Journal of
Clinical Pharmacy and Therapeutics

Journal of Clinical Pharmacy and Therapeutics, 2016 doi: 10.1111/jcpt.12413

Anticholinergic medicines in an older primary care population: a cross-sectional analysis of medicines' levels of anticholinergic activity and clinical indications

P. J. Magin* PhD FRACGP, S. Morgan† MPH&TM FRACGP, A. Tapley‡ MMedStat , C. McCowan§ PhD, L. Parkinson¶ PhD, K. M. Henderson‡ BNurs, C. Muth** MD MPH, M. S. Hammer** MSc, D. Pond* PhD FRACGP, K. E. Mate†† PhD, N. A. Spike‡‡ MBBS FRACGP, L. A. McArthur§§ MBBS FRACGP FACRRM and M. L. van Driel¶¶ PhD FRACGP

**School of Medicine and Public Health, University of Newcastle, Callaghan, NSW, †Elermore Vale General Practice, Newcastle, NSW, ‡GP Synergy, Newcastle, NSW, Australia, §University of Glasgow, Glasgow, UK, ¶School of Human Health and Social Sciences, Central Queensland University, Rockhampton, QLD, Australia, **Institute of General Practice, Johann Wolfgang Goethe University, Frankfurt am Main, Germany, ††School of Biomedical Sciences and Pharmacy, University of Newcastle, Callaghan, NSW, ‡‡Eastern Victoria GP Training, Melbourne, VIC, §§University of Adelaide, Adelaide, SA, and ¶¶School of Medicine, University of Queensland, Brisbane, QLD, Australia*

Received 16 March 2016, Accepted 2 June 2016

Keywords: **anticholinergic agents, elderly, general practitioner, primary care**

SUMMARY

What is known and objectives: **Adverse clinical outcomes have been associated with cumulative anticholinergic burden (to which low-potency as well as high-potency anticholinergic medicines contribute). The clinical indications for which anticholinergic medicines are prescribed (and thus the 'phenotype' of patients with anticholinergic burden) have not been established. We sought to establish the overall prevalence of prescribing of anticholinergic medicines, the prevalence of prescribing of low-, medium- and high-potency anticholinergic medicines, and the clinical indications for which the medicines were prescribed in an older primary care population.**

Methods: **This was a cross-sectional analysis of a cohort study of Australian early-career general practitioners' (GPs') clinical consultations – the Registrar Clinical Encounters in Training (ReCEnT) study. In ReCEnT, GPs collect detailed data (including medicines prescribed and their clinical indication) for 60 consecutive patients, on up to three occasions 6 months apart. Anticholinergic medicines were categorized as levels 1 (low-potency) to 3 (high-potency) using the Anticholinergic Drug Scale (ADS).**

Results: **During 2010–2014, 879 early-career GPs (across five of Australia's six states) conducted 20 555 consultations with patients aged 65 years or older, representing 35 506 problems/diagnoses. Anticholinergic medicines were prescribed in 10·4% [95% CIs 9·5–10·5] of consultations. Of the total anticholinergic load of prescribed medicines ('community anticholinergic load') 72·7% [95% CIs 71·0–74·3] was contributed by Level 1 medicines, 0·8% [95% CIs 0·5–1·3] by Level 2 medicines and 26·5% [95% CIs 24·8–28·1] by Level 3 medicines. Cardiac (40·0%), Musculoskeletal (16·9%) and Respiratory (10·6%) were the most common indications associated with Level 1 anticholinergic prescription. For Level 2 and 3 medicines (combined data), Psychological (16·1%), Neurological (16·1%), Musculoskeletal (15·7%) and Urological (11·1%) indications were most common.**

What is new and conclusion: **Anticholinergic medicines are frequently prescribed in Australian general practice, and the majority of the 'community' anticholinergic burden is contributed by 'low'-anticholinergic potency medicines whose anticholinergic effects may be largely 'invisible' to prescribing GPs. Furthermore, the clinical 'phenotype' of the patient with high anticholinergic burden may be very different to common stereotypes (patients with urological, psychological or neurological problems), potentially making recognition of risk of anticholinergic adverse effects additionally problematic for GPs.**

Correspondence: Professor P. Magin, School of Medicine and Public Health, University of Newcastle, University Drive, Callaghan, NSW 2308, Australia. Tel.: +61 408953872; fax: +61 2 49686733; e-mail: parker.magin@newcastle.edu.au

WHAT IS KNOWN AND OBJECTIVES

Many older patients use medicines with anticholinergic properties. In a recent Australian study, 42% of people over 75 years were taking at least one anticholinergic medicine.[1] That is, they were using a medicine with acetylcholine receptor antagonist activity.[2,3] The degree of anticholinergic effect varies greatly between medicine classes and varies between individual medicines within those classes.[3] Classes of medicines traditionally recognized as being associated with anticholinergic effect include gastrointestinal antispasmodics, medicines used for urinary urge incontinence, antipsychotics, tricyclic antidepressants (which are often used in older patients for non-psychiatric indications, including pain modulation), anti-Parkinsonian medicines and antihistamines.[2–5] These medicines are often grouped as potentially inappropriate for use in the elderly due to their strong anticholinergic effects.[6]

The anticholinergic effect of a medicine may be intrinsic to the intended effect (such as the effect on cholinergic receptors in bladder overactivity) or may be an unintended effect.[2] Anticholinergic effects of medicines in a patient's medicines regimen may be additive, constituting anticholinergic 'burden' or 'load'.[7] Anticholinergic burden has been associated with cognitive impairment,[1,8–12] confusion,[13] falls,[7,14,15] fractures,[16] hospital admission[7,16] and duration of admission,[7,17] impairment in activities of daily living,[9] poorer quality of life,[1] depression,[1,9] incident cardiovascular disease[18] and mortality.[11,18.]

We have previously conducted two studies of the use of anticholinergic medicines by older Australians: a retrospective analysis of prescribing records linked to survey data from a community-based female cohort;[19] and an analysis of the medicines regimens of patients at baseline in a trial of peer education of general practitioners (GPs).[1] The first of these studies linked participants in the cohort study to national prescribing data. The

second involved direct observation and recording of each participant's medicines by nurses visiting participants' homes. In both studies, individual patient anticholinergic burden was driven more by multiple low-potency anticholinergic medicines than by medicines of high anticholinergic potency that clinicians would traditionally be aware of as being 'anticholinergic'.[1,19] Anticholinergic burden may thus be at least partially 'invisible' to clinicians treating older patients. The characteristics of these 'invisible' medicines and the context of their prescription are thus of clinical importance. In neither of these studies (as in most research in this area) was linkage of anticholinergic medicines to indication for their prescription possible.

In this study, we present a secondary analysis of data from a study of early-career GPs' clinical practice (including prescribing). We sought to document the frequency of individual anticholinergic medicines' prescription (both high and low potency) for older patients and the problems/diagnoses for which the anticholinergic medicines were prescribed. We did not aim to calculate individual patients' anticholinergic burden.

METHODS

This was a cross-sectional analysis of data from the Registrar Clinical Encounters in Training (ReCEnT) cohort study. The detailed study methodology has been described elsewhere.[20] Briefly, ReCEnT is an ongoing cohort study of the in-consultation clinical practice of doctors at the beginning of their careers in primary care – general practice registrars (trainees) enrolled with five of Australia's 17 general practice regional training providers (RTPs). Geographically, the five RTPs encompass urban, rural, remote and very remote practices in five of Australia's six states. All registrars in participating RTPs complete data collection as part of their educational programme and may choose to consent to their data being also used for research purposes.

Registrars spend at least three–6-month full-time-equivalent terms in general practice settings. This is the compulsory general practice component of their 3-year training programme. During this general practice component, registrars effectively operate as independent practitioners, although having recourse to the advice and assistance of experienced clinical supervisors. This independence includes prescribing authority (and capacity to order pathology and imaging and make specialist referrals) equivalent to other more senior GPs.

In ReCEnT, participating registrar characteristics and the characteristics of their training practice are documented. Registrars then record the details (including medicines prescribed, supplied or recommended) of sixty consecutive patient consultations, representing approximately 1 week of consultations, each 6-month training term. Data collection is conducted around the mid-point of the term. Each prescribed, supplied or recommended medicine is linked to the problem/diagnosis for which it was prescribed, supplied or recommended.

The analyses in this study used data from ten data collection periods from 2010 to 2014. In each data collection period, participating registrars each recorded 60 consultations. Individual registrars contributed data in up to three separate collection periods.

Outcome factor

The outcome factor of interest was prescribing/recommending/supplying of medicines with anticholinergic effects (hereafter referred to as 'prescribing'). This included recommendations of over-the-counter (OTC) non-prescription medicines and direct supply of medicines (although whether it was prescription, recommendation or supply was not recorded). Medicines were coded via the Anatomical Therapeutic Chemical (ATC) classification system, and medicines with anticholinergic effects were identified using the Anticholinergic Drug Scale (ADS)[21] updated to reflect current Australian medicines availabilities (informed by AMH Australian Medicines Handbook,[19] and a recent review[3]). The ADS categorizes medicines in an ordinal fashion from 0 to 3 (0: 'no known anticholinergic properties'; 1: 'potentially anticholinergic as evidenced by receptor binding studies'; 2: anticholinergic adverse events sometimes noted, usually at excessive doses; and 3: markedly anticholinergic).[21] Scores on the ADS predict clinical outcomes associated with anticholinergic effects[7] and the ADS performs well in this regard compared to other anticholinergic scales.[7] We did not adjust our scoring for drug dose. This has not been shown to provide significantly different results to simple scoring when evaluating association of anticholinergic burden with serum anticholinergic activity[21] and with clinical parameters.[1]

The ADS is usually used to create summary estimates of individual patient anticholinergic burden. We did not have data on individual patients' complete medicines regimens, only data of which medicines were prescribed at that consultation. The focus of this study, then, was to examine overall prescribing of anticholinergic medicines and the conditions for which they are prescribed. This could be seen to represent 'community' rather than 'individual' anticholinergic burden.

Independent variables

Problems managed or diagnoses made during the consultation were coded according to the International Classification of Primary Care, Second Edition classification system (ICPC-2).[22] Individual diseases/problems are categorized in ICPC-2 to seventeen systems-based chapters (cardiovascular, neurological, psychological, urological, etc.).

Analyses

Analyses were undertaken only for patients aged 65 years and older.

We calculated proportions of all prescribed medicines that were rated as 1, 2 or 3 by the ADS. Estimates included 95% confidence intervals, adjusted for clustering of patients within registrar. Similarly, we calculated the proportion of all consultations and the proportion of all problems/diagnoses within this patient group that resulted in prescription of an ADS-defined anticholinergic medicine.

We then calculated the proportion of the overall cumulative ADS-scored anticholinergic burden of the medicines prescribed by all registrars during their collection periods ('community anticholinergic burden') that was due to Level 1, 2 or 3 medicines.

We also identified the most commonly prescribed medicines in each ADS level, the most common problems/diagnoses for which medicines of each ADS level were prescribed, and the proportions of medicines from each ADS level by ICPC-2 disease chapter. For the problem/diagnoses for which anticholinergic medicines were prescribed (in each ADS level), ICPC-2 codes describing clinically equivalent diagnoses were collapsed to single descriptive categories by a clinician member of the research team.

Analyses were programmed with STATA 11·2. (Statacorp, College Station, TX, USA)

Ethics approval

The ReCEnT project has approval from the University of Newcastle Human Research Ethics Committee, Reference H-2009-0323.

RESULTS

Demographics of registrars, patients and practices

A total of 879 individual registrars (response rate 95·3%) participated over the 10 rounds of data collection, 2010–2014. They each participated in one to three rounds of data collection and collectively contributed data from 1953 registrar-rounds, relating to 20 555 consultations with patients aged 65 years or older and to 35 506 problems/diagnoses.

Overall, 66·2% of the registrars were female, with a mean age of 32·6 years. Registrars who undertook their primary medical degree in Australia comprised 78·3% of participants. Participating registrar, practice- and registrar-term demographics are displayed in Table 1.

Prescribing of medicines with anticholinergic effects

A total of 23 308 medicines were prescribed to patients aged 65 years or older. Of these medicines, 2323 were ADS-defined anticholinergic medicines (10·0% of all medicines [95% CIs 9·5–10·5%]). Level 1, Level 2 and Level 3 anticholinergic medicines comprised 8·8%, 0·05% and 1·1%, respectively, of all medicines prescribed (Table 2).

Table 1. Demographics of participating registrars and their practices

Variable	Class	*n* (%) [95% CI]
Registrar variables (*n* = 879)		
Registrar Gender	Male	297 (33·8) [30·7–37·0]
	Female	582 (66·2) [63·0–69·3]
Qualified as a doctor in Australia	No	189 (21·8) [19·1–24·6]
	Yes	680 (78·3) [75·4–80·9]
Registrar age (years)	Mean (SD)	32·6 (6·3)
Registrar-term or practice-term variables (*n* = 1953)		
Registrar Training Term	Term 1	780 (39·9) [37·8–42·1]
	Term 2	698 (35·7) [33·6–37·9]
	Term 3	475 (24·3) [22·5–26·3]
Registrar worked at the practice previously	No	1394 (72·3) [70·3–74·3]
	Yes	533 (27·7) [25·7–29·7]
Registrar works fulltime	No	406 (21·3) [19·5–23·2]
	Yes	1503 (78·7) [76·8–80·6]
Does the practice routinely bulk bill	No	1610 (83·0) [81·2–84·6]
	Yes	331 (17·1) [15·4–18·8]
Number of GPs working at the practice	1–4	650 (34·1) [32·0–36·3]
	5–10+	1254 (65·9) [63·7–68·0]
Rurality of practice	Major city	1117 (57·2) [55·0–59·4]
	Inner regional	543 (27·8) [25·9–29·8]
	Outer regional or remote	293 (15·0) [13·5–16·7]
SEIFA Index (decile) of practice	Mean (SD)	5·4 (2·9)

CI, confidence interval; SD, standard deviation.

Anticholinergic medicines were prescribed in 10·4% [95% CIs 9·8–11·0%] of consultations, for 6·2% [95% CIs 5·9–6·6%] of problems/diagnoses managed (see Table 2).

Using ADS scoring of medicines prescribed, of the total prescribed anticholinergic burden ('community' anticholinergic burden) 72·7% [95% CIs 71·0–74·3%] was contributed by Level 1 medicines, 0·8% [95% CIs 0·5–1·3%] by Level 2 medicines and 26·5% [95% CIs 24·8–28·1%] by Level 3 medicines (Table 2).

The most commonly prescribed anticholinergic medicines, by ADS level, are presented in Table 3, and the most common indications (diagnoses or problems) for which they are prescribed are presented in Table 4.

There was marked variability by ADS level in the ICPC-2 disease chapters for which the anticholinergic medicines were prescribed. For Level 1 medicines, Cardiac (40·0% [95% CI: 36·9–43·2%]), Musculoskeletal (16·9% [95% CI: 15·0–18·9%)) and Respiratory (10·6% [95% CI: 9·2–12·1%]) were the most common ICPC-2 chapters associated with anticholinergic prescription. For Level 2 and 3 medicines (combined data), Psychological (16·1% [95% CI: 12·0–21·2%]), Neurological (16·1% [95% CI: 9·2–17·1%]), Musculoskeletal (15·7% [95% CI: 11·3–21·4%]) and Urological (11·1% [95% CI: 7·8–15·5%]) were the most common ICPC-2 chapters associated with anticholinergic prescription. The relative contributions of all ICPC-2 chapter groupings of problems/diagnoses to each ADS-level prescription are presented in Fig. 1.

WHAT IS NEW AND CONCLUSION

Principal findings and comparison with previous literature

We have demonstrated that the prescription of medicines with anticholinergic properties by Australian GP registrars is common in older patients (10·0% of all medicines and in 10·4% of consultations) and that anticholinergic burden is driven mainly by less potent anticholinergic medicines. This is consistent with previous Australian research examining the issue of anticholinergic use with differing methodological approaches.[19] We found that 72·7% of overall 'community' anticholinergic burden was due to ADS Level 1 medicines. In another Australian study, the contribution of ADS Level 1 medicines to 'individual' anticholinergic burden was 70·5% in patients without dementia and 64·5% in those with dementia.[1]

A singular clinical circumstance where surveillance for possible anticholinergic medicines should be especially rigorous is that of utilization of anticholinergic drugs in patients with dementia treated with cholinesterase inhibitors. In an Australian study of this circumstance,[23] a majority of anticholinergic medications used concurrently with cholinesterase inhibitors were Level 1 medicines.

We found a broad spectrum of indications for the use of medicines with anticholinergic properties, and that this spectrum differs by the level of anticholinergic potency of the individual medicine (as presented in Table 3). The pervasiveness of the use of medicines with low-potency anticholinergic properties across a broad range of indications means that cumulative burden may be relatively 'invisible' to the treating clinician.

Our findings regarding the prescription of individual anticholinergic medicines can be compared with that of previous studies. Whereas there are broad commonalities, it is striking that the most commonly prescribed medicine with anticholinergic properties in our study was warfarin. Warfarin was a commonly prescribed anticholinergic medicine in previous Australian

Table 2. Anticholinergic medicines by Anticholinergic Drug Scale level – number prescribed; number of problems prescribed for; number of consultations prescribed during; and contribution to 'anticholinergic burden'

Anticholinergics	Medications (n = 23 308) n (%) [95% CIs]	Problems[a] (n = 35 506) n (%) [95% CIs]	Consultations[a] (n = 20 555) n (%) [95% CIs]	'Anticholinergic burden' contribution (%) [95% CIs]
All	2323 (10·0) [9·5–10·5]	2208 (6·2) [5·9–6·6]	2136 (10·4) [9·8–11·0]	2835 (100)
Level 1	2061 (8·8) [8·4–9·3]	1968 (5·5) [5·2–5·9]	1904 (9·3) [8·7–9·8]	2061 (72·7) [71·0–74·3]
Level 2	12 (0·05) [0·03–0·09]	12 (0·03) [0·02–0·06]	12 (0·06) [0·03–0·1]	24 (0·8) [0·5–1·3]
Level 3	250 (1·1) [0·9–1·2]	249 (0·7) [0·6–0·8]	247 (1·2) [1·1–1·4]	750 (26·5) [24·8–28·1]

CI, confidence interval.
[a]An individual problem or consultation could be associated with prescription of more than one anticholinergic medicine.

Table 3. Most common individual medicines prescribed from each Anticholinergic Drug Scale level

Level 1 drugs (n = 2061)	n (%)	Level 2 drugs (n = 12)	n (%)	Level 3 drugs (n = 250)	n (%)
Warfarin	539 (26·15)	Carbamazepine	8 (66·67)	Amitriptyline	136 (54·40)
Oxycodone	332 (16·11)	Cyproheptadine	2 (16·67)	Oxybutynin	32 (12·80)
Furosemide	288 (13·97)	Pethidine	2 (16·67)	Promethazine	23 (9·20)
Prednisolone	288 (13·97)			Dosulepin	11 (4·40)
Prochlorperazine	128 (6·21)			Solifenacin	10 (4·00)
Digoxin	77 (3·74)			Doxepin	7 (2·8)
codeine	69 (3·35)			Atropine	6 (2·40)
Oxycodone, combinations	67 (3·25)			Scopolamine	6 (2·40)
Fentanyl	58 (2·81)			Imipramine	5 (2·00)
Morphine	56 (2·72)			Benztropine	2 (0·80)

Table 4. Individual indications (problems or diagnoses[a]) for which each level of anticholinergic medicines was prescribed: most common indications

Level 1 medicines	n (%)	Level 2 medicines	n (%)	Level 3 medicines	n (%)
Atrial fibrillation	219 (11·1)	Epilepsy	2 (16·7)	Bladder instability/incontinence/nocturia	29 (11·7)
Anticoagulation	219 (11·1)	Allergic reaction	1 (8·3)	Neuropathic pain	25 (10·1)
Cardiac failure	140 (7·1)	Migraine	1 (8·3)	Pain (other than back or neuropathic pain)	20 (8·1)
Pain (other than back pain)	140 (7·1)	Peripheral neuropathy	1 (8·3)	Depression	19 (7·7)
Back pain/sciatica	111 (5·6)	Chronic pancreatitis	1 (8·3)	Back pain/sciatica	17 (6·9)
Vertigo/dizziness	87 (4·4)	Lumbar spinal stenosis	1 (8·3)	Dermatitis/eczema	9 (3·6)
Chronic Obstructive Pulmonary Disease	86 (4·4)	Trigeminal neuralgia	1 (8·3)	Headache/migraine	5 (2·0)
Arthritis (including gout) other than osteoarthritis	69 (3·5)			Pruritus	4 (1·6)
Osteoarthritis	63 (3·2)			Anxiety	4 (1·6)
Hypertension	57 (2·9)			Osteoarthritis	4 (1·6)

[a]'Prescriptions'/'renewal of medication' not presented.

studies,[1,19] but not in international studies,[7] using the ADS. The comparison will not reflect differences in use of novel oral anticoagulant medicines as the studies predate their widespread use. The finding may represent relatively aggressive anticoagulant management in older patients in Australia, especially for atrial fibrillation, reflecting national policy.[24] This finding is unlikely to affect the generalizability to other countries of our conclusions regarding the prominence of cardiovascular medicines among anticholinergic medicines as this would persist even with more modest levels of warfarin usage. Also of note was the frequency of prescription of oxycodone in our findings. Oxycodone was among the 10 most commonly used anticholinergic medicines in subjects with high ADS scores in an Australian study,[19] but was not in the most common ADS-rated anticholinergic medicines elsewhere

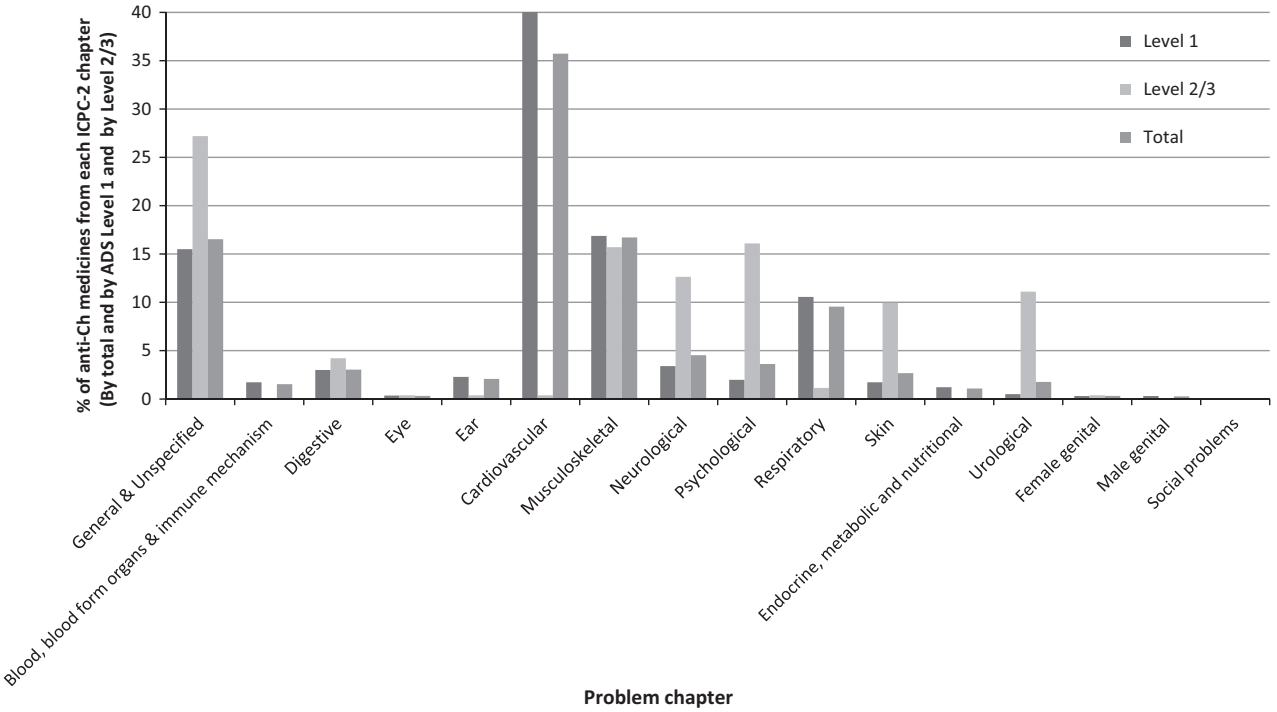

Fig. 1. Level 1, Level 2 and 3 combined, and total anticholinergic medicines, by ICPC-2 chapter.

(although codeine was).[7] This may reflect recent alarmingly steep increases in rates of oxycodone prescribing in Australia, especially to patients aged over 70 years.[25.]

Strengths and limitations

The study has a number of strengths. The response rate is very high for a study of GPs,[26] allowing confidence that we have accurately captured prescription patterns. The major strength is that unlike many studies of anticholinergic medicines, we have close linkage of prescribed medicine to its indication. We also have, unusually in studies of anticholinergic medicines, ascertainment of recommended and physician-supplied as well as prescribed medicines. This is particularly important as several strongly anticholinergic medicines (antihistamines) are over-the-counter medicines which do not require a doctor's prescription in Australia.

The major limitation is that our study elicits 'snapshot' data of consultation content, and we do not collect patients' full medicines regimens. Thus, our estimations of individual medicines' contributions to anticholinergic load are at the population rather than individual patient level, and do not document clustering of anticholinergic medicines within individuals. A further limitation, common to studies in this area, is that *in vivo* anticholinergic effects of medications are inherently difficult to quantify (as is apparent from the many currently used measures of anticholinergic medicines effects)[7] and the updates to the validated ADS that we used in this analysis have not been validated.

Whereas the generalizability to Australian practice is strong (participation by five of Australia's 17 RTPs across five of Australia's six states and encompassing urban, rural, remote and very remote practices), generalizability to those countries with differing health and GP training systems is uncertain.

Implications for practice and future research

Our study demonstrates the high volume of prescription of medicines with anticholinergic effects in general practice – 10% of all prescriptions to those 65 years and over. Thus, adverse effects attributable to anticholinergic burden are potentially a major health issue.

It has been for some time accepted that the propensity to be prescribed highly anticholinergic medications for conditions such as urinary incontinence and chronic neuropathic pain may predispose older patients to high anticholinergic burden.[2] Our study suggests that this known propensity of older patients to anticholinergic adverse effects is further heightened by previously 'invisible' low-level anticholinergic medicines, especially medicines for cardiovascular and musculoskeletal morbidities. Further, the clinical 'phenotype' of the older patient with high anticholinergic burden may often not conform to the 'traditional' phenotype of a patient with urinary incontinence or urgency, neuropathic pain or psychiatric illness. This traditional phenotype is exemplified by a study of anticholinergic medicines pre- and post-hospital admission which ignored Level 1 anticholinergics and considered only Level 2 and 3 anticholinergic medicines.[4] The authors concluded that 'groups of patients [can be] recognised to whom special attention should be paid regarding possible anticholinergic effects of prescribed drugs' and that these groups were patients with 'urinary incontinence and retention, constipation, gastroduodenal ulcer disease as well as neurologic and psychiatric comorbidities'. Although we have not measured individual patient anticholinergic burden, our findings of overall levels and patterns of anticholinergic medicines prescription suggest that many older patients with high anticholinergic burden may have considerable anticholinergic contributions from medicines for cardiac disease or

musculoskeletal pain and that special attention on patients with traditional phenotypes may fail to detect much anticholinergic burden and, potentially, subsequent adverse clinical outcomes.

Most medicines, including anticholinergic medicines, are prescribed by GPs. Whereas the anticholinergic adverse effects of individual 'traditional' high-potency anticholinergic medicines seem to be well appreciated by GPs, the concept of 'anticholinergic burden' is not.[27] Our findings suggest that with the added complexity of multiple 'invisible' anticholinergic medicines in their patients' regimens (across many disease chapters/body systems), GPs' difficulties in this area may be more acute than previously appreciated. They will need support to integrate calculation of anticholinergic burden into their therapeutic decision-making (rather than relying on knowledge of a relatively small number of obviously highly anticholinergic medicines).

Future research could aim to test interventions to alert GPs and other clinicians caring for older patients to individual patients' anticholinergic burden (and to thus prompt review of medicine regimens in response to those alerts).

CONCLUSIONS

Anticholinergic medicines are frequently prescribed in Australian general practice, and the majority of the 'community' anticholinergic burden is contributed by 'low'-anticholinergic potency medicines. GPs will need education and assistance to appreciate the importance of these 'invisible' anticholinergic medicines (and the patient contexts in which they are prescribed, including patient 'phenotype') and to incorporate calculations of individual patient anticholinergic burden into their clinical decision-making. This has the potential to limit patients' anticholinergic burdens and thus reduce the potential for adverse drug effects.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the GP registrars, GP supervisors and practices who have participated in the ReCEnT project.

FUNDING

There was no external funding. The funding of the project was by the participating Regional Training Providers, which are funded by the Australian Commonwealth Government.

CONFLICT OF INTEREST

All authors declare no conflict of interests.

REFERENCES

1. Mate KE, Kerr KP, Pond D *et al.* Impact of multiple low-level anticholinergic medications on anticholinergic load of community-dwelling elderly with and without dementia. *Drugs Aging*, 2015;**32**:159–167.
2. Mintzer J, Burns A. Anticholinergic side-effects of drugs in elderly people. *J R Soc Med*, 2000;**93**:457–462.
3. Gerretsen P, Pollock BG. Drugs with anticholinergic properties: a current perspective on use and safety. *Expert Opin Drug Saf*, 2011;**10**:751–765.
4. Wawruch M, Macugova A, Kostkova L *et al.* The use of medications with anticholinergic properties and risk factors for their use in hospitalised elderly patients. *Pharmacoepidemiol Drug Saf*, 2012;**21**:170–176.
5. Rémillard A. A pharmacoepidemiological evaluation of anticholinergic prescribing patterns in the elderly. *Pharmacoepidemiol Drug Saf*, 1996;**5**:155–164.
6. Stafford AC, Alswayan MS, Tenni PC. Inappropriate prescribing in older residents of Australian care homes. *J Clin Pharm Ther*, 2011;**36**:33–44.
7. Salahudeen MS, Hilmer SN, Nishtala PS. Comparison of anticholinergic risk scales and associations with adverse health outcomes in older people. *J Am Geriatr Soc*, 2015;**63**:85–90.
8. Pasina L, Djade CD, Lucca U *et al.* Association of anticholinergic burden with cognitive and functional status in a cohort of hospitalized elderly: comparison of the anticholinergic cognitive burden scale and anticholinergic risk scale: results from the REPOSI study. *Drugs Aging*, 2013;**30**:103–112.
9. Lampela P, Lavikainen P, Garcia-Horsman JA, Bell JS, Huupponen R, Hartikainen S. Anticholinergic drug use, serum anticholinergic activity, and adverse drug events among older people: a population-based study. *Drugs Aging*, 2013;**30**:321–330.
10. Cai X, Campbell N, Khan B, Callahan C, Boustani M. Long-term anticholinergic use and the aging brain. *Alzheimers Dement*, 2013;**9**:377–385.
11. Fox C, Richardson K, Maidment ID *et al.* Anticholinergic medication use and cognitive impairment in the older population: the medical research council cognitive function and ageing study. *J Am Geriatr Soc*, 2011;**59**:1477–1483.
12. Uusvaara J, Pitkala KH, Kautiainen H, Tilvis RS, Strandberg TE. Detailed cognitive function and use of drugs with anticholinergic properties in older people: a community-based cross-sectional study. *Drugs Aging*, 2013;**30**:177–182.
13. Kalisch EL, Pratt NL, Ramsay EN, Barratt JD, Roughead EE. Multiple anticholinergic medication use and risk of hospital admission for confusion or dementia. *J Am Geriatr Soc*, 2014;**62**:1916–1922.
14. Richardson K, Bennett K, Maidment ID, Fox C, Smithard D, Kenny RA. Use of medications with anticholinergic activity and self-reported injurious falls in older community-dwelling adults. *J Am Geriatr Soc*, 2015;**63**:1561–1569.
15. Nishtala PS, Narayan SW, Wang T, Hilmer SN. Associations of drug burden index with falls, general practitioner visits, and mortality in older people. *Pharmacoepidemiol Drug Saf*, 2014;**23**:753–758.
16. Lu WH, Wen YW, Chen LK, Hsiao FY. Effect of polypharmacy, potentially inappropriate medications and anticholinergic burden on clinical outcomes: a retrospective cohort study. *CMAJ*, 2015;**187**:E130–E137.
17. Uusvaara J, Pitkala KH, Kautiainen H, Tilvis RS, Strandberg TE. Association of anticholinergic drugs with hospitalization and mortality among older cardiovascular patients: a prospective study. *Drugs Aging*, 2011;**28**:131–138.
18. Myint PK, Fox C, Kwok CS, Luben RN, Wareham NJ, Khaw KT. Total anticholinergic burden and risk of mortality and cardiovascular disease over 10 years in 21 636 middle-aged and older men and women of EPIC-Norfolk prospective population study. *Age Ageing*, 2015;**44**:219–225.
19. Parkinson L, Magin PJ, Thomson A *et al.* Anticholinergic burden in older women: not seeing the wood for the trees?. *Med J Aust*, 2015;**202**:91–94.
20. Morgan S, Magin PJ, Henderson KM *et al.* Study protocol: the Registrar Clinical

Encounters in Training (ReCEnT) study. *BMC Fam Pract*, 2012;**13**:50.
21. Carnahan RM, Lund BC, Perry PJ, Pollock BG, Culp KR. The Anticholinergic Drug Scale as a measure of drug-related anticholinergic burden: associations with serum anticholinergic activity. *J Clin Pharmacol*, 2006;**46**:1481–1486.
22. Britt H. A new coding tool for computerised clinical systems in primary care–ICPC plus. *Aust Fam Physician*, 1997;**26**:S79–S82.
23. Robinson M, Rowett D, Leverton A, Mabbott V. Changes in utilisation of anticholinergic drugs after initiation of cholinesterase inhibitors. *Pharmacoepidemiol Drug Saf*, 2009;**18**:659–664.
24. Gadzhanova SV, Roughead EE, Bartlett MJ. Improving cardiovascular disease management in Australia: nPS MedicineWise. *Med J Aust*, 2013;**199**:192–195.
25. Hall WD, Farrell MP. Minimising the misuse of oxycodone and other pharmaceutical opioids in Australia. *Med J Aust*, 2011;**195**:248–249.
26. Bonevski B, Magin P, Horton G, Foster M, Girgis A. Response rates in GP surveys - trialling two recruitment strategies. *Aust Fam Physician*, 2011;**40**:427–430.
27. Magin P, Goode S, Pond D. GPs, medications and older people: a qualitative study of general practitioners' approaches to potentially inappropriate medications in older people. *Australas J Ageing*, 2015;**34**:134–139.

