

Drug management for hypertension in type 2 diabetes in family practice

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ABSTRACT

OBJECTIVE To describe the number and classes of antihypertensive medications prescribed to patients with type 2 diabetes in community family practices, and to estimate the aggressiveness or “dosage intensity” of prescribing for hypertension in these situations.

DESIGN Practice-based, cross-sectional observational study.

SETTING Seventeen rural and urban family practices in the Maritime Family Practice Research Network in Nova Scotia, New Brunswick, and Prince Edward Island.

PARTICIPANTS A total of 670 patients with type 2 diabetes, ranging from 25 to 92 years of age.

MAIN OUTCOME MEASURES Number, classes, and combinations of classes of antihypertensive medications prescribed, as well as an index of each medication’s dosage intensity.

RESULTS Almost 80% of patients studied had hypertension. Participants with hypertension were taking an average of 2.5 medications, and 47.6% were taking 3 or more antihypertensive medications, but only 27.1% reached target blood pressure values of less than 130/80 mm Hg. Older patients took more antihypertensive medications, but there were no differences by sex. More than 90% were taking angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, 66% were taking diuretics, 41% were taking β -blockers, and 38% were taking calcium channel blockers. We cannot describe the sequence in which antihypertensive medication classes were added, but analysis of patients taking multiple drug classes suggests that most patients were started on angiotensin-converting enzyme inhibitors or angiotensin receptor blockers, followed by diuretics, β -blockers, or calcium channel blockers. The most commonly used medications were prescribed at higher than two-thirds the maximum dose effective for hypertension.

CONCLUSION Hypertension is very common among family practice patients with type 2 diabetes; of those patients, few reach target blood pressures. Practice-based strategies to increase dosing and number of medications prescribed might be required.

EDITOR’S KEY POINTS

- Hypertension is a common problem in family practice, and despite improvements in screening and treatment rates in recent years, many patients do not reach target blood pressure (BP) control rates. This is particularly true for patients with type 2 diabetes and hypertension. Inadequate drug treatment is often cited as the reason for poor BP control, so this study sought to explore the number, type, and intensity of hypertension medications prescribed for patients with type 2 diabetes.
- The authors found that despite averaging 2.5 antihypertensive medications per person, at close to maximum dosing, two-thirds of participating patients did not achieve target BP values.
- The authors conclude that practice-based strategies to increase dosing and numbers of drugs prescribed might be required, as is more research about groups of patients who are particularly poorly controlled, but they note that these patients might be resistant to such strategies, owing to the number of medications required to manage their multiple conditions.

This article has been peer reviewed.
Can Fam Physician 2009;55:728-34

Traitement pharmacologique de l'hypertension chez les diabétiques de type 2 en pratique familiale

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RÉSUMÉ

OBJECTIF Décrire le nombre et les classes d'antihypertenseurs prescrits aux diabétiques de type 2 en pratique familiale communautaire et estimer le degré d'agressivité ou d'intensité des doses prescrites pour l'hypertension chez ces patients.

TYPE D'ÉTUDE Étude d'observation transversale effectuée à partir de cliniques.

CONTEXTE Dix-sept cliniques familiales rurales et urbaines du Maritime Family Practice Research Network de la Nouvelle-Écosse, du Nouveau-Brunswick et de l'Île du Prince-Édouard.

PARTICIPANTS Un total de 670 diabétiques de type 2, âgés de 25 à 92 ans.

PRINCIPAUX PARAMÈTRES ÉTUDIÉS Nombre, classes et combinaisons de classes d'antihypertenseurs prescrits, ainsi qu'un indice de l'intensité des doses de chaque médicament.

RÉSULTATS Près de 80% des patients à l'étude étaient hypertendus. Les participants hypertendus prenaient en moyenne 2,5 médicaments et 47,6% en prenaient 3 ou plus, mais seulement 27,1% atteignaient les valeurs cibles de tension artérielle de moins de 130/80 mm Hg. Les plus âgés prenaient davantage de médicaments mais il n'y avait de différence entre les sexes. Plus de 90% recevaient des inhibiteurs de l'enzyme de conversion de l'angiotensine ou des inhibiteurs des récepteurs de l'angiotensine, 66% prenaient des diurétiques, 41% des agents β -bloquants et 38% des inhibiteurs calciques. La séquence dans laquelle les différentes classes d'antihypertenseurs ont été introduits n'a pas été établie, mais l'analyse des patients qui en recevaient plusieurs suggère que la plupart du temps, on a commencé par des inhibiteurs des récepteurs de l'angiotensine, suivis de diurétiques, d'agents β -bloquants ou d'inhibiteurs calciques. Les médicaments les plus fréquemment prescrits l'étaient à plus des deux-tiers de la dose efficace maximale pour l'hypertension.

CONCLUSION L'hypertension est très fréquente chez les diabétiques de type 2 en pratique familiale; parmi ces patients, peu atteignent les tensions artérielles cibles. Il faudrait peut-être envisager des stratégies appliquées à la pratique pour augmenter les doses et le nombre de médicaments prescrits.

POINTS DE REPÈRE DU RÉDACTEUR

- L'hypertension est un problème fréquent en pratique familiale, et malgré des meilleurs taux de dépistage et de traitement au cours des dernières années, bon nombre de patients n'obtiennent pas les valeurs cibles de tension artérielle (TA). Cela est particulièrement vrai pour les diabétiques de type 2 souffrant d'hypertension. On mentionne souvent un traitement pharmacologique inadéquat comme raison de ce mauvais contrôle, de sorte que cette étude a cherché à connaître le nombre, le type et les doses des antihypertenseurs prescrits chez ces patients.
- Les auteurs ont trouvé que malgré une moyenne de 2,5 antihypertenseurs par patient à des doses près du maximum, les deux-tiers des participants n'atteignaient pas les valeurs cibles de TA.
- Les auteurs concluent qu'il pourrait être nécessaire d'adopter des stratégies appliquées à la pratique pour augmenter le nombre et les doses de médicaments prescrits, et d'entreprendre d'autres études sur les groupes de patients dont le contrôle est particulièrement déficient. Ils notent toutefois que ces derniers pourraient ne pas répondre à de telles stratégies en raison des multiples médications que requièrent leurs nombreuses affections.

Cet article a fait l'objet d'une révision par des pairs.
Can Fam Physician 2009;55:728-34

Type 2 diabetes affects 5.1% of Canadians.¹ In addition, the prevalence of hypertension among diabetes patients reportedly ranges from 63%² to 75.8%.³ Both are independent risk factors for cardiovascular disease and together they make a very potent synergistic combination.^{4,5} Effective treatment of hypertension substantially lowers the risk of cardiovascular complications^{4,6,7}; however, hypertension in patients with diabetes presents a difficult challenge, particularly with lowered target blood pressure (BP) values in recent years—only a minority of patients reach those targets. A recent review included 24 observational studies using a BP target value of 130/85 mm Hg or less; a weighted average of 12% of patients reached the target (range 6% to 30%).⁸ Lack of adequate drug treatment is frequently cited as the reason for poor BP control in patients with diabetes, with calls for a more aggressive approach to hypertension management.^{9,10}

In the literature, the number and classes of drugs used are frequently reported as a measure of adequacy of treatment, but little is known about the aggressiveness or intensity of dosages prescribed. Earlier work on intensity focused on the likelihood of a dosage being changed at a clinical encounter.¹¹ While investigating the efficacy of intensive multitherapy in a controlled trial of patients with type 2 diabetes, Ménard et al reported dosages of oral medications as a percentage of the maximum daily dose according to the 1998 *Compendium of Pharmaceuticals and Specialties*.¹² We have adapted this approach, using the highest dose usually effective for hypertension, and applied it to a “usual care” community setting. Our objectives were to describe the number and classes of medications prescribed and to estimate the aggressiveness, or “dosage intensity,” of medications prescribed for patients with type 2 diabetes and hypertension in “real world” community practices for the most commonly used drugs in each of the classes of drugs recommended by the Canadian Hypertension Education Program (CHEP).¹³

METHODS

This practice-based, cross-sectional observational study used patient information extracted from 17 rural and urban family practices in the Maritime Family Practice Research Network in Nova Scotia, New Brunswick, and Prince Edward Island. Family physicians were recruited from among community-based postgraduate teachers affiliated with Dalhousie University's Department of Family Medicine in Halifax, NS, and represented men and women in early, mid, and later stages of their medical careers. Practice settings included solo and group practices, private practices, and community health centres. Ethics approval for the project was granted from each of the 7 research ethics boards with jurisdiction over the participating practices.

Potential participants were patients with type 2 diabetes from those practices. All were eligible to participate if they could understand English and were able to give consent, and were expected to be available for follow-up for more than 1 year. If they consented to enter the study, clinical data captured included the presence or absence of a previous diagnosis of hypertension, the most recent BP reading, all chronic medications prescribed (including dosage), and demographic details. Data were entered into a secure, customized database housed in the Faculty of Medicine at Dalhousie University and were checked for accuracy by one of the authors.

Drugs considered antihypertensive were identified using the World Health Organization (WHO) classification system.¹⁴ For the count of drugs that had antihypertensive effects, we included all drugs, and combinations of drugs, within the following classes: diuretics, β -blockers (BBs), calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitors (ACEIs), angiotensin receptor blockers (ARBs), other antihypertensives (eg, antiadrenergic agents and agents acting on arteriolar smooth muscle), and oral or transdermal organic nitrates. We also included medications such as ethacrynic acid and carvedilol, which are used for other indications but also display antihypertensive effects.

Summary statistics were used to describe the number, classes, and combinations of classes of antihypertensive medications prescribed. Differences in the total number of antihypertensive medications prescribed by sex and age were investigated and χ^2 tests of association were performed.

Although all medications with antihypertensive effects were included in the count described above, to quantify the dosage intensity of medications used, we excluded medications that might have antihypertensive effects but that are not generally indicated in the management of hypertension, such as nitrates, carvedilol, and ethacrynic acid. Using only medications indicated for hypertension and included in the CHEP recommendations for diabetes patients,¹³ we adapted the approach followed by Ménard et al for calculating dosage intensity.¹² We divided the average prescribed daily dose (total dose in milligrams prescribed for a single day) by the upper limit of the range of doses usually effective for hypertension in the 2006 *Compendium of Pharmaceuticals and Specialties*.¹⁵ For example, a dose of 5 mg of ramipril daily is half the maximum (for hypertension) of 10 mg daily, for an index of 0.5.

RESULTS

Our cohort of 670 patients with type 2 diabetes from 17 community practices included 527 (78.7%) participants who had been given a diagnosis of hypertension by their family physicians. Of that subset, 51.6% were men; ages ranged from 25 to 92 years (mean age 64.8 years, SD

11.6). Antihypertensive medications were prescribed for 510 of these patients. Blood pressure and other relevant clinical data are summarized in **Table 1**.

Table 1. Clinical data for participating patients with type 2 diabetes and hypertension*: *N* = 527.

CHARACTERISTIC	NO. OF PATIENTS (%)
Sex	
• Male	272 (51.6)
• Female	255 (48.4)
Age, y	
• <55	97 (18.4)
• 55-64	162 (30.7)
• 65-74	130 (24.7)
• ≥75	138 (26.2)
Systolic BP at target (<130 mm Hg)	175 (33.2)
Diastolic BP at target (<80 mm Hg)	342 (64.9)
BP at target (<130/80 mm Hg)	143 (27.1)
BMI >30	249 (47.2)
Smoking status	
• Current	57 (10.8)
• Past	201 (38.1)
• Never	232 (44.0)
• Unknown	37 (7.0)
No. of comorbidities [†] and complications	
• 0	13 (2.5)
• 1-3	178 (33.8)
• 4-6	221 (41.9)
• ≥7	115 (21.8)

BMI—body mass index, BP—blood pressure.

*Hypertension and type 2 diabetes considered to be the index conditions for these patients.

[†]Other morbidities were counted as comorbidities, with ischemic heart disease, dyslipidemia, metabolic syndrome, arthritis, and gastroesophageal reflux disease occurring in more than 20% of patients.

Physicians prescribed an average of 2.5 (SD 1.3) antihypertensive medications for each patient, which is part of a total average of 6.8 (SD 2.7) chronic medications per patient, resulting in 27.1% of patients reaching the target BP level below 130/80 mm Hg. Almost 47% of patients were prescribed 3 or more antihypertensive medications; χ^2 tests of association indicated significant differences in the numbers prescribed for different age groups ($P < .0001$) but not by sex ($P = .9$) (**Figure 1**). For instance, 58.7% of patients aged 75 years and older were prescribed 3 or more antihypertensive medications, compared with only 30.9% of patients younger than 55 years of age.

More than 90% of patients were prescribed ACEIs (62.8%) or ARBs (28.3%); the next most common classes were diuretics (66%), BBs (40.8%), and CCBs (37.9%). Although these cross-sectional data cannot describe the sequence in which drugs were prescribed, we attempted

to estimate this by tabulating the classes used when patients were taking 1, 2, or 3 drug classes. (This analysis excluded the 17 patients who were not taking antihypertensive drugs and the 91 patients taking 4 or more drug classes, as we wanted to estimate the sequence in the earlier stages of treatment, which are commonly in the domain of primary care physicians.) Angiotensin-converting enzyme inhibitors and ARBs were the foundation for most antihypertensive regimens, ranging from 83.1% in patients taking 1 class of drug to 95.8% of patients taking 3 classes of drugs. Diuretics were included in 61.8% of 2-class and 82.5% of 3-class combinations. β -Blockers and CCBs remained a distant third and fourth, included in 27.0% and 21.1% of 2-class combinations and 60.1% and 53.8% of 3-class combinations, respectively. Data are summarized in **Table 2**.

We also explored the dosage intensity of the medications prescribed. **Table 3**¹⁵ lists the most commonly used drugs in each class and the dosage-intensity index for each. The intensities ranged from a high of 0.97 for ramipril to a low of 0.49 for enalapril.

DISCUSSION

In this cohort of 670 patients with type 2 diabetes in a “real world” setting of community family practices, the prevalence of hypertension was 78.7%, the average BP value was 134.7/73.1 mm Hg, and the proportion at a target below 130/80 was 27.1%. On average, patients were taking 2.5 different antihypertensive medications. The elderly were prescribed more antihypertensive medications, but there were no prescribing differences by sex. Angiotensin-converting enzyme inhibitors, ARBs, and diuretics were the drug classes most prescribed. Eight of the 10 most frequently used drugs were prescribed at 66% or higher of the maximum effective dose for hypertension, with the most common (ramipril) prescribed at 97% of the maximum dose.

The high prevalence of hypertension in our study might be explained, in part, by the use of a lower BP threshold (130/80 mm Hg) to confirm diagnosis. The proportion of our participants at target (27.1%) compares favourably with other observational studies using the same target BP levels (20.4%¹⁶ and 23%¹⁷), but falls short of the 32% achieved in the BP-lowering arm of the Anglo-Scandinavian Cardiac Outcomes Trial.¹⁸

The proportion of patients in our study who reached the diastolic BP target value (64.9%) was much higher than that of those who reached the systolic BP target value (33.2%). This result might be appropriate, as the diastolic BP target of 80 mm Hg or lower is supported by 2 trials (the Hypertension Optimal Treatment study¹⁹ and the United Kingdom Prospective Diabetes Study [UKPDS] 38⁶), whereas the evidence behind the systolic BP target of less than 130 mm Hg is poor (Grade C).²⁰ The

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target might be unrealistic—our practising team members feel it is much harder to achieve.

Campbell et al reported a substantial increase in antihypertensive medication use in Canada since the inception of CHEP, particularly for the classes of medications consistent with the CHEP recommendations.²¹ The predominance of the use of ACEIs and ARBs in the

population we studied, as recommended by CHEP,¹³ supports their conclusion that CHEP has had a positive influence on antihypertensive prescribing trends.²¹ Despite the increasing numbers of drugs used in the treatment of hypertension in diabetes, most patients are not at target. In our study, 47% of patients were prescribed 3 or more drugs compared with 29% in the UKPDS⁶; a

Figure 1. Proportion of patients taking 0, 1, 2, or ≥ 3 antihypertensive medications, by age group and sex: χ^2 tests of association indicate significant differences by age group ($P < .0001$) but not sex ($P = .9$); $n = 527$.

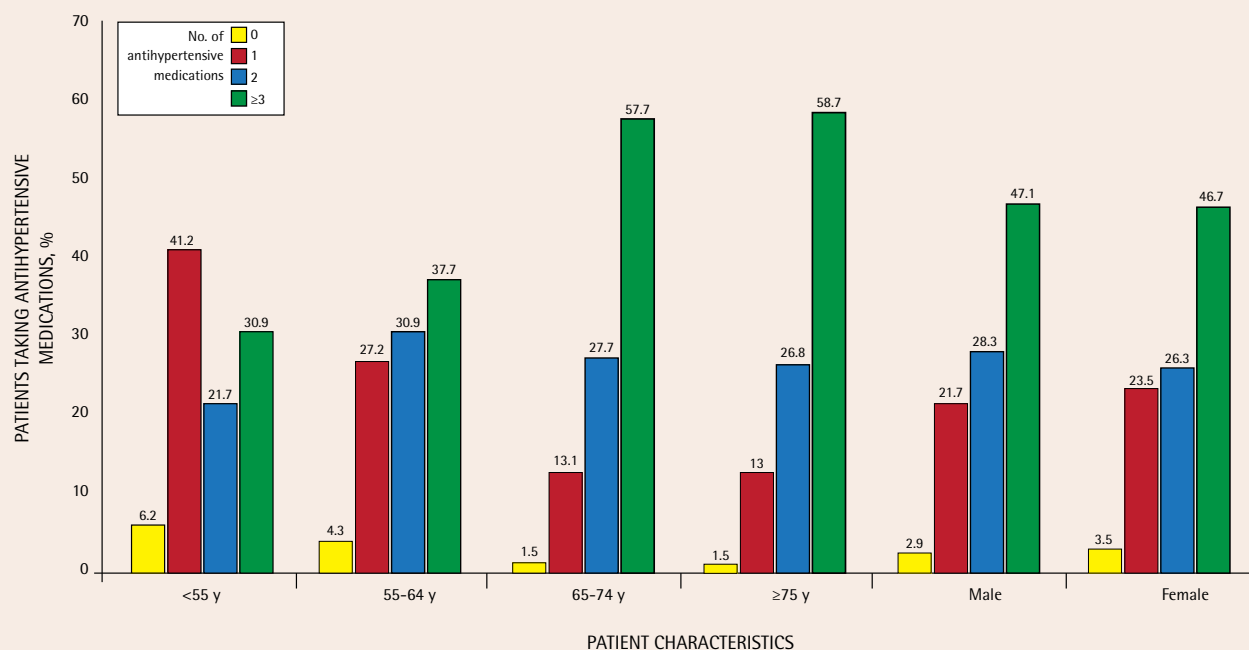


Table 2. Combinations of antihypertensive medications prescribed, from 1 to 3 drug classes: $N = 419$.

NO. OF DRUG CLASSES PRESCRIBED	DRUG CLASSES	NO. OF PATIENTS (%)	CI 95%
1 (n = 124)	ACEI/ARB	103 (83.1)	75.3-89.2
	Diuretic	11 (8.9)	4.5-15.3
	CCB	6 (4.8)	1.8-10.2
	BB	4 (3.2)	0.9-8.1
2 (n = 152)	ACEI/ARB + 1*	136 (89.5)	83.5-93.9
	Diuretic + 1	94 (61.8)	53.6-69.6
	BB + 1	41 (27.0)	20.2-34.8
	CCB + 1	32 (21.1)	14.9-28.4
	Other + 1	1 (0.7)	0.0-3.6
3 (n = 143)	ACEI/ARB + 2*	137 (95.8)	91.1-98.4
	Diuretic + 2	118 (82.5)	75.3-88.4
	BB + 2	86 (60.1)	51.6-68.2
	CCB + 2	77 (53.8)	45.3-62.2
	Other + 2	11 (7.7)	3.9-13.3

ACEI—angiotensin-converting enzyme inhibitors, ARB—angiotensin receptor blocker, BB— β -blocker, CCB—calcium channel blocker, CI—confidence interval.

*Meaning 1 or 2 additional classes (eg, ACEI/ARB + 1 indicates ACEI/ARB and either a diuretic, a BB, or a CCB, etc). A patient taking more than 1 drug class is counted in all relevant categories; therefore, not all percentages add up to 100.

Table 3. Dosage intensity for the 10 most commonly prescribed antihypertensive drugs

DRUG	NO. OF PATIENTS	AVERAGE DAILY DOSE, MG	UPPER LIMIT, MG	INDEX OF INTENSITY*
Ramipril	198	9.7	10	0.97
Hydrochlorothiazide	165	19.2	25	0.77
Metoprolol	102	141.9	200	0.71
Amlodipine	88	8.1	10	0.81
Furosemide	65	55.7	80	0.70
Nifedipine	55	41.5	60	0.69
Atenolol	53	66.0	100	0.66
Lisinopril	47	23.2	40	0.58
Enalapril	47	19.5	40	0.49
Losartan	41	73.8	100	0.74

*Dosage intensity is calculated by dividing the average prescribed daily dose (total dose in milligrams prescribed for a single day) by the upper limit of the range of doses usually effective for hypertension according to the 2006 *Compendium of Pharmaceuticals and Specialties*.¹⁵

similar proportion was prescribed only 1 drug in other studies.²²⁻²⁴ However, our average of 2.5 medications per person might not be enough. A large study reported that an average of 2.9 medications was needed to achieve the target BP of less than 130/80 mm Hg.²⁵ Patients with diabetes are already taking multiple medications for the disease and for comorbidities; our cohort averaged 6.8 medications per person. Any initiative to increase the number of antihypertensive medications will likely meet with resistance from patients.


Diabetes patients have been shown to be treated less intensively for hypertension than patients without diabetes⁹ and they are much more likely to fail to reach target BP levels.^{9,10} In our study, the most commonly used antihypertensive medications were prescribed at approximately two-thirds of the maximum dose usually effective for hypertension. Perhaps physicians should strive to use maximum doses. Yet evidence suggests that 80% of the BP-lowering effect is achieved at “half [the] standard dose,” with minimal adverse effects²⁶; in the clinic setting, side effects are a strong limiting force to prescribing. With increasing pressure to achieve target BP levels, as well as similar pressure from patients to limit medications and minimize side effects, the clinician is faced with formidable choices. Perhaps combination medications, particularly those that have demonstrated synergy, are the answer to reducing patient pressures to limit prescribing while still achieving target BP values.

Limitations

The generalizability of our study might be limited by several issues. Our patients are all residents of the Maritime provinces, which are not as ethnically diverse as the Canadian population.²⁷ There might be a slight bias in patient recruitment, as approximately 25% of our cohort comes from practices whose physicians, at the time of this analysis, had not completed approaching all patients with type 2 diabetes for consent. As a result, sicker patients who visited their physicians

more often might have been included in greater numbers, skewing the results to poorer estimates of BP control. Conversely, physicians willing to participate in such a study might achieve better BP control than other community practitioners. We acknowledge that antihypertensive medications included in this analysis are also used for other indications at different dosages, which might have potentially altered our results. Last, our BP readings were “routine care” office sphygmomanometer pressures, based on previous measurements taken at 17 different practices. We would expect variability across these practices; further, our BP values might be higher than pressures taken with an automated machine that averages several readings at appropriate time intervals when the patient is alone.²⁸

Conclusion

Hypertension is commonly observed in patients with type 2 diabetes in family practice, and it is still not well controlled. Despite averaging more than 2 antihypertensive medications per person, at close to maximum dosing, two-thirds of participating patients did not achieve target BP values. Practice-based strategies to increase dosing and numbers of drugs prescribed might be required, as well as more research about groups of patients who are particularly poorly controlled. 

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Acknowledgment

We are grateful for the advice and support given by **Dr Ingrid Sketris** and **Ms Charmaine Cooke** regarding the drug analysis. We are also grateful to all the patients with type 2 diabetes who consented to participate in this study and to their family physicians who submitted the data to our project office.

Contributors

Drs Putnam, Buhariwalla, and **Lacey** were involved in the conception and design of the study, the acquisition of data, the interpretation of the results, and the drafting of the paper. **Drs Burge, Goodfellow, Goodine, Hall, MacDonald, Murray,** and **Smith** were involved in the conception and design of the study, the acquisition of data, and the interpretation of the results, and reviewed the drafts for intellectual content. **Ms Lawson** was involved in the analysis of the data and reviewed the drafts for intellectual content. **Dr Natarajan** was involved in the interpretation of the results and reviewed the drafts for intellectual content. All authors gave approval of the final draft.

Competing interests

None declared

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