Patient Preference and Adherence

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REVIEW

Methods to Assess Patient Preferences in Old Age Pharmacotherapy – A Systematic Review

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Purpose: The aim of this systematic review was to identify methods used to assess medication preferences in older adults and evaluate their advantages and disadvantages with respect to their applicability to the context of multimorbidity and polypharmacy.

Material and Methods: Three electronic databases (PubMed, Web of Science, PsycINFO) were searched. Eligible studies elicited individual treatment or outcome preferences in a context that involved long-term pharmacological treatment options. We included studies with a study population aged ≥ 65 years and/or with a mean or median age of ≥ 75 years. Qualitative studies, studies assessing preferences for only two different treatments, and studies targeting preferences for life-sustaining treatments were excluded. The identified preference measurement methods were evaluated based on four criteria (time budget, cognitive demand, variety of pharmacological aspects, and link with treatment strategies) judged to be relevant for the elicitation of patient preferences in polypharmacy.

Results: Sixty articles met the eligibility criteria and were included in the narrative synthesis. Fifty-five different instruments to assess patient preferences, based on 24 different elicitation methods, were identified. The most commonly applied preference measurement techniques were "medication willingness" (description of a specific medication with inquiry of the participant's willingness to take it), discrete choice experiments, Likert scale-based questionnaires, and rank prioritization. The majority of the instruments were created for disease-specific or context-specific settings. Only three instruments (Outcome Prioritization Tool, a complex intervention, "MediMol" questionnaire) dealt with the broader issue of geriatric multimorbidity. Only seven of the identified tools showed somewhat favorable characteristics for a potential use of the respective method in the context of polypharmacy.

Conclusion: Up to now, few instruments have been specifically designed for the assessment of medication preferences in older patients with multimorbidity. To facilitate valid preference elicitation in the context of geriatric polypharmacy, future research should focus on suitable characteristics of existing techniques to develop new measurement approaches for this increasingly relevant population.

Keywords: polypharmacy, outcome priorities, multimorbidity, older adults, multiple chronic conditions, patient-centered

Introduction

Incorporating a patient's individual preferences into medical decision-making has improved treatment adherence and patient satisfaction.[1–3] Various medical disciplines, such as oncology, cardiology, or psychiatry, have examined preference-oriented approaches to deliver optimized care.[4–6] Including the patient's priorities seems particularly favorable in clinical settings where sufficient evidence regarding the most effective treatment strategy is lacking.[7]

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The pharmacotherapy of older patients with multiple morbidities is characterized by relevant knowledge gaps due to a paucity of age-related and context-related data.[8] An uncritical adherence to disease-specific clinical practice guidelines in these patients will result in pronounced polypharmacy.[9] In numerous Western societies, prevalence rates between 10.0% and 27.4% have been reported for the chronic intake of 10 and more medicines ("excessive polypharmacy") in adults aged ≥ 65 years.[10–13] Polypharmacy increases the risk of adverse drug reactions[14] and drug-drug interactions.[15] It is independently linked with the number of incident falls experienced by older adults[16] as well as a decline in functionality.[17]

In order to prevent or even reverse the negative effects of polypharmacy, recent articles advocate "deprescribing",[18,19] 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".[20] Including the older patient's treatment preferences has been proposed as a technique to facilitate deprescribing.[21]

Employing reliable and valid preference measurement methods is the prerequisite for evaluating patient preferences and integrating them into long-term health care decision-making. Instruments used in the geriatric setting need to be intelligible and operable for the older and potentially frail adults questioned. A recent systematic review aimed to identify tools suitable for eliciting treatment preferences in aged primary care patients with multimorbidity.[22] The authors found only one tool to be potentially relevant for recording outcome priorities in this context, concluding that there was an urgent need to further develop clinically applicable assessment strategies.[22]

Acting on this need, we carried out a systematic review to identify preference measurement techniques that have been employed to determine the treatment priorities of older patients across various disease and non-disease specific settings, assess both their advantages and disadvantages with respect to their applicability in individuals with polypharmacy, and give recommendations for the development of future preference-based prescribing tools.

Material and Methods

The findings of this systematic review are presented in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[23]

Search Strategy and Information Sources

We searched three electronic databases (PubMed, PsycINFO, and Web of Science) for studies reported in English or German. Abstracts published from the inception of the databases up to October 6, 2017 were considered for inclusion. We based our search strategy on modified versions of two published search strings for the identification of literature on geriatric medicine and patient preferences for treatment outcomes.[24,25] Variations of terms relating to pharmacotherapy and health outcomes were added. The search strategy was adapted for each of the three databases. The complete search string for the PubMed database search is accessible in the Electronic Supplementary Material Table S1. Reference lists of included articles were screened manually for potentially relevant articles.

Eligibility Criteria

Studies were eligible for inclusion if they aimed to identify individual treatment or outcome preferences or priorities of older adults by using a standardized, non-qualitative methodology. We defined preference as the relative "desirability" of a certain option.[26] The medical context of preference elicitation had to involve the pharmacological treatment of chronic conditions, either by directly evaluating preferences for specific medicines or their characteristics or by evaluating preferences for health outcomes potentially achieved with medicines. Studies were included if they addressed an aged population, defined by a cut-off for inclusion of ≥ 65 years. In case the eligibility criteria of individual studies did not exclude younger patients from participation, studies were suitable for inclusion if they reported a mean or median age of participants of ≥ 75 years. We also considered articles that focused on analyzing an aged population as a specific subgroup as stated in the abstract of the respective article. Full-text articles of abstracts not reporting age-related demographic data were only retrieved if the study context referred to diseases or medical problems characteristic of old age. We only included original research journal articles.

Owing to the particular nature and non-therapeutic quality of their setting, studies reporting patient preferences in the context of advance care planning and life-sustaining treatments were excluded. We also excluded studies that assessed preferences for merely two different treatments.

Study Selection

After removal of duplicates, one of the authors (AE) screened study titles and abstracts for eligibility. Full-text articles of potentially suitable abstracts were retrieved and assessed for inclusion independently by two reviewers (AE and AR). Disparities between the reviewing authors were resolved by discussion and through consultation with a third reviewer (SG).

In case of undetermined age-related eligibility, authors of the respective articles were contacted and asked to provide relevant age-related characteristics concerning the study population.

Data Collection Process and Analysis

Two authors (AE or AR) collected data from the included studies using a standardized data extraction form. Besides core study characteristics (year, location, study design, and sample size) extracted information comprised the following items: study population (age, cognitive status, and affective status), study context, preference measurement method used with, if applicable, the name of the specific instrument, and quality criteria including validity testing. Verification of all extracted data was carried out by the second reviewer (AE or AR).

Regarding the nomenclature of the identified preference elicitation techniques we relied primarily on the characterization of the method given by the respective authors. We coined the term "medication willingness" for all not otherwise specified instruments that gave a description of a certain medication and asked the study participants whether or not and, possibly, in what kind of circumstances they were willing to take that specific medication.

The data extraction form was complemented by a short assessment evaluating the adaptability of the identified preference measurement techniques to the context of aged patients with polypharmacy ("polypharmacy assessment"). We aimed at detecting a method that could be used in a routine clinical setting to individualize the medication of older adults with multiple chronic conditions based on the individual patient's preferences. This method would have to reflect the complexity of the context by integrating the majority of the multitude of treatment outcomes and treatment-related considerations innate to geriatric polypharmacy without neglecting the characteristics of the often physically and cognitively frail older population. Therefore, the assessment consisted of four methodological characteristics judged to be of relevance for preference elicitation instruments used in this setting: (1) time budget needed for health care workers to assess patient preferences, (2) level of cognitive demand imposed on the older respondent, (3) representation of a variety of pharmacological aspects including treatment options, and (4) link of recorded preferences with specific pharmacotherapeutic strategies. Each item was evaluated on a three-point scale with the categories "high", "intermediate", "low" (time budget, cognitive demand, and variety of pharmacological aspects) or "distinct", "moderate", "indistinct" (link with treatment strategies). Table 1 summarizes the criteria used to make the allocation to the respective categories. To assess the level of cognitive demand imposed on the respondent, we evaluated the number of cognitive steps needed as well as the assumed amount of time spent to reach an appropriate decision, which is an approach previously used in the optimization of experimental designs for conjoint analysis.[27] Two authors (AE and AR) independently completed the assessment for all 55 identified instruments, analyzing the preference methods as implemented by the respective instruments. Additionally, both reviewers evaluated if the respective preference measurement technique required the respondent to make trade-offs between competing medical problems. Disagreements were settled through consensus discussions. In the case of incomplete presentation of the preference elicitation instrument, authors of the respective articles were contacted and asked to provide additional information.

Due to the heterogeneity and mostly observational design of the eligible studies we did not conduct a meta-analysis but opted to present the collected data as an in-depth narrative summary.

Quality Assessment

Owing to a lack of definite guidance on how to perform an appropriate quality assessment for preference-based studies,[28] the methodological quality of the included studies was evaluated by adapting four criteria from two previously published instruments for patient preference studies.[29,30] Two reviewers (AE, AR) independently assessed whether (1) there was a well-defined question in relation to preferences, (2) the characteristics of the participants were clearly described, (3) the respective methods to assess preferences were clearly explained, and (4) the authors reported quality criteria in relation to the elicitation methods used. We expanded criterion number (2) (characteristics of the participants) to include data on the

Table 1 Assessment Evaluating the Adaptability of the Identified Preference Measurement Instruments to the Context of Aged Patients with Polypharmacy ("Polypharmacy Assessment")

Time budget needed for health care workers to assess patient preferences	▼ — ▲	High: Health care worker present during the complete process of preference elicitation/ Interview mode Intermediate: Partly self-administered, partly completed with the help of a health care worker Low: Self-administered mode (introduction by a health care worker possible)
Level of cognitive demand imposed on respondents	▼ — ▲	High: High number of cognitive steps/high amount of time needed to reach an appropriate decision Intermediate: Intermediate number of cognitive steps/intermediate amount of time needed to reach an appropriate decision Low: Few cognitive steps/short time needed to reach an appropriate decision
Variety of pharmacological aspects represented by the method	▼ — ▲	Low: Method elicits preferences for < 5 different pharmacological aspects (health outcomes, treatment options or procedural characteristics) Intermediate: Method elicits preferences for 5–10 different pharmacological aspects (health outcomes, treatment options or procedural characteristics) High: Method elicits preferences for > 10 different pharmacological aspects (health outcomes, treatment options or procedural characteristics)
Link of recorded preferences with specific (pharmacological) treatment strategies	▼ — ▲	Indistinct: Elicits preferences for very general outcomes or treatment characteristics; no obvious link to a specific treatment Moderate: Elicits preferences (eg for the treatment of specific bodily symptoms or for a related group of medications) that hint towards a larger selection of pharmacotherapeutic strategies or elicits preferences for treatment scenarios (lacking a detailed description of all relevant characteristics) Distinct: Attributes of the preference elicitation task directly linked with specific pharmacological treatment options during the design of the tool or elicits preferences for detailed and specific treatment scenarios

cognitive and affective status of the respondents. Any disparities were resolved by discussion (see Electronic Supplementary Material Tables S2 and S3).

Results

Study Selection

Our database search identified 6786 citations; 358 articles were retrieved for full-text screening and 56 of these articles met the eligibility criteria. Four additional studies were identified by manually searching the reference lists of eligible articles. Figure 1 depicts the PRISMA flow diagram of the screening and selection process.

Study Characteristics

All articles included are listed in Table 2. The majority (86.7 %) of the studies had a cross-sectional design. The research was performed in 12 different countries. Three (5.0%) of the eligible articles were published between 1994 and 1999,[31–33] 19 (31.7%) between 2000 and 2009,[34–52] and 38 (63.3%) between 2010 and 2017 (Table 2). The respective sample size ranged from 13 to 2637 participants. In four of the considered studies, the elicitation of patient preferences was only of minor interest.[39,53–55] One study[56] was a follow-up study of a previously published cross-sectional study.[57] Four studies presumably used the same study sample.[58–61]

Study Populations

Thirty-nine studies met our age-related eligibility criteria by exclusively including adults aged 65 years and older,[32,35,37–39,41,42,44–46,49–60,62–78] 16 by reporting a mean or median age ≥ 75 years,[31,36,40,43,47,48,61,79–87] and 5 by systematically analyzing a subgroup within their overall study population aged 65 years or older.[33,34,88–90] Eleven studies indicated a mean or median age of 80 years or older.[42,47,49,51,52,54,56,57,71,74,79] Thirty-seven studies reported data regarding the cognitive status of their participants.[31,32,35,36,41–44,47,49,51–53,55–61,63–72,74,75,78,80,83,84,90] In 83.8 % of these studies

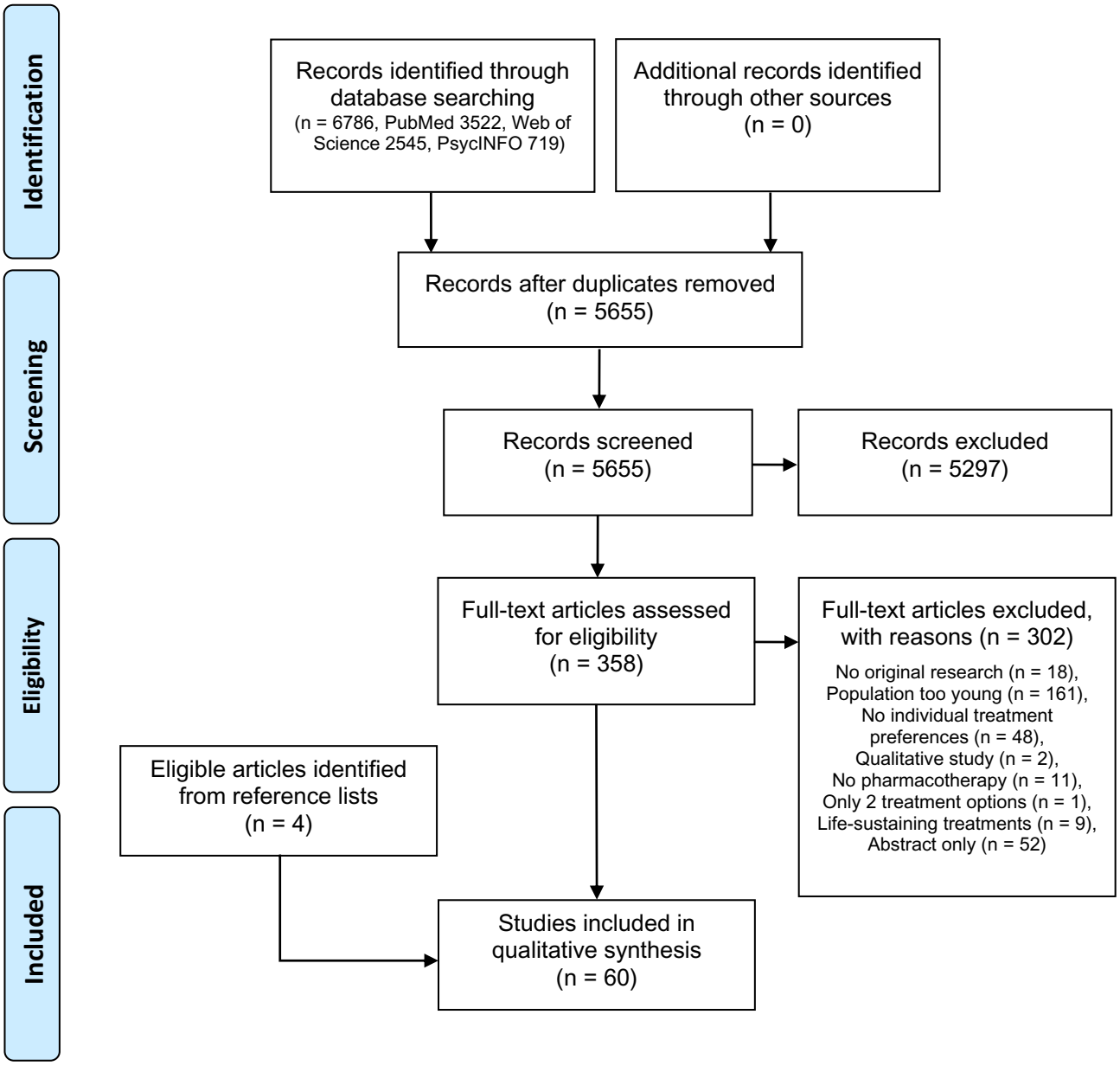

Figure 1 PRISMA flow diagram of the study screening and selection process.

participants were ineligible if one of the following criteria was present: some form of cognitive impairment such as a formal diagnosis of dementia, the failure to meet a specific cut-off on a standardized cognitive assessment, or cognitive problems as suspected by the investigator (Table 2). Seventeen studies detailed the results of a standardized cognitive evaluation of their study population.[32,36,43,51,52,55,66,68–72,74,78,80,83,84] The participants' affective status was considered by 30 studies (Table 2).

Study Context

The majority of the identified 55 instruments were designed to assess patient preferences within a disease-specific or context-specific setting. The most prevalent contexts were various types of cancer (9 tools),[33,41,48,55,66,72,86,90] mental health issues including depression (7 tools),[43,45,67,71,73,75,82,83] cardiovascular prevention (7 tools),[46,47,60,61,63,74,88] stroke prevention in atrial fibrillation (5 tools),[32,42,44,50,80] and age-related macular degeneration (4 tools).[79,81,85,87] Only three tools

Table 2 Characteristics of Included Studies

Study	Study Design	Context	Population				Method [#Instrument Number]	Quality Criteria (Validity, Reliability, Understanding)
			Population - Sample Size	Age	Cognition	Affect		
Akishita et al 2013[62] (Japan)	Cross-sectional	Priorities of health care outcomes	Community-dwelling, functionally independent older adults n = 2637	All aged ≥ 65 years	NC	NC	Rank prioritization [#47]	Reliability: subgroup tested with second version showed similar results
Baxter et al 2016[79] (United Kingdom)	Cross-sectional	Neovascular age-related macular degeneration	Patients with neovascular age-related macular degeneration n = 87 (100 included, 95 completed task, 8 were excluded for not understanding the task)	Mean = 81 years Range = 67 to 94 years	NC	NC	Conjoint analysis [#7]	Validity: 2 additional scenarios to assess validity; Task testing understanding
Böttger et al 2015[80] (Germany)	Cross-sectional	Anticoagulation therapy in atrial fibrillation	Patients with non-valvular atrial fibrillation n = 486 (647 included, 161 did not complete the interview)	Mean (SD) = 73.9 (8.2) years Median = 75.0 years (All included patients: Mean (SD) = 74.2 (8.7) years Median = 75.0 years)	Comorbidity cognitive impairment: 2.9% (all included patients: 3.9%); Comorbidity dementia: 1.0% (all included patients: 1.7%)	Comorbidity depression: 7.6% (all included patients: 8.5%)	Discrete choice experiment [#13]	Validity: 2 additional scenarios to assess validity (results not reported)

Bowling et al 2008[34] (United Kingdom)	Cross-sectional	Angina	Primary care patients with angina* n = 383 (n for the subgroup aged ≥ 75 years not specified) *Only one of the three studies described in the article met the eligibility criteria	Subgroup aged ≥ 75 years	NC	NC	Likert scale-based questionnaire ("The Patients' Preferences Questionnaire") [#23]	Psychometric properties assessed; the final questionnaire was found to be psychometrically sound
Brown et al 2008[35] (USA)	Cross-sectional	Diabetes mellitus type 2	Patients with diabetes mellitus type 2 n = 332 (n = 118 "vulnerable", n = 214 "nonvulnerable", Vulnerable Elders Scale VES-13)	All aged ≥ 65 years Subgroup "vulnerable": mean (SD) = 77 (7) years, subgroup "nonvulnerable": mean (SD) = 73 (5) years	Diagnosis of dementia and scoring less than 17 points on the MMSE were exclusion criteria	Comorbidity depression: 33% of vulnerable, 13% of nonvulnerable participants; assessed with SF-12 (no data reported)	Time trade-off [#51]	No information reported
Carpenter et al 2007[36] (USA)	Longitudinal	Care preferences and life evaluations in older adults with or without dementia	Older adults without or with very mild or mild dementia n = 64 (no dementia n = 31; very mild dementia n = 16; mild dementia n = 17)	Mean (SD) = 74.6 (5.5) years Range = 62 to 87 years	Comparison of patients with and without very mild or mild dementia (Clinical Dementia Rating 0.5–1.0)	Assessment of positive and negative affect (Dementia Quality of Life instrument)	Likert scale-based questionnaire ("Brief Treatment Planning Questionnaire" with additional questions regarding preferences in dementia care) [#24]	Test-retest reliability after one week, stability after one year; individuals with mild dementia had lower reliability than individuals with no dementia or very mild dementia

(*Continued*)

Table 2 (Continued).

Case et al 2013a[58] (USA)	Cross-sectional	Present versus future health - Quantity versus quality of life (Subcontext multimorbidity)	Community-dwelling older adults n = 357	All aged ≥ 65 years Mean (SD) = 76 (7) years	Diagnosis of dementia was exclusion criterion	Depression: 28% in past month	a) Likert scale-based questionnaire ("Time and Outcome [TOP] Scale" → "Attitude Scale") [#25] To assess construct validity: b) Visual analogue scale ("Now vs Later") [#54] c) (Health) Outcome Prioritization Tool [#40]	Construct validity: use of 2 other tools assessing the same trade-offs, analysis of patient characteristics associated with favoring quality over quantity of life, correlation of the 2 subscales; Test-retest-reliability; Internal consistency: Cronbach's α for the 2 subscales
Case et al 2013b[59] (USA)	Cross-sectional	Present versus future health - Quantity versus quality of life (Subcontext multimorbidity)/ Universal health outcomes (Multimorbidity)	Community-dwelling older adults n = 357 (1 did not complete the interview, excluded from analysis)	All aged ≥ 65 years Mean (SD) = 76 (7) years	Diagnosis of dementia was exclusion criterion	Depression (two-item PRIME-MD): 28% in past month	Subcontext multimorbidity: a) Likert scale-based questionnaire ("Attitude Scale") [#25] b) Visual analogue scale ("Now vs Later") [#54] Multimorbidity: c) (Health) Outcome Prioritization Tool [#40]	Acceptability and ease of use assessed quantitatively and qualitatively

Case et al 2014[60] (USA)	Cross-sectional	Primary prevention of myocardial infarction	Community-dwelling older adults n = 353 (357 included, 3 responded "Do not understand the question", 1 had missing data, excluded from analysis)	All aged ≥ 65 years ≥ 75 years: 56%	Diagnosis of dementia was exclusion criterion	NC	a) Likert scale-based questionnaire ("Time and Outcome [TOP] Scale") [#25] b) Visual analogue scale ("Present vs Future Health Prioritization Tool") [#54] c) (Health) Outcome Prioritization Tool [#40] d) "Medication willingness" [#31]	Validity: use of 4 tools assessing the same construct; Understanding of the task
Caughey et al 2017[63] (Australia)	Cross-sectional	Prevention of cardiovascular disease and influence of competing health outcomes (Subcontext multimorbidity)	Ambulatory patients with ≥ 2 chronic conditions n = 15	All aged ≥ 65 years Median (IQR) = 79 (73–86) years	Diagnosis of dementia was exclusion criterion	NC	"Medication willingness" [#32]	Reference to Fried et al 2011a[61]
Cherniack et al 2008[37] (USA)	Cross-sectional	Use of conventional or complementary and alternative medicine in three medical conditions (Colds, insomnia, back pain)	Ambulatory patients of geriatric clinics n = 338	All aged ≥ 65 years Mean = 77.5 years	NC	NC	Questionnaire (only questions 13–15 applicable) [#44]	No information reported

(*Continued*)

Table 2 (Continued).

Chin et al 2008[38] (USA)	Cross-sectional	Diabetes mellitus	Older patients with diabetes n = 473	All aged ≥ 65 years Mean (SD) = 73.7 (5.9) years	NC	SF-12 mental component score: Mean (SD) = 49.9 (6.8)	Time trade-off [#52]	No information reported
Cline & Mott 2003[39] (USA)	Cross-sectional	Preferences for using prescription drugs versus self-treatment strategies (Osteoporosis)	Community-dwelling older women n = 629	All aged ≥ 65 years Mean (SD) = 75.35 (6.23) years	NC	NC	Likert scale-based questionnaire ("Medical Care Preference Scale") [#26]	Reference to previous study examining the validity and reliability of the "Medical Care Preference Scale"; Internal consistency reliability reported
Cranney et al 2001[40] (Canada)	Longitudinal	Osteoporosis	Women with a recent spine or hip fracture n = 10 (subgroup "vertebral fracture") n = 10 (subgroup "hip fracture")	Vertebral fracture: Mean = 75.5 years Range = 65 to 88 years Hip fracture: Mean = 79.5 years Range = 63 to 91 years	NC	Being severely depressed was exclusion criterion; Mean SF-36 Mental health summary score at baseline 43 (vertebral fracture) and 58 (hip fracture)	Feeling Thermometer [#20]	Convergent construct validity: correlation with the HUI2 and the physical health summary of the SF-36; preferences for current health lower in vertebral and hip fracture patients than in wrist or non-fracture patients; Test-retest reliability after 2 weeks; Sensitivity to change
Danner et al 2016[81] (Germany)	Cross-sectional	Age-related macular degeneration	Patients with neovascular age-related macular degeneration n = 86	Median = 75 years	NC	NC	Analytical hierarchy process [#3]	Participants encouraged to "think aloud" during the administration of the instrument to facilitate the interpretation of the quantitative results; Consistency: overall model inconsistency just below 0.2; inconsistency very prevalent at the level of subcriteria

de Vries et al 2015[88] (Netherlands)	Cross-sectional	Antihypertensive medication in diabetes mellitus type 2	Patients with diabetes mellitus type 2 n = 45 (participants in the subgroup aged ≥ 75 years included in the analysis)	Subgroup aged ≥ 75 years: Mean (SD) = 79 (3.6) years	NC	NC	Discrete choice experiment [#14]	Dominant choice set to test understanding of the task: 10 participants (mean age (SD) = 70 (10) years) in the total study sample (n = 161) failed and were excluded from the analysis
Decalf et al 2017[64] (Belgium)	Cross-sectional	Overactive bladder	Community-dwelling and hospitalized older people with and without complaints of overactive bladder n = 276 (informed consent given by 304 people, 28 excluded from analysis)	All aged ≥ 65 years Median (IQR) = 75 (69–80) years ≥ 80 years: n = 71 (26%)	11 participants excluded from the analysis because of suspected cognitive problems	EQ-5D: n = 52 (19%) reported problems on the dimension "Anxiety/ Depression"; this group was found to be unable to make consistent choices in the discrete choice experiment	Discrete choice experiment [#15]	Rationality test with additional choice set to test the participants' understanding of the questionnaire: 3 participants excluded from the analysis because they did not pass the test
Extermann et al 2003[41] (cross-national, France and USA)	Cross-sectional	Cancer (Willingness to undergo chemotherapy)	Cancer outpatients and geriatric outpatients without history of cancer n = 195	All aged ≥ 70 years Mean = 77 years Range = 70 to 95 years	Diagnosis of dementia was exclusion criterion	GDS (Short Form) mean (SD) 2.2–4.9 (2.6–3.7); GDS score not associated with willingness to accept chemotherapy in multivariate analysis	"Medication willingness" [#33]	No information reported
Fraenkel et al 2015[89] (USA)	Cross-sectional	Preference for the status quo in chronic disease (Rheumatoid arthritis)	Patients with rheumatoid arthritis n = 42 (subgroup aged ≥ 65 years)	Subgroup aged ≥ 65 years	NC	NC	Adaptive conjoint analysis [#1]	Content validity/ comprehensibility: literature review + expert opinion

(*Continued*)

Table 2 (Continued).

Fried et al 2011a[61] (USA)	Cross-sectional	Primary prevention of myocardial infarction	Community-dwelling older adults n = 356 (1 participant failed to complete the interview, excluded from the analyses)	Mean (SD) = 76 (7) years	Diagnosis of dementia was exclusion criterion	Depression assessed as "health characteristic"; not associated with willingness to take the preventive medication	"Medication willingness" [#32]	Understanding: 4 participants responded "do not understand" to ≥ 1 scenarios; 4 additional participants gave discrepant responses
Fried et al 2011b[65] (USA)	Cross-sectional	Universal health outcomes (Multimorbidity)	Older adults with hypertension and fall risk n = 81	All aged ≥ 65 years ≥ 85 years: 30%	Diagnosis of dementia was exclusion criterion (Parent study Tinetti et al 2008b[52])	Depressive symptoms (score ≥ 2 on PHQ-2): 43% of participants	(Health) Outcome Prioritization Tool [#40]	Face validity: cognitive interviews with n = 10 participants; Construct validity: association of patient characteristics associated with a preference for life-sustaining treatment with ranking "keeping you alive" as most important; Test-retest reliability after one week evaluated as "fair to poor"; Understanding: rated by interviewers (13% of participants: no/very poor understanding of the task)
Fuller et al 2004[42] (United Kingdom)	Cross-sectional	Stroke prevention (Anticoagulation with warfarin)	Patients attending a general elderly medicine outpatient clinic n = 81	All aged ≥ 65 years Median = 81 years Range = 66 to 97 years	Cognitive impairment was exclusion criterion	NC	"Medication willingness" [#34]	Accompanying qualitative analysis of decision making

Fyffe et al 2008[43] (USA)	Cross-sectional	Depression	Home-care patients n = 28	Mean (SD) = 77 (9.7) years Range = 62 to 95 years	21% scored < 24 on MMSE	25% met criteria for a current depressive disorder (on SCID-I)	Rank prioritization [#48]	Accompanying qualitative analysis of decision making
Girones et al 2012[66] (Spain)	Prospective	Lung cancer	Patients with lung cancer n = 83	All aged ≥ 70 years Mean (SD) = 77 (5.1) years Range = 70 to 91 years ≥ 80 years: 28.9%	26.4% scored < 21 on MMSE	31.3% > 3 on GDS	Direct choice [#9]	Content validity: scenarios based on data from the literature
Gum et al 2010a[82] (USA)	Cross-sectional	Distress (Stress and sadness)	Adults participating in community health screenings n = 140	All aged ≥ 60 years Mean (SD) = 76.48 (7.56) years	NC	Frequency of distress assessed	Choose and rank [#4]	Content validity and comprehensibility pilot tested
Gum et al 2010b[83] (USA)	Cross-sectional	Stress and sadness	Adults receiving home-based aging services n = 142	All aged ≥ 60 years Mean (SD) = 74.7 (8.3) years	Diagnosis of dementia was exclusion criterion; assessed with 3MS (detailed results reported)	Assessed with SCID and BSI-18 (n = 17: any depressive disorder on SCID); assessment of self-identified behavioral health problem	Choose and rank [#4]	See Gum et al 2010a
Hamelinck et al 2016[90] (Netherlands)	Cross-sectional	Early breast cancer	Women with early primary breast cancer n = 29 (subgroup aged ≥ 65 years)	Subgroup aged ≥ 65 years	Presence of cognitive/ mental problems was exclusion criterion	Depression considered as part of assessment for "geriatric health condition"	Probability trade-off technique [#42]	Accompanying qualitative analysis of decision making

(*Continued*)

Table 2 (Continued).

Holbrook et al 2007[44] (Canada)	Cross-sectional randomized trial	Anticoagulation treatment in atrial fibrillation	Patients (family practices, geriatric day clinical program) without atrial fibrillation or warfarin treatment n = 98	All aged ≥ 65 years Mean (SD) = 73.6 (6.1)	Eligible patients were "cognitively intact"	NC	Decision aid [#8]	Validity and reliability pilot tested
Jimenez et al 2012[67] (USA)	Cross-sectional	Mental health	Patients with depression, anxiety or at-risk alcohol abuse n = 2208	All aged ≥ 65 years Mean (SD) in subgroups = 70.5–74.1 (5.0–6.2) years	Parent study: severe cognitive impairment was exclusion criterion (≥ 16 on short Orientation-Memory-Concentration Test)	Eligible participants screened positive for depression, anxiety or at-risk alcohol abuse	Questionnaire ("Cultural Attitudes toward Healthcare and Mental Illness Questionnaire") [#45]	No information reported
Junius-Walker et al 2011[68] (Germany)	Cross-sectional	Multimorbidity	Community-dwelling primary care patients n = 123	All aged ≥ 70 years Mean (SD) = 77.7 (5.4) years	"Limited consent capabilities" was exclusion criterion; Health domain "cognitive malfunction" (Clock-drawing test) problem for 45.5% of participants	Health domain "problems with mood" (depression, mourning) problem for 49.6% of participants	Complex intervention (Geriatric (STEP) assessment + rating of relevant health problems on Likert scale) [#6]	Content validity: geriatric (STEP) assessment covering multiple health domains; development process and feasibility study of STEP assessment referenced
Junius-Walker et al 2012[69] (Germany)	Cluster randomized controlled trial	Multimorbidity	Independently living primary care patients n = 317	All aged ≥ 70 years Mean = 77.2 years	"Limited mental capability" was exclusion criterion; Health domain "cognitive malfunction" (Clock-drawing test) part of STEP assessment (results reported)	Health domain "mood" part of STEP assessment	Complex intervention (Geriatric (STEP) assessment + rating of relevant health problems on Likert scale + priority setting consultation; PrefCheck Intervention) [#6]	Reference to Junius-Walker et al 2011[68]

Junius-Walker et al 2015[70] (Germany)	Cross-sectional	Multimorbidity	Primary care patients n = 826	All aged ≥ 72 years Mean (SD) = 79 (4.4) years	"Inability to consent" was exclusion criterion; Health domain "Cognition" (Clock-drawing test) positive in 31.4% of participants	Health domain "mood" (STEP assessment): problem in 37.5% (mourning), 10.9% (depression), 5.0% (loneliness) and 4.7% (anxiety) of participants	Complex intervention (Geriatric (STEP) assessment + rating of relevant health problems on Likert scale) [#6]	Reference to Junius-Walker et al 2011[68]
König et al 2014[84] (Switzerland)	Cross-sectional	Alzheimer's disease	Patients with mild to moderate Alzheimer's disease n = 126	Mean = 75 years Range = 52 to 91 years	Clinical Dementia Rating score > 6 in ≈ 31% of patients	(Depression considered in parent study, different sample size)	Willingness to pay [#55]	Construct validity: confirmation of predefined hypothesis of altruism
Landreville et al 2001[45] (Canada)	Cross-sectional	Depression	Patients of family medicine clinics n = 200	All aged ≥ 65 years Mean (SD) = 73.13 (5.98) years	NC	Mean (SD) GDS score 6.29 (5.24)	Likert scale (Case descriptions + 3 Treatment descriptions + Modified version of the "Treatment Evaluation Inventory") [#28]	Reference to previous study (validation of case descriptions; validity, test-retest-reliability and internal consistency of modified "Treatment Evaluation Inventory")
Luck-Sikorski et al 2017[71] (Germany)	Cross-sectional	Depression	Primary care patients with and without depression n = 1230	All aged ≥ 75 years Mean (SD) = 80.6 (4.66) years	Presence of moderate or severe dementia was exclusion criterion; Mean (SD) MMSE score 27.3 (2.46)	GDS: 14.0% with mild (score 4–5), 15.9% with moderate (score ≥ 6) depressive symptoms; preferred treatment options analyzed in regard to GDS score	Likert scale + Ranking [#29]	No information reported
Mandelblatt et al 2010[72] (USA)	Prospective cohort study	Breast cancer (Chemotherapy)	Women with invasive nonmetastatic breast cancer n = 801	All aged ≥ 65 years Mean (SD) = 73 (6.1) years Range = 65 to 100 years	Blessed test: 0 errors = 49% (no cognitive impairment); ≥ 1 error = 51%; ≥ 11 errors = exclusion criterion	NC	(Modified) Time trade-off [#53]	Relationship between preferences for chemotherapy and actual receipt of chemotherapy analyzed

(*Continued*)

Table 2 (Continued).

Man-Son-Hing et al 2000[46] (Canada)	Cross-sectional	Primary prevention of stroke and myocardial infarction with aspirin	Primary care patients without manifest atherosclerotic disease and without indication or contraindication for regular aspirin use n = 42	All aged ≥ 65 years Mean = 71 years Range = 65 to 85 years	(Cognitive status was assessed, data not reported)	NC	a) Individualized decision analysis [#21] b) Probability trade-off technique [#43]	Evaluation of the results of both methods by the participants; descriptions of health states previously pilot tested for content and comprehensibility (reference)
Miller et al 1998[31] (USA)	Cross-sectional	Frailty	Older adults (community health clinic, public housing for seniors, geriatric medicine clinics, retirement community) n = 359	All aged ≥ 60 years Mean (SD) = 76.8 (7.4) years	Diagnosis of dementia and "too confused to participate" were exclusion criteria	NC	Likert scale-based questionnaire [#27]	No information reported
Mohlman 2012[73] (USA)	Cross-sectional	Anxiety	Older adults n = 383 (433 surveys received, 50 excluded (incomplete or suspected misunderstanding of instructions))	All aged ≥ 65 years Mean (SD) = 75.21 (7.38) Range = 65 to 97 years Three subgroups: young-old (65–74 years), middle-old (75–84 years), oldest-old (≥ 85 years)	(Pilot tested with non-demented adults; cognition not considered in actual study)	BAI: mean (SD) = 8.46 (5.02); BDI: mean (SD) = 5.98 (6.73); STAI-trait: mean (SD) = 38.99 (11.31)	Direct choice (in response to a scenario) [#10]	Pilot tested

Mueller et al 2016[85] (Germany)	Cross-sectional (after observational period)	Neovascular age-related macular degeneration	Patients with neovascular age-related macular degeneration n = 284 (337 included, 53 excluded from analysis due to incomplete or inconsistent responses)	All aged ≥ 50 years Mean (SD) = 77.4 (7.1) years	NC	NC	Discrete choice experiment [#16]	Additional scenarios and exclusion of participants giving inconsistent responses (no detailed results reported)
Murphy et al 2002[47] (USA)	Cross-sectional	Prevention of myocardial infarction, stroke, hip fracture	Patients of a hospital-based geriatrics clinic n = 409	Mean = 81 years	Patients with dementia and/or inability to fully understand the questions were excluded	Mental illness was exclusion criterion	"Medication willingness" [#35]	Pilot tested; Reproducibility: interview repeated with 30 patients after two months
Muth et al 2016[53] (Germany)	Cluster randomized controlled pilot study	Multimorbidity	Primary care patients with ≥ 3 chronic conditions and ≥ 5 chronic prescriptions n = 100 (94 completed the study)	All aged ≥ 65 years Intervention group: mean (SD) = 75.8 (6.70) Control group: mean (SD) = 75.2 (5.88) Median = 75 years Range = 64 to 93 years	Cognitive impairment (MMSE < 26) was exclusion criterion	GDS score: intervention group: mean (SD) = 2.2 (2.12), control group: mean (SD) = 1.7 (1.89)	Questionnaire ("MediMol" questionnaire; only questions 16–18 applicable) [#46]	No information reported

(*Continued*)

Table 2 (Continued).

Nyman et al 2005[48] (Sweden)	Prospective	Locally advanced prostate cancer	Patients with locally advanced prostate cancer n = 150 (149 completed the questionnaires at entry, 148 at follow-up)	Mean = 75 years Range = 57 to 89 years	("No mental handicap" was inclusion criterion)	NC	Direct choice (after standardized written information) + questionnaire [#12]	Assessment of the patients' satisfaction with the chosen treatment three months after the direct choice
Perret-Guillaume et al 2011[74] (Switzerland)	Cross-sectional	Antihypertensive therapy	Patients hospitalized at a geriatric hospital n = 120	All aged > 70 years Mean (SD) = 83.8 (7.4) years	Presence of cognitive disorders (MMSE < 18) was exclusion criterion; MMSE score ≥ 26 in 55% of participants	GDS 4 items: score = 0/4 in 67% of participants	"Medication willingness" [#36]	Consistency of responses between scenarios reported
Pfisterer et al 2007[49] (Germany)	Cross-sectional	Urinary incontinence	Geriatric inpatients n = 117	All aged ≥ 80 years Mean (SD) = 84.6 (3.9) years	MMSE ≤ 27 was exclusion criterion	NC	Paired comparisons (on 11-point visual analogue scale; information leaflets) [#41]	Pilot tested; Consistency of individual ratings assessed
Protheroe et al 2000[50] (United Kingdom)	Cross-sectional	Atrial fibrillation	Patients with atrial fibrillation n = 97	All aged 70 to 85 years Mean (SD) = 77 (3.9) years	NC	NC	Individualized decision analysis (including ranking of health outcomes and time trade-off exercises) [#22]	No information reported
Raue et al 2011[75] (USA)	Cross-sectional	Depression	Home care patients n = 256	All aged ≥ 65 years Mean (SD) = 78.2 (7.1) years Range = 65 to 96 years	Dementia and/or MMSE ≤ 20 were exclusion criteria	SCID-I; 7% major depression, 9% minor depression; Hamilton Depression Rating Scale; Clinical Anxiety Scale	Choose and rank ("Cornell Treatment Preference Index") [#5]	Reference to previous study examining the association of treatment preferences (assessed with the "Cornell Treatment Preference Index") with various outcomes (eg adherence) in depressed patients

Rochon et al 2014[76] (USA)	Cross-sectional	Osteoarthritis of the knee	Patients with osteoarthritis of the knee n = 58	All aged ≥ 65 years	NC	NC	Adaptive conjoint analysis [#2]	Accompanying qualitative analysis (focus groups with n = 29 participants) of user experience
Schnabel et al 2014[54] (Germany)	Cross-sectional	Complementary and alternative medicine	Older adults (community-dwelling, self-reliant or assisted by home care; residents of retirement or nursing homes) n = 400	All aged ≥ 70 years Mean (SD) = 81.8 (7.4) years	(No detailed data reported, but study population included participants with legal guardian)	NC	Direct choice [#11]	No information reported
Schonberg et al 2014[55] (USA)	Longitudinal	Breast cancer	Women receiving breast biopsy n = 164	All aged ≥ 65 years Age groups 65–74 and ≥ 75 years	Dementia was exclusion criterion; assessed with Short Blessed Test (detailed results reported)	NC	"Medication willingness" [#37]	No information reported
Silverman et al 2013[77] (USA)	Cross-sectional	Osteoporosis	Postmenopausal women at risk for osteoporotic fractures n = 367	All aged ≥ 65 years Means (SD) in 4 subgroups 74.7 (7.1) to 79.7 (7.1) years	NC	Health status assessment including depressive symptoms	a) Rank prioritization [#49] b) Maximum difference scaling [#30]	Pilot tested
Sudlow et al 1998[32] (United Kingdom)	Cross-sectional	Atrial fibrillation (Anticoagulants)	Patients with atrial fibrillation n = 179	All aged ≥ 65 years	MMSE, 26% scoring < 24	NC	"Medication willingness" [#38]	No information reported

(*Continued*)

Table 2 (Continued).

Tinetti et al 2008a[51] (USA)	Cross-sectional	Competing cardiovascular disease, medication symptoms and fall injury outcomes (Subcontext multimorbidity)	Senior housing residents with hypertension and fall risk n = 13	All aged ≥ 70 years Mean (SD) = 83 (9.3) years Range = 71 to 96 years	Cognitive impairment was exclusion criterion (score < 15 on the telephone version of the MMSE); mean (SD) 19 (2.0); median 19; range = 15–21 (of 22 items)	NC	Discrete choice experiment [#17]	Pretest (n = 15); Test-retest reliability; Tested for order effects; Obvious choice task to test understanding (all 13 participants passed)
Tinetti et al 2008b[52] (USA)	Cross-sectional	Competing cardiovascular disease, medication symptoms and fall injury outcomes (Subcontext multimorbidity)	Persons with hypertension and fall risk n = 123 (2 additional individuals failed to complete the choice task and were excluded)	All aged ≥ 70 years Mean (SD) = 81.5 (5.9) years Range = 70 to 96 years	Diagnosis of dementia or MMSE (telephone version) < 15 were exclusion criteria; 21.1% with MMSE < 19; exclusion of individuals who failed a simple choice task (18.4% of otherwise eligible persons)	32.0% with depressive symptoms (score ≥ 2 on PHQ-2)	Discrete choice experiment [#17]	Reference to Tinetti et al 2008a[51]
Uemura et al 2016[86] (Japan)	Cross-sectional	Castration-resistant prostate cancer	Patients with castration-resistant prostate cancer n = 133 (134 included, 1 person excluded from main analyses for giving inconsistent responses)	Mean (SD) = 75.36 (7.39) years	(Participants had to be able to complete the survey by themselves)	NC	Discrete choice experiment [#18]	Additional choice set with dominant scenario to test understanding
van Summeren et al 2016[57] (Netherlands)	Cross-sectional (Pilot study)	Universal health outcomes (Multimorbidity)	Primary care patients with polypharmacy (≥ 5 chronic medications) and multimorbidity (≥ 2 chronic conditions) n = 60	All aged ≥ 69 years Mean (SD) = 83.8 (4.2) years	Cognitive impairment (failing to understand the four health outcomes) was exclusion criterion	NC	(Health) Outcome Prioritization Tool [#40]	Acceptability and practicability (including the patients' understanding of the task) evaluated with semi-structured questionnaires and in-depth interviews

van Summeren et al 2017[56] (Netherlands)	Cross-sectional (Follow-up study)	Universal health outcomes (Multimorbidity)	Primary care patients with polypharmacy (≥ 5 chronic medications) and multimorbidity (≥ 2 chronic conditions) n = 59	All aged ≥ 69 years Median (IQR) = 83 (81–86) years	Cognitive impairment was exclusion criterion	NC	(Health) Outcome Prioritization Tool [#40]	Reference to van Summeren et al 2016,[57] Fried et al 2011b[65] and one additional previous study by Fried et al
Vennedey et al 2016[87] (Germany)	Cross-sectional	Neovascular age-related macular degeneration	Patients with neovascular age-related macular degeneration n = 86	Median = 75 years	NC	NC	Discrete choice experiment [#19]	Pilot tested; Duplicate choice set to test consistency; Participants rated the difficulty of the choice task; Participants encouraged to "think aloud" during the administration of the instrument to facilitate the interpretation of the quantitative results
Voigt et al 2010[78] (Germany)	Cross-sectional	Multimorbidity	Primary care patients n = 35	All aged ≥ 70 years Mean = 77.7 years	Severe dementia was exclusion criterion; Health domain "cognition" part of STEP assessment (detailed results reported)	Health domain "Mood" part of STEP assessment	Complex intervention (Geriatric (STEP) assessment + rating of relevant health problems on Likert scale) [#6]	Content validity: geriatric (STEP) assessment covering multiple health domains; development process of STEP assessment referenced
Yellen et al 1994[33] (USA)	Cross-sectional	Cancer	Cancer patients n = 42 (subgroup aged ≥ 65 years)	Subgroup aged ≥ 65 years: Mean = 70.7 years ≥ 75 years: n = 10	NC	NC	a) "Medication willingness" ("Treatment-Acceptance Vignettes") [#39] b) "Switch-Point Vignettes" [#50]	No information reported

Abbreviations: 3MS, Modified Mini-Mental State Examination; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; Blessed test, Blessed Orientation-Memory-Concentration test; BSI-18, Brief Symptom Inventory-18; EQ-5D, EuroQol 5-Dimensions questionnaire; GDS, Geriatric Depression Scale; HUI2, Health Utilities Index Mark 2; IQR, interquartile range; MMSE, Mini-Mental State Examination; NC, not considered; PHQ-2, Patient Health Questionnaire-2; PRIME-MD, Primary Care Evaluation of Mental Disorders; SCID, Structured Clinical Interview for DSM-III-R; SCID-I, Structured Clinical Interview for DSM-IV Axis I Disorders; SD, standard deviation; SF-12, Medical Outcomes Study 12-Item Short Form Health Survey; SF-36, Medical Outcomes Study 36-Item Short Form Health Survey; STAI-trait, State Trait Anxiety Inventory (trait scale); STEP, Standardized Assessment for Elderly Patients in Primary Care.

were designed for the greater context of multimorbidity: the Outcome Prioritization Tool,[56,57,59,60,65] the complex intervention "PrefCheck" combining a comprehensive geriatric assessment ("STEP assessment") with a health priority evaluation,[68–70,78] and the "MediMol" questionnaire.[53] The latter, however, focuses on the monitoring of various medication-related problems and includes only a minor preference assessment. Four tools concentrated on a specific sub-context of multimorbidity, such as the trade-offs between present and future health (2 tools)[58,59] or the trade-offs between a specific subset of competing health outcomes in multimorbidity (2 tools).[51,52,63] One instrument evaluated a set of general health outcomes for the medical care of older adults.[62]

Methods to Assess Patient Preferences

The most prevalent preference elicitation methods among the 55 identified instruments were "medication willingness" (9 instruments), discrete choice experiments (7 instruments), and Likert scale-based questionnaires (6 instruments) (Tables 2 and 3). Six instruments used ranking exercises, two in combination with a preceding choice of the most relevant options by the participant and one in combination with a Likert scale.[43,62,71,75,77,82,83] A direct choice between different treatment options was employed by four instruments, one using an additional questionnaire.[48,54,66,73] The time trade-off technique and questionnaires were used by three instruments respectively.[35,37,38,53,67,72] Two instruments each used adaptive conjoint analysis,[76,89] the probability trade-off technique,[46,90] or an individualized decision analysis.[46,50] Single instruments applied the analytical hierarchy process,[81] a complex intervention,[68–70,78] traditional conjoint analysis,[79] the format of a decision aid,[44] the feeling thermometer,[40] maximum difference scaling,[77] paired comparisons,[49] switch-point vignettes,[33] a visual analogue scale,[59,60] and willingness to pay.[84] One specific health outcome prioritization tool was evaluated by five different studies.[56,57,59,60,65]

Test Quality of the Instruments to Assess Patient Preferences

The column "quality criteria" in Table 2 gives a short summary regarding the test quality for each of the different instruments as reported in the respective articles. Owing to the large number of studies using literature searches and expert opinions during the design of the preference tools, data on content validity were omitted in favor of further validity or reliability assessments. Five studies evaluated the construct validity of the respective tools by measuring their agreement with other preference instruments or with predefined hypotheses.[40,58,60,65,84] All seven discrete choice experiments and the traditional conjoint analysis used additional choice scenarios to test the participants' understanding of the task as well as the consistency of their answers.[51,64,79,80,85–88] One study targeted criterion validity by inquiring the patients' satisfaction with the treatment that was selected based on the results of the preference elicitation.[48] Nine studies applied qualitative research to aid the interpretation of the quantitative results of the respective preference task.[42,43,57,59,65,76,81,87,90]

Polypharmacy Assessment

The results of our "polypharmacy assessment" are detailed in Table 3. The majority of the instruments (70.9 %) were exclusively tested in interview mode and thus claimed a high amount of time of the respective health care worker. Eighteen instruments were judged to impose a low cognitive demand on the older respondent, 20 to impose an intermediate, and 15 to impose a high cognitive demand. Tools that were rated to present a low cognitive demand primarily used Likert scales, other questionnaires, a direct choice, or ranking exercises with few attributes as their methodological approach. Instruments with a high cognitive demand asked of the respondent to simultaneously trade-off between a large number of attributes or several probability calculations, for example within more complex conjoint analysis-based experiments or during time trade-off tasks. Only three tools evaluated more than 10 pharmacological attributes and were rated to represent a broad variety of aspects.[35,62,68–70,78] The majority of the instruments provided an either distinct (28 tools) or moderate (22 tools) link with a specific drug therapy. The advantages and disadvantages of the various methods showed opposing trends: no tool with a low cognitive demand and only one tool[35] that represented a high variety of pharmacological aspects was rated to provide a distinct link with a specific treatment strategy (Table 3).

No tool was given an ideal rating, and none of the instruments scored more than two positives out of the four ratings. Only seven tools scored at least one positive rating and no negative rating for the criteria "cognitive demand", "variety of pharmacological aspects", and "link with treatment strategies": one analytical hierarchy process,[81] the

Table 3 Results of the "Polypharmacy Assessment" (Assessment Evaluating the Adaptability of the Identified 55 Preference Measurement Instruments to the Context of Aged Patients with Polypharmacy)

	Method	Instrument Number/Study	Time Budget	Cognitive Demand	Variety of Aspects	Link with Treatment	Comments	Trade-Offs
1.	Adaptive conjoint analysis	#1 Fraenkel et al 2015[89]	▼	▼	—	▲		Yes
		#2 Rochon et al 2014[76]	▲	▼	—	▲		Yes
2.	Analytical hierarchy process	#3 Danner et al 2016[81]	▼	—	—	▲		Yes
3.	Choose and rank	#4 Gum et al 2010a,[82] 2010b[83]	▼	▲	▼	—		Yes
		#5 Raue et al 2011[75]	▼	▲	▼	—		Yes
4.	Complex intervention	#6 Junius-Walker et al 2011,[68] 2012,[69] 2015,[70] Voigt et al 2010[78]	▼	▲	▲	—		No
5.	Conjoint analysis	#7 Baxter et al 2016[79]	▼	▼	—	▲		Yes
6.	Decision aid	#8 Holbrook et al 2007[44]	▼	—	▼	▲		Yes
7.	Direct choice (between different options)	#9 Girones et al 2012[66]	▼	Insufficient data	▼	▲		No
		#10 Mohlman 2012[73]	—	▲	▼	—		No
		#11 Schnabel et al 2014[54]	▲/▼	▲	▼	—		No
8.	Direct choice + Questionnaire	#12 Nyman et al 2005[48]	▲	Insufficient data	▼	▲		Yes
9.	Discrete choice experiment	#13 Böttger et al 2015[80]	▼	—	—	▲		Yes
		#14 de Vries et al 2015[88]	▲	▼*	—	▲	*Cognitive demand: 6 attributes, changing probability data within attribute levels, 3 options per choice set	Yes
		#15 Decalf et al 2017[64]	▲/▼	—	▼	—*	*Link with treatment: link to treatment strategies only at the level of side effects	Yes
		#16 Mueller et al 2016[85]	▼	—	▼	▲		Yes
		#17 Tinetti et al 2008a,[51] 2008b[52]	▼	—	▼	▲		Yes
		#18 Uemura et al 2016[86]	▲	▼*	—	▲	*Cognitive demand: 6 attributes, changing probability data within attribute levels	Yes
		#19 Vennedey et al 2016[87]	▼	—	—	▲		Yes
10.	Feeling thermometer	#20 Cranney et al 2001[40]	▼	—	—	—		Yes

(*Continued*)

Table 3 (Continued).

	Method	Instrument Number/Study	Time Budget	Cognitive Demand	Variety of Aspects	Link with Treatment	Comments	Trade-Offs
11.	Individualized decision analysis	#21 Man-Son-Hing et al 2000[46]	▼	—*	▼	▲	*Cognitive demand: assessment of health states on visual analogue scale	No
		#22 Protheroe et al 2000[50]	▼	▼*	▼	▲	*Cognitive demand: ranking of 9 health states + time trade-off	Yes
12.	Likert scale	#23 Bowling et al 2008[34]	Insufficient data	▲	▼	—		No
		#24 Carpenter et al 2007[36]	▼	▲	Insufficient data*	Insufficient data*	*Missing information regarding exact questionnaire items	No
		#25 Case et al 2013a,[58] 2013b,[59] 2014[60]	▼	—	▼	—	"Attitude Scale"/"Time and Outcome Preference (TOP) Scale"	Yes
		#26 Cline & Mott 2003[39]	▲	▲	▼	▼		No
		#27 Miller et al 1998[31]	▲/▼	▲	▼	—		No
		#28 Landreville et al 2001[45]	▲/▼	—	▼	—		No
13.	Likert scale + Ranking	#29 Luck-Sikorski et al 2017[71]	▼	▲	▼	—		Yes
14.	Maximum difference scaling	#30 Silverman et al 2013[77]	▲/▼	—	—	▲		Yes
15.	"Medication willingness"	#31 Case et al 2014[60]	▼	—	▼	▲	Single question regarding preventive medication	No
		#32 Version 1: Fried et al 2011a[61] Version 2: Caughey et al 2017[63]	▼	▼	—/▼*	▲	*Version 2 (Caughey et al 2017) covers also competing health outcomes	Yes
		#33 Extermann et al 2003[41]	▲	—	▼	▲		Yes
		#34 Fuller et al 2004[42]	▼	—	—	▲		Yes
		#35 Murphy et al 2002[47]	▼	—	▼	—		Yes
		#36 Perret-Guillaume et al 2011[74]	▼	▼	▼	▲		Yes
		#37 Schonberg et al 2014[55]	▼	▲	▼	—		No
		#38 Sudlow et al 1998[32]	▼	▲	▼	—		No
		#39 Yellen et al 1994[33]	▼	▼	▼	▲	"Treatment-Acceptance Vignettes"	Yes
16.	Outcome Prioritization Tool	#40 Case et al 2013b,[59] 2014,[60] Fried et al 2011b,[65] van Summeren et al 2016,[57] 2017[56]	▼	—	▼	—/▼*	*Link with treatment: items vary in practical implications	Yes

(*Continued*)

Table 3 (Continued).

	Method	Instrument Number/Study	Time Budget	Cognitive Demand	Variety of Aspects	Link with Treatment	Comments	Trade-Offs
17.	Paired comparisons	#41 Pfisterer et al 2007[49]	▼	—	▼	—		Yes
18.	Probability trade-off technique	#42 Hamelinck et al 2016[90]	▼	▼	▼	▲		Yes
		#43 Man-Son-Hing et al 2000[46]	▼	▼	▼	▲		Yes
19.	Questionnaire	#44 Cherniack et al 2008[37]	—	▲	▼	—	Only part of the questionnaire assesses preferences, items 13 to 15 considered	No
		#45 Jimenez et al 2012[67]	▼	▲	▼	—		No
		#46 Muth et al 2016[53]	▼	▲	—	—	Only part of the "MediMol" questionnaire assesses preferences, items 16 to 18 considered	No
20.	Rank prioritization	#47 Akishita et al 2013[62]	▲	—	▲	▼		Yes
		#48 Fyffe et al 2008[43]	▼	▲	▼	—		Yes
		#49 Silverman et al 2013[77]	▲/▼	▲	▼	—		Yes
21.	Switch-Point Vignettes	#50 Yellen et al 1994[33]	▼	▼	▼	▲		Yes
22.	Time trade-off	#51 Brown et al 2008[35]	▼	▼	▲	▲		Yes
		#52 Chin et al 2008[38]	▼	▼	—	▲		Yes
		#53 Mandelblatt et al 2010[72]	▼	▼	▼	—		Yes
23.	Visual analogue scale	#54 Case et al 2013b,[59] 2014[60]	▼	▲	▼	▼	"Now vs Later"/ "Present vs Future Health Prioritization"	Yes
24.	Willingness to pay	#55 König et al 2014[84]	▼	—	▼	▲		Yes

Notes: Time budget = Time budget needed for health care workers to assess patient preferences; Cognitive demand = Level of cognitive demand imposed on respondents; Variety of aspects = Variety of pharmacological aspects represented by the method; Link with treatment = Link of recorded preferences with specific (pharmacological) treatment strategies; Trade-offs = Instrument requires the respondent to make trade-offs between competing medical problems (Yes or No).
▼→ Negative rating: High (time budget, cognitive demand), Low (variety of aspects), Indistinct (link with treatment); — → Intermediate/Moderate rating: Intermediate (time budget, cognitive demand, variety of aspects), Moderate (link with treatment); ▲ → Positive rating: Low (time budget, cognitive demand), High (variety of aspects), Distinct (link with treatment); ▲/▼ Low or High (time budget); —/▼Intermediate or Low (variety of aspects), Moderate or Indistinct (link with treatment).

complex intervention "PrefCheck",[68–70,78] two discrete choice experiments,[80,87] the maximum difference scaling,[77] one example of "medication willingness",[42] and the "MediMol" questionnaire[53] (Table 3). The analytical hierarchy process, maximum difference scaling as well as discrete choice experiments are well-established methods to measure preferences.[77,80,81,87] "PrefCheck" is a complex intervention, specifically designed to assess health priorities in older primary care patients.[68] It is based on a validated comprehensive geriatric assessment.[68] No data regarding the validity or reliability of the instrument have been reported for the "MediMol" questionnaire.[53]

Methodological Quality of Included Studies

The results of the quality assessment are depicted in the Electronic Supplementary Material Table S3. Four studies failed to give a comprehensive description of the preference measurement method used.[36,48,66,89]

Discussion

To our knowledge, this is the first review to both systematically identify methods used to assess medication preferences in older adults and to rate their potential in regard to preference elicitation within the context of polypharmacy. We aimed at determining methods that could support an individualized prescribing process by including the patient's medication preferences.

We identified 55 different instruments that have been applied to evaluate patient preferences in old age pharmacotherapy, based on 24 different methods to determine preferences. Apart from "medication willingness", a term that we originally coined to specify a group of not otherwise characterized instruments that directly elicited the participant's willingness for the use of a certain medication, we found that discrete choice experiments, Likert scale-based ratings, and ranking exercises were the most commonly employed elicitation methods in older adults. This finding is in line with data from a non-age-specific investigation on the integration of patient preferences in clinical decision-making that listed rating scales, ranking exercises as well as discrete choice experiments amongst the most prevalent methods.[91]

Only a minority of the eligible instruments targeted the context of multimorbidity-related polypharmacy. In addition to the Outcome Prioritization Tool identified in a review on preference elicitation in older primary care patients with multiple conditions,[22] we found two further tools that were specifically designed to assess multimorbidity-related patient preferences. The complex intervention "PrefCheck" combines the geriatric "STEP assessment" with a Likert scale-based individual health priority evaluation by the patients and their general practitioners followed by a priority-setting consultation. It focusses on general health problems, with medication-related aspects being one part of an extensive evaluation including social and financial issues. Because it is based on a comprehensive geriatric assessment, this approach is time-consuming but might be practicable in settings routinely collecting the respective data. The reliability of the "PrefCheck"-related health priority evaluation is yet to be determined.[68] The second additional instrument identified, the "MediMol" questionnaire, does not primarily focus on measuring patient preferences but incorporates the elicitation of universal health priorities into the assessments of various medication-related issues. Neither the "PrefCheck" intervention nor the "MediMol" questionnaire allow for trade-offs between competing health outcomes.

To identify further preference measurement techniques that could serve as a basis for future tools to allow for preference-based individualized prescribing in polypharmacy, we conducted a thorough evaluation of all 55 identified preference elicitation instruments and analyzed their advantages and disadvantages with the help of four relevant characteristics ("time budget", "cognitive demand", "variety of pharmacological aspects", and "link with treatment strategies"). In order to meet the time constraints imposed by routine medical practice, tools for the measurement of patient preferences should reduce the amount of time the physician needs to invest in preference elicitation. However, the vast majority of the instruments in our review were tested in interview mode and as such did not offer any time-saving benefits. To allow for large-scale application outside of separately funded study settings, future tools need to be simple and usable to be self-administered by the older patient and future research should particularly address the feasibility of self-administration. Alternatively, one might advocate integrating the standardized elicitation of patient preferences into the comprehensive geriatric assessment, thereby providing a time frame for this important task within the routine geriatric setting.

Besides the "PrefCheck" intervention and the "MediMol" questionnaire only five other instruments showed no negative rating and at least one positive rating for the remaining three criteria "cognitive demand", "variety of pharmacological aspects", and "link with treatment strategies". Two discrete choice experiments were among these five favorable tools.[80,87] Typical for this method, these two instruments were designed to directly link the measured patient preferences to a specific drug therapy, revealing one of the advantages of this approach. Both tools balanced the cognitive demand of their choice tasks and the number of attributes within the choice sets by defining simple attribute levels, refraining from confronting the participants with risk reduction percentages, and using visual aids such as pictographs or a clear questionnaire layout. The cognitive demand of a discrete choice

experiment is expected to increase with the number of attributes included in the choice task and the maximum number of attributes to consider is generally given as six to seven.[92] This restricted number of health outcomes or other pharmacotherapy-related aspects that could be represented in the instrument seems to limit the profitable use of the method in multimorbidity-related polypharmacy. However, future tools aiming at preference-based individualized prescribing might combine the actual discrete choice experiment with an individual preselection of the relevant attributes by the patient. The indirect scenario-based approach of preference measurement is thought to be challenging for the respondent and none of the seven discrete choice experiments in this review was rated to impose a low cognitive demand on the participant. However, research indicates that simple discrete choice experiments with a reduced number of choice sets might be successfully completed even by older adults with mild cognitive impairment.[93] The cognitive demand for the older participant and its impact on the feasibility of the instruments need to be evaluated in more depth in order to clarify whether the potential of this popular method of preference elicitation is developable or limited in old-age polypharmacy. Similar considerations might apply to the analytical hierarchy process[81] and the maximum difference scaling[77] which, according to the standards of our assessment, impose an intermediate cognitive demand on the respondent. To date, little evidence in regard to the measurement of patient preferences exists for either of these methods. The last approach rated as possibly favorable in polypharmacy, a version of "medication willingness",[42] differs from the aforementioned techniques in that it would require developing a reasoned algorithm of adding or altering variables of a medication scenario and repeatedly asking the patients whether or not they would be willing to take the specified drug therapy.

Interestingly, the Outcome Prioritization Tool, which was previously identified as potentially relevant for measuring treatment preferences in older patients with multiple conditions,[22] did not tend towards an overall favorable rating on our "polypharmacy assessment". This evaluation was based on the time-consuming design as an interview tool, the intermediate level of cognitive demand owing to the need of multiple trade-offs, the limited number of health outcomes incorporated in the instrument, and a moderate to unclear link of the recorded priorities with a specific drug therapy. The latter evaluation is substantiated by the results of a recent study that suggested that primary care physicians might find it difficult to translate the patient's preference for the general outcome "maintaining independence" to a certain change in his or her medication.[56]

Several limitations of this systematic review should be addressed. Despite our comprehensive search strategy, potentially eligible articles might not have been identified. The four methodological criteria for the "polypharmacy assessment" were developed by our research group instead of being derived from a thorough literature review and accompanying expert interviews. Due to the unique characteristics of pharmacotherapy we limited our eligibility criteria to exclude studies without any long-term drug therapy-related aspects. It might be possible, that published methods assessing patient preferences within non-pharmacological contexts, eg surgery, could also offer some potential in relation to preference elicitation in polypharmacy.

Conclusion

To our knowledge, this is the first systematic review offering a comprehensive overview of instruments used to assess patient preferences in old age pharmacotherapy. No ideal method for practicable and valid elicitation of patient preferences in the context of geriatric polypharmacy could be identified. By evaluating the existing preference measurement instruments on four criteria salient for successful preference-based individualized prescribing in polypharmacy, the findings of this systematic review can guide future research in polypharmacy-related patient preferences and provide relevant information for the development of new and more appropriate measurement approaches.

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