Updating and validating quality prescribing indicators for use in Australian general practice

ABSTRACT

Objective: To update and validate quality prescribing indicators (QPIs) for Australian general practice.

Design and Setting: The study comprised two phases: (1) developing a preliminary list of potential QPIs based on the 2006 National Prescribing Service (NPS) MedicineWise indicators, published literature, international indicators and guidelines, and through qualitative focus group discussions; and (2) validating the proposed QPIs through a two-round online survey using the Delphi technique.

Participants: The Delphi panel included four general practitioners, four pharmacists and two clinical pharmacologists.

Main outcome measures: The Delphi panel rated the potential QPIs for their validity, importance and feasibility using a 1-10 Likert scale.

Results: In the first round, all proposed QPIs presented as 'prescribing rules' achieved high scores regarding validity, importance and feasibility (median $\geq$ 7/10 without disagreement, except one with median feasibility of 6.5). No rule was eliminated and three new rules were introduced. Rules were reworded into 'prescribing indicators' for the second round, which resulted in 35 indicators being accepted and two indicators being eliminated. Seven drug-drug interactions, all of which received high scores in the first round, were also included in the final set of QPIs.

Conclusion: Forty-two QPIs were nominated for use in Australian general practice, based on their validity, importance and feasibility. If implemented in practice, these QPIs have the potential to assist in efforts to improve the quality and safety of medicines management.

Keywords: general practice, medication-related problem, drugs, quality indicator, prescribing, quality of care.

WHAT IS KNOWN ABOUT THE TOPIC?

- Medication-related problems (MRPs) are an important cause of patient harm in Australia and are increasingly recognised in general practice through clinical audits, medication reviews and the observations of embedded pharmacists.
- Quality prescribing indicators (QPIs) have been used to identify MRPs that most significantly affect patient outcomes , and play a vital role in the improvement of quality and safety in healthcare.
- Globally, QPIs have been developed and are continually used and updated in many countries, such as the US and UK.
- In Australia, QPIs for general practice were developed by NPS MedicineWise in 2006 but had no planned review cycle. Therefore, the current QPIs are significantly outdated.

WHAT DOES THIS PAPER ADD?

- This paper introduces an updated and validated list of quality prescribing indicators (QPIs) for use in Australian general practice.
- The QPIs have the potential to assist in efforts to improve the quality and safety of medicines management by enabling users to measure and benchmark prescribing activities.
- The QPIs are ready for use in further research to test their applicability before they are widely implemented.

INTRODUCTION

Medication-related problems (MRPs) are an important cause of patient harm, even in highly developed healthcare systems, such as that existing in Australia. It has been reported that approximately 2% to 3% of hospital admissions in Australia are medication-related, with around 50% of these being considered preventable (Roughead and Semple 2009).

In general practice, MRPs are increasingly recognised through clinical audits, medication reviews and the observations of embedded pharmacists (Benson *et al.* 2018; Harris 2018). In a 2015-16 report of general practice activity, 11.2% of patients had experienced an adverse drug event (ADE) in the previous 6 months and about 6% of these resulted in a hospital admission (Britt *et al.* 2016). Inappropriate prescribing and under-prescribing of therapeutically beneficial medications appear to be compounded in the elderly and those with common chronic conditions, such as cardiovascular disease and diabetes. In an Australian community study of older men aged 74-80 years, the rate of potentially inappropriate prescribing was 49% and the rate of medication under-utilisation was 57%. In this group, one consequence of under-prescribing of cardiovascular drugs was an association with an increased risk of cardiovascular events (Beer *et al.* 2011). Another study, conducted over a period of 13 years with 251,305 Australians aged 65 years and older, found the rate of patients having inappropriate medication exceeded 40% annually (Price *et al.* 2014).

Reducing MRPs is essential for the improvement of quality and safety in healthcare. To optimise the impact and cost-effectiveness, efforts need to be targeted at MRPs that most significantly affect patient outcomes. Quality prescribing indicators (QPIs) have been developed to "measure the performance of health care providers in several key dimensions related to the appropriate use of drugs" (World Health Organization 1993). Such QPIs can help

identify gaps, prompt interventions, detect impact of changes and ultimately improve the quality and safety of practice (Duerden *et al.* 2011). QPIs could be applied through a cycle of audit and feedback (Avery *et al.* 2011; NPS 2006; Spencer *et al.* 2014). A Cochrane review confirmed audit and feedback improved professional practice, with a large effect on prescribing, citing an improvement of 13% (Ivers *et al.* 2012). Additionally, in Australian general practice, using indicators for audit and to provide feedback was found to be effective in improving cardiovascular disease management (Gadzhanova *et al.* 2013) and the optimal use of metformin and insulin in diabetes (Gadzhanova *et al.* 2011). Indicators also have the capacity to reduce costs in primary care (Meltzer and Chung 2014). However, as the clinical evidence base, health priorities and available treatments change over time, any existing indicators should be periodically reviewed and the need for new indicators considered (Kontopantelis *et al.* 2014; Meltzer and Chung 2014).

In the United Kingdom, QPIs for general practice have been used for over 4 decades and are periodically updated (Avery *et al.* 2011; Duerden *et al.* 2011; Spencer *et al.* 2014). Similarly, other countries, such as Sweden (Fastbom and Johnell 2015) and the USA (The American Geriatrics Society 2015), also have a process for updating their QPIs. In contrast, the Australian QPIs developed by NPS MedicineWise (NPS 2006) had no planned review cycle. These 21 QPIs (8 structural and 13 process) are now significantly out of date and this may explain the current low utilisation rates. Revision of these QPIs may increase their utility and fulfil the goal of reducing contemporary MRPs. Therefore, our aim was to update and validate QPIs for use in Australian general practice using the Delphi technique, which has been validated for determining healthcare quality indicators (Boulkedid *et al.* 2011).

METHODS

There were two phases in this study: preparing a preliminary list of potential QPIs (phase one) and validating the list of potential QPIs using the Delphi technique (phase two).

Preparing a preliminary list of potential QPIs

The list was constructed by reviewing the 2006 NPS MedicineWise indicators and introducing new indicators based on currently available international indicators (Appendix 1) and guidelines, and drug-drug interactions. Additionally, four focus group discussions with Australian GPs and a general practice based-pharmacist were used to identify topics that were considered to be important to general practice for inclusion into the list of potential QPIs. All proposed QPIs were compared with current Australian therapeutic guidelines (eTG complete available at https://tgldcdp.tg.org.au/etgcomplete) and recent international literature. Subsequently, the research team, which consisted of four experienced pharmacists and one GP, modified or eliminated indicators that were considered irrelevant to current practice in Australia.

Available international indicators were identified through a systematic search of the PubMed and Embase databases. Search terms were (inappropriate prescribing OR inappropriate prescription OR inappropriate prescriptions OR inappropriate medication OR inappropriate medications) AND (scale OR scales OR instruments OR indicator OR indicators OR tool OR tools OR toolkit OR toolkits OR criteria). The search was limited from 01/01/2003 to 15/04/2017, to English articles and applicable to human subjects aged 65 years old or older. This narrowed the search to the population most susceptible to adverse events with drugs. Articles that described criteria to assess hazardous or inappropriate prescribing and articles

describing updated versions of published indicators were included. Exclusion criteria were articles describing indicators for a specific disease or a healthcare setting other than general practice.

Drug-drug interaction indicators were also selected from these international sources, as well as three other published lists of drug interactions (Appendix 2). The research team identified the interactions that were included in most of the sources and in accordance with ADEs reported in an Australian study (Parameswaran Nair *et al.* 2017).

Validating the potential QPIs list

A group of experts was recruited via personal invitation and advertisements in healthcare professional newsletters, to help validate the proposed QPIs. The final expert panel comprised four GPs, four pharmacists and one clinical pharmacologist from Australia, and one clinical pharmacologist from New Zealand. They were selected based on peer recommendations, membership of the Australasian Pharmaceutical Science Association (APSA) and/or Australasian Society of Clinical and Experimental Pharmacologists and Toxicologists (ASCEPT), and having at least 5 years of clinical experience with a practical understanding of the general practice context. Some of these experts also had previous experience in indicator development and quality measurement. Selection of panel members also sought to ensure variation in gender and distribution between urban and rural areas. Information sheets were provided to, and consent forms obtained from, panel participants.

The validation process was conducted using the Delphi technique, a communication method to achieve a consensus of opinion through a series of questionnaire rounds with an anonymised summary of the group's responses fedback after each round. The technique was chosen because

it does not require face-to-face meetings, which was more practical than either the RAND/UCLA or nominal group techniques, due to the cost and geographic distribution of our participants (Campbell *et al.* 2002).

The process was a two-round survey, conducted online using LimeSurvey. In the first round, proposed QPIs were presented as 'prescribing rules' (Table 1). Each panellist rated these rules for their validity, importance and feasibility of measurement. Free-text comments were also allowed in this round, to explore panellists' viewpoints on the rules. In the second round, the 'prescribing rules' were converted into 'indicators' (Table 1). Feedback from the previous round's responses (represented as mean, median and frequency distribution) was attached and the panellists were asked to reflect on this information before rating the indicators. Each indicator was rated for their validity and feasibility. A Likert scale of 1 = inappropriate to 10 = appropriate was used in both rounds. Table 1 presents the definitions of 'prescribing rule', 'indicator', rating criteria and an example of a conversion from prescribing rule to indicator. We determined in advance that two rounds would likely be sufficient as in most published studies consensus is reached after two rounds and too many rounds may exhaust participants and decrease the response rate (Keeney *et al.* 2011). For any QPIs that did not reach consensus after two rounds, the research team proposed internal discussion until a consensus was reached.

Table 1: Definition of prescribing rule, indicator and rating criteria.

Definition of 'prescribing rule' and 'indicator'	
	Definition
Prescribing rule	A rule is an evidence based statement that guides a particular prescribing action.
Indicator	An indicator is a measure of quality presented as percentages of observed prescribing actions in a sample of clinical encounters
Example of converting from prescribing rule to indicator: - Prescribing rule: 'Prescribe pneumococcal vaccine at least once for patients aged more than 65 years'. - Indicator: 'Percentage of patients older than 65 years who are NOT prescribed pneumococcal vaccine'.	
Definition of rating criteria	
	Definition
Validity	An indicator is VALID if it measures a real medication-related problem (i.e. it is definitive, with well-accepted evidence).
Importance	An indicator is IMPORTANT if it measures a prevalent problem in general practice, and by addressing it could improve quality and safety.
Feasibility	An indicator is FEASIBLE if the extent of the problem can be easily measured (e.g. by using data extracted from GPs' clinical software).

Data analysis and defining consensus

Data were analysed using SPSS version 23 (Armonk, NY: IBM Corp.). Rating scores were summarised using descriptive statistics, such as means, medians, standard deviations and percentile. Free-text comments were optional and were evaluated by the research team on a case by case basis.

The ratings were classified into three levels: appropriate, uncertain and inappropriate, as below. A consensus was reached when the indicator was rated as appropriate or inappropriate, with indicators rated as appropriate being included in the final list and indicators rated as inappropriate being eliminated. A consensus was not reached when the indicator was rated as uncertain, which was re-rated in the second round or discussed internally by the research team.

Appropriate: median score >= 7 and less than one-third of respondents rating the indicator within the 1-3 range.

Inappropriate: median score <= 3 and less than one-third of respondents rating the indicator within the 7-10 range.

Uncertain: 3 < median score < 7, OR median score >= 7 (or <= 3) and one-third or more of respondents rating the indicator within the 1-3 range (or 7-10 range).

RESULTS

The systematic search identified 2,260 articles (1,198 from PubMed and 1,062 from Embase). Removal of duplicates, and title and abstract screening resulted in 120 relevant articles. Full-text screening resulted in 14 final sets of international prescribing indicators. These sets are listed in Appendix 1.

The response rate from the panel was 100% in the first round and 90% (one pharmacist dropped out) in the second round. In the first round, there were 31 proposed prescribing rules; nine were derived from the original NPS MedicineWise indicators and 22 were derived from international indicators. All prescribing rules were regarded by the panel as valid and important for use as QPIs (median score ≥ 7 with less than one-third of respondents rating the indicator within the 1-3 range). All rules also reached consensus with high scores regarding feasibility, except one regarding inhaled corticosteroids for patients with chronic obstructive pulmonary disease (COPD), that was rated uncertain (median = 6.5) (Table 2). This rule was kept for re-rating in the second round. In short, no prescribing rule was eliminated after first round.

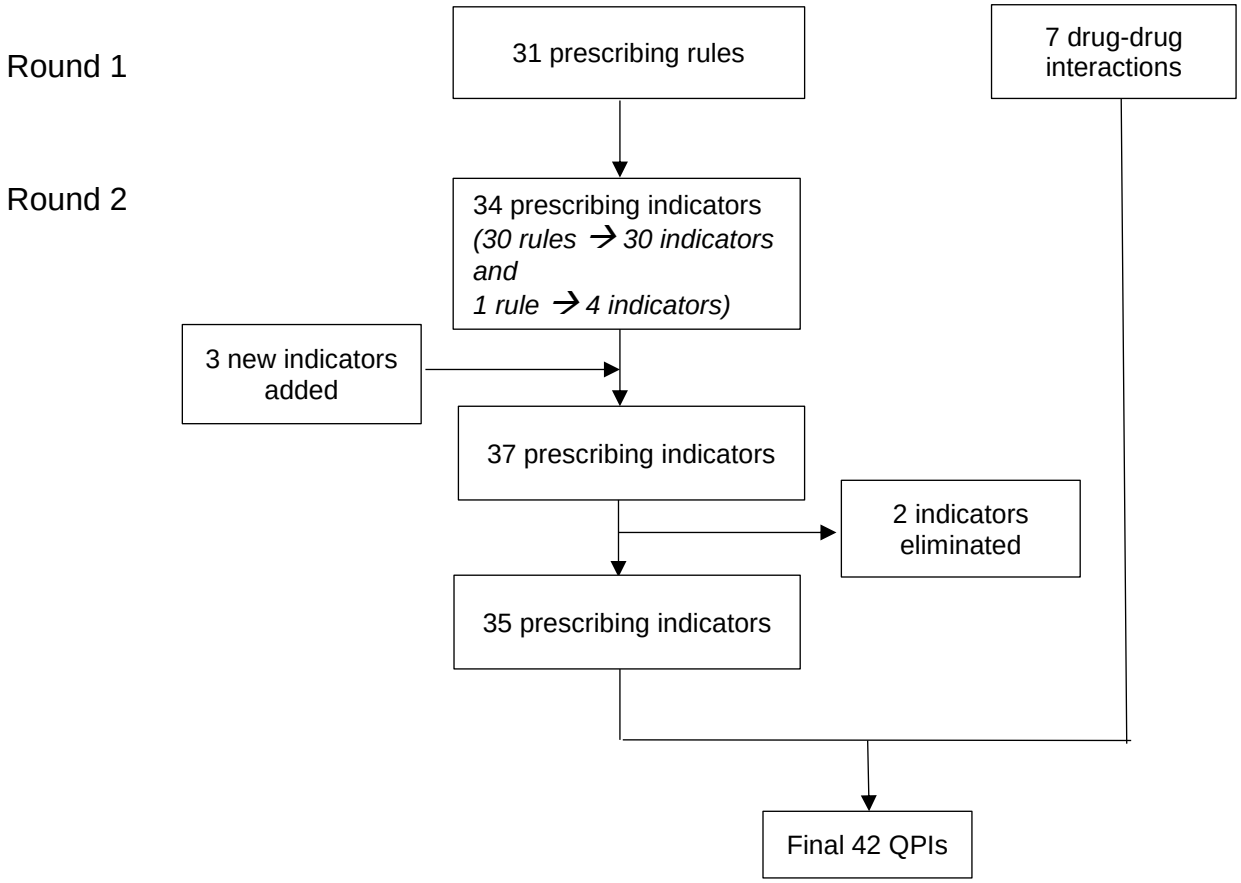
In preparation for the second round, the prescribing rules were reworded into ‘indicators’. One prescribing rule was considered lengthy and complex, and so was separated into four indicators, to improve clarity. Three new indicators were also recommended by the panel and added to the

list. This resulted in 37 indicators at the entry of the second round (Figure 1). In this round, 35 indicators reached consensus with high scores regarding validity and feasibility (median score ≥ 7 with less than one-third of respondents rating the indicator within the 1-3 range). There was one indicator that did not reach consensus for validity and one indicator that did not reach consensus for feasibility (Table 2) and both of these were then eliminated by the research team.

There were also seven prescribing rules regarding drug-drug interactions. All of them reached consensus with high scores in all three aspects (median score ≥ 7) in the first round. These were all accepted for inclusion in the final set of QPIs without changes.

Free-text comments revealed some concerns regarding the feasibility of some QPIs (Table 4). Additionally, one panellist commented that it would be easier to implement QPIs if they were simplified to avoid patient subgroups, e.g. measure patients taking anticholinergics rather than patients with dementia taking anticholinergics.

198 Figure 1: Flowchart illustrating validating process.



199 The final QPIs, comprising 42 indicators, are presented in Table 3, with their corresponding

200 prescribing rules and rating scores through the two rounds.

201 Table 2: Eliminated indicators

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Indicator	Round 1 Median (Interquartile Range)			Round 2 Median (Interquartile Range)	
	Validity	**Importance**	**Feasibility**	**Validity**	**Feasibility**
Percentage of patients with osteoporosis, who have been prescribed systemic corticosteroids.	-	-	-	***8.00**** ***(5)***	9.00 (1)
Percentage of patients with COPD who have been prescribed an inhaled corticosteroid when they do NOT have asthma/COPD overlap syndrome and do NOT have FEV1 ≤50% of predicted and repeated exacerbations.	9.00 (1.5)	8.50 (2)	***6.50*** ***(4)***	9.00 (1)	***7.00**** ***(4)***
* one-third or more of respondents rated the indicator within the opposite 1-3 range					

203 Table 3: Final QPIs with their corresponding prescribing rules and rating scores through two Delphi rounds.

No	Indicator	Prescribing rule	Round 1 Median (Interquartile Range)			Round 2 Median (Interquartile Range)		
			V	I	F	V	I	F
1	Percentage of patients aged over 65 years who have been prescribed two or more drugs with anticholinergic effects concomitantly.	Avoid prescribing two or more drugs with anticholinergic effects concomitantly for patients aged over 65 years.	8.00 (1.75)	8.00 (1)	8.00 (2)	8.00 (1)	-	8.00 (1)
2	Percentage of patients aged over 65 years who have been prescribed either tricyclic antidepressants, antipsychotics with strong anticholinergic effects or urological antispasmodic agents.	Avoid prescribing tricyclic antidepressants, antipsychotics with strong anticholinergic effects or urological antispasmodic agents for patients aged over 65 years.	8.50 (1.75)	8.00 (0)	9.00 (1.75)	9.00 (1)	-	9.00 (0)
3	Percentage of patients aged over 65 years with extrapyramidal symptoms caused by antipsychotics, who have been prescribed anticholinergic antiparkinsonian agents.	Avoid prescribing anticholinergic antiparkinsonian agents for patients aged over 65 years to prevent or treat extrapyramidal symptoms caused by antipsychotics.	9.00 (2.5)	7.50 (1.75)	9.00 (1.5)	8.00 (2)	-	7.00 (3)
4	Percentage of patients aged over 65 years with cognitive impairment/dementia, delirium or chronic constipation, who have been prescribed drugs with strong anticholinergic effects (except inhaled anticholinergics).	Avoid prescribing drugs with strong anticholinergic effects (except inhaled anticholinergics) for patients aged over 65 years with cognitive impairment/dementia, delirium or chronic constipation.	9.00 (1.75)	8.00 (1.75)	8.00 (2.5)	9.00 (0)	-	8.00 (1)
5	Percentage of patients aged over 65 years with lower urinary tract symptoms and/or benign prostatic hyperplasia, who have been	Avoid prescribing drugs with strong anticholinergic effects (except urological antispasmodic agents) for	8.00 (1.5)	8.00 (2.5)	8.00 (1.5)	8.00 (1)	-	8.00 (3)

	prescribed drugs with strong anticholinergic effects (except urological antispasmodic agents for lower urinary tract symptoms).	patients aged over 65 years with lower urinary tract symptoms and/or benign prostatic hyperplasia.						
6	Percentage of patients aged over 65 years with a history of narrow angle glaucoma, who have been prescribed drugs with strong anticholinergic effects.	Avoid prescribing drugs with strong anticholinergic effects for patients aged over 65 years with a history of narrow angle glaucoma.	8.00 (1)	7.00 (1)	7.00 (1.5)	8.00 (1)	-	7.00 (1)
7	Percentage of patients receiving anticholinesterase drugs (donepezil, galantamine, rivastigmine), who have been prescribed drugs with strong anticholinergic effects concomitantly.	Avoid prescribing anticholinesterase drugs (donepezil, galantamine, rivastigmine) and drugs with strong anticholinergic effects concomitantly.	8.50 (3)	8.50 (3.25)	9.50 (1)	8.00 (2)	-	9.00 (2)
8	Percentage of patients with a non-specific URTI[a] prescribed an antibiotic.	Avoid prescribing an antibiotic for patients with a non-specific URTI[a]	10.00 (0.75)	9.00 (1)	9.00 (2.75)	10.00 (1)	-	9.00 (2)
9	Percentage of children aged 6 months to 12 years who had acute otitis media for less than 2 days without systemic symptoms, prescribed an antibiotic.	Avoid prescribing antibiotics for children aged 6 months to 12 years who have had acute otitis media for less than 2 days without systemic symptoms.	10.00 (0.75)	8.50 (1.75)	8.00 (2)	10.00 (1)	-	8.00 (2)
10	Percentage of cases of non-specific URTI[a], pharyngitis, tonsillitis, acute otitis media, sinusitis or acute bronchitis with prescriptions of cephalexin.	Avoid prescribing cephalexin for non-specific URTI[a], pharyngitis, tonsillitis, acute otitis media, sinusitis or acute bronchitis.	9.50 (1.75)	9.00 (3.5)	8.00 (2.5)	9.00 (1)	-	8.00 (2)
11	Percentage of patients with type II diabetes and hypertension and any degree of albuminuria who are NOT prescribed an ACEI or ARB[b].	Prescribe an ACEI or ARB for patients who have type II diabetes and hypertension and any degree of albuminuria[b].	9.50 (1)	9.00 (2)	9.50 (2)	9.00 (1)	-	9.00 (3)

12	Percentage of patients with a history of acute coronary syndrome who are NOT prescribed an antiplatelet agent (or anticoagulant), statin and ACEI or ARB.	Prescribe an antiplatelet agent (or anticoagulant), statin and ACEI or ARB for patients who have had acute coronary syndrome.	10.00 (1)	10.00 (1)	9.00 (1)	9.00 (1)	-	9.00 (2)
13	Percentage of patients prescribed an antihypertensive agent who are NOT at their target blood pressure.	Patients prescribed antihypertensive therapy should achieve target blood pressure.	9.50 (2)	9.00 (1.75)	8.50 (4.25)	9.00 (1)	-	7.00 (2)
14	Percentage of patients with heart failure with reduced ejection fraction (systolic heart failure) who are NOT prescribed an ACEI or ARB, and a beta-blocker[b].	Prescribe an ACEI or ARB and a beta-blocker for patients with systolic heart failure (LVEF < 40%)[b].	10.00 (0.5)	9.50 (1.25)	9.00 (2.25)	9.00 (2)	-	9.00 (2)
15	Percentage of patients prescribed benzodiazepines where continuous usage exceeds 4 weeks.	Avoid prescribing benzodiazepines for more than 4 weeks.	9.00 (2)	8.00 (3)	9.00 (0)	9.00 (1)	-	9.00 (2)
16	Percentage of patients with asthma receiving a long-acting beta2-agonist who are NOT prescribed an inhaled corticosteroid concomitantly.	Avoid prescribing a long-acting beta2-agonist without co-prescribing an inhaled corticosteroid for patients with asthma.	9.50 (1)	9.00 (1.5)	9.00 (0.75)	9.00 (1)	-	9.00 (1)
17	Percentage of patients with chronic atrial fibrillation receiving an oral anticoagulant who are prescribed antiplatelet agent(s) concomitantly.	Avoid prescribing antiplatelet agent(s) in combination with an oral anticoagulant (vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitor) for patients with chronic atrial fibrillation.	10.00 (1)	10.00 (1)	9.50 (1)	9.00 (1)	-	9.00 (3)
18	Percentage of patients with non-valvular chronic atrial fibrillation who are NOT prescribed an oral anticoagulant.	Prescribe an oral anticoagulant (vitamin K antagonist, direct thrombin inhibitor or factor Xa inhibitors) for patients (without contraindications) with non-valvular atrial fibrillation and a CHA_2DS_2–VASc score ≥2.	9.00 (2)	9.00 (1.5)	9.00 (1.75)	9.00 (1)	-	9.00 (1)

19	Percentage of patients with moderate to severe COPD, who are NOT prescribed a regular inhaled long-acting beta-2 agonist or an inhaled long-acting muscarinic antagonist.	Prescribe a regular inhaled long-acting beta-2 agonist or an inhaled long-acting muscarinic antagonist for patients with moderate to severe COPD.	8.00 (3.75)	8.00 (3.5)	8.50 (1.75)	9.00 (2)	-	8.00 (1)
20	Percentage of patients with mild to moderate COPD, who have been prescribed systemic corticosteroid as a maintenance therapy.	Avoid prescribing systemic corticosteroids in one of following conditions: + as a maintenance therapy for mild to moderate COPD. + as a long-term monotherapy (>3 months) for rheumatoid arthritis. + for osteoarthritis (except intra-articular corticosteroids for short-term relief of a flare or acute deterioration in symptoms) + for patients with osteoporosis.	9.00 (1.75)	9.00 (0.75)	9.00 (2.75)	7.00 (2)	-	7.00 (2)
21	Percentage of patients with rheumatoid arthritis, who have been prescribed systemic corticosteroids continuously for more than 3 months.					9.00 (2)	-	8.00 (2)
22	Percentage of patients with osteoarthritis, who have been prescribed systemic corticosteroids (except intra-articular corticosteroids).					9.00 (2)	-	9.00 (1)
23	Percentage of patients with a documented history of coronary, cerebral or peripheral vascular disease, who are NOT prescribed a statin.	Prescribe a statin as secondary prevention for patients with a documented history of coronary, cerebral or peripheral vascular disease, unless the patient's status is end-of-life or age is > 85 years.	10.00 (1.75)	9.00 (2)	8.50 (1.75)	9.00 (2)	-	9.00 (1)
24	Percentage of patients who are prescribed a short-acting muscarinic antagonist and a long-acting muscarinic antagonist in combination.	Avoid prescribing a short-acting muscarinic antagonist and a long-acting muscarinic antagonist in combination.	9.00 (2)	8.00 (2.5)	9.50 (1.75)	8.00 (3)	-	9.00 (2)
25	Percentage of patients with persistent non-cancer pain, who are prescribed strong opioids as monotherapy.	Avoid prescribing strong opioids as monotherapy in the management of persistent non-cancer pain.	9.00 (2)	9.00 (1)	8.00 (1.75)	9.00 (1)	-	8.00 (1)

26	Percentage of patients with osteoarthritis pain and taking NSAID for more than 3 months, who have NOT tried regular paracetamol.	Avoid prescribing NSAID for long-term use (>3 months) for symptom relief of osteoarthritis pain where regular paracetamol has not been tried.	8.50 (2.5)	8.50 (1)	7.00 (1.75)	8.00 (2)	-	8.00 (2)
27	Percentage of patients aged more than 65 years who are NOT prescribed seasonal influenza vaccine annually.	Prescribe seasonal trivalent influenza vaccine annually.	10.00 (3.5)	8.00 (3.25)	10.00 (0.75)	10.00 (2)	-	9.00 (2)
28	Percentage of patients aged more than 65 years who are NOT prescribed pneumococcal vaccine.	Prescribe pneumococcal vaccine at least once for patients aged more than 65 years.	9.50 (1.75)	8.50 (2)	10.00 (1)	9.00 (2)	-	9.00 (0)
29	Percentage of patients receiving a long-term systemic corticosteroid (>= 3 months), who have NOT been prescribed a bisphosphonate.	Prescribe a bisphosphonate for patients who have severe osteopenia or osteoporosis (BMD T-score of -1.5 or less) and who are prescribed a long-term (>=3 months) systemic corticosteroid at a dose equivalent to or greater than prednisolone 7.5 mg per day.	9.00 (1.75)	9.00 (0.75)	8.00 (2)	9.00 (1)	-	9.00 (1)
30	Percentage of patients with documented osteoporosis and/or patients with previous history of fracture due to minimal trauma, who have NOT been prescribed an anti-resorptive agents.	Prescribe an anti-resorptive agents for elderly patients (>= 70 years old) with documented osteoporosis (BMD T-score of -2.5 or less) and/or patients with previous history of fracture due to minimal trauma.	9.00 (2)	8.50 (1)	8.00 (2.5)	9.00 (2)	-	9.00 (4)
31	Percentage of patients with heartburn or mild to moderate GORD or oesophagitis, who are prescribed a PPI at full therapeutic dosage for more than 8 weeks.	Avoid prescribing a PPI at or above full therapeutic dosage for more than 8 weeks for patients with heartburn or mild to moderate GORD or oesophagitis, and whose symptoms have resolved (excludes the situation of prophylaxis e.g. when using anticoagulation in a patient with a history of	9.00 (1.75)	8.00 (2)	9.00 (1)	8.00 (2)	-	8.00 (2)

		gastrointestinal bleeding; or long-term use of NSAID)						
32	Percentage of patients with behavioural and psychological symptoms of dementia, who are prescribed antipsychotic medications.	Avoid prescribing antipsychotic medications for patients with behavioural and psychological symptoms of dementia unless symptoms are severe and non-pharmacological treatments have failed.	9.50 (1.75)	9.00 (0.75)	8.00 (3.75)	8.00 (3)	-	8.00 (3)
33	Percentage of patients with congestive heart failure, who have been prescribed NSAIDs or COX-2 inhibitors.		-	-	-	9.00 (2)	9.00 (2)	8.00 (2)
34	Percentage of patients with low absolute cardiovascular risk, who have been prescribed statins for primary prevention.		-	-	-	8.00 (3)	7.00 (2)	8.00 (2)
35	Percentage of patients taking antipsychotic medicines who receive appropriate monitoring[c] for the development of metabolic side effects within 1 year.		-	-	-	9.00 (1)	9.00 (1)	8.00 (1)
Drug – Drug Interactions[d]								
36	ACEI or ARB ←→ Potassium supplement or Potassium-sparing diuretics or Aldosterone antagonist		9.00 (2.5)	8.00 (3.75)	8.90 (0.75)	-	-	-
37	ACEI ←→ ARB		9.50 (2)	8.50 (1.75)	9.30 (0.75)	-	-	-
38	Beta blocker ←→ Verapamil		9.50 (1.75)	10.00 (1.75)	9.40 (1)	-	-	-
39	Diuretic ←→ NSAID ←→ ACEI or ARB (“Triple Whammy”)[e]		8.00 (1.75)	8.50 (2)	9.00 (1.75)	-	-	-
40	NSAID ←→ vitamin K antagonist or direct thrombin inhibitor or factor Xa inhibitors		9.00 (2.5)	8.50 (2.5)	9.00 (0)	-	-	-

41	Lithium ←→ Diuretics or NSAID or ACEI or ARB	8.00 (1.75)	7.00 (1.75)	9.00 (0)	-	-	-
42	Concomitant prescription of three or more drugs within the groups of centrally-acting analgesics, antipsychotics, antidepressants and/or benzodiazepines	8.50 (1.75)	8.00 (1)	9.00 (0)	-	-	-

[a] Non-specific URT includes patients with the common cold and rhinosinusitis.

[b] Exclude patients with contraindication to ACEI/ARB or beta-blocker.

[c] Appropriate monitoring includes waist circumference, weight and blood pressure, serum lipid measurements and fasting blood glucose.

[d] Interaction between two groups of drugs or drug classes is presented as “group 1 ←→ group 2”.

[e] Triple Whammy: a drug interaction between three groups of drugs, that can result in acute renal failure.

V = Validity, I = Importance, F = Feasibility.

ACEI = angiotensin-converting-enzyme inhibitor; ARB = angiotensin II receptor blocker; NSAID = nonsteroidal anti-inflammatory drug; BMD = bone mineral density; COPD = chronic obstructive pulmonary disease; FEV-1 = forced expiratory volume in 1 second; GORD = gastro-oesophageal reflux disease; URTI = upper respiratory tract infection.

Table 4: Feasibility concerns from the first round's comments

1) Poor documentation of drugs and laboratory tests.
2) Lack of coding for diagnoses and drugs.
3) Difficulty in determining indications for some drugs (e.g. systemic corticosteroids).
4) Difficulty in determining duration of symptoms (e.g. gastroesophageal reflux).
5) Problems tracking medicines purchased over-the-counter.
6) Difficulty in measuring the practice of multiple clinicians and/or in multiple settings.

DISCUSSION

Our study produced a list of 42 QPIs for use in Australian general practice. The QPIs cover a wide range of contemporary prescribing areas and problems (e.g. anticholinergic burden, cardiovascular disease, asthma, osteoporosis), as well as several important drug-drug interactions. They were verified for their validity, importance and feasibility in general practice by an expert panel of stakeholders (GPs, pharmacists and clinical pharmacologists).

Indicators to assess appropriateness of prescribing have been developed in many countries (Kaufmann *et al.* 2014). Some are notable for their systematic and continuous approach in the development and updating of data, such as the Beers indicator in the USA (The American Geriatrics Society 2015) and the STOPP/START indicator in Europe (O'Mahony *et al.* 2015). While these tools can be implemented in any settings, a set of indicators specific for general practice has also been developed and recently updated in the UK (Avery *et al.* 2011; Spencer *et al.* 2014). In Australia, a set of Quality Use of Medicines Indicators for the hospital setting was updated in 2014 (ACSQHC and NSW Therapeutic Advisory Group 2014) while the QPIs for general practice have not been updated since their original development in 2006. Our work is, therefore, in line with international and local attempts to build and maintain a contemporary tool to assist in quality and safety improvement initiatives.

Our QPIs for the general practice setting were similar to that determined, using similar methodology, in a recent UK general practice study (Spencer *et al.* 2014). In both studies there was an emphasis on indicators related to specific conditions (namely cardiovascular, respiratory, musculoskeletal and neurological conditions), on drug interactions and laboratory measurement to detect harm. In our study there was more focus on indicators related to anticholinergc load and the elderly. However, the similarities suggest that such indicators might apply to primary care globally.

A strength of our study was that we developed a list of QPIs with high validity, based on international indicators, recent guidelines, literature and expert opinion. Although our QPIs gained high rates of consensus in feasibility, free-text comments revealed that it could be difficult to routinely implement some QPIs in practice. For example, paracetamol can be purchased over-the-counter, so it is difficult to track if patients with osteoarthritis had tried it before they had been prescribed a long-term NSAID. Nevertheless, the high rating scores indicate an optimism from the panel for implementation of these QPIs in the future.

Our study has some limitations. We limited our literature search to the elderly so valuable indicators specific to younger patient groups may have been missed. However, this was countered by incorporating disease topics related to the younger population through the qualitative focus group discussions and from reviewing the old NPS MedicineWise indicators. Secondly, we did not hold a formal discussion process between rounds. This was because consensus was reached in nearly all cases after the first round. While this could technically have been the end-point of the survey, the second round augmented panellists' opinion, hence our final result. However, for the reproduction of research method, we highlighted standard feedback with group results, comments and individual scores compared with group averages

(Boulkedid *et al.* 2011). Thirdly, characteristics of the panellists, such as their expertise, scope of practice and experience, may affect the result. Although we addressed these in selection criteria in accordance with guidelines and standard methodology, there is no universal 'gold standard' for recruiting panellists. Lastly, only one out of four pharmacists in the panel was a pharmacist working in a general practice. Nevertheless, the other pharmacists have a long-term experience working closely with general practice and one pharmacist of the research team is also a general practice pharmacist. This ensured relevant expertise of the panel.

Our QPIs enable users (GPs, pharmacists or other stakeholders) to measure and benchmark prescribing activities. They serve two main functions: (1) to help identify potential MRPs at an individual practice level, and hence prompt action to change and improve; and (2) to compare performance over time, e.g. before and after an improvement initiative is implemented. However, before the QPIs can be implemented widely, a study to test their applicability should be conducted. Due to limited resources in general practice and risk of indicator overload, initially focussing on indicators considered high risk is recommended in such field trials. The increasing use, and acceptance of, practice-embedded community pharmacists in Australia is an essential step in achieving active utilisation of prescribing indicators and should be considered in future studies.

CONCLUSION

This study generated 42 contemporary QPIs for use in Australian general practice, based on their validity, importance and feasibility. Using them as a benchmark in audit and feedback could help improve the quality and safety of prescribing in primary care.

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APPENDIX 1

International indicators identified by systematic search

No	Indicators	Year introduced, Country of origin	Description
1	Beers indicator [1]	2015, USA	Lists of potentially inappropriate drug that should be avoided or use with caution in people aged 65 years or older. The lists are categorized as (1) drugs to avoid in general, (2) drugs to avoid with specific diseases/syndromes, (3) drugs to be used with caution, (4) non-anti-infective drugs that require dose adjustment based on kidney function and (5) non-anti-infective drug-drug interaction
2	ACOVE indicator [2]	2006, USA	The set is to access care for “vulnerable elders”, who are at higher risk of mortality or functional decline over a period of 2 years. There are 392 indicators divided in 26 conditions, covering 4 domains of care (screening and prevention, diagnosis, treatment, and follow-up and continuity).
3	Basger’s indicator [3, 4]	2008, Australia	A list of 41 prescribing indicators for Australian elders aged >= 65 years.
4	Laroche’s indicator [5]	2007, France	A list of 34 medications, classified into 29 drugs/ drug class to be avoided in all people aged >= 75 years, and 5 drugs to be avoided in specific medical conditions.
5	Norwegian General Practice criteria (NORGEP) [6]	2009, Norway	A list of 36 criteria to assess inappropriate prescription in general practice for people aged >= 70 years. The list is divided into 21 inappropriate single drugs and drug dosages, and 15 inappropriate drugs combinations.
6	Screening Tool of Older Persons' potentially inappropriate Prescriptions (STOPP), and Screening Tool to Alert doctors to Right Treatment (START) [7]	2015, Europe	A list of 80 indicators to assess potentially inappropriate prescribing (STOPP) and a list of 34 indicators to identify prescribing omission in elderly patient aged >= 65 years old (START). Indicators in both lists are classified according to physiological systems.

7	EU(7)-PIM list [8]	2015, Europe	A list of 282 medications from 34 therapeutic groups to be used as a screening tool to identify potentially inappropriate medication for older people.
8	Austrian indicator [9]	2012, Austria	A list of 73 drugs to be avoided in geriatric patients due to lack of evidence and/or unfavourable risk-benefit profile.
9	Fit for The Aged list (FORTA) [10]	2015, Germany	A list of long-term and most frequently used medications for older patients, which includes 273 drugs belonging to 29 diagnoses/ indication. The drugs are labelled as A (indispensable), B (beneficial), C (questionable) or D (avoid) according to evidence of safety and efficacy and appropriateness for older patients.
10	Ghent Older People's Prescriptions community Pharmacy Screening (GheOP3S) tool [11]	2016, Belgium	A list of 83 drugs/drug classes to be used as a screening tool in community pharmacy to identify potentially inappropriate prescribing in older patients. The list is divided into 5 parts: (1) potentially inappropriate drugs, independent of diagnosis; (2) potentially inappropriate drugs, dependent on diagnosis; (3) potential prescribing omissions; (4) drug– drug interactions and (5): general care-related items in the community pharmacy.
11	Lindblad's indicator [12]	2006, USA	A list of 28 important drug-disease interaction that cause harmful clinical impact in patients aged >=65 years.
12	Maio's indicator [13]	2010, Italy	A list of 23 inappropriate medications for elder aged >=65 years, which is classified into: 17 drugs that should be always avoided, 3 drugs that are only appropriate in certain circumstances, and 3 drugs that have some indications but are often subject to inappropriate use.
13	The PRISCUS list [14]	2010, Germany	A list of 83 drugs in 18 drug classes that are potentially inappropriate for elderly patients. Precautions when these drugs are used was also provided.
14	Shrank's quality-of-care indicators [15]	2006, USA	One hundred thirty-three quality indicators were derived from RAND's Quality Assessment Tools Systems and validated. The indicators were used to assess four domains of prescribing: appropriate medication prescribing, avoidance of inappropriate medications, medication monitoring, and medication education and documentation.

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APPENDIX 2

Published lists of drug interactions

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