  |              |            |         |         |         |
| Reeve et al, 2018 Australia  | 21          | Outpatient, adults aged 18+ years, taking ≥1 medication, with a diagnosis of mild cognitive impairment or dementia. Caregivers | 77<sup>c</sup> | 48         | 7<sup>c</sup> | N       | Y, the rPATD questionnaire for older adults was used to develop the rPATDcog questionnaire |
| Study                  | Country   | Setting                        | Sample Size | Age Range | Drugs | Language  | Notes                                           |
|------------------------|-----------|--------------------------------|-------------|------------|-------|-----------|------------------------------------------------|
| Scott et al, 2019,63    | UK        | Hospital setting, aged 70+ years, with physical frailty or co-morbidities | 87          | 45         | 8     | N         | Y, Q10 minor changes to fit the UK context regarding cost of medicines |
| Tegegn et al, 2018,56   | Ethiopia  | Outpatient, aged 65+ years, taking ≥1 medication | 70          | 45         | 3     | Y, Amharic | Y, translated and modified to a 4-point Likert scale (deleted unsure) |

a Implied in the article: a translated questionnaire was based on comparative research (van Marum et al, 2016)

b Regular and medications taken as required
Mean

Discrepancy in the manuscript text and table

This reference contains results from two cohorts; one of these cohorts was published separately (and so are reported separately: Reeve 2013). Data presented here is from the second cohort only (community pharmacy participants).

This is an abstract

This is an editorial comment

Including supplements

Combined PATD and rPATD questions, for clarity we have classified this reference as using the rPATD questionnaire
Table 2: PATD questionnaire results

| Study   | Q1. I feel that I am taking a large number of medications | Q2. I am comfortable with the number of medications that I am taking | Q3. I believe that all my medications are necessary | Q4. If my doctor said it was possible, I would be willing to stop one or more of my regular medications | Q5. I would like to reduce the number of medications that I am taking | Q6. I feel that I may be taking one or more medications | Q7. I would accept taking more medications for my health conditions | Q8. I have a good understanding of the reasons I was prescribed each of my medications | Q9. Having to pay for my medications would play a role in my willingness to stop one or more of them | Q10. I believe one or more of my medications is giving me side effects |
|---------|----------------------------------------------------------|---------------------------------------------------------------------|--------------------------------------------------|------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|-------------------------------------------------|-----------------------------------------------|-----------------------------------------------------------------------------|---------------------------------------------------------------------------|-------------------------------------------------------------------------|
| Anderson| 60                                                      | 95                                                                  | 19                                               |                                                                                                             | 29                                                                  |                                                                                                           |                                                              |                                                                                           |                                                                          |                                                                         |
|               | et al, 2020 | Aoki et al, 2019 | Candela et al, 2019 (thesis) | Cross et al, 2020 | Frankowski et al, 2019 | Galazzi et al, 2016 | Gillespie et al, 2019 | Goulding |
|---------------|-------------|------------------|-------------------------------|-------------------|-----------------------|----------------------|-----------------------|----------|
|                | 21,22       | 68               |                               | 54                | 53                    | 59                   | 49                    | 60       |
| Aoki et al, 2019 |             |                  |                               | 88                | 77                    | 78                   | 88                    | 74       |
| (thesis) 59    |             |                  |                               | 82                | 77                    | 78                   | 88                    | 74       |
| Candela et al, 2019 | 41         | 61               | 90                            | 82                | 51                    | 97                   | 43                    | 43       |
| Aoki et al, 2019 |             |                  |                               | 72                | 38                    | 47                   | 49                    | 44       |
| Candela et al, 2019 | 8           | 71               |                               | 16                | 47                    | 70                   | 30                    | 36       |
| Cross et al, 2020 | 54         | 86               | 76                            | 62                | 15                    | 12                   | 18                    | 30       |
| Frankowski et al, 2019 | 53         | 70               | 64                            | 12                | 64                    | 12                   | 18                    | 44       |
| Galazzi et al, 2016 | 59         | 87               | 78                            | 70                | 15                    | 70                   | 70                    | 44       |
| Gillespie et al, 2019 | 49         | 80               | 80                            | 64                | 20                    | 64                   | 66                    | 22       |
| Goulding       | 60          | 76               | 81                            | 56                | 37                    | 56                   | 37                    | 44       |
| Author(s)            | Year | Values |
|----------------------|------|--------|
| unpubished data      |      |        |
| Hao et al., 2018     | 33   | 46     |
| Hendrix et al., 2019 | 26   | 49     |
| Kalogianis et al., 2016 | 27   | 40     |
| Ng et al., 2017      | 53   | 60     |
| Qi et al., 2015      | 29   | 71     |
| Reeve et al., 2014   |      | 48     |
| (thesis)             |      | 48,a   |
| Reeve et al., 2014   | 30,a | 65     |

Downloaded from https://academic.oup.com/biomedgerontology/advance-article/doi/10.1093/gerona/glab222/6352400 by guest on 27 August 2021
| Year   | Study Details               | Values | Values | Values | Values | Values | Values | Values | Values |
|--------|----------------------------|--------|--------|--------|--------|--------|--------|--------|--------|
| 2013   | (PATD development & results) | 17,32  |        |        |        |        |        |        |        |
| 2018   | Saraswathy et al.           | 49     | 17     | 43     |        |        |        |        |        |
| 2018   | Schiøtz et al.              | 81     | 65     | 79     | 85     | 82     | 11     | 71     | 85     | 18     | 40     |
| 2017   | Sirois et al.               | 51     | 81     | 84     | 69     | 51     | 22     | 81     | 91     | 33     | 26     |
| 2018   | Turner et al.               | 56     | 85     | 92     | 86     | 66     | 22     | 48     | 97     | 18     | 26     |
| 2016   | Ul Haq et al.               | 55     |        |        |        |        |        |        |        |        |        |
|               | 0-10% | 11-20% |
|---------------|-------|--------|
| Van Marum *et al*, 2016 | 68    | 38     |
| Whitty *et al*, 2018 | 61    | 43     |

*a* This reference contains results from two cohorts; one of these cohorts was published separately (and so are reported separately: Reeve 2013). Data presented here is from the second cohort only (community pharmacy participants).

*b* This is an abstract.

*c* Mean.

*d* Strongly agree + agree + unsure grouped for questions 2, 3, 7 & 8 in this study.
Table 3. Older adults’ results from the rPATD questionnaire

| Study         | Globa Involvement | Globa Burden | Appropriateness | Concerns about stopping |
|---------------|------------------|--------------|-----------------|------------------------|
|               | Q1 Q2 Q3 Q4 Q5 Q6 Q7 | Q8 Q9 Q1 Q1 Q1 Q1 Q1 | Q1 Q1 Q1 Q1 Q1 Q1 Q1 | Q1 Q1 Q2 Q2 Q2 Q2 Q2 |
| Cardwell et al, 2020 | 62 |              |                 |                        | 90 |
| Edelman, 2019 46,47,a |              |              |                 |                        | 79 91 |
| Gnjidic et al, 2019 25 |              |              |                 |                        | 93 |
| Kua C-H et al, 2020 52 |              |              |                 |                        | 89 61 |
| Kua K et      |              |              |                 |                        | 88 64 |

AGREE % (strongly agree & agree)
|          | 2019       | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     | 2019     |
|----------|------------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| Lundby et al, 2019 | 93 10 0 | 86 63   | 44 27   |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Major et al, 2019 | 93 76 59 77 73 49 | 56 11 38 44 18 32 24 20 23 18 17 50 38 18 11 |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Martinez et al, 2020 | 90 97 10 10 10 10 93 30 43 33 17 33 20 10 13 7 33 40 43 20 3 |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Ng et al, 2019 | 67 |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Nusair et al, 2020 | 79 80 92 74 75 86 90 60 59 41 58 57 34 38 23 43 24 19 27 26 25 15 |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Paque et al, 2019 | 84 46 46 39 77 47 85 36 12 13 20 15 23 25 10 20 15 13 27 19 16 8 |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
| Reeve et al, 2019 | 92 96 97 94 97 96 88 38 16 40 23 10 20 15 12 24 9 16 36 21 15 4 |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |          |
Q1. Overall, I am satisfied with my current medicines

Q2. I like to be involved in making decisions about my medicines with my doctors

Q3. I have a good understanding of the reasons I was prescribed each of my medicines

Q4. I like to know as much as possible about my medicines

Q5. I always ask my doctor, pharmacist or other health care professional if there is something I don’t understand about my medicines
Q6. I know exactly what medicines I am currently taking, and/or I keep an up to date list of my medicines

Q7. If my doctor said it was possible, I would be willing to stop one or more of my regular medicines

Q8. I feel that I am taking a large number of medicines

Q9. Taking my medicines every day is very inconvenient

Q10. I spend a lot of money on my medicines

Q11. Sometimes I think I take too many medicines

Q12. I feel that my medicines are a burden to me

Q13. I would like to try stopping one of my medicines to see how I feel without it

Q14. I would like my doctor to reduce the dose of one or more of my medicines

Q15. I feel that I may be taking one or more medicines that I no longer need

Q16. I believe one or more of my medicines may be currently giving me side effects

Q17. I think one or more of my medicines may not be working

Q18. I have had a bad experience when stopping a medicine before
Q19. I would be reluctant to stop a medicine that I had been taking for a long time.

Q20. If one of my medicines was stopped I would be worried about missing out on future benefits.

Q21. I get stressed whenever changes are made to my medicines.

Q22. If my doctor recommended stopping a medicine I would feel that he/she was giving up on me.

\textsuperscript{a} Mostly reported factor scores

\textsuperscript{b} This is an
abstract

c  This is an editorial comment

d  Combined PATD and rPATD questions, for clarity we have classified this reference as using the rPATD questionnaire

| Not reported | 0-10% | 11-20% | 21-30% | 31-40% | 41-50% | 51-60% | 61-70% | 71-80% | 81-90% | 91-100% |
|--------------|-------|--------|--------|--------|--------|--------|--------|--------|--------|---------|
Table 4. Associations with the primary outcome question “If my doctor said it was possible, I would be willing to stop one or more of my regular medicines”

| Source, year | Variables (statistical significance, direction of association) |
|--------------|---------------------------------------------------------------|
|              | Age | Number of medications | Number of chronic health conditions | Gender (female) | Education level | Access discount medications<sup>a</sup> (yes) |
| **PATD**     |     |                  |                                  |               |               |                                               |
| Aoki <i>et al</i>, 2019<sup>60</sup> | S, + | S, +               | S, +                            | NS            | NS            | /                                              |
| Gillespie <i>et al</i>, 2019<sup>24</sup> | /   | NS                 | /                               | /             | /             | /                                              |
| Hao <i>et al</i>, 2018<sup>53</sup> | S, – | /                  | /                               | NS            | /             | /                                              |
| Kalogianis <i>et al</i>, 2016<sup>27</sup> | /   | NS                 | /                               | /             | /             | /                                              |
| Qi <i>et al</i>, 2015<sup>29</sup>    | NS  | NS                 | /                               | /             | /             | /                                              |
| Reeve <i>et al</i>, 2013             | NS  | NS                 | NS                              | /             | /             | /                                              |
| (PATD development + results)<sup>17,32</sup> |     |            |                                  |               |               | S, –                                          |
| Reeve <i>et al</i>, 2014 (thesis)<sup>50,b</sup> | NS  | NS                 | /                               | /             | /             | /                                              |
| ul Haq <i>et al</i>, 2016<sup>61</sup> | S, + | NS                 | /                               | /             | /             | NS                                            |
| Study Reference | Result | NS | S<sup>c</sup> | / | NS | NS | / |
|-----------------|--------|----|--------------|---|----|----|---|
| Kua C-H <i>et al</i>, 2020<sup>52</sup> | NS | S<sup>c</sup> | / | NS | NS | / |
| Kua <i>et al</i>, 2019<sup>54</sup> | S, + | NS | / | NS | S, – | / |
| Ng <i>et al</i>, 2017<sup>55</sup> | S, – | / | / | / | / | / |
| Reeve <i>et al</i>, 2019 (rPATD results)<sup>18,31</sup> | NS | NS | / | NS | NS | S, + |
| Reeve <i>et al</i>, 2018<sup>42</sup> | NS | S, + | S, + | NS | NS | NS |
| Tegegn <i>et al</i>, 2018<sup>56</sup> | NS | / | NS<sup>d</sup> | NS | NS | / |
| **TOTAL EXAMINED** | **11** | **10** | **4** | **6** | **5** | **4** |
| **TOTAL SIGNIFICANT** | **5** | **3** | **2** | **0** | **1** | **2** |

/ = Not examined

NS = Not significant

S = Significant

+ = Increasing/higher variable (or Female gender, or possession of a medication concession card) associated with increasing willingness to deprescribe

– = Decreasing/lower variable (or Male gender, or no medication concession card) associated with increasing willingness to deprescribe
a Participants had a medication concession card or drug cost was covered/fully subsidised

b This reference contains results from two cohorts; one of these cohorts was published separately (and so are reported separately: Reeve 2013). Data presented here is from the second cohort only (community pharmacy participants)

c Unclear if the direction of the finding is ‘+’ or ‘-‘; significant difference was found between groups (1-5, 6-10 and >10), but authors report “No significant differences in sub-group analysis”

d Charlson Comorbidity Index
Figure 1. Forest plots of proportion of participants who agreed or strongly agreed with the question “If my doctor said it was possible, I would be willing to stop one or more of my medicines”

Figure 1a. Forest plot patients

| Study                | Events | Total | Proportion | 95%-CI | Weight |
|----------------------|--------|-------|------------|--------|--------|
| Saraswathy 2018      | 126    | 257   | 0.49       | [0.43; 0.55] | 3.0%   |
| ul Haq 2016          | 113    | 207   | 0.55       | [0.48; 0.61] | 2.9%   |
| Goulding 2020        | 32     | 58    | 0.55       | [0.42; 0.68] | 2.6%   |
| Kua 2019             | 340    | 502   | 0.68       | [0.64; 0.72] | 3.1%   |
| Aoki 2019            | 1006   | 1483  | 0.68       | [0.65; 0.70] | 3.1%   |
| Sirois 2017          | 89     | 129   | 0.69       | [0.61; 0.77] | 2.8%   |
| Frankowski 2019      | 36     | 47    | 0.77       | [0.63; 0.88] | 2.4%   |
| Kalogianis 2016      | 183    | 231   | 0.79       | [0.74; 0.84] | 3.0%   |
| Tegegn 2018          | 258    | 316   | 0.82       | [0.77; 0.86] | 3.0%   |
| Candela 2019         | 173    | 210   | 0.82       | [0.77; 0.87] | 2.9%   |
| Kua 2020             | 511    | 615   | 0.83       | [0.80; 0.86] | 3.1%   |
| Hendrix 2019         | 118    | 142   | 0.83       | [0.76; 0.89] | 2.9%   |
| Hao 2018             | 185    | 222   | 0.83       | [0.78; 0.88] | 3.0%   |
| Ikeji 2019           | 16     | 19    | 0.84       | [0.64; 0.98] | 1.9%   |
| Schi..tz 2018        | 85     | 100   | 0.85       | [0.77; 0.91] | 2.8%   |
| Paque 2019           | 115    | 135   | 0.86       | [0.79; 0.91] | 2.9%   |
| Reeve 2019           | 331    | 386   | 0.86       | [0.82; 0.89] | 3.0%   |
| Turner 2018          | 421    | 489   | 0.86       | [0.83; 0.89] | 3.1%   |
| Lundby 2019          | 137    | 159   | 0.86       | [0.80; 0.91] | 2.9%   |
| Cross 2020           | 44     | 50    | 0.88       | [0.77; 0.96] | 2.5%   |
| Grillmade 2019       | 37     | 42    | 0.88       | [0.76; 0.96] | 2.4%   |
| Reeve 2014           | 68     | 77    | 0.88       | [0.80; 0.95] | 2.7%   |
| Gillespie 2019       | 121    | 141   | 0.88       | [0.82; 0.93] | 2.9%   |
| Reeve 2018           | 1752   | 1981  | 0.88       | [0.87; 0.90] | 3.1%   |
| Qi 2015              | 160    | 180   | 0.89       | [0.84; 0.93] | 2.9%   |
| Galazi 2016          | 89     | 100   | 0.89       | [0.82; 0.94] | 2.8%   |
| Cardwell 2019        | 86     | 96    | 0.90       | [0.83; 0.95] | 2.8%   |
| Nusair 2020          | 323    | 358   | 0.90       | [0.87; 0.93] | 3.0%   |
| Reeve 2013           | 92     | 100   | 0.92       | [0.86; 0.97] | 2.8%   |
| Whitty 2018          | 49     | 53    | 0.92       | [0.84; 0.98] | 2.5%   |
| Edelman 2019         | 115    | 124   | 0.93       | [0.87; 0.97] | 2.8%   |
| Martinez 2020        | 28     | 30    | 0.93       | [0.81; 1.00] | 2.2%   |
| Ng 2017              | 127    | 136   | 0.93       | [0.89; 0.97] | 2.9%   |
| Anderson 2020        | 69     | 73    | 0.95       | [0.88; 0.99] | 2.7%   |
| Scott 2019           | 73     | 75    | 0.97       | [0.92; 1.00] | 2.7%   |
| Van Marum 2016       | 39     | 40    | 0.98       | [0.90; 1.00] | 2.4%   |

Random effects model 93359
Heterogeneity: $I^2 = 95\%, \chi^2 = 0.0189, p < 0.01$

$0.84 \, [0.81; \, 0.88] \, 100.0\%$
Figure 1b. Forest plot caregivers

| Study     | Events | Total | Proportion | 95%-CI     | Weight |
|-----------|--------|-------|------------|------------|--------|
| Kua 2019  | 34     | 52    | 0.65 [0.51; 0.78] | 14.4%      |
| Paque 2019| 127    | 161   | 0.79 [0.72; 0.85] | 21.4%      |
| Scott 2019| 58     | 72    | 0.81 [0.70; 0.89] | 16.6%      |
| Reeve 2019| 168    | 205   | 0.82 [0.76; 0.87] | 22.5%      |
| Kua 2020  | 385    | 442   | 0.87 [0.84; 0.90] | 25.1%      |
| **Random effects model** | **932** |       | **0.80 [0.74; 0.86]** | **100.0%** |

Heterogeneity: $I^2 = 77\%$, $\tau^2 = 0.0051$, $p < 0.01$