Original Articles



Cardiovascular risk management in chronic kidney disease in general practice (the AusHEART study)

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Abstract

Background. Chronic kidney disease (CKD) is common and increasing in prevalence. Adverse outcomes of CKD can be prevented through early detection and treatment. There is limited data on the awareness of CKD and the quality of care offered to patients with CKD in the primary care setting. The objectives of this study were to assess the prevalence, general practitioner (GP) awareness and extent of current evidence–practice gaps in the management of CKD in Australian primary care.

Methods. The Australian Hypertension and Absolute Risk Study (AusHEART) was a nationally representative, cluster stratified, cross-sectional survey among 322 GPs. Each GP was asked to provide data for 15–20 consecutive patients (age \geq 55 years) who presented between April and June, 2008. The main outcome measures were CKD prevalence based on proteinuria and decreased estimated glomerular filtration rate. Evidence–practice gaps in management of patients with CKD were identified.

Results. Among a total of 4966 patients with kidney function test data, 1845 (37%) had abnormal kidney function. Of the 1312 patients with abnormal kidney function known to the GP at the time of visit, only 235 were correctly identified as having CKD. GPs under-estimated cardiovas-cular (CV) risks in patients with CKD when compared with the prevailing guidelines at the time of survey and the recent national guidelines, particularly in later stages of CKD. Among CKD patients not prescribed blood pressure-lowering agents or lipid-lowering agents, treatment was indicated as per relevant guidelines in 51 and 46%, respectively. For CKD patients who were already prescribed blood pressure-lowering and lipid-lowering agents, 61 and 50%, respectively, did not meet the treatment targets recommended by the relevant guidelines.

Conclusions. CKD is common, significantly under-recognized and under-treated in primary care. Effort to increase awareness and provide opportunities for improved screening and assessment should improve the management and outcome of these patients at high risk of CV disease. Keywords: chronic kidney disease; vascular risk; general practice, primary care; evidence-based practice

Introduction

Chronic kidney disease (CKD), defined by the presence of kidney damage (proteinuria) or reduced kidney function [estimated glomerular filtration rate (eGFR) < 60 mL/min/ $1.73m^2$] [1], is estimated to affect between 10 and 15% of the adult population [2–5]. Among high-risk populations, including people with diabetes mellitus, the prevalence is substantially higher [6]. With an increasing prevalence of diabetes and an ageing population, the number of patients affected by CKD is projected to rise significantly [5, 7].

Apart from the direct long-term health consequences of CKD, such as the need for renal replacement therapy, CKD is also recognized as an independent risk factor for cardiovascular (CV) morbidity and mortality [8–12]. The risks of CV mortality and morbidity and the need for renal replacement therapy increases with increasing severity of CKD [13–15], although individuals with CKD are far more likely to die than to require renal replacement therapy [14]. The management of CV risk factors is therefore fundamental to the management of people with CKD.

With 85% of Australians visiting a general practitioner (GP) each year [16], the potential for GPs to play a crucial role in the detection and management of patients with CKD is vast. However, data on the prevalence of CKD in patients attending primary care practices are sparse. In addition, little is known about the management of patients with CKD in this setting. In a cross-sectional, Australian primary care-based sample of patients aged \geq 55 years, we assessed the prevalence of CKD, its associated risk factors and degree of awareness of CKD among GPs. In addition, we examined the proportion of patients achieving recommended treatment targets aimed at preventing CV events and slowing the progression of kidney disease.

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Materials and methods

Selection of investigators and study population

The Australian Hypertension and Absolute Risk Study (AusHEART) [17] was a cross-sectional, cluster-stratified survey of patients attending primary care practices which was undertaken to explore the management of CV risk in Australian adults aged \geq 55 years. We randomly selected 534 GP investigators who expressed interest in participation, in a stratified manner to ensure that state and urban/rural splits reflected the distribution of the adult population (using 2004 national census data). Each participating GP was asked to recruit 15–20 consecutive patients, irrespective of the reason for the consultation, between April and June 2008.

For each eligible consenting patient, GPs were required to complete a one-page questionnaire on CV risk factors, medical history (including CKD-yes, no and unknown) and currently prescribed CV medication. They were asked to perform blood pressure (BP) recordings on the right arm using an appropriately sized cuff and an Omron HEM-907 BP monitor where one was available. If certain key CV risk factors, including fasting blood lipids, blood glucose, eGFR, urine dipstick (Microalbustix, Bayer) or urinary albumin creatinine ratio (ACR), had not been measured within the time frame recommended by the national guidelines for preventive activities in general practice, the GPs were requested to repeat these tests and record the results to allow a 'forced capture' of CV risk factor levels in all registered patient. In addition, GPs were asked to estimate the 5-year risk of a CV event in each of their patients without specifying how this should be determined. The 5-year CV risk was also determined centrally for each patient without cardiovascular disease (CVD) (defined as previous myocardial infarction, stroke, peripheral arterial disease, revascularization, transient ischaemic attack or angina), using the 1991 Framingham risk equation which is based on age, sex, smoking status, BP, cholesterol levels, diabetes and left ventricular hypertrophy. Adjustments were then made to this estimate according to two guidelines-the National Heart Foundation (NHF) Hypertension Management Guide for Doctors 2004 guideline [18] (the prevailing guideline at the time of data collection), and the most recent guideline on absolute CVD risk assessment the Australian National Vascular Disease Prevention Alliance (NVDPA) guideline [19] based on the information provided by the GPs. Box 1 indicates the adjustment criteria, above Framingham equation-based risk estimates, for these guidelines. The calculated 5-year CV risk was then classified into 'low' (<10%), 'moderate' (10-15%) and 'high' (≥15%) categories. Patients with established CVD were separately classified.

CKD definition

CKD was defined according to the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines [1], which are based on presence of kidney damage (proteinuria) or reduced kidney function: Stages 1–2 CKD was defined as eGFR \geq 60 mL/min/1.73m² and proteinuria (laboratory ACR >2.5 mg/mmol in men or >3.5 mg/mmol in women or >3.4 mg/mmol

Box 1. Guideline adjustments to Framingham risk estimates

NHF 2004 guidelines, patients with an associated clinical condition [Aboriginal/Torres Strait Islander/Maori or Pacific Islander origin, aged \geq 75 years, diabetes, CKD, aortic disease, left ventricular hypertrophy, vascular disease, ultrasonic or radiological evidence of atherosclerotic plaque, hypertensive retinopathy (Grade II or more)] were assigned a risk of 15% if the calculated risk was lower. The guidelines also recommend increasing the risk by 5% (once only) in patients where it is likely that the Framingham equations under-estimate risk (BMI \geq 30 kg/m², total cholesterol > 8.5 mmol/L, SBP > 170 mmHg and DBP > 100 mmHg, first degree relative with CVD before 60 years old).

National Vascular Disease Prevention Alliance guidelines, adults with (diabetes and aged >60 years, diabetes with microalbuminuria, moderate or severe CKD with eGFR <45 mL/min/1.73m², systolic BP ≥180 mmHg, diastolic BP ≥110 mmHg, serum cholesterol >7.5 mmol/L) were classified into the high-risk category as they are considered already at increased risk (high) and estimation of risk is not required.

from urinary dipstick); Stage 3 eGFR <60 and \geq 30 mL/min/1.73m²; Stages 4–5 eGFR <30 mL/min/1.73m².

Reduced kidney function and kidney damage

Patients with an eGFR of $<60 \text{ mL/min}/1.73\text{m}^2$ were defined as having reduced kidney function. The presence and level of proteinuria was assessed using the laboratory ACR on a urine sample from the previous 12 months. If this was unavailable, the presence and level of proteinuria was based on urine dipstick (Microalbustix) test result.

Albuminuria levels were stratified, on the basis of K/DOQI guidelines [1], as normoalbuminuria (urinary dipstick protein ≤ 3.4 mg/mmol, ACR ≤ 3.5 mg/mmol in women or ≤ 2.5 mg/mmol in men); microalbuminuria (urinary dipstick protein > 3.4 mg/mmol, urinary ACR of 3.5–35 mg/mmol in women or 2.5–25 mg/mmol in men) or macroalbuminuria (urinary ACR > 35 mg/mmol in women or >25 mg/mmol in men).

Ethics approval

The study was approved by the Royal Australian College of General Practitioners (RACGP) National Research and Evaluation Ethics Committee. All patients gave written informed consent to participate in the study.

Statistical methods

Descriptive statistics were reported as proportions, means or medians. Differences between included and excluded patients were tested using the χ^2 -test for categorical variables and *t*-test for differences between means. Differences between the stages of CKD were conducted using a trend analysis calculated using logistic regression for categorical variables and a one-way analysis of variance for differences between means. Agreement between GP estimates of risk and centrally calculated estimates were evaluated using SASv9.1 (Cary, NC: SAS Institute Inc, 2002–2003). All statistical analyses were conducted using STATA version 10.1 (Stata Corporation, College Station, TX).

Results

Of the 534 GPs selected to participate in the study, 322 (60%) GPs participated actively, providing data for a total of 5293 patients. When compared with the GP workforce, the active contributors were more likely to be female (40% active GPs versus 35% GP workforce, P < 0.05), older (78% >45 years versus 66%, P < 0.001) and from a rural/remote area (36% versus 26%, P < 0.001).

Due to missing kidney function or missing urine protein data in people with eGFR >60 mL/min/1.73m², 191 and 136 people, respectively, were excluded from these analyses; as it was not possible to classify these 327 (6%) patients according to their CKD stage. These patients had similar clinical characteristics to the overall study population. Of the 4966 patients with kidney function data available for analyses, 3558 patients had renal function performed in the 12 months previous to the study visit and the remaining 1408 had it provided by the GP after the study visit as recommended by the guidelines. Patients who had their renal function measured later were less likely to have a history of diabetes (20% versus 23%; P = 0.002). Urinary data were available for 3852 (78%) of the 4966 patients with kidney function data, 1092 (28%) based on ACR and 2760 (72%) based on urine dipstick. The patients with missing (36) or with too dilute urinary samples to determine urine protein levels (1078 patients) were more likely to be female (69 versus 52%), less obese (28 versus 35%) with less diabetes (10 versus 26%) and CVD (25 versus 31% all P < 0.001) than those with urinary data.

Table 1.	Patient	characteristics	by	stage	of	CKD ^a
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	Total $(n = 4966)$	No CKD (<i>n</i> = 3121)	Stages 1–2 (<i>n</i> = 984)	Stage 3 (<i>n</i> = 793)	Stages 4–5 $(n = 68)$	P-value ^b
Female	2770 (56%)	1798 (58%)	444 (45%)	492 (62%)	36 (53%)	0.001
Age, years	68 ± 9	66 ± 8	68 ± 9	73 ± 9	73 ± 9	< 0.001
Metropolitan areas	3240 (65%)	2040 (65%)	640 (65%)	516 (65%)	44 (65%)	0.82
Current smoker	400 (8%)	266 (9%)	80 (8%)	48 (6%)	6 (9%)	0.16
Diabetes mellitus	1103 (22%)	572 (18%)	272 (28%)	223 (28%)	36 (53%)	< 0.001
Established CVD	1462 (29%)	762 (24%)	330 (34%)	335 (42%)	35 (51%)	< 0.001
Systolic BP, mmHg	136 ± 17	135 ± 16	137 ± 17	136 ± 17	137 ± 21	0.007
Diastolic BP, mmHg	76 ± 10	77 ± 10	77 ± 11	74 ± 11	73 ± 11	0.005
$BMI > 30 \text{ kg/m}^2$	1611 (32%)	986 (32%)	329 (33%)	269 (34%)	27 (40%)	0.07
Waist circumference (cm)	98 ± 25	97 ± 23	99 ± 14	100 ± 41	102 ± 14	< 0.001
Triglycerides (mmol/L)	1.52 ± 0.80	1.48 ± 0.78	1.55 ± 0.82	1.63 ± 0.85	1.53 ± 0.68	0.002
Cholesterol (mmol/L)	4.96 ± 1.04	5.04 ± 1.03	4.87 ± 1.03	4.80 ± 1.03	4.39 ± 1.04	0.997
LDL (mmol/L)	2.84 ± 0.92	2.92 ± 0.92	2.76 ± 0.90	2.68 ± 0.90	2.47 ± 0.92	0.73

^aData are mean \pm SD or number (%) and the percentages are based on non-missing values. Missing values were <5% in all categories, total missing values smoking (20), diabetes (35), systolic BP (4), diastolic BP (3), BMI (137), Waist circumference (140), triglycerides (78), cholesterol (63), LDL (181). LDL, low-density lipoprotein; BMI, body mass index.

^bP-values for the trend test from no CKD across the stages of CKD.

Table 1 shows the characteristics of the 4966 patient study population according to stage of CKD. Of the 3852 patients with urinary albumin data, 1087 (28%) had microalbuminuria and 179 (5%) macroalbuminuria. Overall, the estimated frequency of CKD was 37%: 984 (20%) with Stages 1-2 CKD, 793 (16%) Stage 3 CKD and 68 (1.4%) Stages 4-5 CKD. Clinical variables that were associated with CKD included age, diabetes, established CV disease, BP and waist circumference (Table 1). Compared to patients without CKD, patients with CKD tended to have higher triglyceride levels and lower high-density lipoprotein, low-density lipoprotein and total cholesterol levels. As shown in Figure 1, the proportion of patients with moderate to advanced CKD (CKD Stages 3-5) increased with age, while the frequency of earlier stage CKD was similar among the different age groups.

CKD awareness gap

Of those 3558 with their eGFR recorded and available to the GP at the time of the visit, 1312 had measurements consistent with abnormal kidney function. Among these with abnormal kidney function, the CKD box was ticked 'yes' for 235 (18%) patients, 'no' for 1062 (81%) and 'unknown' for 15 (1%). Figure 2 shows the GPs' level of awareness among these 1312 patients according to stages of CKD. Appreciation of abnormal kidney function increased with increasing severity of CKD, however, even for those with Stages 4-5 CKD; only two-thirds of the patients were correctly identified.

CV risk assessment

In 3504 patients without established CV disease, the GPs took an estimation and there was sufficient data to calculate risk in 89% (3115). They tended to over-estimate risk of CV disease in patients without CKD and under-estimate the risk in patients with CKD, in particular in later stages of CKD (Figure 3), when their estimates were compared to the risk estimates obtained using NHF 2004 guidelines or the NVDPA guideline.

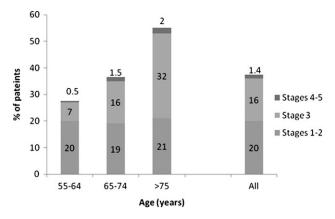


Fig. 1. Prevalence CKD according to age.

Prescribing of CV medication

Use of CV protective therapies (lipid-lowering agents, BPlowering agents and antiplatelet agents) in those with abnormal kidney function recorded and available to their GP prior to the study visit, according to stage of CKD is shown in Figure 4. There was increasing use of these medications with increasing severity of CKD.

Management of patients with proteinuria

Of the 1285 patients with abnormal urinary protein excretion levels, 964 (75%) were receiving BP-lowering therapy. Of these, 776 (81%) were receiving renin-angiotensin-aldosterone system (RAAS) blockers. There was no significant difference in use of RAAS blockers between those with microalbuminuria and macroalbuminuria. In the remaining 321 (25%) patients with proteinuria who were not on any BP-lowering agent, 222 (69%) had BP levels >130/85 and 119 (37%) had BP levels >140/90.

Management of BP

The most commonly used BP-lowering agents for patients with CKD were angiotensin II receptor blockers followed by

angiotensin-converting enzyme inhibitors, calcium channel blockers, diuretics and beta blockers, respectively. The mean number of BP-lowering agents used per patient is shown in Figure 5.

Among the 1406 CKD patients who were on a BP-lowering agent, 856 (61%) were not achieving the recommended target BP level (defined as $\leq 125/75$ mmHg for patients with proteinuria, $\leq 130/85$ mmHg for those with coronary heart disease, diabetes, stroke, transient ischemic attack, macroalbuminuria or known CKD, or <140/90 mmHg for all others), (Figure 6). Of the 439 with CKD who were not on BP-lowering medication, therapy was indicated for 224 (51%). The overall prescribing and treatment gap affected 59% of CKD patients (Figure 6). The corresponding prescribing and treatment gap for non-CKD patients was 52% (P < 0.001). The overall management gap was similar irrespective of whether CKD was recognized by the GP.

Management of lipids

A significant treatment gap in lipid management was also found. Of the 1755 patients with CKD who had lipid data available for evaluation, 940 (54%) were receiving lipidlowering medication. The overall prescribing and treatment gap affected 1102 (64%) of CKD patients, based

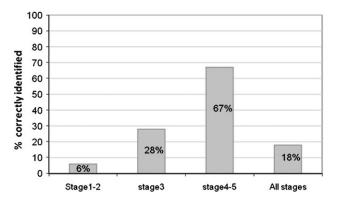
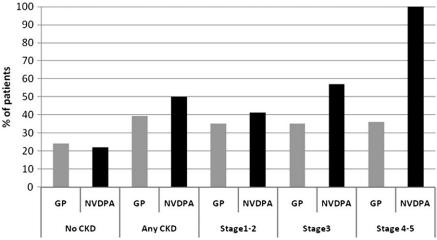


Fig. 2. GPs' recognition of CKD among those with kidney function recorded and available to GPs at the time of study visit.



on targets defined as <2 mmol/L for patients with CVD or <2.5 mmol/L for all others [20]. The corresponding prescribing and treatment gap for non-CKD patients was 71% (P = 0 < 0.001).

Antiplatelet therapy

In patients with a history of CVD, 73% of the CKD and 67% of the non-CKD participants were receiving antiplatelet therapy (P = 0.13).

Discussion

This study provides new evidence of the high prevalence of CKD among Australian older adults in a representative sample of primary care practices. There were significant gaps in GPs' adherence to preventative guidelines, recognition of CKD, assessment and management of the associated high CV disease risk and management of risk factors for the progression of CKD. Opportunistic screening and detection of CKD, with evidence-based management of CV and renal risk, in people aged >55 years presenting to GPs could reduce the burden of disease in older Australians and in the community as a whole.

Several studies have documented poor awareness of CKD among the general public [21, 22]. Other studies have also reported poor documentation of CKD in patient records [23]. This might be due to the asymptomatic nature of CKD, poor general awareness of CKD risk factors and complications and sub-optimal screening of the high-risk population as seen in this study. Implementation of automatic laboratory reporting of eGFR has been suggested as a way of improving GP recognition and awareness of CKD [24, 25]. This study, conducted several years after implementation of nationwide automated eGFR reporting to GPs, suggests that implementation of this strategy alone is insufficient to change clinical practice.

Our data extend current evidence regarding the evidencepractice gap in the management of CKD [26-28]. In general, previous research has reviewed the management of select groups of people with CKD; either people with advanced

Fig. 3. Percentage of patients without known CVD estimated to have 'high' 5-year CV risk by GPs and NVDPA guidelines according to stage of CKD [Patients at any stage of CKD were classified as high risk based on NHF 2004 guidelines (the prevailing guidelines at the time of this survey)].

CKD who are recruited on the basis of their attendance at specialist clinics [26, 27], or sub-groups who, for a range of reasons including having an inter-current illness, have had their renal function measured in primary care [28] or are

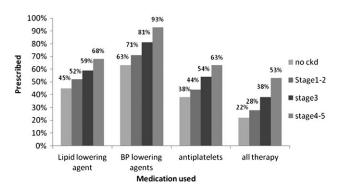


Fig. 4. Use of CV medications according to stage of CKD in patients without established CVD whose kidney function were known to their GP.

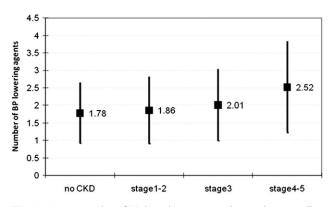


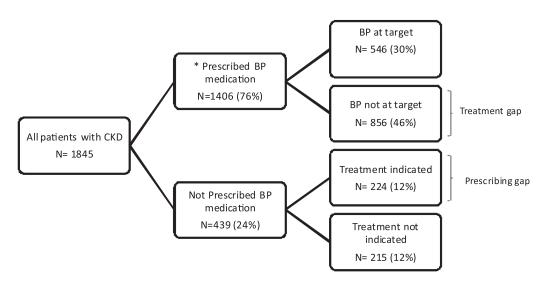
Fig. 5. Average number of BP-lowering agents used per patient according to stage of CKD, (bars represent standard deviations).

known to have diabetes [6, 29]. This study provides evidence regarding the management of CKD within a nationally representative sample of people attending primary care.

An important finding from this study was that the majority of CKD patients did not meet BP targets that are recommended by the relevant guidelines, despite good evidence that BP lowering is an effective strategy to slow progression of CKD and to reduce the risk of CV complications in patients with CKD [15, 30, 31]. There are several potential explanations for this finding: poor adherence to guidelines recommending screening of high-risk individuals for CKD, poor recognition of CKD, lack of familiarity with the recommended BP targets for patients with CKD and the challenges of controlling BP in patients with CKD in primary care. This latter factor is supported by the finding that study participants with CKD were less likely to achieve targets compared to individuals without CKD, even though they were receiving a greater average number of BP-lowering medications.

Although the effectiveness of lipid lowering for the primary prevention of CV events in patients with CKD had not been definitively established at the time of this study, statins had been shown to be well tolerated, effective in lowering lipid concentrations and beneficial in the secondary prevention of CV events [32] in patients with CKD. There is ongoing debate regarding the role of statins in slowing the progression of CKD [32–34]. In this study, we found that the majority of patients with CKD were not treated to targets based on the relevant guidelines. Thus, two main therapeutic options for reducing CV risk and prevention of CKD progression would appear to be sub-optimally implemented in primary care.

There are several potential explanations for the finding of a substantial prescribing gap for patients with CKD. To begin with, as CKD patients are likely to be on multiple medications [35, 36], there may be some reluctance on their part or of their GPs to add new medications because of



*BP levels were missing for 4 patients who were prescribed BP lowering medications. % were based on all values. Target values are based on NHF 2004 guidelines

Fig. 6. Prescribing and treatment gaps among patients with CKD.

potential side effects and perceived drug interactions. Some other factors might include an underestimation of CV risk in CKD patients as we have demonstrated in this study, a lack of familiarity with the safety of medications for CV disease in patients with CKD where altered pharmacokinetics is common, the perception that medications have an altered balance of risks and benefits in patients with CKD and the relative paucity of direct evidence of benefits of such treatment in patients with CKD. One prime example being the lack of evidence of effectiveness of lipid lowering in primary prevention of CVD in CKD patients until the recent publication of the results of the SHARP study [37]. Australia provides universal access to subsidized medications through the Pharmaceutical Benefits Scheme (PBS). Access to and utilization of medications is not affected by insurance coverage and thus socioeconomic status is unlikely to be the cause of the management gaps demonstrated in this study.

One of the strengths of this study is that a large representative sample of primary care patients was included using standardized protocols and data collection tools. In addition, this is one of only a few studies that have examined the prevalence and management of CKD in a high risk, community-based population where there are many opportunities for screening, detection and treatment. We recognize, however, several weaknesses to consider in the interpretation of the results. Firstly, as the evaluation of kidney disease was based on a single assessment of eGFR and urine sample, we may have over-estimated the number of patients with a permanent abnormality of renal function and thus the true prevalence of CKD in this cohort. In addition, a number of patients (n = 327, 6.1%) with missing kidney function data were excluded from the analysis, and they may have had a lower CKD risk category, thus skewing the data. However, as they constituted only a small proportion of all participants and their clinical characteristics were overall similar to those of the overall group, it is unlikely that their exclusion has significantly affected the findings. A majority of the urinary albumin data were based on dipstick analysis, which has a relatively high false-positive rate and potentially would have over-estimated the number of patients with albuminuria. Finally, as this study was conducted during routine clinic care, and BP and other parameters were only measured at a single point in time, we may have underestimated the frequencies of various risk measures and have not taken account of how GPs' decisions on the initiation and changes in the therapy are made on the basis of a series of measurements.

In summary, this study suggests that opportunistic screening of high-risk individuals in primary care might identify many people with previously undiagnosed CKD. Such opportunistic screening of people at high risk, including those with hypertension, diabetes mellitus, a family history of CKD and those over the age of 50, within routine primary care consultations, might prove highly cost effective [7, 38]. Extrapolation of the AusHEART study findings to the Australian and other countries' populations attending primary care suggests a heavy burden of CKD in older people compounded by a large evidence–management gap for these patients. In light of these findings, strategies to increase awareness of CKD among GPs and improve the management of risk factors for adverse outcomes require development, implementation and evaluation.

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Conflict of interest statement. All authors have completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that (i) E.H., A.P., C.A., A.C. and J.C. have received an unrestricted educational grant support from Servier Laboratories Australia for this study: J.C. has also received grant support from Servier for PROGRESS and ADVANCE clinical trials: A.W. is an employee of Servier Australia in the submitted work; (ii) A.P., C.A., A.C. and J.C. have received speaker fees and travel assistance from Servier Australia for speaking at scientific meetings; E.H. has received travel assistance from Servier Australia to attend a scientific meeting; J.C. is a member of the Servier International Diabetes Advisory Board; (iii) A.W.'s spouse is an employee of Bristol Myers Squibb and M.R.'s spouse is an employee of Novartis, all other authors' spouses, partners or children have no financial relationships that may be relevant to the submitted work and (iv) all authors have no other financial or nonfinancial interests that may be relevant to the submitted work.

(See related article by Levin. Ongoing gaps in CKD and CVD care: reevaluating strategies for knowledge dissemination. *Nephrol Dial Transplant* 2012; 27: 1282–1284.)

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