

# Validation of prescribing appropriateness criteria for older Australians using the RAND/UCLA appropriateness method

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## ABSTRACT

**Objective:** To further develop and validate previously published national prescribing appropriateness criteria to assist in identifying drug-related problems (DRPs) for commonly occurring medications and medical conditions in older ( $\geq 65$  years old) Australians.

**Design:** RAND/UCLA appropriateness method.

**Participants:** A panel of medication management experts were identified consisting of geriatricians/pharmacologists, clinical pharmacists and disease management advisors to organisations that produce Australian evidence-based therapeutic publications. This resulted in a round-one panel of 15 members, and a round-two panel of 12 members.

**Main outcome measure:** Agreement on all criteria.

**Results:** Forty-eight prescribing criteria were rated. In the first rating round via email, there was disagreement regarding 17 of the criteria according to median panel ratings. During a face-to-face second round meeting, discussion resulted in retention of 25 criteria after amendments, agreement for 14 criteria with no changes required and deletion of 9 criteria. Two new criteria were added, resulting in a final validated list of 41 prescribing appropriateness criteria. Agreement after round two was reached for all 41 criteria, measured by median panel ratings and the amount of dispersion of panel ratings, based on the interpercentile range.

**Conclusions:** A set of 41 Australian prescribing appropriateness criteria were validated by an expert panel. Use of these criteria, together with clinical judgement and other medication review processes such as patient interview, is intended to assist in improving patient care by efficiently detecting potential DRPs related to commonly occurring medicines and medical conditions in older Australians. These criteria may also contribute to the medication management education of healthcare professionals.

## INTRODUCTION

Drug-related problems (DRPs) in older people ( $\geq 65$  years old) are common.<sup>1–4</sup> They may result in drug treatment goals not being

## ARTICLE SUMMARY

### Article focus

- Drug-related problems (DRPs) are common in older people. They may result in drug treatment goals not being achieved and/or the occurrence of adverse drug events.
- The aim of this study was to further develop and validate a previously published list of prescribing appropriateness criteria for use in older people which may be used to improve the quality of the Australian medication review process, and for quality assessment and education in medicine use.

### Key messages

- The use of medication assessment criteria is one method to assist in identifying DRPs. Criteria developed elsewhere may have little or no applicability to the Australian healthcare environment.
- Validation of proposed Australian prescribing appropriateness criteria for older people was accomplished using a two-round-modified Delphi method, resulting in agreement for all criteria as measured by median panel ratings, and the amount of dispersion of panel ratings, based on the interpercentile range.
- Use of these criteria, together with other Australian medication review processes, may assist in improving patient care in a variety of settings by efficiently identifying DRPs to common medical conditions and commonly used medicines. They may also contribute to the medication management knowledge of healthcare professionals through education programmes and by use in daily practice, and for the evaluation of the quality of pharmaceutical care in older people.

### Strengths and limitations of this study

- A validated consensus method was used involving an expert medication management panel of varied specialisation. Criteria were based on established evidence—practice gaps and degree of disease burden imposed on the healthcare system, and were written with the aim of conciseness and clarity.
- Further developmental work is required to assess the usefulness of these criteria, which only included commonly occurring medicines and medical conditions.

achieved and/or disproportionately high numbers of serious adverse medication events due to polypharmacy.<sup>5–7</sup> DRPs can occur for many reasons such as undertreatment, inadequate monitoring of medicines, poor medicine or dose selection, duplication of medicines or factors to do with the way the patient uses the medicine.<sup>2 3 8–12</sup> Methods to identify and reduce DRPs include healthcare professional-directed educational interventions,<sup>13</sup> comprehensive geriatric assessment,<sup>14</sup> discontinuation of multiple medications,<sup>15 16</sup> electronic health record clinical decision support targeted towards certain diseases or drugs,<sup>17 18</sup> and the use of medication assessment criteria, which usually consist of explicit (ie, criterion-based rather than implicit or judgement-based) lists of prescribing recommendations for various drugs and/or disease states.<sup>13 19–22</sup>

In Australia, identification and resolution of DRPs are intended to be considered when patients are interviewed by an accredited pharmacist as part of the Home Medicines Review programme.<sup>23</sup> This programme aims to provide the sophistication lacking in the application of explicit measures alone, as it takes into account other issues such as the patients history and personal preferences, and is targeted towards patients who may be (among other reasons) currently taking  $\geq 5$  regular medicines, attending a number of different doctors, or have recently been discharged from hospital.<sup>24</sup>

In 2008, we proposed a list of 48 prescribing appropriateness criteria (45 explicit and three implicit) aimed at improving detection of DRPs as part of the Australian medication review process.<sup>25</sup> These criteria were intended to be applied alongside the patient interview in order to prompt appropriate history taking, particularly with respect to commonly occurring medical conditions and medicines. Similar criteria derived outside Australia have been found to have application in a variety of settings and for a variety of uses, such as in the training of healthcare professionals and in the evaluation of the quality of healthcare.<sup>19 26–29</sup> Our criteria were based on the most frequent medicines prescribed to Australians, and the most frequent medical conditions for which older Australians ( $\geq 65$  years old) consult medical practitioners. Australian medication and disease state resources and guidelines were used to provide content validity.<sup>25</sup> However, unlike our criteria, other prescribing criteria or tools have combined evidence with expert opinion to provide face validity.

The aim of this study was to further develop our list of criteria, supplementing it with recommendations for comorbidity and the oldest old where possible, and adding new criteria where necessary through expert consensus. In older patients, the importance of traditional outcomes, such as discrete clinical events or mortality, may be secondary to maintaining physical or cognitive function or relief of symptoms.<sup>30</sup> Because of this, optimal care requires clinical decision support tools that consider issues such as patient preferences, frailty, cost and comorbidities.<sup>31</sup> Additionally, few criteria target the

oldest old<sup>32</sup> (generally regarded as people older than 85 years), where evidence may be poor, and preventive interventions may be encouraged in patients who have already exceeded an average lifespan.<sup>33 34</sup>

To further develop and validate our criteria list, we identified a panel of medication management experts, and chose the RAND/UCLA appropriateness method, which has been described as the best method for systematically combining recommendations from clinical guidelines, with the opinion of healthcare providers.<sup>35</sup>

## METHODS

### Ethics

Ethics approval was obtained from the Human Research Ethics Committee of the University of Sydney.

### Criteria development

In 2008, we identified the 50 highest-volume Australian Pharmaceutical Benefits Scheme (PBS) medicines prescribed, and the 40 most common reasons for older Australians to seek or receive healthcare. Healthcare information was obtained using the BEACH (Bettering The Evaluation and Care of Health) programme, which continuously collects information about the clinical activities in general practice in Australia.<sup>36</sup> We then used Australian medication information sources to identify both optimal and inappropriate medication management of these common conditions.<sup>25</sup> In Australia, medication availability and use are largely determined by the PBS.<sup>37</sup> In October 2011, commonly used medications and medical conditions were checked and updated using the BEACH programme to ensure that criteria content was current. Changes in evidence, product information, Australian consensus documents, evidence-based publication recommendations or clinical practice guidelines relating to our criteria were noted for evaluation by an expert medication management panel. The criteria were designed to provide guidance on the process of care wherever it occurred—community, hospital, residential home, care home or nursing home. Major considerations in their development were likely accessibility of data from the patient, their medical notes and/or their healthcare professional(s), conciseness and clarity of wording, and provision of a practical number of criteria. Most were explicit to enable consistent application, with additional notes provided for interpretation where necessary. They were written as a statement of the kind of medication management that should or should not occur, to simplify comprehension and facilitate uptake.<sup>25</sup>

### Validation of criteria: participants

We recruited a multidisciplinary group of medication management experts to review, update and rate the criteria, consisting of geriatrician/pharmacologists, clinical pharmacists and disease management advisors to organisations that produce Australian evidence-based

therapeutic publications. This resulted in a round-one panel of 15 members. The geriatricians consisted of two professors of geriatric medicine; an associate professor of clinical pharmacology and aged care; a research fellow in geriatric medicine and a hospital staff geriatrician. Clinical pharmacists consisted of a residential medication management review pharmacist; a home medicines review pharmacist; four hospital-based pharmacists (two team leaders, one director and one education and training pharmacist) and a professor of aged care (pharmacy). Disease management advisors to Australian evidence-based therapeutic organisations consisted of Therapeutic Guidelines,<sup>38</sup> Australian Medicines Handbook<sup>39</sup> and the New South Wales Therapeutic Advisory Group.<sup>40</sup>

### Choice of the RAND/UCLA appropriateness method

We chose the RAND/UCLA appropriateness method, a two-round modified Delphi method<sup>41</sup> to select the most appropriate criteria. Unlike the Delphi method, which generally involves multiple questionnaire-driven rounds to obtain convergence of opinion, the RAND method involves an initial individual rating round, and a second face-to-face round. This method has been shown to produce results that have face, construct and predictive validity.<sup>42–43</sup> Systematically combining available evidence with expert opinion can create quality criteria where best evidence may be lacking.<sup>44</sup>

While most lists of prescribing criteria are based on expert consensus, this has often been achieved through mail surveys rather than face-to-face meetings.<sup>32–35–45</sup> Although face-to-face meetings restrict panel size, they allow discussion to resolve misinterpretations, introduce new evidence and improve clarity of criteria between rating rounds. We ensured our panel comprised different specialities, as less disagreement has been found among same-specialty panels.<sup>46</sup> We addressed concern regarding potential intimidation due to dominant panel personalities by choosing a moderator experienced in the development of these criteria and in facilitating small group discussion. This may also have assisted with conflict-of-interest issues. We used both the median panel rating and the amount of dispersion of panel ratings to identify agreement or disagreement. While it has been acknowledged that discrepancies between these two methods may occur,<sup>41</sup> our aim was to achieve agreement for all accepted criteria for both methods after second round discussion.

### RAND/UCLA appropriateness method round one

In October 2011, candidate panel members were emailed an explanation of the project and an invitation to participate. After acceptance, they were emailed a rating sheet consisting of 48 criteria, and asked to rate each on a nine-point scale. Ratings of 1–3 were classified as inappropriate, with a rating of one indicating the greatest degree of inappropriateness. Ratings of 7–9 were classified as appropriate, with a rating of nine indicating the

greatest degree of appropriateness. Ratings of 4–6 were classified as neither appropriate nor inappropriate. Appropriate was defined as ‘the expected health benefit exceeds the expected negative consequences by a sufficiently wide margin that criteria are worth following, exclusive of cost’. They also received a description of the way in which the criteria had been derived, and a comparison with other prescribing criteria.<sup>25–32</sup> Panel members were requested to amend the wording or delete, update or identify missing criteria as required. Upon return of the rating sheets, results were tabulated. Agreement was based on four or less panellists rating outside the three-point region containing the median (1–3; 4–6; 7–9), and disagreement was based on five or more panellists rating in each extreme (1–3 and 7–9), as per the RAND/UCLA protocol for a 15-member panel.<sup>41</sup>

### Rand/UCLA appropriateness method round two

In November 2011, a face-to-face meeting of the expert panel, chaired by a panel moderator experienced in facilitating group discussions and criteria development, met to discuss the results of round one and re-rate each of the criteria and any potential additional criteria. One pharmacist, one staff geriatrician and a disease management advisor for a therapeutics publication could not attend, resulting in a 12-member panel. For this meeting, each panel member was provided with a copy of the results from round one. This consisted of the frequency distribution of ratings of all panellists across the nine-point scale, the overall panel median rating for each of the criteria and, for each panellist, an annotation of how they had rated each of the criteria. Scores from other panel members were not revealed. Depending on panellists votes, panel agreement or disagreement was also stated for each of the round one criteria. Additionally, the 30th and 70th percentiles adjusted for symmetry were computed for each of the criteria, as it has been found that when ratings were symmetric with respect to the middle (five on the 1–9 scale), the inter-percentile range (IPR) required to label an indication as disagreement was smaller than when they were asymmetric with respect to the middle (values far from five on the 1–9 scale). Agreement after round two occurred when the IPR adjusted for symmetry (IPRAS) was greater than the IPR.<sup>41</sup>

We used the median method to present data at the face-to-face meeting, as it provided a clear visual interpretation of the ratings for each criterion. By the end of the meeting, our aim was to ensure that there was agreement between the median method and the inter-percentile method for all accepted criteria.

Discussion at round two occurred on the level of agreement for each of the criteria. In addition, discussion was facilitated on the wording of each of the criteria to improve clarity and decide whether agreement would be reached. The definitions of agreement and disagreement were adjusted for the smaller second round 12 member panel.<sup>41</sup> Agreement was reached when three or

less panel members voted outside the three-point region containing the median, or when the IPRAS was greater than the IPR. Disagreement was determined when four or more panellists rated in each extreme (1–3 and 7–9). Each of the criteria were then discussed irrespective of whether there was agreement or disagreement, with panellists having the opportunity of changing their ratings if, for example, misinterpretation had occurred because of the way in which the criteria had been written, or if new evidence had become available, or if criteria had been interpreted in the light of a panellist's own clinical experience. Each panel member consented to audio recording of the discussion. Values for the median, IPR and IPRAS<sup>41</sup> were computed using SPSS V.20 (SPSS, Chicago, Illinois, USA).

## RESULTS

After round one, there was agreement for the appropriateness of 31 of the 48 criteria, and disagreement for 17 criteria. Of the 31 criteria for which there was agreement, discussion at round two resulted in 17 criteria being amended and retained, 2 criteria being deleted and 12 criteria accepted with no change. Of the 17 criteria for which there was disagreement, discussion at round two resulted in eight criteria being amended and retained, seven criteria being deleted and two criteria accepted with no change. Two new criteria were added, resulting in a total of 41 validated criteria.

An example of how the RAND/UCLA method was applied to each of our criteria is described in table 1 for criterion one. The larger the IPRAS, the less asymmetric are the ratings. For example, 13 of 15 panellists at round one rated indicator 14 with a score of 8 or 9, for which the IPRAS was 8.35.

Table 2 lists the median panel ratings, the amount of dispersion of panel ratings, and whether there was

agreement or disagreement for the original criteria and the validated criteria. It also lists the amendments made by the panel to the original criteria, and the reasons for these amendments. There was 100% agreement for both median panel ratings and dispersion of panel ratings for the validated criteria. Table 3 contains the final list of validated criteria, arranged according to disease states. Table 4 lists usage information judged to be necessary for certain criteria.

## DISCUSSION

This study identified a panel of medication management experts to discuss and validate a set of 41 prescribing appropriateness criteria for commonly used medicines and medical conditions in older ( $\geq 65$  years) Australians. Panel discussion resulted in retention of 39 of the originally proposed 48 criteria, with 25 being reworded, and 14 accepted with no change. These criteria do not simply represent a list of medications to avoid in the elderly, but also address issues such as the need for additional therapy (eg, criteria 23 and 34, table 3), additional tests (eg, criteria 18–20, table 3), ineffective treatment (eg, criteria 22 and 37, table 3) and medication monitoring (eg, criteria 10 and 20, table 3). They were designed to contribute to the Australian quality use of medicines process.<sup>94</sup> The information required to apply these criteria may be obtained from the patients or their carer, and patient medical notes and/or their healthcare professional.<sup>95</sup> It may also be provided by a Home Medicines Review referral form from the patients' general practitioner.<sup>23</sup> Owing to their currency and the nature of their development, we expect these criteria to make a significant contribution to the detection of DRPs in the Australian healthcare environment. For example, in a review of prescribing indicators for two conditions,<sup>36</sup> which are common in older people in Australia—type 2

**Table 1** An example of the application of the RAND/UCLA appropriateness method to one criterion (criterion one) from round one

Nine-point scale where 1–3=inappropriate, 4–6=neither appropriate nor inappropriate, 7–9=appropriate	Number of panellists rating this criterion (n=15)	Calculations, interpercentile range method <sup>41</sup>	Interpretation
1		30th percentile=7.0	This criterion was accepted according to the median method because four or less panellists voted outside the three-point region containing the median. The IPRAS (6.1) was greater than the IPR (1.0) indicating no disagreement. The larger the IPRAS, the less asymmetric the ratings
2		70th percentile=8.0, interpercentile range	
3	1	(IPR)=70th–30th percentile)=1.0,	
4		IPR central point (IPRCP)=30th	
5	1	+70th percentile divided by 2=7.5	
6	1	Asymmetry index (AI)=(5–IPRCP)	
7	5	(as an absolute value)=2.5	
8	5	IPRAS=(2.5+(AI×1.5))=6.1,	
9	2	where 2.5 is the IPR required for disagreement when perfect symmetry exists, and 1.5 is the correction factor for asymmetry	
	Median=7.0		

**Table 2** Changes made to original criteria according to agreement, disagreement and panel discussion

Criteria number	Original prescribing appropriateness criteria for older (≥65 years) Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement; D=disagreement), n=15		Validated prescribing appropriateness criteria for older (≥65 years) Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement, D, disagreement), n=12		Amendment/reason
1	Patient taking an antihypertensive is at their target blood pressure	7	A	1.00, 6.10	A	Patient taking an antihypertensive is at the target blood pressure appropriate for them	8	A	1.10, 7.52	A	'Appropriate for them' added. Current blood pressure guidelines may not be appropriate for all older patients <sup>47-49</sup> . For example, in the oldest old <sup>50</sup> ; in palliative care; and for those who are/ become hypotensive and/or fall <sup>51 52</sup>
2	Patient at high risk of a cardiovascular event is taking a statin	7	A	1.00, 6.10	A	Patient at high risk of a recurrent cardiovascular event is taking a statin	8	A	1.00, 6.10	A	'Recurrent' added to ensure use in secondary prevention of cardiovascular events rather than primary prevention, where evidence is less clear, especially in the oldest old <sup>33 53-57</sup>
3	Patient with IHD or a history of MI is taking a β-blocker	8	A	2.00, 6.85	A	Patient with CHD or a history of MI is taking a β-blocker	7	A	1.00, 6.10	A	'CHD' replaced 'IHD'. The term 'coronary heart disease' is preferred over 'ischaemic heart disease'
4	Patient with IHD or a history of MI is taking an antiplatelet agent unless on an oral anticoagulant	8	A	1.00, 7.60	A	Patient with CHD or a history of MI is taking an antiplatelet agent unless on an oral anticoagulant	8	A	1.00, 7.60	A	'CHD' replaced 'IHD'. The term 'coronary heart disease' is preferred over 'ischaemic heart disease'
5	Patient with heart failure is taking a β-blocker	7	A	1.00, 6.10	A	Patient with stable HF-LVSD is taking a β-blocker	8	A	0.10, 6.78	A	Description of heart failure amended. The use of β-blockers is contraindicated in unstable heart failure. The optimal treatment of HFPEF is uncertain at this time <sup>58 59</sup>
6	Patient with heart failure is taking an ACEI or A2A	8	A	2.00, 6.85	A	Patient with stable HF-LVSD is taking an ACEI or A2A	9	A	1.00, 7.60	A	Description of heart failure amended. The optimal treatment of HFPEF is uncertain at this time <sup>58 59</sup>
7	Patient with heart failure is NOT taking medications which may exacerbate heart failure	9	A	1.00, 7.60	A	Patient with HF-LVSD or HFPEF is NOT taking medications which may exacerbate heart failure	9	A	0.10, 8.27	A	Description of heart failure amended. The types of medicines contraindicated in HF-LVSD and HFPEF may not be identical <sup>60 61</sup>

Continued

Table 2 Continued

Criteria number	Original prescribing appropriateness criteria for older (≥65 years) Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement; D=disagreement), n=15		Validated prescribing appropriateness criteria for older (≥65 years) Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement, D, disagreement), n=12		Amendment/reason
8	Patient with heart failure or hypertension is NOT taking high sodium medications	8	D	2.20, 5.50	A	Deleted	–	–	–	–	High sodium medicines (among others) in heart failure are addressed by indicator 7. In hypertension, they are addressed as lifestyle modifications <sup>62 63</sup>
9	Patient with AF is taking an oral anticoagulant	7	D	2.0, 5.35	A	Patient with AF is taking an oral anticoagulant or an antiplatelet agent, depending upon stroke risk and bleeding risk	8	A	0.10, 6.93	A	An antiplatelet agent may be appropriate for patients at low risk of stroke. Bleeding risk may determine choice of antithrombotic agent <sup>49 64 65</sup>
10	Patient with AF taking an anticoagulant has an INR between 2 and 3	8	A	2.20, 6.70	A	Patient taking warfarin for AF has an INR between 2 and 3	9	A	1.00, 7.60	A	New anticoagulants like rivaroxaban and dabigatran do not require INR monitoring
11	Patient with a history of non-haemorrhagic stroke or TIA is taking an antiplatelet agent unless on an anticoagulant	8	A	1.00, 7.60	A	Patient with a history of non-haemorrhagic stroke or TIA is taking an antiplatelet agent unless on an anticoagulant	9	A	1.00, 7.60	A	No change
12	Patient with risk factors for myopathy is NOT taking 40 mg or more per day of simvastatin or atorvastatin	7	D	3.00, 4.60	A	Patient with risk factors for statin-induced myopathy is not taking a high-potency statin	8	A	1.10, 7.52	A	The use of all high dose of high-potency statins together with risk factors may increase the likelihood of myopathy <sup>49 66 67</sup>
13	Patient with cardiovascular disease is NOT taking an NSAID	7	A	1.20, 5.95	A	Patient with cardiovascular disease is NOT taking an NSAID	8	A	1.10, 6.18	A	No change

Continued

**Table 2** Continued

Criteria number	Original prescribing appropriateness criteria for older (≥65 years) Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15				Validated prescribing appropriateness criteria for older (≥65 years) Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12				Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement, D, disagreement), n=12	Amendment/reason
		9	A	0.00, 8.35	A		9	A	0.00, 8.35	A		
14	Patient with cardiovascular, respiratory disease or diabetes who smokes has been offered smoking cessation therapy	9	A	0.00, 8.35	A	Patient with cardiovascular, respiratory disease or diabetes who smokes has been offered smoking cessation options	9	A	0.00, 8.35	A	'Therapy' implies pharmacotherapy, whereas repeated counselling/ psychotherapy may be preferred to avoid the risks associated with polypharmacy	
15	Patient with type 2 diabetes and hypertension and albuminuria is taking an ACEI or A2A	8	A	2.00, 6.85	A	Patient with type 2 diabetes and hypertension and albuminuria is taking an ACEI or A2A	9	A	1.00, 7.60	A	No change	
16	Patient with diabetes at high risk of a cardiovascular event is taking an antiplatelet agent unless on an anticoagulant	7	D	2.20, 5.50	A	Patient with diabetes at high risk of a cardiovascular event is taking an antiplatelet agent unless on an anticoagulant	9	A	1.00, 7.60	A	No change	
17	Patient with diabetes is NOT taking a medication which may increase or decrease blood glucose concentrations	5	D	2.20, 3.70	A	Patient with diabetes receiving medications that may affect glycaemic control is having regular monitoring of blood glucose concentrations	9	A	1.00, 7.60	A	Increased awareness and monitoring may require adjustment of hypoglycaemic medication doses, depending on the need to continue interacting medicines. For example, the start of oral corticosteroids may worsen diabetes control <sup>39</sup>	
18	Patient with diabetes has had an HbA1c measurement within the previous 6 months	8	A	1.20, 7.45	A	Patient with diabetes has had an HbA1c measurement within the previous 6 months	8	A	1.00, 7.60	A	No change	
19	Patient taking metformin for diabetes has had the dose adjusted for creatinine clearance	8	A	1.20, 7.45	A	Patient taking metformin for diabetes has had the dose adjusted for renal function	9	A	1.00, 7.60	A	Creatinine clearance may represent only one of the methods used to determine renal function	

Continued

Table 2 Continued

Criteria number	Original prescribing appropriateness criteria for older (≥65 years) Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement; D=disagreement), n=15		Validated prescribing appropriateness criteria for older (≥65 years) Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement, D, disagreement), n=12		Amendment/reason
20	Patient taking metformin for diabetes is NOT concurrently taking glibenclamide	6	D	2.40, 3.85	A	Deleted	–	–	–	–	Glibenclamide is an uncommonly used hypoglycaemic
21	Patient with OA pain interfering with daily activities has been trialled on paracetamol 2–4 g/day	8	A	2.00, 6.85	A	Patient with OA pain interfering with daily activities has been trialled on regular paracetamol 2–4 g/day	9	A	0.40, 8.05	A	'Regular' paracetamol added to improve quality of indicator
22	Patient taking analgesic(s) does NOT have pain that interferes with daily activities	7	D	3.2, 4.75	A	Patient taking analgesic (s) has had the dose(s) titrated in order to avoid pain that interferes with daily activities	8	A	2.00, 6.85	A	Indicator rephrased to improve clarity
23	Patient taking an opioid is on prophylactic treatment for constipation	8	A	2.00, 6.85	A	Patient taking a regular opioid is on prophylactic treatment for constipation	9	A	1.00, 7.60	A	'Regular' use added as 'when required' use may not always require prophylactic treatment
24	Patient with risk factors for impaired renal function is NOT taking an NSAID	8	A	1.00, 7.60	A	Patient with risk factors for impaired renal function is NOT taking an NSAID	8	A	1.00, 7.60	A	No change
25	Patient is NOT concurrently taking an ACEI or A2A, diuretic and NSAID (excluding low-dose aspirin)	9	A	1.00, 7.60	A	Patient is NOT concurrently taking an ACEI or A2A, diuretic and NSAID (excluding low-dose aspirin)	9	A	1.00, 7.60	A	No change
26	Patient with sleep disturbance or anxiety has NOT been taking benzodiazepines for >4 weeks	8	A	1.20, 7.45	A	Patient has NOT been taking benzodiazepines for >4 weeks	9	A	1.00, 7.60	A	'Sleep disturbance or anxiety' deleted. Benzodiazepines increase the risk of oversedation, ataxia, confusion, falls, respiratory depression and short-term memory impairment, and are recommended for short-term use only <sup>39</sup>

Continued



**Table 2** Continued

Criteria number	Original prescribing appropriateness criteria for older (≥65 years) Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15				Validated prescribing appropriateness criteria for older (≥65 years) Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12				Amendment/reason
		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement; D=disagreement), n=15									
27	Patient with depression is NOT taking anticholinergic-type antidepressants	7	D	1.00, 4.60	A	Deleted	–		–	–	The issue of anticholinergic burden is addressed by indicator 32
28	Patient with a history of falls is NOT taking psychotropic medications	8	A	1.00, 6.10	A	Patient with a history of falls is NOT taking psychotropic medications	8	A	1.40, 6.40	A	No change
29	Patient taking an SSRI is NOT concurrently taking medications known to increase the risk of GI bleeding	7	D	2.20, 5.20	A	Deleted	–		–	–	Redundant indicator. This issue would be identified by indicator 47
30	Patient taking an SSRI is NOT concurrently taking other medications that may contribute to serotonin toxicity	8	A	2.20, 6.70	A	Patient taking an SSRI is NOT concurrently taking other medications that may contribute to serotonin toxicity	8	A	1.40, 6.40	A	No change. Retained by panel due to its potential significance, despite the use of indicator 47
31	Patient with dementia is NOT receiving anticholinergic medication	8	A	1.20, 7.45	A	Patient with dementia is NOT receiving anticholinergic medication	8	A	1.00, 7.60	A	No change
32	Patient is NOT taking more than one medication with anticholinergic activity	8	A	0.2, 6.70	A	Patient is not taking medication with SIGNIFICANT anticholinergic activity	8	A	0.40, 7.15	A	Rewording focuses on the issue of anticholinergic burden
33	Patient taking a PPI is NOT taking a medication that may cause dyspepsia	7	D	3.20, 4.45	A	Patient taking a PPI is NOT taking a medication that may cause dyspepsia unless prescribed for gastroprotection	8	A	0.40, 7.15	A	'Unless prescribed for gastroprotection' added to improve the accuracy of the indicator

Continued

Table 2 Continued

Criteria number	Original prescribing appropriateness criteria for older (≥65 years) Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement; D=disagreement), n=15		Validated prescribing appropriateness criteria for older (≥65 years) Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement, D, disagreement), n=12		Amendment/reason
34	Patient with COPD is NOT taking benzodiazepines	7	D	3.00, 6.10	A	Patient with COPD is NOT taking benzodiazepines	8	A	1.00, 6.10	A	No change
35	Patient with asthma using an inhaled LABA is also using an inhaled corticosteroid	9	A	0.20, 8.20	A	Patient with asthma using an inhaled LABA is also using an inhaled corticosteroid	9	A	1.00, 7.60	A	No change
36	Patient using salbutamol or terbutaline inhaler more than three times per week for reversible airways disease has been prescribed an ICS	9	A	1.00, 7.60	A	Patient using salbutamol or terbutaline inhaler more than three times per week for reversible airways disease has been prescribed an ICS (except for exercise-induced asthma)	9	A	0.40, 8.05	A	'Except for exercise-induced asthma' added to improve the accuracy of the indicator
37	Patient with asthma is NOT taking a medication that may worsen asthma	7	A	1.20, 6.25	A	Patient with asthma is NOT taking a medication that may worsen asthma	8	A	1.00, 7.60	A	No change
38	Female patient with recurrent UTIs has been prescribed intravaginal oestrogen	5	D	2.00, 3.85	A	Deleted	–	–	–	–	Evidence for this indicator was judged to be poor <sup>68</sup>
39	Patient with a creatinine clearance <60 ml/min is NOT receiving nitrofurantoin for UTI	8	A	2.00, 6.85	A	Patient with a UTI is not receiving nitrofurantoin or hexamine for prophylaxis or acute treatment	8	A	1.00, 7.60	A	Hexamine and nitrofurantoin are not recommended for the prophylactic or acute treatment of UTI in older patients <sup>39 49</sup>
40	Patient with a creatinine clearance <50 ml/min is NOT receiving hexamine for UTI prophylaxis	8	A	1.20, 6.25	A	Deleted	–	–	–	–	Hexamine and nitrofurantoin are not recommended for the prophylactic treatment of UTI in older patients <sup>39 49</sup>

Continued

**Table 2** Continued

Criteria number	Original prescribing appropriateness criteria for older Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement; D=disagreement), n=15		Validated prescribing appropriateness criteria for older Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement, D, disagreement), n=12		Amendment/reason
41	Patient with an URTI is NOT receiving antibiotics	7	D	3.00, 4.60	A	Patient with a non-specific URTI is NOT receiving antibiotics	8	A	1.00, 7.60	A	'Non-specific' added to improve the accuracy of the indicator
42	Patient with osteoporosis who is not receiving at least 600 IU vitamin D daily from dietary sources is receiving supplementation with vitamin D	8	D	3.20, 4.75	A	Deleted	–	–	–	–	This indicator is covered by indicator 44 and an expanded footnote
43	Patient with osteoporosis who is not receiving at least 1200 mg of calcium daily from dietary sources is receiving calcium supplementation	8	A	1.60, 5.95	A	Deleted	–	–	–	–	This indicator is covered by indicator 44 and an expanded footnote
44	Patient with osteoporosis is receiving antiosteoporotic medication	7	A	1.00, 6.10	A	Patient with osteoporosis is receiving appropriate antiosteoporotic medication	8	A	0.40, 7.15	A	'Appropriate' added and an expanded footnote to include calcium and vitamin D
45	Patient using topical corticosteroids does NOT have itch or discomfort that interferes with daily activities	6	D	2.00, 5.35	A	Patient using topical corticosteroids for contact or allergic dermatitis does not have itch or discomfort that interferes with daily activities	–	–	–	–	This indicator was deleted by the panel because there was no identification of the diagnosis/condition being treated. However, contact and allergic dermatitis is one of the top 40 most frequently managed problems by general practitioners in patients ≥65 years old in Australia, <sup>36</sup> so this indicator was re-worded by the authors

Continued

Table 2 Continued

Criteria number	Original prescribing appropriateness criteria for older Australians published in 2008 <sup>25</sup>	Rating by median method <sup>41</sup> (median value, A, agreement; D, disagreement), n=15		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement; D=disagreement), n=15		Validated prescribing appropriateness criteria for older Australians as a result of this study	Rating by median method <sup>41</sup> (median value, A, agreement, D, disagreement), n=12		Rating by IPRAS <sup>1</sup> method <sup>41</sup> (IPR value, IPRAS value, A, agreement, D, disagreement), n=12		Amendment/reason
46	Patient has received influenza and pneumococcal vaccination	9	A	1.00, 7.60	A	Patient has received influenza and pneumococcal vaccination	9	A	0.00, 8.35	A	No change
47	Patient has no <i>significant</i> medication interactions (agreement between two medication interaction databases)	8	D	3.00, 6.10	A	Patient has no <i>clinically significant</i> medication interactions (agreement between two medication interaction databases)	8	A	0.40, 7.15	A	'Clinically' added to improve the accuracy of the indicator
48	Patient has had no <i>significant</i> change in medications in the previous 90 days	5	D	1.20, 3.25	A	Deleted	–		–		It was preferred to transfer this information to the explanatory text of the article
New						Patient taking thyroid hormone replacement therapy has had a serum TSH measurement within the previous 12 months					Thyroid disease is a common medical condition managed by GPs in older Australians <sup>36 69</sup>
New						Patient with coronary heart disease is taking an ACEI or A2A					ACEIs or A2As reduce the risk of cardiovascular events <sup>70 71</sup> . However, a high incidence of comorbid disease in CHD (commonly arthritis or respiratory disease) or other clinical factors (eg, dizziness or falls, cognitive impairment, use of >5 medicines, patient preference) may be more important in determining medication priorities <sup>72</sup>

ACEI, ACE inhibitor; AF, atrial fibrillation; A2A, angiotensin 2 receptor antagonist; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; HbA1c, glycosylated haemoglobin; HF-LVSD, heart failure with left ventricular systolic dysfunction; HFPEF, heart failure with preserved ejection fraction; GI, gastrointestinal; GP, general physician; ICS, inhaled corticosteroid; IHD, ischaemic heart disease; INR, international normalized ratio; IPR, interpercentile range; IPRAS, interpercentile range adjusted for symmetry; LABA, long-acting  $\beta$  agonist; MI, myocardial infarct; NSAID, non-steroidal anti-inflammatory drug; OA, osteoarthritis; PPI, proton pump inhibitor; SSRI, selective serotonin reuptake inhibitor; Statin, HMG-coenzyme A reductase inhibitor; TIA, transient ischaemic attack; TSH, thyroid stimulating hormone; UTI, urinary tract infection; URTI, upper respiratory tract infection.

**Table 3** Validated prescribing appropriateness criteria for older Australians ( $\geq 65$  years) for commonly used medications and medical conditions\*, †, ‡ (\*for usage information for certain criteria, see table 4)

Criteria number	Validated criteria
1	Patient taking an antihypertensive is at the target blood pressure appropriate for them*
2	Patient at high risk of a recurrent cardiovascular event is taking a statin*
3	Patient with CHD or a history of MI is taking a $\beta$ -blocker
4	Patient with CHD or a history of MI is taking an antiplatelet agent unless taking an oral anticoagulant*
5	Patient with CHD is taking an ACEI or A2A*
6	Patient with stable heart failure with HF-LVSD is taking a $\beta$ -blocker
7	Patient with stable heart failure with HF-LVSD is taking an ACEI or A2A*
8	Patient with HF-LVSD or HFPEF is NOT taking medications which may exacerbate heart failure*
9	Patient with AF is taking an oral anticoagulant or an antiplatelet agent, depending on stroke risk and bleeding risk*
10	Patient taking warfarin for AF has an INR between 2 and 3
11	Patient with a history of non-haemorrhagic stroke or TIA is taking an antiplatelet agent unless taking an anticoagulant
12	Patient with risk factors for statin-induced myopathy is not taking a high dose of a high-potency statin*
13	Patient with cardiovascular disease is NOT taking an NSAID
14	Patient with cardiovascular, respiratory disease or diabetes who smokes has been offered smoking cessation options*
15	Patient with type 2 diabetes and hypertension and albuminuria is taking an ACEI or A2A
16	Patient with diabetes at high risk of a cardiovascular event is taking an antiplatelet agent unless on an anticoagulant
17	Patient with diabetes taking medications that may affect glycemic control is receiving regular monitoring of blood glucose concentrations*
18	Patient with diabetes has had an HbA1c measurement within the previous 6 months*
19	Patient taking metformin for diabetes has had the dose adjusted for renal function*
20	Patient taking thyroid hormone replacement therapy has had a serum TSH measurement within the previous 12 months
21	Patient with OA pain interfering with daily activities has been trialled on regular paracetamol 2–4 g/day
22	Patient taking analgesic(s) has had the dose(s) titrated in order to avoid pain that interferes with daily activities
23	Patient taking a regular opioid is on prophylactic treatment for constipation
24	Patient with risk factors for impaired renal function is NOT taking an NSAID*
25	Patient is NOT concurrently taking an ACEI or A2A, diuretic and NSAID (excluding low-dose aspirin)
26	Patient has NOT been taking benzodiazepines for >4 weeks*
27	Patient with a history of falls is NOT taking psychotropic medications*
28	Patient taking an SSRI is NOT concurrently taking other medications that may contribute to serotonin toxicity*
29	Patient with dementia is NOT receiving anticholinergic medication*
30	Patient is not taking medication with SIGNIFICANT anticholinergic activity*
31	Patient taking a PPI is NOT taking a medication that may cause dyspepsia unless prescribed for gastroprotection*
32	Patient with COPD is NOT taking benzodiazepines
33	Patient with asthma using an inhaled LABA is also using an inhaled corticosteroid
34	Patient using salbutamol or terbutaline inhaler more than three times per week for reversible airways disease has been prescribed an ICS (except for exercise-induced asthma)
35	Patient with asthma is NOT taking a medication that may worsen asthma*
36	Patient with a UTI is not receiving nitrofurantoin or hexamine for prophylaxis or acute treatment
37	Patient with a non-specific URTI is NOT receiving antibiotics*
38	Patient with osteoporosis is receiving appropriate antiosteoporotic medication*
39	Patient has received influenza and pneumococcal vaccination
40	Patient using topical corticosteroids for contact or allergic dermatitis does not have itch or discomfort that interferes with daily activities
41	Patient has no <i>clinically significant</i> medication interactions (agreement between two medication interaction databases)*

\*These criteria are intended to be used by appropriately trained and qualified health professionals, as a tool to assist in making medication management decisions as part of the medication review process.

†Prior to the start of any medication, the contraindications and precautions for that medication should be considered.

‡The intended result of using these criteria is the reasonable and appropriate medication management of individual patients, rather than the systematic application of these criteria to all patients irrespective of other considerations.

A2A, angiotensin 2 receptor antagonist; ACEI, ACE inhibitor; AF, atrial fibrillation; CHD, coronary heart disease; COPD, chronic obstructive pulmonary disease; HbA1c, glycosylated haemoglobin; HF-LVSD, heart failure with left ventricular systolic dysfunction; HFPEF, heart failure with preserved ejection fraction; ICS, inhaled corticosteroid; INR, international normalised ratio; LABA, long-acting  $\beta$  agonist; MI, myocardial infarct; NSAID, non-steroidal anti-inflammatory drug; OA, osteoarthritis; PPI, proton pump inhibitor; SSRI, selective serotonin reuptake inhibitor; TIA, transient ischaemic attack; TSH, thyroid stimulating hormone; UTI, urinary tract infection; URTI, upper respiratory tract infection.

**Table 4** Criteria usage information

Criteria number	Description of issue	Details
1	Blood pressure targets (mm Hg)	Proteinuria >1 g/day (with or without diabetes) <125/75. CHD, diabetes, chronic kidney disease, proteinuria (>300 mg/day), stroke or TIA<130/80. Others <140/90. <sup>39</sup> Current blood pressure guidelines may not be appropriate for all older patients, such as the oldest old; in palliative care; and for those who are/become hypotensive and/or fall <sup>47 49–52 73</sup>
2	Patients at high risk of a cardiovascular event (>15% within the next 5 years)	Age >75 years; history of diabetes, moderate or severe chronic kidney disease (persistent proteinuria, GFR<60 ml/min, eGFR<45 ml/min/1.73 m <sup>2</sup> ), hypercholesterolaemia (familial, TC>7.5 mmol/l), SBP≥180 or DBP≥110 mm Hg, ISH (SBP≥160 and DBP≤70 mm Hg), CHD, stroke, TIA, PAD, heart failure, aortic disease, LVH, family history of premature CVD. <sup>39 74</sup> The benefits of statins and risks of adverse effects are uncertain towards the end of life <sup>75</sup>
4	Antiplatelet agents and oral anticoagulants	Antiplatelet agents: aspirin, clopidogrel, dipyridamole and ticlopidine. Oral anticoagulants: dabigatran, phenindione, rivaroxaban and warfarin
5	Use of ACEI or A2A in CHD	A high incidence of comorbid disease in CHD (typically arthritis and/or respiratory disease) or other clinical factors (eg, dizziness or falls, cognitive impairment, use of >5 medicines, patient preference) may be considerations in determining medication prescribing priorities <sup>30 34 72</sup>
8	Medications that may exacerbate heart failure	HF-LVSD: anti-arrhythmic medicines (except for heart failure-specific β-blockers and amiodarone), non-dihydropyridine calcium-channel blockers (eg, verapamil or diltiazem), clozapine, corticosteroids, NSAIDs (excluding low-dose aspirin), thiazolidinediones, TNF-α inhibitors, topical β-blockers (when added to systemic β-blockers), tricyclic antidepressants. <sup>49 76 77</sup> HFPEF: venodilators (eg, isosorbide dinitrate), potent arterial vasodilators (eg, hydralazine), digoxin (unless AF), excessive use of diuretics. Note; verapamil and diltiazem may improve diastolic function in HFPEF <sup>60</sup>
9	Stroke risk and bleeding risk	Stroke risk can be calculated using CHADS <sub>2</sub> or CHA <sub>2</sub> DS <sub>2</sub> -VASc. <sup>78</sup> Risk factors for coumarin-related bleeding complications: advanced age, uncontrolled hypertension, history of MI or IHD, cerebrovascular disease, anaemia or a history of bleeding, concomitant use of aspirin/polypharmacy <sup>79</sup>
12	Risk factors for statin myopathy; high dose of high-potency statins	Age >70 years, presence of disease states (diabetes, hypothyroidism, renal and hepatic disease), concurrent use of ciclosporin, fibrates, CYP3A4 inhibitors (eg, diltiazem, macrolides, protease inhibitors, verapamil (except for pravastatin and rosuvastatin), severe intercurrent illness (infection, trauma and metabolic disorder), dose≥40 mg daily. High dose of high-potency statins ; ≥40 mg atorvastatin or simvastatin; >10 mg rosuvastatin <sup>39 80</sup>
14	Smoking cessation options	Counselling (extended, brief, telephone), support services (professional, family, social, work), pharmacotherapy
17	Medications that may affect glycaemic control	Increase blood glucose: baclofen, clozapine, ciclosporin, glucocorticoids, haloperidol, olanzapine, paliperidone, phenytoin, protease inhibitors, quetiapine, risperidone, sirolimus, tacrolimus and tricyclic antidepressants. Decrease blood glucose: excessive alcohol, disopyramide, perhexiline, quinine, trimethoprim/sulphamethoxazole <sup>39</sup>
18	Six-monthly HbA1c measurements	Treatment intensification in response to less than optimally controlled HbA1c may be inappropriate in patients with limited life expectancy or in frail older patients <sup>81 82</sup>
19	Metformin dose	Based on creatinine clearance: 60–90 ml/min, maximum 2 g daily; 30–60 ml/min, maximum 1 g daily; <30 ml/min avoid use. <sup>39</sup> Based on eGFR: review dose if eGFR<45 ml/min/1.73 m <sup>2</sup> ; avoid if eGFR<30 ml/min/1.73 m <sup>2</sup> <sup>83</sup>
24	Risk factors for impaired renal function	Volume depletion, age >60 years, salt-restricted diet, concomitant use of ACEIs, A2As, ciclosporin or aspirin, GFR ≤60 ml/min, cirrhosis, heart failure <sup>84</sup>
26	Benzodiazepine use	Benzodiazepines increase the risk of oversedation, ataxia, confusion, falls, respiratory depression and short-term memory impairment, and are recommended for short-term use only <sup>39</sup>
27	Falls and psychotropic medications	Psychotropic medications=antidepressants (all), anxiolytics/hypnotics, antipsychotics. <sup>85 86</sup> Medications causing (postural) hypotension

Continued

Table 4 Continued

Criteria number	Description of issue	Details
28	Medications that may contribute to serotonin syndrome	(eg, cardiovascular medicines) or cognitive impairment (eg, opioids) may also increase the risk of falls <sup>49 87</sup> Antidepressants: desvenlafaxine, duloxetine, St John's wort, MAOIs (including moclobemide), SSRIs, TCAs, venlafaxine. Opioids: dextromethorphan, fentanyl, pethidine, tramadol. Others: selegiline, linezolid, lithium, tryptophan <sup>39</sup>
29 and 30	Medications with significant anticholinergic activity	Amantadine, amitriptyline, atropine*, belladonna alkaloids*, benzhexol, benztropine, biperiden, brompheniramine*, chlorpheniramine, chlorpromazine, clomipramine, clozapine, cyclizine, cyclopentolate, cyproheptadine*, darifenacin, dexchlorpheniramine*, dimenhydrinate*, diphenhydramine*, disopyramide, dothiepin, doxepin, glycopyrrolate, homatropine, hyoscine* (butylbromide or hydrobromide), imipramine, ipratropium (nebulised), mianserin, nortriptyline, olanzapine, orphenadrine, oxybutynin, pericyazine, pheniramine*, pimozone, pizotifen, prochlorperazine, promethazine*, propantheline, solifenacin, tiotropium, tolterodine, trimipramine, triprolidine*, tropicamide (*available over-the-counter in Australia) <sup>39</sup>
31	Medications that may cause dyspepsia	Drugs with anticholinergic effects, aspirin, benzodiazepines, bisphosphonates, calcium channel antagonists, oral corticosteroids, dopaminergic drugs, doxycycline, erythromycin, ferrous sulphate, nitrates, NSAIDs, potassium chloride (slow release) <sup>38 39 49 88</sup>
35	Medications that may worsen asthma	Aspirin, $\beta$ -blockers (including eye drops), carbamazepine, echinacea, NSAIDs, royal jelly <sup>39 89</sup>
38	Non-specific URTI	Acute bronchitis, pharyngitis, tonsillitis, non-suppurative otitis media and sinusitis <sup>38</sup>
39	Appropriate antiosteoporotic medication	RDI of calcium from dietary sources and/or supplements=1300–1500 mg daily. RDI for vitamin D from sunlight and/or dietary sources and/or supplements=600 IU daily. Antiosteoporotic medication=bisphosphonates, calcitriol, denosumab, HRT, raloxifene, strontium, teriparatide. <sup>39</sup> Evidence for fracture risk reduction in women $\geq 75$ years is either absent or lacking in NVF for alendronate, risedronate and teriparatide, and in HF for alendronate, risedronate, zoledronic acid and teriparatide. There are no data available for denosumab in VF, NVF or HF. <sup>90</sup> The optimal duration of bisphosphonate therapy is uncertain. Evidence supports the use of strontium for 5 years, raloxifene for 4 years and zoledronic acid and denosumab for 3 years. Exposure to teriparatide should be limited to 18 months. <sup>91</sup> Data are limited for non-ambulatory patients and those with significant comorbidities. <sup>92</sup> It should be noted that bone strength is only one of many determinants of fracture risk <sup>93</sup>
42	Clinically significant medication interactions	Medication interactions that may interfere with the outcome of therapy

A2A, angiotensin 2 receptor antagonist; ACEI, ACE inhibitor; AF, atrial fibrillation; CHADS<sub>2</sub>, cardiac failure, hypertension, age, diabetes, stroke (doubled); CHA<sub>2</sub>DS<sub>2</sub>-VASc, cardiac failure or dysfunction, hypertension, age over 75 years (doubled), diabetes, stroke (doubled), vascular disease, age 65–74 years, sex category (female); CHD, coronary heart disease; CVD, cardiovascular disease; DBP, diastolic blood pressure; GFR, glomerular filtration rate; HF, hip fracture; HF-LVSD, heart failure with left ventricular systolic dysfunction; HFPEF, heart failure with preserved ejection fraction; HRT, hormone replacement therapy; IHD, ischaemic heart disease; ISH, isolated systolic hypertension; LVH, left ventricular hypertrophy; MAOI, monoamine oxidase inhibitor; MI, myocardial infarct; NSAID, non-steroidal anti-inflammatory drug; NVF, non-vertebral fracture; PAD, peripheral arterial disease; RDI, recommended daily intake; SBP, systolic blood pressure; SSRI, selective serotonin reuptake inhibitor; TC, total cholesterol; TCA, tricyclic antidepressant; TIA, transient ischaemic attack; TNF, tumour necrosis factor; URTI, upper respiratory tract infection; VF, vertebral fracture.

diabetes and cardiovascular disease<sup>96 97</sup>—disease-oriented and drug-orientated criteria such as ours have shown good content, face, concurrent and predictive validity and operational feasibility, as well as use for internal and external quality assessment in both ambulatory and hospital care.<sup>35</sup> Evidence–practice gaps in Australia have been identified in other areas besides diabetes and cardiovascular disease, such as in asthma, pain and vaccination status.<sup>9 98–101</sup> The existence of these gaps formed part of the developmental process for these criteria.

### Prescribing appropriateness tools in Australia

Appropriateness of prescribing has been assessed by measures that are explicit or implicit, in an effort to identify and reduce DRPs.<sup>102</sup> In Australia, both types of measures have been used.<sup>103–107</sup> However, they have been imported into the Australian healthcare environment, with consequent shortcomings related to both the intrinsic nature of the measure, as well as environment compatibility issues. For example, in a study evaluating the impact of Home Medicine Reviews on

appropriateness of prescribing, a significant number of recommendations made regarding the need for monitoring and addition of missing therapy were found to have no impact on explicitly derived scores using the Medication Appropriateness Index,<sup>103</sup> due to the intrinsic shortcomings of this tool. This is not a tool that gives precise guidance in relation to specific medicines.<sup>13</sup>

The Beers criteria,<sup>108</sup> perhaps the tool most widely used to assess inappropriate prescribing in older people, has been used in Australia, but requires modification to exclude medicines not listed for government subsidy.<sup>107</sup> This is because medicine availability and use in Australia is largely determined by the Australian Pharmaceutical Benefits Scheme<sup>37</sup>. Other Australian studies have found that some medicines listed as inappropriate by Beers may be appropriate for certain older people according to Australian practice;<sup>105</sup> many medicines listed by Beers are not available in Australia; and that some medicines considered inappropriate in Australia are not listed by Beers.<sup>106</sup> Disagreement between Beers and other criteria, such as the improving prescribing in the elderly tool, have been identified.<sup>109</sup>

The Beers criteria was recently updated,<sup>22</sup> with approximately half the medicines listed being unavailable in Australia. Further, almost three quarters of the diseases or syndromes listed are not among the 40 problems most frequently managed in patients over 65 years of age by Australian general practitioners.<sup>97</sup> Beers still contains recommendations to avoid some medicines that are recommended for certain older people in Australia such as amiodarone, and it has recently been shown that rhythm control in older patients with atrial fibrillation may be more effective than rate control in reducing mortality over the long term.<sup>110</sup> Reviews of explicit and implicit criteria have identified these and other problems such as failure to address drug–drug interactions and drug duplication, errors in recommendations, underrepresentation of certain drug categories, inclusion of infrequently prescribed drugs, criteria that are inapplicable for all situations, disagreement between criteria and lack of organisation of criteria.<sup>45 102 111</sup>

This has resulted in the development by others of criteria more suited to their own particular healthcare environment.<sup>112 113</sup> Nationally based criteria have been described as the most desirable type of criteria, as they do not necessitate adaptation to local guidelines or national formularies before they can be used with confidence.<sup>32</sup> In 2008, we therefore sought to construct and validate a set of prescribing appropriateness criteria relevant to the Australian healthcare environment. Our development process differed from most other tools<sup>21 108 112–117</sup> as it did not initially involve a consensus panel, which has now been addressed. This development process also resulted in criteria unavailable in other tools such as monitoring, underprescribing, need for additional tests, evaluation of smoking and vaccination status, and certain drug interactions.<sup>32 45 102</sup> Because we have generally named drug classes rather

than specific drugs (table 3), and targeted common medical conditions found in older patients,<sup>118 119</sup> we anticipate that our work may have some international usefulness.

Despite a desire in Australia to develop decision support tools to improve healthcare quality,<sup>120</sup> progress has consisted of the development of a limited number of non-age specific structure and process indicator lists for use in hospitals and general practice.<sup>40 121–123</sup> Many of these lists require updating.<sup>32 113 124</sup> Currently, there is no Australian prescribing appropriateness criteria list to assist in improving medication management in older people. The usefulness of such an approach has been acknowledged, together with other approaches such as medication review.<sup>125</sup>

### Co-morbidity

Over 80% of older Australians have three or more chronic conditions,<sup>96</sup> with Australian general practitioners shown to be dealing more frequently with patients presenting with three or four problems in the year 2009–2010 compared with 2000–2001.<sup>126</sup> Comorbidity is associated with poor quality of life, physical disability, high healthcare use, multiple medicines with consequent increased risk of adverse drug events, fragmentation of care and increased mortality.<sup>119 127</sup> Yet most Australian guidelines for chronic diseases do not modify or discuss the applicability of their recommendations to older patients with multiple comorbid conditions.<sup>34</sup> This situation is not restricted to Australia.<sup>127 128</sup> Because the risk of harm in older patients increases in proportion to the number of treatments prescribed, prioritisation of therapeutic goals is necessary. For example, coronary heart disease (CHD) is an important morbidity in Australia<sup>77 96</sup> for which treatment with ACE inhibitors or angiotensin 2 antagonists has been recommended to reduce the risk of cardiovascular events.<sup>70 71</sup> Other criteria derived outside Australia such as STOPP/START do not include this recommendation.<sup>21</sup> However, the presence of comorbidity in CHD (commonly arthritis or respiratory disease) or other clinical factors (such as dizziness, falls or patient preference) may mean that medicines such as these are never started, due to consideration of other factors. While we wished to identify problems such as these, the ultimate decision regarding medicine use should always be made on a case-by-case basis based on clinical experience, a discussion between the healthcare professional and the patient, and best available evidence.<sup>72</sup> Issues such as these may run counter to recommendations of disease-specific, evidence-based guidelines.<sup>34</sup> Addition of our criteria with this associated usage information (table 4) to the implicit processes of Australian medication review may assist in addressing the problem of comorbidity.

### The oldest old

Knowledge about the state of health and function of the oldest old is limited,<sup>129</sup> with research on their drug use



being scarce, and often based on small and selected samples without comparison with other age groups.<sup>130 131</sup> We know that older patients in general are underrepresented in clinical trials, so that disease-specific guideline recommendations based on evidence may not apply to older cohorts.<sup>34</sup> For example, undertreatment with anti-osteoporotic medicines has been identified as a significant evidence–practice gap in Australia.<sup>98</sup> While STOPP/START criteria recommend calcium and vitamin D supplements,<sup>21</sup> no recommendations for more specific medicines are made. Further, evidence available for fracture risk reduction has been reported to differ with age.<sup>90</sup> Similarly, blood pressure targets appropriate for older patients may not be appropriate for the oldest old,<sup>50</sup> with adverse effects for antihypertensives found to be among the most frequent in centenarians.<sup>132</sup> Issues regarding the oldest old appear in [table 4](#), criteria 1, 2, 9, 18 and 39. We have attempted to achieve the advantages of using mostly explicit criteria, such as ease of application, with the addition of application information ([tables 2 and 4](#)) unavailable in our previous criteria set.

### Rationale for the use of the RAND/UCLA appropriateness method

The RAND/UCLA appropriateness method has been used to rate lists ranging up to over 3000 indications, where panellists have been asked to use the clinical literature and their best clinical judgement to assess the appropriateness of performing a procedure. To do this, they have rated various clinical scenarios.<sup>46</sup> While the number and type of our criteria may differ to this, similar criteria have been developed using the RAND/UCLA method. For example, in the development of indicators for patients undergoing total hip or total knee replacement, 1 of the 68 indicators stated that for such patients, ‘deep venous thrombosis prophylaxis should be provided for a minimum of 2 weeks after hospital discharge’.<sup>43</sup> In the development of indicators for hazardous prescribing for general physicians (GPs) using this method, 1 of the 34 indicators identified the hazardous use of ‘NSAID in a patient with heart failure’.<sup>44</sup> We therefore followed a similar protocol.

### Nature of decision support tools

Panel members emphasised that criteria may not provide definitive answers, instead indicating potential problems that might need addressing, due to a perceived unacceptable variation in care.<sup>133</sup> While performance indicators are designed to measure the result of statements made in clinical practice guidelines, these guidelines often provide recommendations for care independent of other considerations such as multiple comorbidities, advanced age, frailty, patient preferences, disease burden or limited life expectancy.<sup>134–136</sup> In such cases, less stringent goals, deprescribing or non-prescription may be more

appropriate.<sup>15 81 137</sup> For example, a frail older patient with multiple comorbidities and one or more functional impairments may have a life expectancy of approximately 2 years or less.<sup>75</sup> This raises the question of whether failure to intensify treatment<sup>81</sup> or to underuse evidence-based therapies<sup>138</sup> reflects appropriate clinical judgement or an inappropriate care gap. The panel felt strongly that use of indicators, guidelines or criteria providing clinical decision support should never replace critical thinking in patient care.<sup>139</sup>

### Strengths and weaknesses

We have followed a recommended approach<sup>120</sup> by suggesting criteria for which high-quality evidence exists linking best practice with improved outcomes; where there are established evidence–practice gaps<sup>98 99</sup>; and where the health conditions impose the greatest burden on the healthcare system. We used a validated consensus method, an expert panel of varied specialisation, and criteria written with the aim of conciseness and clarity.

In addition to face and content validity, these validated criteria, much like performance indicators, will require further developmental work to provide evidence of their acceptability, operational feasibility, reliability and degree of predictive validity.<sup>35 133</sup> Some of this work has already started with the original criteria.<sup>95</sup> Further, these criteria only cover commonly occurring medicines and medical conditions. In addition, judgements made by an expert panel may not be representative of all healthcare professionals.

### Intended use

These validated criteria are intended for use by healthcare providers to enhance the quality of the Australian medication review process, for quality improvement, educational purposes and internal audit. They are also intended for external quality assessment, such as use by policy makers and for public reporting. Stakeholder involvement will be critical to facilitate local uptake and encourage further research into the effects on health outcomes.<sup>125</sup>

### CONCLUSION

This study validated 41 prescribing appropriateness criteria to assist in identifying DRPs in older ( $\geq 65$  years) Australians. These criteria are intended to represent an addition to the medication management skill set that includes consideration of limited life expectancy, evidence base in the oldest old, drug burden and care coordination, patient and care-giver education, empowerment for self management, and shared decision-making. These skills are far from a ‘do everything for everyone’ philosophy, where aggressive treatment may encourage more care, not more appropriate care.<sup>31 135</sup> Despite the presence of clinical decision support tools, healthcare

providers need to know how to think about clinical problems, not just what to think.<sup>139</sup>

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