Medication appropriateness tool for co-morbid health conditions in dementia: consensus recommendations from a multidisciplinary expert panel

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Abstract

Background: Medication management for people living with dementia is a complex task as it is unclear what constitutes optimal medication management in this population due to the shifting focus of health priorities and the balance between the benefits and harms of medications.

Aim: This study sought expert opinion to create a consensus list to define appropriate medication management of co-morbidities for people with dementia.

Methods: This study used the Delphi technique. We invited multidisciplinary experts in geriatric therapeutics including pharmacists, doctors, nurse practitioners, a patient advocate and a psychologist to participate. Participants were asked to engage into three or more rounds of questioning. Round 1 was a questionnaire comprised of one question defining dementia and seven open-ended questions about appropriate management of co-morbidities in people with dementia. Two investigators qualitatively analysed the responses to questions from Round 1 using thematic analysis. The results of this analysis were provided to participants as statements in the Round 2 survey. The participants were asked to rate their agreement with each statement on a 5-point Likert scale. The median and interquartile range (IQR) were calculated for the responses to each statement. Consensus was pre-specified as an IQR less than or equal to 1. Statements where consensus was not achieved were presented to participants in Round 3. The Round 2 median and IQR values were provided and participants were again asked to rate their agreement with each statement on a 5-point Likert scale. The statements where participants agreed or strongly agreed were included in the Medication Appropriateness Tool for Co-morbid Health conditions in Dementia criteria.

Results: Fifty-seven experts agreed to participate in the study, of whom 58% were pharmacists and 36% were medical practitioners. Fifty-five participants completed the Round 1 (95% response rate). A total of 128 statements was included in the Round 2 survey. Consensus was reached on 93 statements in Round 2 (n = 48 responders, 84% response rate) and on 18 statements in Round 3 (n = 43 responders, 75% response rate). The participants reached consensus on 111 of 128 statements. Of these statements, 67 statements were included in the Medication Appropriateness Tool for Co-morbid Health conditions in Dementia criteria. The statements were in the broad themes of preventative medication, symptom management, disease progression, psychoactive medication, treatment goals, principles of medication use, side-effects and medication reviews.

Discussion: This research provides consensus-based guidance for clinicians who manage co-morbid health conditions in people with dementia.

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Conflict of interest: None.

Introduction

Dementia is a life-limiting disease with an average survival time of less than 5 years from diagnosis.[1,2] It is the third leading cause of death and the leading cause of disability burden in adults aged 65 years and over in Australia.[3,4] Co-morbidities and polypharmacy are common in people with dementia, though evidence is scarce for medication safety, tolerability and efficacy in this population.[5–7]

People with dementia have as many co-morbidities as their peers (cognitively intact people of a comparable age) and take a mean of five or more medications daily.[8–14] However, people with dementia are more likely than their peers to use certain medication classes, such as antihypertensives, laxatives, diuretics, antidepressants and antipsychotics.[15,16] This medication use may reflect risk factors for dementia and common co-morbidities such as cardio and renovascular disease.[6,17–19]

Age-related pharmacokinetic changes occur in all older people,[20–22] and an altered blood-brain permeability in people with dementia means that they may be more sensitive to neurological and cognitive effects of medications than their peers.[23,24] These pharmacokinetic changes are additional to drug-disease interactions that occur in dementia.[25] The safety profile and efficacy of many medications in people with dementia are undetermined due to their active exclusion from 85% of published clinical trials.[26] Furthermore, the tendency for people with dementia to under-report disease-related symptoms means that it is likely they also under-report side-effects.[27]

Research in people with dementia focuses on treatments that prevent or delay dementia onset and/or progression and manage dementia-specific symptoms,[28] such as the neuropsychiatric or behavioural symptoms common in people with dementia.[29,30] Evidence for the efficacy of these medications is conflicting,[31,32] and the harms of some, such as antipsychotics and benzodiazepines, make them potentially inappropriate in this population.[33]

Despite the frequency of co-morbidities and medication use among people with dementia, appropriate medication management in this life-limiting condition is infrequently studied and poorly understood. Studies of antihypertensives, hypoglycaemics, statins and anti-inflammatories mainly assess their ability to delay dementia onset.[34–41] After dementia onset, medication appropriateness to manage co-morbidities is complicated by a relative absence of evidence.[5–7] Preventive treatments may require a treatment time to benefit that exceeds life expectancy,[42] or may target treatment goals that are not relevant to the individual or their families.[43] This is combined with a shifting focus on the priorities of healthcare in this patient cohort and the balance between the benefits and harms of medicines.[44]

Medication management is subsequently complicated for people with dementia, and careful consideration should be given to initiation and continuation of all medications. Medication management decisions for people with dementia are often based on data collected in younger adults or peers, which may not be generalisable or relevant to this population. The existing explicit prescribing criteria developed for older people do not account for the additional complexities of dementia or its life-limiting nature.[45–49] Consensus-based guidance specifically for people with dementia would assist clinicians with decision-making in this population.[50,51] This study aimed to elicit opinion and gain consensus on appropriate medication management of co-morbidities in people with dementia. The intended outcome was to create a consensus-based list of statements to define appropriate medication management of co-morbidities in people with dementia named the Medication Appropriateness Tool for Co-morbid Health conditions in Dementia (MATCH-D) criteria.

Methods

The methods for this study have been previously described in detail, [52] and are briefly described here.

Ethical approval was granted from the University of Western Australia's Human Research Ethics Committee (HREC) (reference: RA/4/1/7172).

Expert panel selection

Clinical and research based experts with relevant backgrounds were eligible for inclusion on the multidisciplinary expert panel. Participants were identified using a multipronged approach.[52] Relevant professional associations and networks were approached to distribute an advertisement for recruitment to their membership. Individuals identified as potentially eligible participants through their peer-reviewed publications, participation in relevant conferences or peer-nominated, were sent personalised letters of invitation to participate. Conflicts of interest were declared and assessed.

Data collection

The Delphi technique consisted of three rounds (Fig. 1), which were administered via Qualtrics: Online Survey Software & Insight Platform.[53] A cover sheet that stated the intention of the rounds was included.

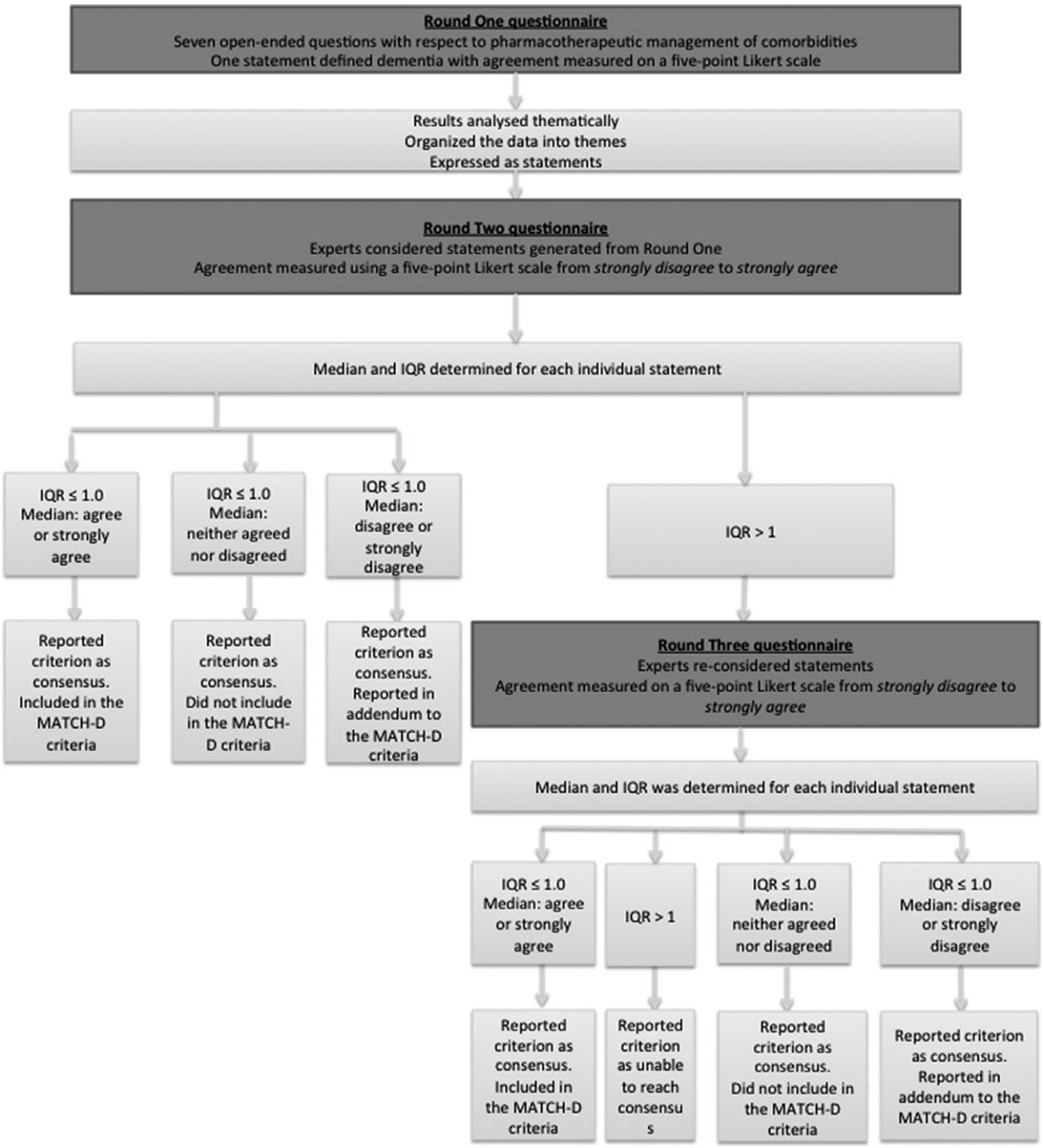

Figure 1 Flow chart to illustrate the process of the three rounds of the Delphi technique.

Round 1 – survey design

The survey questions were developed by three investigators (AP, CEB and KP). The Round 1 questionnaire asked seven open-ended questions with respect to pharmacotherapeutic management of co-morbidities for people with dementia. The questionnaire included one statement that measured agreement on a 5-point Likert scale. This statement was to define dementia. The questions asked the expert panelists their opinion on the approach to medication management of co-morbidities for people with dementia (Supporting Information, Appendix S1).

Round 1 – survey pilot

The survey was piloted with all the investigators (three pharmacists, a general practitioner and a geriatrician/clinical pharmacologist). Adjustments were made to the questions and format of the survey based on their feedback. The pilot process was repeated with five senior clinical pharmacists in November 2014. The survey was further adjusted based on their feedback.

Round 1 – survey administration

The survey was administered to the expert panel in May and June 2015.

Round 1 – data analyses

The responses to the open-ended questions collected during Round 1 were analysed thematically. Two researchers independently coded the data using content analysis to organise the data into themes and collaborated to discuss any disagreement to reach a consensus.

The Round 1 analysis was used to develop statements to present to participants in the Round 2 survey. Statements were amalgamated where the researchers agreed that the statements had the same or very similar meaning.

Rounds 2 and 3

Round 2 – survey design

The Round 2 survey consisted of statements generated in response to the open-ended questions in the Round 1 survey. Participants were asked to state the extent to which they agree with the statements using a 5-point Likert scale from *strongly disagree* to *strongly agree*.

Statements with quantitative thresholds were repeated with different sensitivities to clarify agreement where relevant. For example, participants were asked if they agreed with the statements that a medication review (otherwise known as a medicines use review (MUR)) should be triggered by (i) five or more medications, (ii) eight or more medications and (iii) ten or more medications.

Statements were referenced to early, mid and late stages of dementia. The stages were defined for the participants as:

> Early-stage dementia: "mild cognitive impairment with a preserved ability to self-care and undertake activities of daily living."
>
> Mid-stage dementia: "moderate cognitive impairment with physical function often preserved. People with mid-stage dementia may be living with support in the community or a low-care residential aged care setting."
>
> Late-stage dementia: "severe cognitive impairment and declining function (inability to recognise loved ones, unable to ambulate independently, incontinent of urine or faeces)."

Round 3 – survey design

Statements to which agreement was reached in Round 2 were removed from the survey for Round 3. The remaining statements to which the agreement was not reached in Round 2 were resubmitted to the panel in the Round 3 survey.

Rounds 2 and 3 – survey administration

The Round 2 survey was administered in September and October 2015, and the Round 3 survey was administered in November 2015.

Rounds 2 and 3 – data analyses

The quantitative data (responses to the Likert scales) were entered into SPSS v22 (IBM, Armonk, NY, USA) for Macintosh statistical software for analysis.[54]

To undertake the quantitative analysis, the Likert scale responses were coded numerically as: *strongly disagree* = 1, *disagree* = 2, *neither agree nor disagree* = 3, *agree* = 4 and *strongly agree* = 5. Descriptive statistics were undertaken on the entire data set to determine the median and interquartile range (IQR) for each statement. Where the median was not a whole number, it was rounded to the nearest whole unit so that it remained consistent with a response of strongly disagree, disagree, neither agree nor disagree, agree or strongly agree.

Definition of consensus

Consensus for an individual statement was pre-defined as an IQR less than or equal to 1.[52]

Statement synthesis for the MATCH-D criteria

The statements were condensed to produce the final MATCH-D criteria. Statements were included in the MATCH-D criteria for clinical application where the participant consensus was agreed or strongly agreed. Statements were not included in the MATCH-D criteria where the participants reached agreement that they neither agreed nor disagreed, disagreed or strongly disagreed.

Statements where participants agreed that it was relevant for early, mid and late stage dementia were combined to indicate that these remained relevant regardless of dementia stage. These were collated under the heading 'all stages'. For statements with multiple quantitative thresholds, we reported the lowest of the thresholds

where more than one response elicited the same consensus-based response (i.e. agree or strongly agree).

Results

The multidisciplinary expert panel consisted of 57 experts with qualifications and experience in relevant fields (Fig.2; Table 1).

Definition of people with dementia for the criteria

Experts agreed on the draft definition in Round 1 but suggested modifications in free text comments. They agreed on the refined definition in Round 2. The final consensus definition of dementia for use in the criteria was:

> Dementia is a clinical syndrome characterised by a chronic progressive decline in neurocognitive function, specifically affecting memory, cognition, language, behaviour, emotional control, and social functioning beyond the expected effects of physiological ageing and not attributable to an intercurrent illness. The specific signs and symptoms of dementia and the rate of progression vary accordingly to the aetiology and individual. One or more aetiology may be present at the same time; the most common forms of dementia are Alzheimer's, vascular, Lewy body, and fronto-temporal dementia.

Agreement on the proposed criteria

The panel considered 128 statements in eight domains for the Round 2 survey. Consensus was reached on 93 (73%) of the 128 proposed statements considered by the expert panel in Round 2: disagree (n = 4), neither agree nor disagree (n = 8), agree (n = 45) and strongly agree (n = 36).

The panel considered 36 statements for the Round 3 survey. Consensus was reached on 19 (53%) of the 36 proposed statements that were re-administered in Round 3: disagree (n = 8), neither agree nor disagree (n = 1) and agree (n = 4).

Table 1 Participant characteristics

Age	20–29 years	n = 4, 7%
	30–39 years	n = 15, 26%
	40–49 years	n = 15, 26%
	50–59 years	n = 16, 28%
	60–69 years	n = 7, 12%
Gender	Male	n = 21, 37%
Qualifications as an expert	Authored one or more papers connected to medicine use in older people in the last 10 years?	n = 28, 49%
	Credentialed in an area related to medicine use in older people (CGP, AACP, Geriatrician etc.)	n = 39, 68%
	Practised in a relevant field for 5 or more years?	n = 48, 85%
	Participated in an invitation only symposium or focus group related to geriatric medicine use	n = 29, 51%
	Received a personally addressed letter inviting you to participate in this study.	n = 36, 63%
Health profession or background	Pharmacist	n = 33, 58%
	General practitioner	n = 4, 7%
	Clinical pharmacologist	n = 1, 2%
	Geriatrician	n = 9, 16%
	Physician	n = 5, 9%
	General medicine physician	n = 1, 2%
	Research psychologist	n = 1, 2%
	Registered nurse	n = 2, 4%
	Nurse practitioner	n = 1, 2%
	Patient advocate	n = 1, 2%
Work environment	Research based	n = 8, 14%
	Practice based	n = 28, 49%
	Both research and practice based	n = 20, 35%
	Research, education and practice based	n = 1, 2%
Years experience in managing pharmacotherapy for people living with dementia	Under 5 years	n = 14, 25%
	5–10 years	n = 9, 16%
	11–20 years	n = 16, 28%
	21–30 years	n = 11, 19%
	31 + years	n = 4, 7%

Numbers are n (%). AACP, Australian Association of Consultant Pharmacy; GCP, Certified Geriatric Pharmacist.

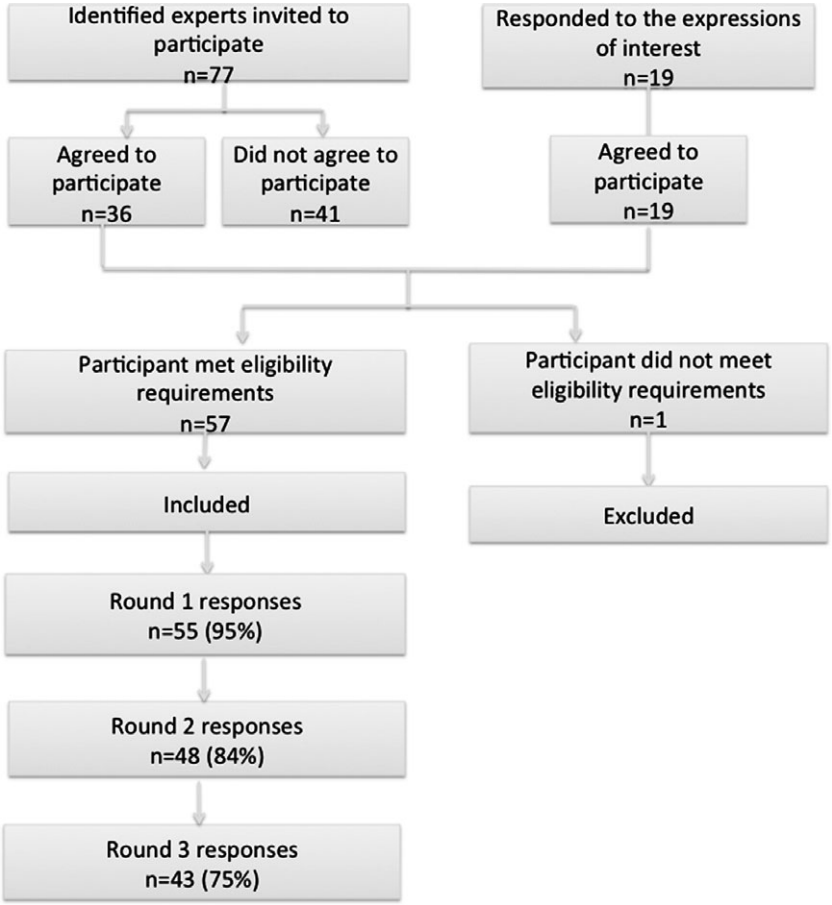

Figure 2 Recruitment flowchart.

The expert panel reached consensus on 111 statements (Supporting Information, Table S1) and did not reach consensus on 17 statements (Supporting Information, Table S2).

Statement synthesis for the MATCH-D criteria

The 85 statements on which consensus agreement was achieved were condensed into 67 statements across eight categories to create the MATCH-D criteria (Appendix S2).

The MATCH-D criteria include a one-page addendum to present the condensed statements for the statements where the consensus was to disagree with the statement (Appendix S2, p. 5).

Discussion

This paper reports consensus statements that describe appropriate medication management in people with dementia. We convened a large multidisciplinary panel of experienced clinicians with backgrounds in pharmacy, medicine and nursing for this project. The expert panel generated a list of statements that provide guidance on appropriate treatment goals in people with dementia and important discussion points for patient-centered care. The MATCH-D statements give specific consensus-based advice on symptom management, prescribing to reduce the risk of future events, medications to slow dementia progression, psychoactive medications, the experience of side-effects and the indications for a medication review in people living with dementia.

Medication management for people with dementia has often been focused on improving cognitive function and reducing symptoms of the dementia.[17] Australia released clinical guidelines on the management of dementia in May 2015.[55] These guidelines describe the use of anticholinesterase inhibitiors and memantine for dementia progression and pharmacological management of behavioural and psychological symptoms of dementia with antipsychotics, antidepressants, anxiolytics, mood stabilisers and melatonin.[55] They do not provide guidance on the pharmacological management of co-morbidities except where they may affect behavioural and psychological symptoms. Evidence assessing co-morbidities among people with dementia remains focused on prevalence and assessment of quality

of care.[17] Our study complements existing dementia guidelines by describing appropriate pharmacological management of co-morbidities as dementia progresses.

One of the strong messages from our expert panel was the importance of a person-centered approach to pharmacological management in people with dementia. Medication management needs to focus on treatment goals that are relevant to the individual and their families, as older adults vary in their preferences for treatment when they consider the potential risks and benefits of medication management.[43,56] It is important that people with dementia are involved in decisions about their own care,[57] and that the wishes of caregivers or family are also considered in the decision-making process.[58,59]

General prescribing criteria for older adults do not specifically consider the particularities of a progressive, life-limiting nature of dementia.[45–49] We anticipated that this project would generate a list of appropriate and inappropriate medications for managing co-morbidities in dementia, similar to other existing explicit prescribing criteria in older people such as the Beers and STOPP/START criteria.[60,61] However, the expert responses to the Round 1 questions emphasised individualising treatment and the importance of reviewing treatments for co-morbidities as the dementia progresses. The MATCH-D criteria reported here may add value if used alongside other prescribing criteria designed for older adults and provide health professionals with guidance on when it may be appropriate to de-prescribe specific medications for co-morbidities in people with dementia.[62] The MATCH-D criteria also provide guidance on specific issues to discuss with patients and their families when individualising care in dementia.

This study has several strengths. The panel was large with experts from a variety of health professional fields and we had a high response rate to our initial approach (95% participation in Round 1). We used carefully worded open-ended questions in the initial round to avoid biasing or limiting the possible responses. Two investigators independently analysed the Round 1 responses to increase the objectivity of the process. Existing consensus-based criteria for older people have been criticised for a lack of transparency in the methods.[63] A strength of the current study is that the methods were transparent with a pre-specified published protocol.[52] A weakness of this study is that Round 1 did not generate statements on the anticipated list of appropriate and inappropriate medications as specified in the protocol. As such, we did not anticipate the process of condensing a large number of statements in our protocol. However, this demonstrates that the Round 1 questions did not limit possible responses.

Conclusion

More work is required to evaluate whether the MATCH-D criteria are useful in clinical practice. In addition, the MATCH-D criteria may need to be refined or amended for clinical application. In the current version of MATCH-D, we have included statements where there was consensus disagreement in their original format as an addendum (e.g. 'Health professions should conceal medication in food or drink if [a person with dementia] refuses to take medications' and 'Regular medicines intended for symptom relief should be continued indefinitely in people who are unable to reliably report symptom recurrence' and 'the wishes and needs of family and carers should take priority over those of the person living with dementia'). It is uncertain without further research whether the inverse of these statements would be ratified.

More research is also needed to determine whether applying the MATCH-D criteria in the clinical setting will improve health outcomes and quality of life for people with dementia. However, the strong message from our experts is that medication management in people with dementia should be individualised to match the person's changing treatment goals as the disease progresses.

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Supporting Information

Additional supporting information may be found in the online version of this article at the publisher's web-site:

Appendix S1 Round one survey.

Appendix S2 Medication appropriateness tool for comorbid health conditions in dementia (MATCH-D).