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Audit-based education lowers systolic blood pressure in chronic kidney disease: the Quality Improvement in CKD (QICKD) trial results

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Strict control of systolic blood pressure is known to slow progression of chronic kidney disease (CKD). Here we compared audit-based education (ABE) to guidelines and prompts or usual practice in lowering systolic blood pressure in people with CKD. This 2-year cluster randomized trial included 93 volunteer general practices randomized into three arms with 30 ABE practices, 32 with guidelines and prompts, and 31 usual practices. An intervention effect on the primary outcome, systolic blood pressure, was calculated using a multilevel model to predict changes after the intervention. The prevalence of CKD was 7.29% (41,183 of 565,016 patients) with all cardiovascular comorbidities more common in those with CKD. Our models showed that the systolic blood pressure was significantly lowered by 2.41 mm Hg (CI 0.59–4.29 mm Hg), in the ABE practices with an odds ratio of achieving at least a 5 mm Hg reduction in systolic blood pressure of 1.24 (CI 1.05–1.45). Practices exposed to guidelines and prompts produced no significant change compared to usual practice. Male gender, ABE, ischemic heart disease, and congestive heart failure were independently associated with a greater lowering of systolic blood pressure but the converse applied to hypertension and age over 75 years. There were no reports of harm. Thus, individuals receiving ABE are more likely to achieve a lower blood pressure than those receiving only usual practice. The findings should be interpreted with caution due to the wide confidence intervals.

Kidney International (2013) **84**, 609–620; doi:10.1038/ki.2013.96; published online 27 March 2013

KEYWORDS: blood pressure; clinical trial; glomerular filtration rate; hypertension; kidney disease; quality of health care

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Received 3 June 2012; revised 16 January 2013; accepted 17 January 2013; published online 27 March 2013

Chronic kidney disease (CKD) can be managed in primary care

Internationally, the management of stages 1–3 CKD is carried out in primary care; however, there is scope to improve the coordination and quality of care.^{1–3} CKD is more common with increasing age, and in females but the proportion of males increases with declining renal function;^{4,5} with males more likely to develop proteinuria.⁶ CKD differs across ethnic groups,^{7,8} and with increased deprivation.⁹ It is also associated with heart disease,¹⁰ heart failure, hypertension (HT), and diabetes.¹¹ Intervention in CKD is needed because untreated CKD associated with an increased risk of cardiovascular morbidity and mortality,^{12–14} hospitalization,¹⁵ and progression to renal failure.^{16,17} Strict control of systolic blood pressure (SBP) is known to slow progression;^{18,19} and may be cost effective.^{20,21} CKD was added to the UK's pay-for-performance (P4P) (Quality Outcomes Framework) scheme for primary care in April 2006. This scheme uses routine data to determine the level of case ascertainment, on a disease register, and sets financially incentivized quality indicators. The CKD indicator includes a treatment target of keeping blood pressure (BP) below 140/85 mm Hg preferentially using angiotensin-modulating drugs in the presence of proteinuria.

Uncertainty about CKD and its management

Despite all that is known about CKD, there is uncertainty about how to improve the quality of care. A systematic review of interventions in CKD concludes that other than for people with diabetes, there is a lack of research evidence about how best to develop services. Primary care clinicians feel they lack knowledge and confidence in its management. CKD is usually diagnosed using a four-item formula (age, gender, serum creatinine, and ethnicity) to estimate glomerular filtration rate; and from the presence of proteinuria or albuminuria. The condition has a range of different underlying pathological and ageing processes leading some clinicians to speculate that is merely a biochemical

construction rather than a disease *per se*.^{22–24} A Cochrane review of the use of angiotensin-modulating drugs, the main recommended treatment, in early CKD reports uncertainty about their value,^{25,26} other than for people with CKD and diabetes.²⁷ In addition, a systematic review of interventions in CKD concludes that again, other than for people with diabetes, there is a lack of research as to how services to support management should be developed.^{28,29}

An appropriate quality improvement (QI) intervention

Audit-based education (ABE) is a QI intervention developed over the last 15 years, which provides education, peer support, and documents the gap between achievement and guidelines. This is a complex, non-judgmental, educational intervention underpinned by the use of information technology to extract and make comparisons between practices and against evidence-based guidelines; details in Box 1.³⁰ In observational studies, this intervention improves the quality of cardiovascular disease management.^{31,32} The theoretical basis for this intervention is that audit and feedback, and professional meetings are known to have small but positive effects on quality.^{33,34} Any change that takes place might be explained by control theory,³⁵ which suggests that this is most likely if feedback is accompanied by a target or action plan,³⁶ ideally in writing.³⁷

Rationale for the study

A systematic review identified very few studies involving QI interventions to lower SBP in CKD, and those there were largely focused on high-risk groups, including ethnic minorities with interventions largely carried out by nurses and pharmacists.¹⁸ A subsequent diagnostic analysis, using focus groups, found primary care teams are uncertain about whether CKD was really a disease, disliked its diagnosis based on estimate glomerular filtration rate and found it very difficult to explain the condition to patients.²²

Aim

We carried out this study to determine whether ABE might be effective in addressing the quality gap in CKD management using reduction in SBP as the primary outcome measure of improved management.

RESULTS

Recruitment and sample size

We over-recruited into the trial, anticipating that more practices would drop out than did. The registered practice populations consisted of 691,504 registered people. The mean age of the population was 41.1 years (s.d. 22.36 years) and the mean index of multiple deprivation 17.4 (s.d. 13.66, Supplementary Table S6 online). There were 30 practices in the ABE arm with a mean list size of 9082; 32 practices in the guidelines and prompts (G&P) arm with a mean list size of 6992; and 31 practices in usual practice (UP) arm with a mean list size of 6300 (Table 1). During the course of the study, 10.6% of the population died or left the trial practices. Ethnicity was recorded for around half the population and

Box 1 | Components of audit-based education (ABE)

1. Anonymized extraction of the data set required to report any whether there was any quality improvement. The usual components are:
 - a. Denominator to allow standardization of prevalence.
 - b. Subset of people with the target condition—to create a virtual disease register.
 - c. Clinically relevant comorbidities, risk factors, and treatment.
2. Processing that data to make it informative and providing comparative feedback combined with academic detailing. A key feature is presenting comparative feedback comparing practices at twice yearly meetings held within a locality/primary care organization. These meetings are called Data Quality Workshops (DQW), generally locally led with a consultant of the relevant discipline attending as a specialist resource.
3. In addition to the presentation at the DQW practices are provided two additional printed aids:
 - a. 'Laminate'—a single laminated A4 page summary of the practice demographics and case ascertainment compared with others who attended the DQW. This is for the practice notice board or other prominent location (we recommend wherever they take their breaks).
 - b. Workbook—a slide by slide explanation of the DQW presentation—and what the data means for their practice, compared with their peers and any evidence-based guidance.
4. Running local searches in the practices to provide lists of patients that need to be targeted for intervention. These lists are usually generated by individual GP. Experiential learning is that audit lists of up to 150 per 10,000 registered patients result in change.
5. Supporting education about the evidence-base and providing coding or other training is provided as required.
6. Participants have been encouraged to contribute to the future development of the ABE program.

ABE is an intervention developed over 10 years ago; its aim is to provide feedback about performance against guidance. ABE includes feedback about quality compared with peers in a workshop setting usually led by a local GP with a specialist available as an expert resource, and also supported by academic detailing. ABE usually also identified lists of patients within the practices needing intervention.

69% of these had white ethnicity (Table 1). There were statistically significant differences between the population arms in demographics and proportions with cardiovascular comorbidities (Supplementary data files online).

Class of CKD by study arm

The crude prevalence of CKD for the trial population (aged 18 years and over) was 9.84% for women, 4.74% for men, and 7.29% for the population. The age-standardized rates (based on the 2001 UK National Census) were 9.84% (95% confidence interval (CI) 9.73–9.95%), 3.69% (95% CI 4.66–4.81%), and 7.29% (95% CI 7.22–7.36%), respectively.

The CKD cases with before and after BP readings, included in our analysis, ($n = 23,311$) had a mean age of 75.1 years: 75.1 years in the ABE arm ($n = 9333$); 74.7 years in G&P ($n = 6871$); 75.3 years in the UP arm ($n = 7107$, Table 2).

The mean deprivation score for the CKD cases was 15.8 and ethnicity was recorded for 60.6%; there were statistically significant differences in these between the study arms. The

Table 1 | Baseline characteristics of the population in each study arm

	Audit-based education	Guidelines and prompts	Usual practice	All practices total	Statistical test
<i>List sizes for trial practices</i>					NPar χ^2
Trial population					
Patients	272,467 (39.4%)	223,730 (32.4%)	195,307 (28.24%)	691,504 (100%)	<i>P</i> < 0.001
Mean list size	9082	6992	6300	7436	
Adult population					
Patients	223,847 (39.6%)	181,318 (32.1%)	159,851 (28.29%)	565,016 (100%)	<i>P</i> < 0.001
Mean list size	7462	5666	5156	6075	
<i>Demographics of population</i>					
Age (years)					
<i>n</i>	272,467 (39.4%)	223,730 (32.4%)	195,307 (28.24%)	691,504 (100%)	ANOVA
Mean	41.4	40.1	41.8	41.1	<i>P</i> < 0.001
s.d.	22.3	22.2	22.6	22.4	
Gender					
Female	135,305 (49.7%)	110,600 (49.4%)	98,457 (50.4%)	344,362 (49.8%)	Pearson χ^2
Male	137,162 (50.3%)	113,130 (50.6%)	96,850 (49.6%)	347,142 (50.2%)	<i>P</i> < 0.001
Multiple deprivation index score					
<i>n</i>	250,832 (38.9%)	208,577 (32.3%)	185,651 (28.8%)	645,060 (100%)	ANOVA
Mean	16.1	20.5	15.6	17.4	<i>P</i> < 0.001
s.d.	13.1	14.7	12.6	13.7	
<i>Ethnicity for population</i>					Pearson χ^2
Not recorded or not stated	155,035 (56.9%)	96,946 (43.3%)	104,723 (53.6%)	356,704 (51.6%)	<i>P</i> < 0.001
White	75,249 (27.6%)	82,851 (37.0%)	71,547 (36.6%)	229,647 (33.2%)	
Mixed	2607 (1.0%)	3737 (1.7%)	1483 (0.8%)	7827 (1.1%)	
Asian or Asian British	25,088 (9.2%)	26,925 (12.0%)	8289 (4.2%)	60,302 (8.7%)	
Black or black British	11,875 (4.4%)	10,306(4.6%)	6857 (3.5%)	29,038 (4.2%)	
Chinese or other ethnicity	2613 (1.0%)	2965 (1.3%)	2408 (1.2%)	7986 (1.2%)	
Trial practices (<i>n</i>)	272,467 (100.0%)	223,730 (100.0%)	195,307 (100.0%)	691,504 (100.0%)	
<i>Comorbidities</i>					Pearson χ^2
Diabetes	10,969 (4.9%)	9465 (5.2)	7322 (4.6)	27,756 (4.9)	<i>P</i> < 0.001
Hypertension	35,513 (15.9)	27,216 (15.0)	25,680 (16.1)	88,409 (15.6)	<i>P</i> < 0.001
Heart failure	1659 (0.7)	1581 (0.9)	1313 (0.8)	4553 (0.8)	<i>P</i> < 0.001
Peripheral vascular disease	1341 (0.6)	1342 (0.7)	1147 (0.7)	3830 (0.7)	<i>P</i> < 0.001
Ischemic heart disease	8491 (3.8)	6654 (3.7)	6266 (3.9)	21,411 (3.8)	<i>P</i> < 0.001
Cerebrovascular disease	2472 (1.1)	2302 (1.3)	1994 (1.2)	6768 (1.2)	<i>P</i> < 0.001

Abbreviation: ANOVA, analysis of variance.

Complete case analysis including deaths and leavers during the trial.

Bold values indicate the total of the three columns to the left.

proportion of people with HT and stroke was not significantly different between the arms of the study, but the proportions of other comorbidities were significantly different (Table 1). All the cardiovascular comorbidities were more common in the CKD cases than in the general population. The prevalence of diabetes was 4.9% in the practices' overall adult population and 19.2% in the CKD cases; HT 15.6% versus 71.4%; heart failure 0.8% versus 5.8%; peripheral vascular disease 0.7% versus 4.0%; cerebrovascular disease (stroke or transient ischemic attack (TIA)) 1.2% versus 6.3% for the overall population and CKD cases population respectively.

Fall in SBP between study arms

Mean SBP fell by 4.91 (95% CI 4.51–5.32) mm Hg in the ABE arm, by 4.20 (95% CI 3.71–4.68) mm Hg in G&P, and 3.71 (95% CI 3.25–4.17) mm Hg in UP (Table 3). The fall was greatest with increasing age, the biggest reduction being in people over 75 years. Across all age bands the reduction in BP was greatest in the ABE arm of the study (Figure 1). When we compared the reduction in the ABE arm with pooled data from the other two arms the reduction in SBP is 0.96 mm Hg

(95% CI 0.439–1.429). There was no difference in the time period between observations between the SBP measures in the three arms of the study. The median and interquartile range between the BP readings by study arm were 943 days (833–1035), 941 days (829–1036), and 937 days (826–1031) for ABE, G&P, and UP arms, respectively.

A greater proportion of people in the ABE arm (12.3%) were at target post intervention compared with G&P (9.2%) and UP (9.3%, Table 4). The proportion of people with a > 5 mm Hg reduction in SBP was 47.1% in ABE, 45.9% in G&P, and 45.3% in the UP arm. The odds ratio (OR) of achieving a > 5 mm Hg reduction in ABE compared with UP, was 1.24 (95% CI 1.053–1.450, *P* = 0.010). People with ischemic heart disease (IHD) also, had an increased OR 1.132 (95% CI 1.01–1.27; *P* = 0.033); whereas people treated with 'other' antihypertensives (i.e., non-angiotensin-modulating drugs) and those over 75 years old had OR suggesting they were less likely to achieve a > 5 mm Hg reduction in SBP (Table 5).

Change in process and outcome measures

Within the ABE arm, there was a greater switch to using angiotensin-modulating antihypertensive therapy (angioten-

Table 2 | Baseline characteristics of the CKD cohort with repeat SBP data

	Audit-based education	Guidelines and prompts	Usual practice	All practices total	Statistical test
<i>List sizes for trial practices</i>					NPar χ^2
Trial population					
Patients	272,467	223,730	195,307	691,504	$P < 0.001$
Mean list size	9082.2	6991.6	6300.2	7435.5	
Adult population					
Patients	204,124	159,261	140,822	504,207	$P < 0.001$
Mean list size	6804.1	4976.9	4542.6	5421.6	
<i>Demographics of CKD cohort</i>					
Age (years)					
<i>n</i>	9333 (40.04%)	6871 (29.48%)	7107 (30.49%)	23,311 (100%)	ANOVA
Mean	75.08	74.69	75.32	75.04	$P = 0.079$
s.d.	11.85	11.92	11.68	11.82	
Gender					
Female	6145 (65.84%)	4506 (65.58%)	4760 (66.98%)	15,411 (66.11%)	Pearson χ^2
Male	3188 (34.16%)	2365 (34.42%)	2347 (33.02%)	7900 (33.89%)	$P = 0.023$
Multiple Deprivation Index score					
<i>n</i>	9333 (40.04%)	6871 (29.48%)	7107 (30.49%)	23,311 (100%)	ANOVA
Mean	15.38	17.76	14.38	15.77	$P < 0.001$
s.d.	12.45	13.47	10.61	12.30	
<i>Ethnicity for CKD cohort</i>					Pearson χ^2
Not recorded or not stated	4416 (47.32%)	2069 (30.11%)	2701 (38.00%)	9186 (39.41%)	$P < 0.001$
White	3878 (41.55%)	3863 (56.22%)	4011 (56.44%)	11,752 (50.41%)	
Mixed	45 (0.48%)	85 (1.24%)	27 (0.38%)	157 (0.67%)	
Asian or Asian British	565 (6.05%)	550 (8.00%)	143 (2.01%)	1258 (5.40%)	
Black or black British	386 (4.14%)	279 (4.06%)	204 (2.87%)	869 (3.73%)	
Chinese or other ethnicity	43 (0.46%)	25 (0.36%)	21 (0.30%)	89 (0.38%)	
Trial practices (<i>n</i>)	30 (32.26%)	32 (34.41%)	31 (33.33%)	93 (100%)	
<i>Comorbidities CKD cohort</i>					Pearson χ^2
Diabetes	1814 (19.44%)	1405 (20.45%)	1263 (17.77%)	4482 (19.23%)	$P < 0.001$
Hypertension	6725 (72.06%)	4949 (72.03%)	4979 (70.06%)	16,653 (71.44%)	$P < 0.001$
Heart failure	527 (5.65%)	444 (6.46%)	373 (5.25%)	1344 (5.77%)	$P < 0.001$
Peripheral vascular disease	347 (3.72%)	296 (4.31%)	293 (4.12%)	936 (4.02%)	$P = 0.001$
Ischemic heart disease	1973 (21.14%)	1485 (21.61%)	1428 (20.09%)	4886 (20.96%)	$P = 0.011$
Cerebrovascular disease	550 (5.89%)	444 (6.46%)	468 (6.59%)	1462 (6.27%)	$P < 0.001$

Abbreviations: ANOVA, analysis of variance; CKD, chronic kidney disease; SBP, systolic blood pressure. Bold values indicate the total of the three columns to the left.

Table 3 | Change in systolic BP by arm of study

Systolic BP	<i>n</i>	Mean (mm Hg)	s.d. (mm Hg)	s.e.m. (mm Hg)
<i>ABE</i>				
Before	9333	138.98	17.73	0.18
After		134.06	16.21	0.17
Change		4.91	19.96	0.21
<i>G&P</i>				
Before	6871	139.05	18.81	0.23
After		134.85	16.54	0.20
Change		4.20	20.61	0.25
<i>UP</i>				
Before	7107	139.37	18.20	0.22
After		135.66	16.42	0.19
Change		3.71	19.81	0.24
<i>Total</i>				
Before	23,311	139.12	18.20	0.12
After		134.78	16.38	0.11
Change		4.33	20.12	0.13

Abbreviations: ABE, audit-based education; BP, blood pressure; G&P, guidelines and prompts; UP, usual practice.

sin-converting enzyme inhibitors (ACE) and angiotensin receptor blockers), and a lower rate of mortality and onset of cardiovascular disease compared with the other two arms.

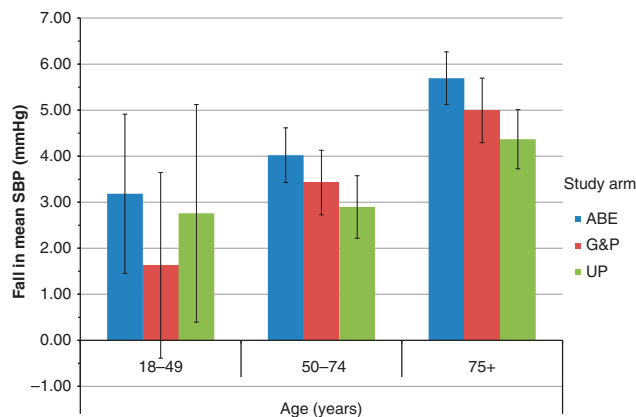


Figure 1 | Fall in mean blood pressure (BP) by study arm between before and after time periods with increasing age. ABE, audit-based education; G&P, guidelines and prompts; UP, usual practice.

6.5% ($n = 1058$) in the ABE arm; 6.9% ($n = 712$) in G&P arm; and 5.8% ($n = 623$) people were switched to from non-ACE to ACE antihypertensive medicines. The annualized incidence of new cardiovascular disease by arm was 2.4% ($n = 364$), 2.7% ($n = 285$), and 3.0% ($n = 325$) for ABE, G&P,

Table 4 | Proportion of people reaching BP target by arm

		Status afterward			Total	Before (% at target)	After (% at target)	Difference (% difference)
		Off target	On target	Missing				
<i>Audit-based education</i>								
Status before	Off target	2327	2376	1167	5870	49.0	61.1	12.0
	On target	1267	3258	1317	5842			
	Missing	531	927	1886	3344			
	Total	4125	6561	4370	15,056			
<i>Guidelines and prompts</i>								
Status before	Off target	1729	1678	567	3974	50.2	59.5	9.2
	On target	1046	2393	663	4102			
	Missing	410	620	1292	2322			
	Total	3185	4691	2522	103,98			
<i>Usual practice</i>								
Status before	Off target	1977	1740	654	4371	47.6	56.8	9.3
	On target	1084	2287	680	4051			
	Missing	451	680	1278	2409			
	Total	3512	4707	2612	10,831			

Abbreviations: ABE, audit-based education; BP, blood pressure; G&P, guidelines and prompts; UP, usual practice. In all, 12.3% more are at target post intervention with ABE, 9.2% with G&P, and 9.3% with UP.

Table 5 | A multilevel logistic model to predict impact of arm of study and other factors on reduction in systolic BP > 5 mm Hg

Model performance	AIC = 11,851 BIC = 11,916		Log likelihood = - 5916		Deviance = - 5916		ROC C stat = 0.625
Random effects:							
Groups	Name	Variance	s.d.				
National practice ID	(Intercept)	0.043	0.206				
Fixed effects	Estimate	s.e.	Pr(> z)	OR	Lower 95% CI	Upper 95% CI	
(Intercept)	1.035	0.127	0.000	2.815	2.193	3.613	
Study arms: audit-based education	0.211	0.082	0.010	1.235	1.053	1.450	
Study arms: guidelines and prompts	0.098	0.085	0.250	1.103	0.933	1.303	
Systolic BP (z scored)	1.193	0.036	<0.001	3.297	3.072	3.539	
Gender: male	0.086	0.048	0.071	1.090	0.993	1.198	
IHD	0.124	0.058	0.033	1.132	1.010	1.268	
Non-angiotensin-modulating antihypertensive drugs	- 0.118	0.052	0.024	0.889	0.802	0.985	
Aged over 75	- 0.288	0.115	0.012	0.750	0.598	0.939	

Abbreviations: AIC, Akaike’s information criterion; BIC, Bayesian information criterion; BP, blood pressure; CI, confidence interval; CVA, cerebrovascular accident; IHD, ischemic heart disease; IMD, index of multiple deprivation; OR, odds ratio; PVD, peripheral vascular disease; ROC C stat, receiver operating characteristic area under the curve statistic; TIA, transient ischemic attack.

The estimate represents the change in SBP because of study arm or other variable.

Not in the model: IMD quartile, PVD, CVA, TIA, hypertension, heart failure, angiotensin-modulating drugs, Afro-Caribbean ethnicity, general practice list size.

and UP arms, respectively ($\chi^2 P=0.015$). Renal function improved marginally more in the ABE arm, mean difference 1.99 ml/min; compared with an improvement of 1.95 and 1.96 ml/min in G&P and UP arms. Median estimate glomerular filtration rate improved from 53 to 54 ml/min. The mortality by arm was: 5.0% ($n=828$), 7.8% ($n=954$), and 6.6% ($n=812$) for ABE, G&P, and UP, respectively.

Multilevel model to explore reduction in SBP by study arm

The multilevel models using linear mixed models (LMMs) showed a statistically significant greater likelihood of lowering BP by around 2.4 mm Hg in the ABE arm of the trial compared with the UP arm (Table 6). The changes within the G&P arm compare with UP crossed parity, and were not

significant. The interclass cluster correlation (ICC) value of 0.061 for the model was higher than that (ICC + 0.03) used in the sample size calculation reported in our protocol.³⁸

The LMM suggested that ABE lowered SBP by 2.41 mm Hg (95% CI 0.593–4.285, Table 6). Deprivation quartile, peripheral vascular disease, cerebrovascular accident and transient ischemic attack, angiotensin-modulating drugs, and general practice list size were excluded from the models as they had no significant impact. In addition to ABE, male gender, IHD, and chronic heart failure were independently associated with an increased lowering SBP; whereas the converse effect was found in people with a diagnosis of HT, and in people treated with non-angiotensin-modulating HT therapy (non-ACE HT Px), Afro-Caribbean ethnicity, and

Table 6 | A multilevel model to predict impact of arm of study and other factors on final SBP

Model performance					
AIC = 87,638	BIC = 87,732	Log likelihood = -43,806	Deviance = 87,617	REML deviance = 87,612	ICC = 0.05
Random effects					
Groups	Name	Variance	s.d.		
National practice ID	(Intercept)	10.878	3.2982		
Residual		241.097	15.5273		
Fixed effects					
	Estimate	Lower 95% CI	Upper 95% CI	s.e.	Pr(x > 0)
(Intercept)	136.565	134.517	138.608	1.063	< 0.001
Study arms: audit-based education	- 2.408	- 4.285	- 0.593	0.979	0.012
Study arms: guidelines and prompts	- 0.925	- 2.845	0.963	0.984	0.329
Previous systolic BP (z scored)	2.856	2.558	3.164	0.155	< 0.001
Gender: male	- 1.208	- 1.856	- 0.559	0.328	0.000
IHD	- 0.841	- 1.632	- 0.049	0.403	0.038
Hypertension	1.359	0.576	2.163	0.401	0.001
Heart failure	- 1.651	- 3.117	- 0.153	0.743	0.026
Non-angiotensin-modulating antihypertensive drugs	1.245	0.434	2.033	0.409	0.002
Afro-Caribbean	2.548	0.635	4.386	0.964	0.009
Aged over 75	2.097	0.546	3.631	0.794	0.008

Abbreviations: AIC, Akaike’s information criterion; BIC, Bayesian information criterion; BP, blood pressure; CI, confidence interval; CVA, cerebrovascular accident; IHD, ischemic heart disease; ICC, interclass cluster correlation; IMD, index of multiple deprivation; OR, odds ratio; PVD, peripheral vascular disease; REML, restricted maximum likelihood; TIA, transient ischemic attack.

The estimate represents the change in SBP because of study arm or other variable. Not in the model: IMD quartile, PVD, CVA, TIA, angiotensin-modulating drugs, general practice list size.

age over 75 years old. All other age bands were excluded as they had no significant influence on the model.

DISCUSSION

Principal findings

We found that practitioners exposed to the ABE intervention are more likely to achieve a greater reduction SBP in their patients with CKD than those practitioners exposed to UP; patients in the ABE arm also had a greater chance of achieving a > 5 mm Hg reduction in SBP. A higher proportion of people in the ABE were changed to angiotensin-modulating antihypertensive therapy. Also, people in the ABE arm had fewer cardiovascular events and lower mortality. There was no evidence that G&P improved care or changed practice. G&P was not associated with having a significant reduction in BP. However, the differences between the arms were small, and much lower than the anticipated reduction. We also found that use of other antihypertensive therapy (i.e., which does not act on the angiotensin system) was associated with a higher SBP at the end of the trial; and being less likely to achieve ≥ 5 mm Hg reduction in SBP.

Across all three arms people aged over 75, of Afro-Caribbean ethnicity, those treated with other (non-angiotensin-modulating) hypertensive therapy, and with a diagnosis of HT were less likely to achieve SBP target and reduce SBP. Conversely, ABE, male gender, IHD, chronic heart failure, and larger practices were associated with a higher chance of reaching target.

The study was over-recruited, and no practices withdrew post-randomization. Generally, there was a much higher prevalence of cerebrovascular disease among people with CKD.

Implications of the findings

Despite widespread skepticism among practitioners as to the significance of a CKD diagnosis in older people practices continued to allow access to their records even if they did not fully participate in their study arm intervention for the duration of the study. The participant general practices appeared willing to join and maintain involvement with improvement science projects. The reduction in SBP achieved, although small, under 3 mm Hg, is likely to have a significant clinical impact at the population level. Although this reduction in SBP is small and around a third of that achieved by treatment with BP lowering therapy, it is known that at the population level a reduction of 5 mm Hg produces a reduction of about 34% in stroke and 21% in IHD.³⁹

The study outcomes should lead practitioners to reflect on how they treat different patient groups. People with IHD and chronic heart failure may have been perceived to be at higher risk and treated more aggressively as a result. There are large numbers of older people with HT and early CKD many of whom are female who may not be classified as high risk by many general practitioners. It is possible that clinicians were treating these people to the P4P target for HT (SBP of 145 mm Hg) ignoring their CKD.

Caution should be exercised in the interpretation of these findings because the CIs around the finding of benefit from ABE were wide. However, we have demonstrated that ABE appears to be effective in improving the proportion of people who achieve a reduction in SBP in primary care. If a similar effect is confirmed in other studies then we would be more optimistic of the effectiveness of this intervention. The use of ACE was promoted within the ABE, and it is possible that

accounted for the improvement in this arm of the trial. Although we noted a lower incidence of vascular events and mortality we have not demonstrated any effect related to variables rejected from the model.

ABE should be considered as an intervention by those seeking to improve quality. Sending out academic detailing in G&P did not appear to change practice. Based on these findings, it cannot be recommended as a QI strategy.

Comparison with the literature

Although the trial set out to follow the CONSORT recommendations for randomized controlled trials⁴⁰ we did not achieve an even distribution of practice characteristics, demographic, and comorbidities between study arms. Our simple block randomization led to there being differences between the study arms. In a future study, we would use allocation techniques that achieve a better baseline balance.⁴¹

The findings contrast with the findings of a study exploring the variation in incidence of renal replacement therapy. This study showed that deprivation, non-white ethnicity, diabetes, and non-achievement of P4P BP target in CKD, were predictor variables of progression to renal replacement.⁴²

A number of other interventions to improve CKD management have been reported but these have mainly looked at their impact on referral rather than on BP management.⁴³

ABE has many of the characteristics of an effective intervention to improve quality in primary care. It is tailored, educational, and multifaceted.⁴⁴ ABE also includes some of the features of the chronic care model: principally better use of practice information systems to prepare proactive practice teams looking to engage and change their quality of service delivery.⁴⁵ As more information about how to effect change becomes available, ABE may be developed further, or alternatively more likely candidates to drive change may be adopted.⁴⁶

Limitations of the method

We did not fully implement ABE as designed. A general practitioner from the study team was not always present at the feedback meetings, although where this happened we tried to at least give individual feedback to that practice. The majority of attendees at ABE sessions were general practitioners or practice nurses from non-neighboring practices so the data were fed back to groups from practices who were meeting for the first time. No 'local queries' were run to identify individual patients requiring intervention for practices. This important aspect of the intervention was omitted as a decision of the wider study team who were concerned about the delays in ethics and in recruitment early in the study. However, this omission is likely to have lessened the effect of the intervention: a study of HT management, which compared audit-based feedback with audit plus details of patients risk achieved a greater reduction in BP in the latter group.⁴⁷ We could also have examined pulse pressure rather than SBP the latter may be a better predictor of progression in CKD.⁴⁸

It is possible that changes in end-digit preference in recording BP may have influenced the recording of BP⁴⁹ and repeated measures may result in regression to the mean;⁵⁰ but these effects would be expected to have an equal effect on each arm of the study. Also, the use of only two BP readings, the two furthest apart in the study period, may have resulted in a loss of fidelity compared with using more. However, this maximized the number of people we could include in the study.

Proteinuria is an independent risk factor for cardiovascular risk in CKD and an important effect modifier for intervention; incomplete recording in people with CKD meant we could not look at this as an additional variable.⁵¹

The power of the analysis was restricted by inter-practice variation in demographics and cardiovascular comorbidity. We cannot report yet on the cost effectiveness of ABE as an intervention but are due to conduct an economic analysis.

Call for further research

Further studies are needed to test the effectiveness of ABE, perhaps in those people with CKD at highest risk, for example, those with proteinuria or declining renal function. It may have been better to have chosen a stepped wedge design. This would have been ethically simpler, as all arms are exposed to the same intervention components, and may have overcome some of the initial delays in recruitment.⁵²

CONCLUSIONS

ABE is a responsive tool to feedback clinically led customized analyses to improve quality. Here we demonstrate, in the first trial of an educational intervention underpinned by information technology, its potential to improve chronic disease management in primary care. Further work is required to determine the generalizability and cost-effectiveness of this approach.

MATERIALS AND METHODS

Trial design

The quality improvement in CKD (QICKD) trial was a three-arm cluster randomized study with an intervention period of 2 years,³⁸ approved by research ethics committees and registered with a clinical trials database.⁵³ The QICKD trial compared two QI interventions G&P and ABE, with UP.

Setting

We carried out this study in UK primary care. This is a setting that lends itself to this type of research.⁵⁴ There is a registration-based system (patients only register with one practice). Practices are computerized and electronic patient record (EPR) systems are used almost universally at the point of care.⁵⁵ Repeat prescribing data are complete and electronic links to pathology labs means that test results are sent directly into practice EPR systems. The UK primary care P4P scheme rewards quality based on routinely collected data measures; this in turn has further improved data quality.⁵⁶ P4P was first introduced in April 2004, mainly targeted on vascular disease, with CKD domain added in 2006. The provision of a common data extraction platform for the different brands of EPR systems (MIQUEST—Morbidity Information Query and Export Syntax) make conducting this type of study more straightforward. We

became involved with CKD in collaboration with renal specialists interested in identifying people with CKD from general practice computer records.⁵⁷ We demonstrated this process was valid⁵⁸ and could be used to define the United Kingdom prevalence of CKD.⁵⁹ The reliability of the diagnosis improving after 2006 when national quality control system was put in place,⁶⁰ although there may be some disparity in creatinine testing.⁶¹

Participants

The study participants were health-care professionals who managed people with CKD in the study practices. Between December 2007 and May 2008, we recruited practices that had the same EPR system for at least 5 years. Where they changed EPR system we were able to map patients from one system to the next by anonymous data linkage based on year of birth, gender, date of registration, and date of last BP recording. Two rounds of follow-up data collections were conducted after the intervention: between 1 May 2009 and 29 September 2009; and between 1 April 2010 and 29 July 2010. We defined the people with CKD as those with an estimated glomerular filtration rate of <60 ml/min (stages 3–5 CKD) based on two readings at least 90 days apart, whenever available. This fits with international guidance and smoothes the effect of creatinine fluctuation.⁵ We used the Modified Diet in Renal Disease four-item equation. We restricted our analysis to the group of adults, people over 18 years old, who fulfilled these criteria between 1 July 2007 and 30 June 2008 7.29% (41,183/565,016; 95% CI 7.22–7.36%) of the registered population at the start of the study were labeled the 'CKD cases.' We included in the analysis people with CKD who had raised BP, or a diagnosis of HT, or cardiovascular comorbidities treated using antihypertensive agents.

Interventions

G&P involved the sending of academic detailing,⁶² printed information containing local guidelines on CKD management,⁶³ and providing access to an information website. This was subsequently revised to the provision of national guidance following the publication of CKD guidelines by the National Institute for Health and Clinical Excellence (NICE). This intervention was designed to be typical of low cost methods used by the NHS used to prompt practitioners about quality. ABE (Box 1) was largely implemented as planned. However, we did not include 'local queries', which provide practices with lists of patients with CKD who are suboptimally managed; additionally this arm did not receive ABE in addition to G&P as originally planned, until the second year. In our protocol, we intended that ABE would be provided in addition to G&P rather than as an alternative.³⁸

Sample size/power calculation

Our intention was to recruit a sample to finish the study with 25 practices per arm. We identified practices for the study by first recruiting renal centers willing to take part in the study. This was because the G&P intervention and ABE arms required the agreement and participation of the local renal center. We identified renal centers wishing to participate in Leicester, Birmingham, Cambridge, southwest London, and Surrey and Sussex. We then recruited practices in these areas via a range of sources including through dedicated practice liaison managers, teaching practice networks, and the local Primary Care Research Networks.

The study was powered to detect a >3 mm Hg difference in SBP between the group. Using a sample data set of 30 practices, we

estimated that the variation between practice means has a s.d. of 3.77 mm Hg. Assuming this sample of 30 practices to be representative of the study practices in terms of their size and number of CKD patients, we estimated that a sample size of 25 practices per intervention group was required to detect a difference of 3 mm Hg at the 5% level with a power of 80%.

Randomization (including blinding)

A total of 138 practices expressed interest in the project although 16 did not progress to randomization (Figure 2). The reasons for this were: outside the participating health service locality ($n=3$); not consented before we closed recruitment ($n=4$); withdrew pre-randomization ($n=4$). Five practices were allocated to an in-depth process evaluation arm. A randomization sequence was created in Microsoft Excel. As practices were recruited a centralized recruitment list was appended on a weekly basis and practices assigned a unique sequential study number. Newly recruited practices were then allocated to each of the three study arms at random in blocks of nine. Once each successive block was filled, the practices were informed of their allocation. Once the total study practice cohort recruitment was completed 10 practices from each arm were randomly allocated per study arm to become questionnaire practices. These practices received questionnaires about their confidence and competence in managing CKD. They were not included in this analysis. Investigators were blinded to the study arm allocation during analysis, and arms were designated by a number within the database.

Data

We extracted data from general practice EPR systems using MIQUEST⁶⁴ and aggregated the data using well-established methods.⁶⁵ We have made our data dictionary, an online lookup tool, which lists every variable extracted online, publicly available.⁶⁶

From within the total population ($N=951,764$), we identified deaths and leavers from the practices ($n=109,701$, 11.5%) and excluded them from the study (Figure 2).

We report the completeness of recording of study variables (Supplementary data file), demographics, and key comorbidities. Demographics include: age, index of multiple deprivation score,⁶⁷ and ethnicity by study arm. We mapped ethnicity codes to the National Statistics 5+1 categories using a mapping process developed in-house.⁶⁸ We additionally captured any coding suggestive of African-Caribbean ethnicity as this group has a special correction factor in the formula used to estimate kidney function.⁶⁹ We also record the proportion of people at baseline with diabetes having corrected miscoding, and misdiagnosis;⁷⁰ as the thresholds for SBP are different for those with diabetes. We also report the prevalence of five other cardiovascular co morbidities: IHD, HT, chronic heart failure, peripheral vascular disease, and cerebrovascular disease.

Outcomes

We report the effect of the intervention arm, compared with UP and other likely predictor variables on reduction in SBP over the period of the study. We compared the earliest BP measure in the first year of the study with the latest recorded in the last. We checked to see if there was any difference in the time interval between the earliest and latest SBP reading by arm, reporting median and interquartile range.

We used 'Z-score' to transform BP. This is a standard methodology for transforming a continuous variable by

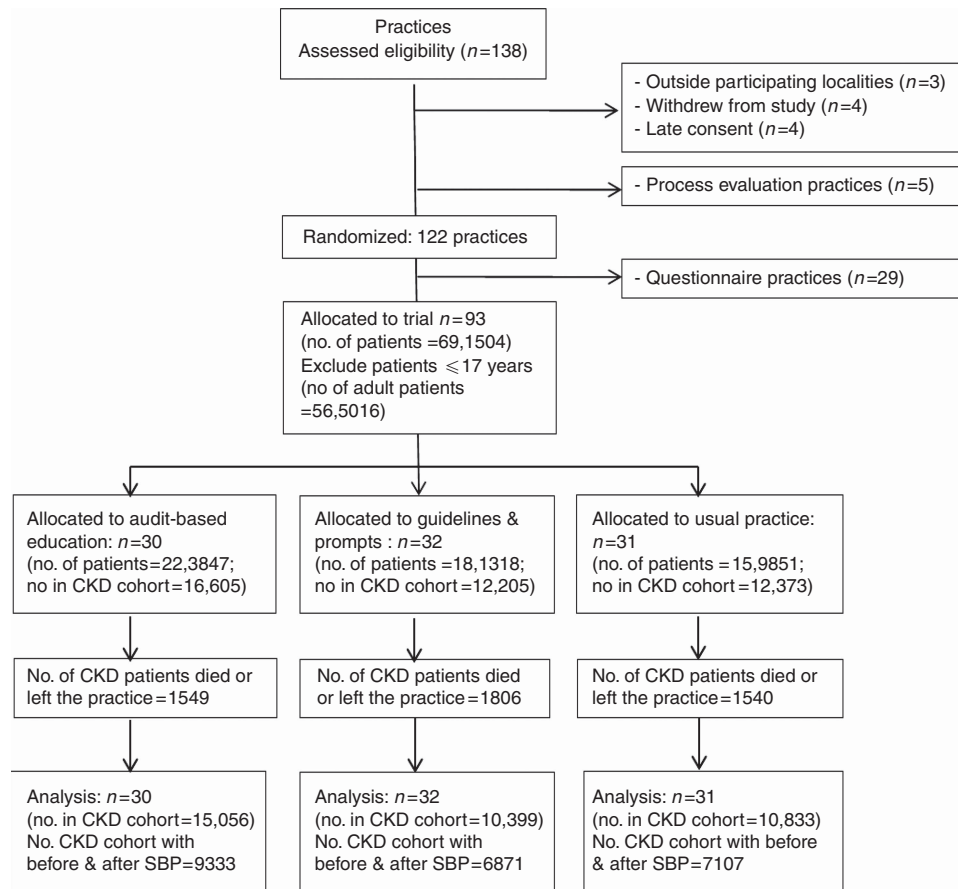


Figure 2 | CONSORT (2010) flow diagram of practice recruitment and exclusion in the quality improvement in chronic kidney disease (QICKD) trial. SBP, systolic blood pressure.

$(x - \text{mean}(x))/\text{s.d.}(x)$. The resultant variable has a mean of zero and a s.d. of 1; making SBP more readily combined with variables with binary values. We also reported incident cases of cardiovascular disease and HT, and any change in renal function as measured using estimate glomerular filtration rate.

Statistical methods

We report data using the mean and s.d. and s.e.m. where appropriate. For non-normally distributed data, we report the median and inter-quartile range. We quote prevalence as a percentage of the population aged 18 years and over with 95% CIs. We used Pearson's χ^2 to report any differences in the proportion of people in each study arm.

The secondary outcome measure is a binary outcome, whether a patient achieved the target BP according to NICE guidelines⁶³ or a reduction of ≥ 5 mmHg we implemented a simple multilevel logistic regression model,⁷¹ using ORs as a measure of effect size.

We developed multilevel models using LMMs fitted using restricted maximum likelihood; we applied our models to the whole study arm with CKD and paired BPs. These models were used to explore the influence of the study arms whilst controlling for age, deprivation, sex, ethnicity, diabetes, and cardiovascular disease and differences in practice size between arms. Our approach included checking for collinearity between variables. This approach was adopted instead of the originally planned analysis of variance because of difference in baseline characteristics between the study arms in particular in the age-sex distribution. These baseline

differences included a difference in practice size, which we have included in the analysis, as this might affect quality achievement.⁷²

The LMM looked at the impact of potential predictor variables on reduction of SBP. These LMM were developed using R Statistical package software 2.14 (www.r-project.org) with the *lme4* add in.⁷³ By default, *lme4* fits the model using restricting maximum likelihood. Across all arms of the trial, patients were nested within their general practice using a random intercept. Model selection was performed following Maindonald and Braun's approach, which aims to maximize the log likelihood, by backward stepwise elimination of variables.⁷⁴ We used Markov Chain Monte Carlo methods to estimate the 95% credible interval for the estimates obtained by this method; these are broadly similar to confidence intervals, and we report them as such.

DISCLOSURE

SdeL led the expert reference group for the development of the Quality and Outcomes Framework (QOF) CKD indicator. A P4P chronic disease management program. Subsequently lead author for NHS Employers/British Medical Association Frequently Asked Questions about CKD, now in its third edition; and General Practitioner Advisor to NICE for CKD indicator. Funding to write three articles and give two invited conference lectures in last 5 years. HG was an expert advisor to QOF, co-author CKD FAQs, honoraria for lectures to General Practitioners. AT co-authored CKD frequently asked questions. NT was deputy on NICE clinical guideline development group for CKD guidance 2008. Funding to write eight articles and develop

on-line learning materials for early management of CKD in last 5 years. KH co-authored for NHS Employers/British Medical Association Frequently Asked Questions about CKD, now in its third edition; Member of NICE CKD clinical guideline develop group; Honoraria received for lectures to General Practitioners on CKD. The remaining authors declared no competing interests.

ACKNOWLEDGMENTS

The following patients and practices contributed to the study. Bernie Stribling initially, then Jo Moore, project managers. Gabreilla Gomez (GG) for initial support with the application. Michael Nation (MN) Director Kidney Research UK for input into the initial protocol development and support throughout the study. Nigel Hague, who wrote all the initial study data extraction queries and attended some ABE workshops. Azhar Farooqi for leadership of the northern ABE; Iain Crinson for methodological advice for the process evaluation; Fiona Reid for statistical support and Andre Ring for data collection. Nigel Mehdi and Mark Bradley of Mehdi-Ward for their assistance with setting up the database and assistance with databases upload and query utilities; Antonios Ntasioudis who worked extensively with the project data. This work was funded by the Health Foundation and Edith Murphy Trust; National Institute for Health Research (NIHR) research portfolio supported participant practices; Edith Murphy Foundation. The Joint Research Office at St George's, University of London and St George's Healthcare Trust for supporting the application and sponsorship of the research.

AUTHOR CONTRIBUTIONS

SdeL conceived the idea for a smaller scale trial of ABE as a QI intervention in CKD with GG. Worked with NM, to develop the final successful funding application. Lead author for the protocol, supported HG with the ethics application. PI, strongly engaged in all parts of the trial and the lead author of the final write-up. HG worked with the principal investigator to develop initial funding application, co-authored protocol, led ethics application, senior study investigator strongly engaged in all parts of the trial, and made significant contribution to papers. SJ assisted with overall design of the analysis plan. Supervision and direction of the final analysis for this paper and conducted some of the analyses; including the development of the multilevel models. A significant contribution to the papers. TC worked with the principal investigator to design the data set and queries, led data analysis team, organized, and developed the academic input into ABE and made significant contribution to papers. JvV conducted much of the data processing and contributed to the design of the database and data handling methods. Conducted the block randomization. Some basic descriptive results for the analysis and supporting SJ in developing and testing the multilevel models. AT is an active member of the study team throughout. Assistance with recruitment, ABE in the south of England. Major input into the process evaluation, and the reliability of the interventions. Contribution to the analysis and papers. NT is an active member of the study team throughout. Recruited and liaised with participating practices in southern localities, organized, and ran ABE interventions in southern localities, reviewed manuscript. NJ is an active member of the study team throughout. Recruited and liaised with participating practices in northern localities, organized, and ran ABE interventions in northern localities, reviewed manuscript and contributed to final write-up. OD contributed as a member of the local study team, using clinical knowledge to interpret and quality assure study findings and outputs. IR active member of the study team throughout. Assistance with recruitment, ABE in the south of England. Contribution to the analysis and papers. AM extensive assistance with the statistical review and response to reviewers'

comments. KH worked with the principal investigator to develop initial funding application, co-authored protocol, senior study investigator strongly engaged in all parts of the trial, and made significant contribution to papers. SdeL is the guarantor for this paper. The Joint Research Office of St George's, University of London and St George's Healthcare Trust were the research sponsors. They fulfilled the role of the sponsor as required to submit an NHS research ethics application ensuring that the research team had appropriate arrangements in place. We are able to make available the table of results used to carry out the analysis reported in this paper.

SUPPLEMENTARY MATERIAL

Table S1. Data collection dates from participating practices.
Table S2. Number of practices, total population, and mean list for study joiner, deaths and leavers and questionnaire and process evaluation practices.
Table S3. Proportion of practice population complete data.
Table S4. Proportion of practice population with records in the key diagnostic and management variables.
Table S5. Proportion of chronic kidney disease (CKD) cases with records in the key diagnostic and management variables.
Table S6. Population mean age by arm of study, and mean deprivation index.
Table S7. Population ethnicity by study arm.
Table S8. Prevalence of common cardiovascular comorbidities by study arm in the trial practices.
Table S9. Ethnicity recording in the adult population in the trial practices.
Table S10. a–b Baseline characteristics of the chronic kidney disease (CKD) cohort.
Table S11. a–d Incidence of hypertension by study arm and for the chronic kidney disease (CKD) cohort by study arm.
Table S12. a–b Renal function recording.
Table S13. Change in renal function (measured as estimate glomerular filtration rate (eGFR)) between study arms.
Table S14. Incident cases of cardiovascular disease by study arm for the population and chronic kidney disease (CKD) cases.
Table S15. a–d Change to taking an angiotensin-modulating antihypertensive medicine.
Table S16. a–c Death and leavers.
Table S17. Difference in time between first and last blood pressure (BP) reading by arm of study.
Table S18. a–d Absolute change in systolic blood pressure (SBP).
Table S19. Baseline characteristics of each study arm population.
Table S20. a–b Change in diastolic blood pressure (BP).
Table S21. a–b Change in pulse pressure.
Table S22. Multilevel model using pulse pressure as an alternative primary outcome measure.
Table S23. a–b Sensitivity/missing values—simulation of patients achieving a reduction of 5 mm Hg in systolic blood pressure.
 Supplementary material is linked to the online version of the paper at <http://www.nature.com/ki>

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