BMJ Open

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Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-005480
Article Type:	Research
Date Submitted by the Author:	14-Apr-2014
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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Renal medicine, Health policy, Epidemiology
Keywords:	EPIDEMIOLOGY, Chronic renal failure < NEPHROLOGY, End stage renal failure < NEPHROLOGY, PUBLIC HEALTH

Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010

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Abstract

Objectives
To determine whether the prevalence of CKD in England has changed over time.

Design
Cross-sectional analysis of nationally representative Health Survey for England (HSE) random samples.

Setting
England 2003 and 2009/2010.

Survey participants
13,896 Adults aged 16+ participating in HSE, adjusted for sampling and non-response, 2009/10 surveys combined.

Main outcome measure
Change in prevalence of eGFR <60ml/min/1.73m^2 (as proxy for stage 3-5 chronic kidney disease [CKD]), from 2003 to 2009/10 based on a single serum creatinine measure using IDMS traceable enzymatic assay in a single laboratory; eGFR derived using MDRD and CKDEPI eGFR formulae.

Analysis
Multivariate logistic regression modelling to adjust time changes for socio-demographic and clinical factors (body mass index, hypertension, diabetes, lipids).

Results
National prevalence of low eGFR (<60) decreased from 9.6% to 6.0% using MDRD (P<0.001) and from 7.6% in 2003 to 5.2% in 2009/10 using CKDEPI (p<0.001). Prevalence decreased within each age and gender group for both formulae. Prevalence of both obesity and diabetes increased in this period, there was a decrease in hypertension. The fully adjusted odds ratio for eGFR<60ml/min/1.73m^2 was 0.49 (0.42-0.57) comparing 2009/10 with 2003 using the MDRD equation, and was similar using the CKDEPI equation.

Conclusion
The prevalence of a low eGFR indicative of CKD in England has decreased over this seven year period, despite rising prevalence of obesity and diabetes, two key causes of CKD. Hypertension prevalence declined and blood pressure control improved but this did not appear to explain the fall. Periodic assessment of eGFR and albuminuria in future HSEs is needed to evaluate trends in CKD.

Article Summary

Strengths & Limitations of this study

- This study uses of nationally representative samples, with later HSEs pooled over two years to increase numbers and precision of estimates. The surveys used standardised protocols for measurement by trained interviewers and nurses, with all samples were tested in the same laboratory with standardised assays.
- Another strength of the study is that the analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. Weighting was introduced for both surveyed periods to reduce response bias and account for missing data.
- The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. The study was also limited by a single sample was tested for serum creatinine in each survey, therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown.
- Another weakness is that prevalence of stage 4/5 CKD is likely to be underestimated as the HSE may not fully account for some in whom more severe CKD (stage 4/5) will be more common.

- The absence of albuminuria data in the 2003 HSE is another major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of RAS inhibition).

Total word count n=3225

Introduction

Chronic kidney disease (CKD) is recognised as a global public health problem.[1] CKD is defined and staged using the estimated glomerular filtration rate (eGFR) and markers of kidney damage, mainly albuminuria.[2] Both eGFR and albuminuria are strong independent risk factors for all-cause and cardiovascular disease (CVD) mortality, and progression to end-stage renal disease (ESRD), which may require renal replacement therapy (RRT) by dialysis or transplantation.[3] In England in 2010 the prevalence of RRT was 832 per million population, a 3% increase from 2009; NHS costs of RRT were estimated at £780 million for 2009/10, and the total cost at £1.45 billion, a nearly threefold increase on estimated costs for 2002.[4,5]

The population prevalence of CKD in England was reported for the first time using data on eGFR and albuminuria in the nationally-representative Health Surveys for England (HSE) 2009 and 2010, though there had previously been estimates based on routine testing using primary care data.[6,7] In the combined 2009/2010 HSE, 6% of men and 7% of women had eGFR <60ml/min/1.73m^2 (equivalent to CKD stage 3-5 if chronic) with a strong age gradient.[8] The prevalence of low eGFR increased in the US, based on National Health and Nutrition Examination (NHANES) surveys between 1988-2004, even after adjusting for adverse trends in risk factors (obesity, diabetes, hypertension), but little is known about CKD prevalence trends in England.[9,10,11]

Information on prevalence change is needed to assess the impact of trends in underlying determinants, and of strategies to prevent and manage CKD. Several policy initiatives have been introduced in England that have had an impact on prevention, detection and management of CKD. The National Service Framework for Renal Services 2004/05 led to national reporting of eGFR by clinical biochemistry laboratories from 2006,[12] the General Practice pay for performance Quality Outcomes Framework (QOF) included targets for CKD management from 2006/07,[13] and the NHS Vascular Checks Programme, introduced in 2009, includes screening for CKD (stage 3-5) in people aged 35-74 with newly identified type 2 diabetes or hypertension.[14] This study therefore aimed to compare the prevalence of CKD in the HSE 2003 with the combined HSE 2009-10 and to relate this to any changes in prevalence of risk factors for CKD, particularly obesity, diabetes and hypertension, over this period.

Methods

Full details of the conduct of the HSE, measurement of non-CKD variables and response rates are shown in the 2003, 2009 and 2010 Health Survey for England reports.[15,16] Survey participants within private households were selected using a multistage stratified random probability sample. Household response rates were 73% in HSE2003 and 68%/66% in HSE 2009/2010. In co-operating households, 90% and 89%/86% of adults completed an interview questionnaire while 70% and 62%/57% respectively consented to a nurse visit, of whom 74%-76% provided a blood test. The HSE 2003 contained 18,533 individuals and data from HSE 2009 and HSE 2010 were combined to provide a larger sample size of 13,065 individuals. This totalled 31,598 individuals for the combined 2003, 2009 and 2010 HSEs. Eligible participants were individuals aged 16 years and older who had a valid serum creatinine value. This left 7,850 individuals from the 2003 HSE and 6,046 individuals from the combined 2009/10 HSEs, leaving a total of 13,896 individuals for analysis.

Age was grouped into five categories: 16-34, 35-54, 55-64, 65-74 and 75+. There were four separate ethnic groupings: White, South Asian, Black and Other. Socio-economic factors included: i) occupation National Statistics Socio-Economic Classification (NS-SEC, divided into three categories: managerial and professional occupations; intermediate occupations and routine and manual occupations); ii) qualifications grouped as: degree or equivalent; below degree (other qualification) and none (no qualification); iii) household tenure (own vs renting); iv) access to motor vehicle (none vs. any).

Smoking status was defined as current, ex-smoker or never smoked. Hypertension was defined as doctor-diagnosed (pre-existing diagnosis), survey-defined (identified as having high blood pressure (BP, systolic ≥140mmHg and/or diastolic ≥90mmHg and/or taking medication for hypertension) at the survey examination), and 'total' (doctor + survey diagnosed). Survey-defined diabetes was glycated haemoglobin (HBA1c) ≥6.5% at nurse visit. Glycated haemoglobin data are presented for those with and without diagnosed diabetes. Body mass index (BMI) was defined as normal (<25kg/m^2), overweight (≥25, <30kg/m^2), and obese (≥30kg/m^2). Waist circumference was classified as: <94cm, 94–102cm (high), and >102cm (very high) for men, and <80cm, 80–88cm (high) and >88cm (very high) for women. For South Asian men, the waist circumference was classified as: <90cm, 90–102cm (high), and >102cm (very high). High density lipoprotein (HDL) cholesterol and total cholesterol were treated as continuous variables.

To investigate medication use, we examined the use of diuretics, ß-blockers, renin-angiotensin system (RAS) inhibitors (angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)), calcium channel blockers, and other anti-hypertensives in those with doctor diagnosed hypertension, doctor diagnosed diabetes and eGFR <60ml/min/1.73m^2, and use of lipid lowering agents in the whole population. In 2003, 47% of respondents answered yes to whether they were taking any medication, and 50% in 2009/10.

Serum creatinine was assayed using an isotope dilution mass spectrometry (IDMS) traceable enzymatic assay in a single laboratory (Clinical Biochemistry Department at the Royal Victoria Infirmary (RVI), Newcastle-upon-Tyne). Both the Modified Diet in Renal Disease (MDRD) equation (in routine use in the UK) and the newer Chronic Kidney Disease Epidemiology Collaboration (CKDEPI) equation (which provides better risk prediction and is recommended for use in international guidelines) were used to define CKD.[2,17] eGFR values were derived using the standard equations.[18,19]

Details of laboratory analysis, internal quality control, and external quality assurance are provided in the HSE 2009/10 documentation, with these methods replicated in the 2003 HSE.[8] The HSE 2003 samples had been stored, frozen at -40^{o}C, then thawed for

measurement in 2012. Such freezing does not affect creatinine levels.[20] eGFR was classified as below 60ml/min/1.73m^2 or equal to or greater than 60ml/min/1.73m^2.

Samples were assayed for serum creatinine over a 19 month time period with two different batches of tri-level Internal Quality Control (IQC) material. HSE 2009 and 2010 samples were analysed with Batch 1 or Batch 2 IQC, HSE 2003 samples were analysed with Batch 2 IQC. The creatinine assay was stable over time with IQC results very close to expected target values. Batch 1 IQC gave mean (SD) creatinine concentrations of 56(0.6),167(1.3) and 586(4.9) umol/L for levels 1,2 and 3 respectively compared with target means of 56, 167 and 588 umol/L. Batch 2 material gave mean(SD) creatinine concentrations of 51(1.1),175(2.2) and 597(5.6)umol/L for levels 1,2 and 3 respectively compared with target means of 51, 175 and 599 umol/L. We compared the change in mean serum creatinine in people aged 20-39 without any diabetes or any hypertension as per Coresh at al.[9]

Statistics

Patient characteristics were compared between the 2003 and 2009/10 HSEs using chi-squared tests for categorical variables and Mann Whitney U tests for non-normally distributed continuous variables. eGFR<60ml/min/1.73m^2 prevalence in 2003 and 2009/10 was compared across age and sex groupings. BP levels were compared in all, in those with diagnosed hypertension and in those with eGFR<60ml/min/1.73m^2; glycated haemoglobin (HBA1c) was compared in all participants and in those with doctor-diagnosed diabetes. Binary logistic regression models were used to examine the relationships between eGFR<60ml/min/1.73m^2 and age, sex and socioeconomic and clinical factors to determine if there were significant differences between the two survey time periods. The dependent variable were CKDEPI and MDRD equation eGFR <60ml/min/1.73m^2 (indicative of stage 3-5 CKD). Four models were produced for each: 1) Age-sex adjusted; 2) model 1 plus socio-economic status and ethnicity; 3) model 2 plus behavioural, lipid levels (HDL and total cholesterol) and clinical variables except hypertension, 4) Model 3 plus doctor-diagnosed hypertension. Interactions between period and both diabetes and hypertension were tested.

Sensitivity analyses were performed by replacing doctor-diagnosed diabetes with HBA1c and replacing doctor-diagnosed hypertension with diastolic and systolic blood pressure. Non-response and blood sample weights were used in all analyses to address issues with missing data. All analyses were performed using IBM SPSS Statistics version 20.

Results

The final sample for the study comprised of 13,896 individuals aged 16+ who had a valid serum creatinine value. Comparing the characteristics of these participants between the 2003 and 2009/10 surveys, the age structure, gender, NS-SEC and car ownership were similar while educational level improved and there was an increase in rented tenure (Table 1). Prevalence of diabetes however classified increased, as did obesity. In contrast, smoking and hypertension prevalence decreased.

There were significant increases in BMI, waist circumference and HBA1c in the population though no change in HBA1c in those with diagnosed diabetes (Table 2). Median BP levels (both systolic and diastolic) fell in all groups including those with diagnosed hypertension, doctor-diagnosed diabetes and with eGFR<60ml/min/1.73m^2. Median total and HDL cholesterol fell in both men and women.

The distribution of serum creatinine was shifted to the left in 2009/10; 1.7% values were greater than 130μmol/L in 2003, but only 0.1% in 2009/10 (Figure 1). Mean serum creatinine decreased, leading to an increase in mean eGFR using both MDRD and CKDEPI formulae (Table 2). Mean serum creatinine for those aged 20-39 without doctor diagnosed hypertension or diabetes fell significantly from 74.8μmol/L (SD 14.8) in 2003 to 71.4μmol/L (SD 14.3) in 2009/10 (p<0.001).

The proportion of individuals with MDRD eGFR<60ml/min/1.73m^2 decreased from 9.6% in 2003 to 6.0% in 2009/10 (p<0.001) and with eGFR <45ml/min/1.73m^2 from 2.4% to 1.4% (p<0.001). Corresponding figures for CKDEPI were 7.6% and 5.2% (p<0.001) and 2.2% and 1.4% (p=0.001). Prevalence of low eGFR fell in all age and gender groups and with either CKDEPI or MDRD equations (Figure 2).

There was an increase in the mean number of anti-hypertensive agents taken in individuals with: doctor-diagnosed hypertension (1.19 in 2003 to 2.01 in 2009-10), doctor-diagnosed hypertension and doctor-diagnosed diabetes (1.47 to 2.57); MDRD eGFR <60ml/min/1.73m^2 (1.26 to 1.77); and CKDEPI eGFR < 60ml/min/1.73m^2 (1.29 to 1.93). The proportion taking RAS inhibitors in individuals with doctor-diagnosed diabetes, doctor-diagnosed hypertension, MDRD eGFR <60ml/min/1.73m^2 or CKDEPI eGFR < 60ml/min/1.73m^2 also increased, as did overall lipid lowering agent use (Appendix 1).

The age-sex adjusted odds ratio (OR) of having low eGFR (MDRD eGFR<60ml/min/1.73m^2) in 2009/10 compared with 2003 was 0.52 (95% confidence interval (CI) 0.45-0.60) (Table 3). This pattern was maintained on further adjustment for potential confounding factors (Table 3) and when using CKDEPI eGFR (Table 4).

Sensitivity analyses replacing doctor-diagnosed diabetes with HBA1c and doctor-diagnosed hypertension with diastolic and systolic BP made little difference to the adjusted ORs. No interactions between period and diabetes or hypertension were identified.

Discussion

These analyses show that CKD prevalence in England estimated by serum creatinine based equations in England decreased from 2003 to 2009/10. This decrease was seen across all age groupings, for CKD defined by both MDRD and CKDEPI eGFR equations (though more pronounced for the MDRD equation), and despite increased prevalence of both diabetes and obesity.[21] Using the CKDEPI equation in place of MDRD to define CKD resulted in a lower prevalence of CKD. Whilst it reduces overall prevalence, the CKDEPI equation identifies more individuals aged 75+ with CKD compared with the MDRD equation.[22,23]

The HSE 2003, 2009 and 2010 were nationally representative samples, with the 2009/10 data pooled over two years to increase numbers and precision of estimates. The age-sex characteristics of the different study periods sampled were similar. The surveys used standardised protocols for measurement by trained interviewers and nurses. All samples were tested in the same laboratory with standardised assays. The analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. Weighting was introduced for both surveyed periods to reduce response bias and account for missing data.

The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. However the use of new, cross-sectional samples enables measurement of general population CKD prevalence at different time points. A single sample was tested for serum creatinine in each survey, and therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown. Given the individual variation in kidney function, more extreme values will be averaged out on repeated testing (regression to the mean), reducing the prevalence of low eGFR.[24] The results may therefore slightly overestimate the prevalence of CKD. Despite high numbers of participants, there were too few cases from the key minority ethnic groups to give robust data on ethnic differences in prevalence of CKD; over 90% of the participants for both survey periods were white (data not shown). South Asians and Black groups have higher rates of renal replacement but have been found to have lower prevalence of CKD than Caucasians.[25,26]

Prevalence of stage 4/5 CKD is likely to be underestimated as, whilst the HSE is able to adjust for non-response among the general population in private households, it may not fully account for some in whom more severe CKD (stage 4/5) will be more common. This includes people who were not able to give a blood or urine sample because of poor health and those who did not participate due to concurrent illness or hospitalisation, as well as those in residential care.

The absence of albuminuria data in the 2003 HSE is a major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of RAS inhibition).[3] We have therefore been unable to estimate changes in prevalence of albuminuria per se, in all CKD (stages1-5), and fully assess prevention and management.

The fall in eGFR could be due i) chance ii) artefact of differences in the serum creatinine measurement, iii) changes in serum creatinine production rather than excretion by the kidney, iv) residual confounding by differences in sample characteristics not adjusted for by sample weighting, v) true fall in eGFR. The period effects were highly statistically significant making chance unlikely. The 2003 assay results data were from stored sera, however this should be stable for creatinine even after long storage.[20] Moreover, if the 2003 serum creatinine had been underestimated this would have reduced any fall over the period. The two sets of samples were analysed in multiple analytical runs over a 19 month time period, which could lead to differences in results, however during this time period the internal quality control data indicates that the assay was accurate compared with assigned target values

and stable, with no indication of assay drift with time. Artefact due to serum creatinine measurement changes does not seem to be the explanation. A fall in serum creatinine over time independent of kidney function could be due to less muscle mass (leading to lower serum creatinine production); there is no evidence for this and it seems unlikely to have occurred at the population level. A fall in dietary protein consumption from cooked meat could also lead to fall in serum creatinine. Cooked meat consumption has been shown to increase serum creatinine in small case studies of volunteers and of patients with diabetic nephropathy and hence national guidance is to avoid eating cooked meat for 12 hours before a blood test for creatinine[27] but this was not done in HSE. We used the HSE study design and non-response weights and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics differences is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences.

Key risk groups for developing CKD are those with hypertension and or diabetes especially if they have albuminuria. In this study there was evidence of modest reductions in the prevalence of hypertension, better control of hypertension in key groups, and greater use of RAS inhibitors which have anti-proteinuric as well as BP lowering effects, though the period changes in eGFR remained after correction for changes in hypertension prevalence. There is evidence from some studies using HSE, primary care databases and QOF data,[28-30] though not all,[31] of improved hypertension control in the last decade. However there are ethnic disparities with poorer control of BP in Black and South Asians who have higher risk of progression to need RRT.[32] Population salt consumption also fell during the last decade which is likely to have influenced population BP.[33,34] CKD prevalence could fall too if those identified with moderate CKD were treated more aggressively, especially those with hypertension and or albuminuria, leading to increased eGFR in some people to above 60ml/min/1.73m^2. The limited HSE data suggest better BP control and greater use of RAS inhibitors in those with eGFR <60ml/min/1.73m^2. Karunetatne et al examined BP control in those with and without CKD in a primary care population in Kent and showed that BP control had improved in CKD patients over time pre- and post the introduction of QOF and that it was greater than in non-CKD hypertensive patients. They also showed increased use of RAS inhibitors and other anti-hypertensive agents in CKD patients.[35] Whilst there was a small fall in population lipid levels and some evidence of increased statin use, this would not be expected to lead to a reduced incidence of CKD, and our period changes were not altered by adjusting for lipid levels.[36]

There are limited data from other countries with which to compare these findings. Coresh et al analysed the US NHANES surveys of 1988-1994 and 1999-2004, which both collected albuminuria and eGFR data. Both prevalence of albuminuria and MDRD eGFR <60ml/min/1.73m^2 increased, the latter from 5.6% to 8.1%.[8] The albuminuria increase was explained by changes in levels of obesity, diabetes and hypertension, whereas this adjustment only partly explained eGFR falls. Changes in population serum creatinine explained most of the remainder of the eGFR changes; this was analysed by comparing the mean serum creatinine in young people aged 20-39 without diabetes or hypertension and this had increased across the surveys.[9] The authors suggested that this rise in serum creatinine could be due to residual laboratory assay differences or to changes in dietary protein or muscle mass. Grams et al showed that prevalence of eGFR<60ml/min/1.73m^2 had also increased using the same survey data when eGFR was estimated using Cystatin C, a marker of kidney function that is independent of muscle mass, and this was not explained by changes in demography, hypertension, diabetes or obesity, suggesting a true increase in low eGFR.[37]

If this change in prevalence in England is true, then based on the HSE 2003 age-sex-specific estimates and 2001 and 2011 Census data, the estimated number of CKD cases (for those aged 16 and over) would be 3.77 million based on the MDRD equation, falling by

1.18 million for 2009/10. Equivalent figures for CKDEPI eGFR <60ml/min/1.73m^2 are 2.98 million and 0.75 million respectively. The impact of such changes would be twofold: a reduced pool of patients at risk of progressing to need RRT; and a contribution to falling cardiovascular incidence and mortality. The former is supported by stabilised acceptance rates onto RRT in England.[4]

Conclusions

The prevalence of a low eGFR appears to have decreased in England from 2003 to 2009/10, despite increases in obesity and diabetes. It is unclear why this has occurred and it is difficult to infer directly that this is due to current policies to improve prevention of CKD and the identification and management of people with CKD. There is a need for repeated national prevalence estimates to further assess CKD patterns over time, including measures of albuminuria and of Cystatin C, both of which were available in HSE 2009 and 2010.

What is already known on this topic

- eGFR and albuminuria are strong independent risk factors for progression to end-stage renal disease (ESRD), which may require costly renal replacement therapy (RRT)
- Prevalence of low eGFR has increased over time in countries such as the US, even after adjustment for adverse trends in CKD risk factors
- Little is known about CKD prevalence trends in England

What this study adds

- Prevalence of a low eGFR indicative of CKD in England has decreased from 2003 to 2009/10, despite increasing prevalence of diabetes and obesity
- This pattern of prevalence of low eGFR was maintained even after adjustment for potential mediating and confounding factors
- A future need for repeated national prevalence estimates, that includes measures of albuminuria and Cystatin C, is required to further assess CKD patterns over time.

Contributors: GA was involved in the analysis and interpretation of the data. PR drafted the paper. GA, PR, SF and GM made substantial contributions to the study conception and design. JM co-ordinated the Health Surveys for England. DO provided background information on CKD policy. JD conducted the laboratory analyses. All authors critically reviewed the paper and were involved in the drafting and approval of the manuscript. GA is the guarantor.
Funding: Kidney function testing in the Health Surveys for England was funded by NHS Kidney Care. GA is funded by a University of Southampton PhD scholarship.
Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.
Ethical approval: Approval was obtained from the London Multi-Centre Research Ethnics Committee for the 2003 survey (HSE 2003 ref MREC/02/2/72) and approval was obtained from the Oxford B Research Ethics Committee for both 2009 and 2010 surveys (HSE 2009 ref 08/H0605/103, HSE 2010 ref 09/H0605/73).
Transparency: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
Data sharing: The HSE 2003, 2009 and 2010 are archived with the UK Data Service. Creatinine measurements for the HSE 2003 undertaken for this study will be archived in due course.

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Table 1. Comparison of prevalence of categorical measures in 2003 and 2009/10[1]

Variable	Category	2003		2009-10		Chi-squared test
		Number	%	Number	%	p-value
All	Aged 16+	7850[2]	100.0	6046[2]	100.0	-
Age	16-34	2425	31.0	1847	30.6	p = 0.441
	34-54	2790	35.7	2129	35.3	
	55-64	1126	14.4	886	14.7	
	65-74	813	10.4	639	10.6	
	75+	662	8.5	539	8.9	
	Missing	0	-	0	-	
Ethnicity	White	7226	92.5	5244	90.7	**p < 0.001**
	South Asian	332	4.3	243	4.2	
	Black	144	1.8	154	2.7	
	Other	108	1.4	139	2.4	
	Missing	0	-	0	-	
Sex	Male	3795	48.6	2961	49.0	p = 0.803
	Female	4020	51.4	3080	51.0	
	Missing	0	-	0	-	
Qualification	Degree	1375	17.6	1295	22.5	**p < 0.001**
	Below degree	4551	58.3	3296	57.0	
	None	1874	24.0	1191	20.6	
	Missing	11	-	3	-	
NSSEC	Highest	2514	33.7	1894	34.8	p = 0.434
	Middle	1674	22.4	1203	22.1	
	Lowest	3273	43.9	2343	43.1	
	Missing	350	-	345	-	
Car Ownership	Yes	6460	82.7	4728	81.7	p = 0.168
	No	1348	17.3	1056	18.3	
	Missing	2	-	1	-	
Tenure	Own	5878	75.4	3955	68.5	**p < 0.001**
	Rent	1914	24.6	1817	31.5	
	Missing	11	-	13	-	
Smoking	Current	1960	25.2	1210	21.0	**p < 0.001**
	Ex	1877	24.1	1429	24.8	
	Never	3951	50.7	3126	54.2	
	Missing	22	-	20	-	
Body mass index	Normal /underweight (<25kg/m^2)	2867	39.2	1956	36.8	**p < 0.001**
	Overweight (25-30 kg/m^2)	2868	39.2	2047	38.5	
	Obese (>30kg/m^2)	1587	21.7	1314	24.7	
	Missing	489	-	469	-	
Waist Circumference	Low (<94cm male, <80cm female)	3060	39.8	2120	37.1	**p < 0.001**
	High (94-102cm male, 80-88cm female)	1929	25.1	1347	23.6	

	Very High (>102cm male, >88cm female)	2703	35.1	2242	39.3	
	Missing	118	-	77	-	
Doctor diagnosed Diabetes	Yes	305	3.9	322	5.3	**p < 0.001**
	No	7504	96.1	5715	94.7	
	Missing	6	-	2	-	
Survey diagnosed Diabetes	Yes (HBA1c ≥6.5%)	296	3.8	316	5.5	**p < 0.001**
	No (HBA1c <6.5%)	7401	96.2	5417	94.5	
	Missing	113	-	52	-	
Total Diabetes	Yes	406	5.2	446	7.4	**p < 0.001**
	No	7405	94.8	5585	92.6	
	Missing	0	-	0	-	
Doctor diagnosed Hypertension	Yes	2118	27.2	1501	25.0	**p = 0.003**
	No	5662	72.8	4527	75.0	
	Missing	36	-	10	-	
Survey diagnosed Hypertension	Yes	2065	31.5	1545	29.2	**p = 0.019**
	No	4499	68.5	3744	70.8	
	Missing	1246	-	496	-	
Total Hypertension	Yes	2866	36.7	2062	34.2	**p = 0.004**
	No	4933	63.3	3968	65.8	
	Missing	12	-	0	-	
eGFR CKDEPI	<45 (ml/min/1.73m^2)	176	2.2	81	1.4	**p = 0.001**
	<60 (ml/min/1.73m^2)	594	7.6	303	5.2	**p < 0.001**
	Missing	0	-	0	-	
eGFR MDRD	<45 (ml/min/1.73m^2)	186	2.4	80	1.4	**p < 0.001**
	<60 (ml/min/1.73m^2)	751	9.6	349	6.0	**p < 0.001**
	Missing	0	-	0	-	

[1] Weighted for non-response (unless stated otherwise)
[2] Not weighted

Table 2. Weighed Comparison of continuous measures in 2003 and 2009-10

Variable	Category	2003	2009-10	Mann Whitney U test
		Median value (IQR)	Median value (IQR)	p value
Serum Creatinine (µmol/L)	Median value	76.0 (66.0 to 87.0)	72.0 (62.0 to 83.0)	**p<0.001**
eGFR (ml/min/1.73m^2)	MDRD	84.7 (72.2 to 98.7)	90.3(77.1 to 104.7)	**p<0.001**
	CKDEPI	94.3 (78.6 to 109.7)	98.6 (84.0. to 112.5)	**p<0.001**
BMI (kg/m^2)	All	26.2 (23.3 to 29.4)	26.6 (23.5 to 30.0)	**p<0.001**
	Male	26.6 (24.0 to 29.4)	27.0 (24.2 to 29.9)	**p=0.001**
	Female	25.7 (22.7 to 29.5)	26.1 (23.1 to 30.0)	**p<0.001**
Waist circumference (cm)	All	90.6 (81.1 to 100.0)	92.0 (81.6 to 101.7)	**p<0.001**
	Male	95.8 (88.0 to 104.0)	96.7 (88.2 to 105.0)	p=0.052
	Female	84.6 (76.4 to 94.0)	86.3 (77.3 to 96.7)	**p<0.001**
Systolic BP (mmHg)	All	125.5 (115.5 to 138.0)	124.5 (114.0 to 136.0)	**p<0.001**
	Dr-diagnosed HT	135.5 (124.0 to 149.5)	134.0 (122.2 to 145.5)	**p<0.001**
	Dr-diagnosed DM	134.5 (122.5 to 148.0)	131.8 (120.0 to 143.5)	**p<0.001**
	CKD (CKDEPI)	139.5 (126.0 to 154.5)	131.8 (119.0 to 143.5)	**p<0.001**
	CKD (MDRD)	137.0 (123.0 to 151.0)	129.2 (118.0 to 142.5)	**p<0.001**
Diastolic BP (mmHg)	All	73.0 (65.5 to 80.5)	72.5 (65.5 to 80.)	**p<0.001**
	Dr-diagnosed HT	77.5 (70.0 to 85.5)	76.0 (68.0 to 83.5)	**p<0.001**
	Dr-diagnosed DM	72.0 (64.5 to 80.5)	71.50 (64.5 to 78.5)	**p<0.001**
	eGFR<60 (CKDEPI)	72.0 (64.5 to 80.5)	68.5 (60.5 to 76.0)	**p<0.001**
	eGFR<60 (MDRD)	73.0 (65.5 to 81.5)	69.0 (61.5 to 76.8)	**p<0.001**
Glycated Hb (%)	All	5.20 (5.00 to 5.50)	5.30 (5.10 to 5.70)	**p<0.001**
	Dr-diagnosed DM	6.90 (5.90 to 8.20)	6.90 (5.90 to 8.30)	p=0.846
HDL Cholesterol (mmol/L)	All	1.50 (1.20 to 1.70)	1.40 (1.20 to 1.70)	**p<0.001**
	Male	1.30 (1.20 to 1.60)	1.30 (1.10 to 1.50)	**p<0.001**
	Female	1.60 (1.40 to 1.90)	1.60 (1.30 to 1.90)	**p=0.046**
Total Cholesterol (mmol/L)	All	5.40 (4.70 to 6.20)	5.20 (4.40 to 5.90)	**p<0.001**
	Male	5.40 (4.70 to 6.20)	5.10 (4.30 to 5.90)	**p<0.001**
	Female	5.40 (4.70 to 6.20)	5.20 (4.50 to 6.00)	**p=0.001**

Figure 1. Distribution of serum creatinine (μmol/L) for 2003 and 2009/10 survey data. Serum creatinine categories are grouped in bands of 5 μmol/L from 40μmol/L to 130μmol/L. Serum creatinine values <40 μmol/L and those >130μmol/L are grouped together.

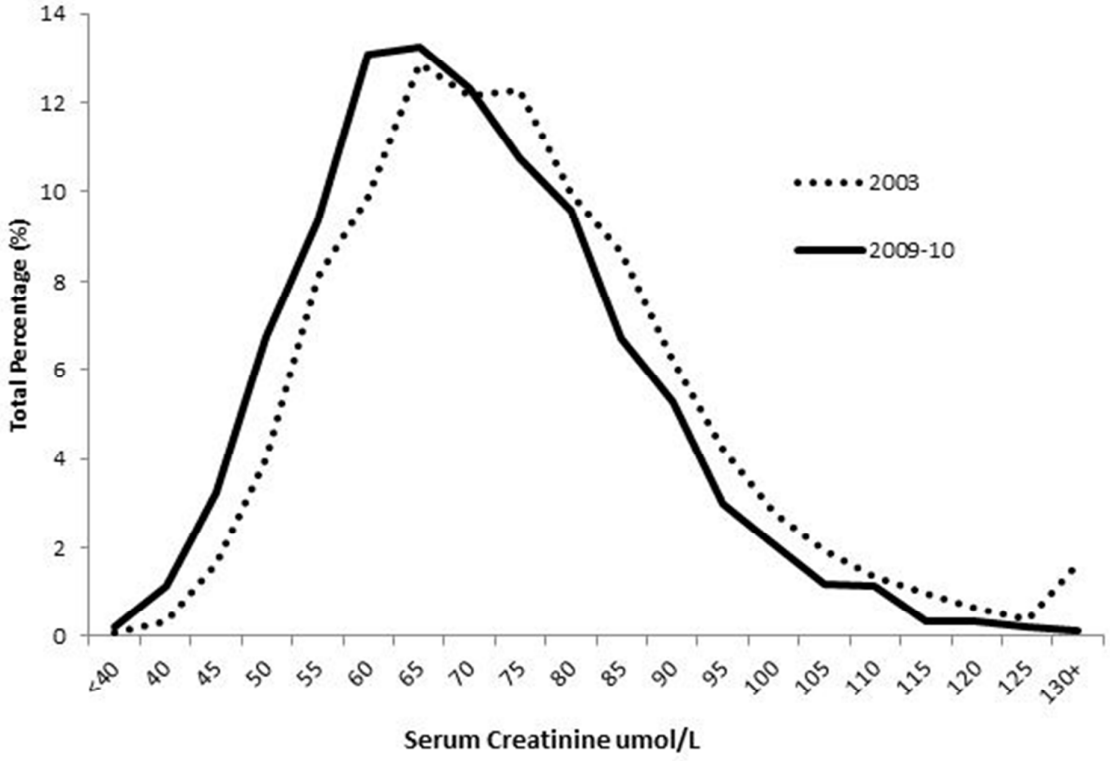
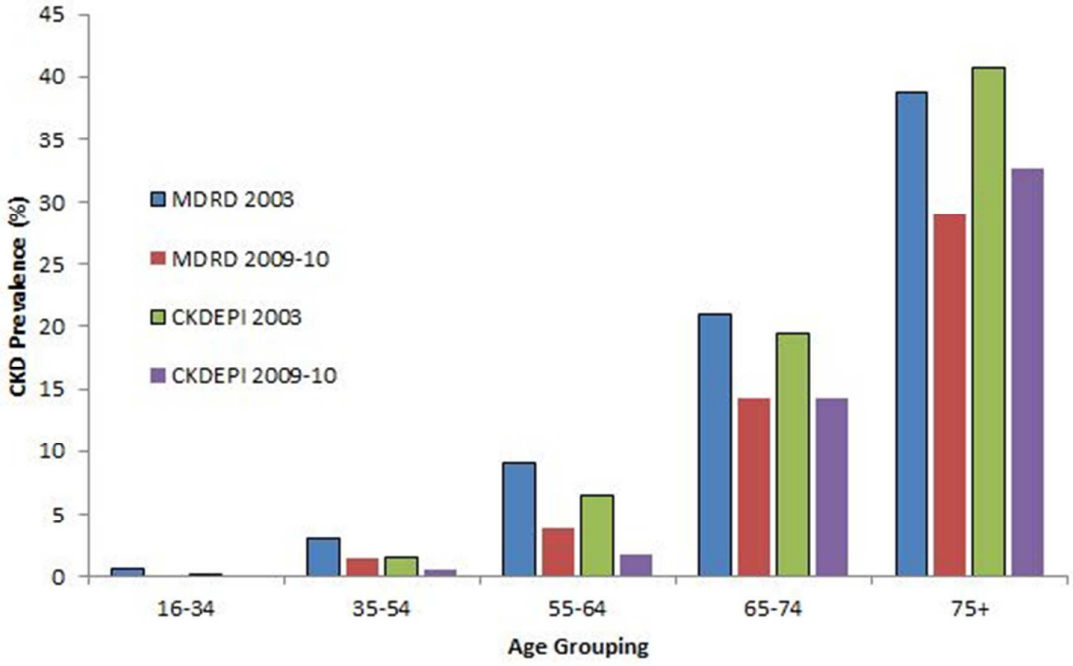


Figure 2. Comparison of low eGFR (<60ml/min/1.73m^2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender

Male



Female

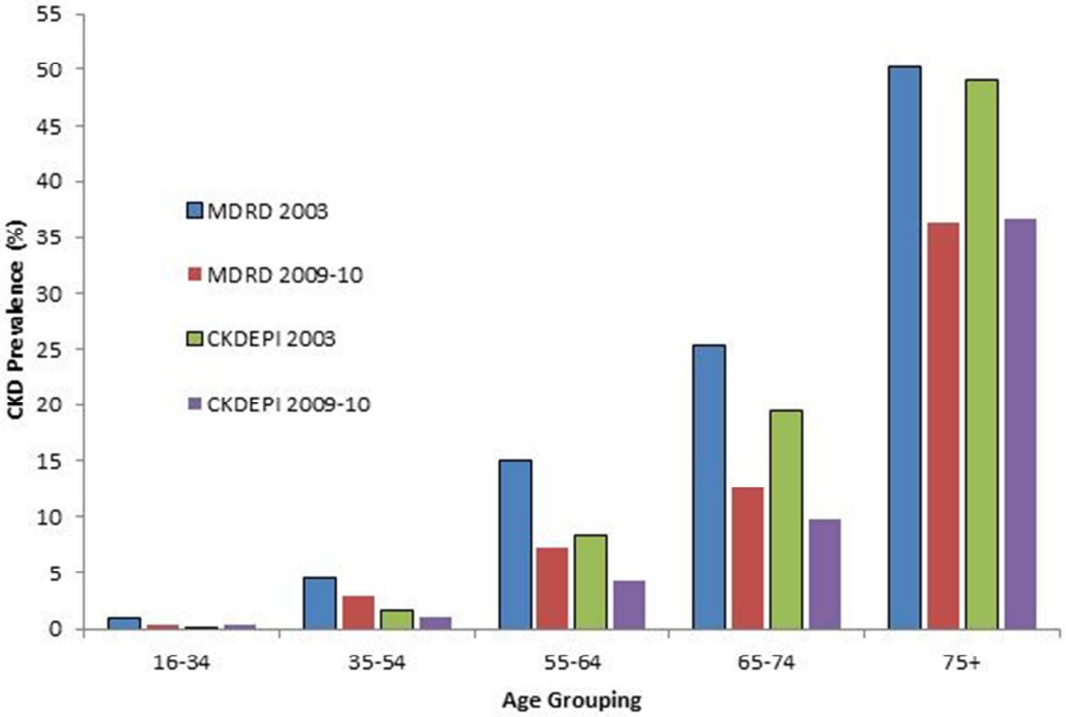


Table 3. Prevalence and associations of low eGFR (<60ml/min/1.73m^2) by MDRD equation with adjustment for socio-demographic and clinical factors

Variable		MDRD				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	9.6	1	1	1	1
	2009-10	6.0	**0.52 (0.45 – 0.60)****	**0.53 (0.44 – 0.62)****	**0.48 (0.41 – 0.57)****	**0.49 (0.42 – 0.57)****
Age	16-34	0.6	1	1	1	1
	35-54	3.0	**5.8 (3.7-9.0)****	**5.7 (3.5-9.1)****	**5.2 (3.3 – 8.2)****	**5.0 (3.2 – 7.9)****
	55-64	9.2	**19 (12 – 30)****	**17 (11 – 28)****	**14 (9 – 23)****	**13 (8 – 20)****
	65-74	19.0	**44 (28 – 68)****	**39 (24 – 63)****	**31 (20 – 50)****	**28 (17 – 44)****
	75+	40.3	**127 (83 – 196)****	**109 (69 – 175)****	**88 (55 – 140)****	**76 (48 – 122)****
Sex	Male	6.3	1	1	1	1
	Female	9.8	**1.45 (1.26 – 1.68)****	**1.39 (1.19 – 1.62)****	**1.45 (1.23 – 1.70)****	**1.43 (1.22 – 1.67)****
Ethnic	White	8.6	-	1	1	1
	South Asian	2.3	-	0.63 (0.32 – 1.26)	0.74 (0.41 – 1.34)	0.72 (0.40 – 1.32)
	Black	2.7	-	0.73 (0.32 – 1.69)	0.41 (0.17 – 1.02)	0.40 (0.16 – 1.01)
	Other	2.4	-	1.19 (0.46 – 3.08)	0.92 (0.36 – 2.30)	0.93 (0.37 – 2.34)
Tenure	Own	8.3	-	1	1	1
	Rent	7.6	-	1.13 (0.93 – 1.36)	1.11 (0.92 – 1.34)	1.10 (0.91 – 1.33)
Education	Degree Level	3.1	-	1	1	1
	Below degree	5.9	-	1.29 (0.98 – 1.70)	**1.34 (1.03 – 1.74)***	**1.33 (1.02 – 1.74)***
	None	18.2	-	**1.43 (1.06 – 1.93)***	**1.50 (1.14 – 1.99)****	**1.50 (1.13 – 1.98)****
Smoking	Never	7.7	-	-	1	1
	Ex-Smoker	12.8	-	-	1.23 (0.97 – 1.55)	1.20 (0.94 – 1.53)
	Current Smoker	4.3	-	-	1.22 (0.96 – 1.57)	1.19 (0.94 – 1.51)
BMI (kg/m^2)	Normal (<25)	4.3	-	-	1	1
	Overweight (25-30)	8.8	-	-	**1.57 (1.30 – 1.90)****	**1.51 (1.25 – 1.83)****
	Obese (>30)	10.6	-	-	**1.80 (1.47 – 2.21)****	**1.65 (1.33 – 2.03)****
HDL Cholesterol	Continuous	-	-	-	**0.53 (0.41 – 0.68)****	**0.54 (0.43 – 0.69)****
Total Cholesterol	Continuous	-	-	-	0.95 (0.88 – 1.11)	0.96 (0.90 – 1.12)
Doctor diagnosed Diabetes	No	7.5	-	-	1	1
	Yes	19.9	-	-	1.42 (0.95 – 2.12)	1.31 (0.88 – 1.97)
Doctor diagnosed Hypertension	No	5.1	-	-	-	1
	Yes	16.5	-	-	-	**1.47 (1.23 – 1.75)****

[1]Prevalence for combined 2003 and 2009-10 HSE
[2]Adjusted for age and sex

[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Table 4. Prevalence and associations of low eGFR (<60) by CKDEPI equation with adjustment for socio-demographic and clinical factors

Variable		CKDEPI				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	7.6	1	1	1	1
	2009-10	5.2	**0.57 (0.48-0.67)****	**0.59 (0.49 – 0.71)****	**0.52 (0.43 – 0.63)****	**0.52 (0.43 – 0.62)****
Age	16-34	0.1	1	1	1	1
	35-54	1.3	**8.4 (3.7 – 19.2)****	**7.5 (3.3 – 17.1)****	**9.1 (3.7 – 22.1)****	**8.7 (3.6 – 21.2)****
	55-64	5.6	**38 (17.4 – 86.0)****	**31 (14 – 69)****	**38 (16 – 91)****	**33 (14 – 81)****
	65-74	16.3	**128 (58 – 292)****	**104 (47 – 231)****	**119 (50 – 269)****	**103 (43 – 247)****
	75+	41.0	**465 (212 – 1019)****	**356 (160 – 790)****	**420 (175 – 1003)****	**357 (149 – 857)****
Sex	Male	5.6	1	1	1	1
	Female	7.6	**1.17 (1.01 – 1.37)***	1.11 (0.93 – 1.32)	**1.37 (1.09 – 1.70)****	**1.36 (1.09 – 1.67)****
Ethnic	White	7.0	-	1	1	1
	South Asian	1.7	-	0.80 (0.36 – 1.79)	0.66 (0.30 – 1.99)	0.63 (0.29 – 1.97)
	Black	2.3	-	0.90 (0.35 – 2.34)	0.47 (0.16 – 1.87)	0.44 (0.14 – 1.56)
	Other	1.6	-	1.13 (0.33 – 3.88)	1.42 (0.22 – 2.89)	1.44 (0.24 – 3.03)
Tenure	Own	6.5	-	1	1	1
	Rent	6.8	-	**1.31 (1.07 – 1.62)***	**1.30 (1.04 – 1.59)***	**1.29 (1.05 – 1.59)***
Education	Degree Level	2.1	-	1	1	1
	Below degree	4.4	-	1.32 (0.94 – 1.84)	1.23 (0.87 – 1.79)	1.24 (0.86 – 1.81)
	None	16.2	-	1.42 (0.99 – 2.02)	1.32 (0.95 – 1.85)	1.33 (0.97 – 1.86)
Smoking	Never	6.2	-	-	1	1
	Ex-Smoker	10.7	-	-	1.20 (0.90 – 1.59)	1.17 (0.81 – 1.44)
	Current Smoker	3.1	-	-	0.99 (0.70 – 1.41)	0.96 (0.68 – 1.45)
BMI (kg/m^2)	Normal (<25)	3.4	-	-	1	1
	Overweight (25-30)	6.8	-	-	**1.43 (1.15 – 1.78)****	**1.36 (1.09 – 1.70)****
	Obese (>30)	8.6	-	-	**1.78 (1.40 – 2.25)****	**1.72 (1.27 – 2.04)****
HDL Cholesterol	Continuous	-	-	-	**0.49 (0.37 – 0.66)****	**0.49 (0.37 – 0.65)****
Total Cholesterol	Continuous	-	-	-	0.95 (0.89 – 1.03)	0.97 (0.90 – 1.04)
Doctor diagnosed Diabetes	No	6.0	-	-	1	1
	Yes	18.4	-	-	**1.59 (1.02 – 2.48)***	1.49 (0.96 – 2.33)
Doctor diagnosed Hypertension	No	3.8	-	-	-	1
	Yes	14.5	-	-	-	**1.40 (1.14 – 1.72)****

[1]Prevalence for combined 2003 and 2009-10 HSE
[2]Adjusted for age and sex

[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Appendix 1: Medication use in key subgroups who reported yes to taking doctor prescribed medication

		2003				2009-10		
Group	**Drug type**	**Number**	**Yes (%)**	**No (%)**		**Number**	**Yes (%)**	**No (%)**
Any Doctor-diagnosed hypertension	**Diuretics**	2118	523 (24.7%)	1595 (75.3%)		1501	378 (25.2%)	1123 (74.8%)
	ß-Blockers		419 (19.8%)	1699 (80.2%)			249 (16.6%)	1252 (83.4%)
	Calcium channel blockers		324 (15.3%)	1794 (84.7%)			357 (23.8%)	1144 (76.2%)
	RAS inhibitors		1027 (48.5%)	1091 (52.5%)			932 (62.1%)	569 (37.9%)
Any Doctor-diagnosed diabetes	**RAS inhibitors**	305	172 (56.4%)	133 (43.6%)		322	199 (61.8%)	123 (38.2%)
eGFR <60ml/min/1.73m^2 MDRD	**RAS inhibitors**	751	386 (51.4%)	365 (48.6%)		349	205 (58.7%)	144 (41.3%)
eGFR <60ml/min/1.73m^2 CKDEPI	**RAS inhibitors**	594	351(59.1%)	243 (40.9%)		303	199 (65.7%)	104 (34.3%)
All	**Lipid lowering**	7810	484 (6.2%)	7326 (93.8%)		5786	770 (13.3%)	5016 (86.7%)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	4,5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, 16
		(b) Indicate number of participants with missing data for each variable of interest	16
Outcome data	15*	Report numbers of outcome events or summary measures	16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	21,22,23
		(*b*) Report category boundaries when continuous variables were categorized	16,17
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8,9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-005480.R1
Article Type:	Research
Date Submitted by the Author:	21-Aug-2014
Complete List of Authors:	Aitken, Grant; University of Southampton, Geography and Environment Roderick, Paul; University of Southampton, Academic Unit of Primary Care and Population Sciences Fraser, Simon; University of Southampton, Academic Unit of Primary Care and Population Sciences Mindell, Jenny; UCL (University College London), Epidemiology and Public Health O'Donoghue, Donal ; Salford Royal NHS Foundation Trust, Renal Medicine Day, Julie; Royal Victoria Infirmary, Department of Clinical Biochemistry Moon, Graham; University of Southampton, Geography and Environment
Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Renal medicine, Health policy, Epidemiology
Keywords:	EPIDEMIOLOGY, Chronic renal failure < NEPHROLOGY, End stage renal failure < NEPHROLOGY, PUBLIC HEALTH

Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010

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Abstract

Objectives
To determine whether the prevalence of CKD in England has changed over time.

Design
Cross-sectional analysis of nationally representative Health Survey for England (HSE) random samples.

Setting
England 2003 and 2009/2010.

Survey participants
13,896 Adults aged 16+ participating in HSE, adjusted for sampling and non-response, 2009/10 surveys combined.

Main outcome measure
Change in prevalence of eGFR <60ml/min/1.73m^2 (as proxy for stage 3-5 chronic kidney disease [CKD]), from 2003 to 2009/10 based on a single serum creatinine measure using IDMS traceable enzymatic assay in a single laboratory; eGFR derived using MDRD and CKDEPI eGFR formulae.

Analysis
Multivariate logistic regression modelling to adjust time changes for socio-demographic and clinical factors (body mass index, hypertension, diabetes, lipids). A correction factor was applied to the 2003 HSE serum creatinine to account for a storage effect.

Results
National prevalence of low eGFR (<60) decreased within each age and gender group for both formulae except males aged 65-74. Prevalence of both obesity and diabetes increased in this period, there was a decrease in hypertension. Adjustment for demographic and clinical factors led to a significant decrease in CKD between the surveyed periods. The fully adjusted odds ratio for eGFR<60ml/min/1.73m^2 was 0.75 (0.61-0.92) comparing 2009/10 with 2003 using the MDRD equation, and was similar using the CKDEPI equation 0.73 (0.57-0.93).

Conclusion
The prevalence of a low eGFR indicative of CKD in England appeared to decrease over this seven year period, despite rising prevalence of obesity and diabetes, two key causes of CKD. Hypertension prevalence declined and blood pressure control improved but this did not appear to explain the fall. Periodic assessment of eGFR and albuminuria in future HSEs is needed to evaluate trends in CKD.

Article Summary

Strengths & Limitations of this study

- This study used nationally representative samples, with later HSEs pooled over two years to increase numbers and precision of estimates. The surveys used standardised protocols for measurement by trained interviewers and nurses, with all samples tested in the same laboratory with standardised assays.
- Another strength of the study is that the analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. Weighting was introduced for both surveyed periods to reduce response bias and account for missing data. A correction factor was applied to 2003 HSE data to adjust for the shift in measured creatinine due to sample storage.
- The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. The study was also limited by a single sample was tested for serum creatinine in each survey, therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown.
- The prevalence of stage 4/5 CKD is likely to be underestimated as the HSE may not fully account for some people in whom more severe CKD (stage 4/5) will be more common.
- The absence of albuminuria data in the 2003 HSE is another major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of renin-angiotensin system (RAS) inhibition).

Total word count n=3,844

Introduction

Chronic kidney disease (CKD) is recognised as a global public health problem.[1] CKD is defined and staged using the estimated glomerular filtration rate (eGFR) and markers of kidney damage, mainly albuminuria.[2] Both eGFR and albuminuria are strong independent risk factors for all-cause and cardiovascular disease (CVD) mortality, and progression to end-stage renal disease (ESRD), which may require renal replacement therapy (RRT) by dialysis or transplantation.[3] In England in 2010 the prevalence of RRT was 832 per million population, a 3% increase from 2009; NHS costs of RRT were estimated at £780 million for 2009/10, and the total cost at £1.45 billion, a nearly threefold increase on estimated costs for 2002.[4,5]

The population prevalence of CKD in England was reported for the first time using data on eGFR and albuminuria in the nationally-representative Health Surveys for England (HSE) 2009 and 2010, though there had previously been estimates based on routine testing using primary care data.[6,7] In the combined 2009/2010 HSE, 6% of men and 7% of women had eGFR <60ml/min/1.73m^2 (equivalent to CKD stage 3-5 if chronic) with a strong age gradient.[8] The prevalence of low eGFR increased in the US, based on National Health and Nutrition Examination (NHANES) surveys between 1988-2004, even after adjusting for adverse trends in risk factors (obesity, diabetes, hypertension), but little is known about CKD prevalence trends in England.[9,10,11]

Information on prevalence change is needed to assess the impact of trends in underlying determinants, and of strategies to prevent and manage CKD. Several policy initiatives have been introduced in England that have had an impact on prevention, detection and management of CKD. The National Service Framework for Renal Services 2004/05 led to national reporting of eGFR by clinical biochemistry laboratories from 2006,[12] the General Practice pay for performance Quality Outcomes Framework (QOF) included targets for CKD management from 2006/07,[13] and the NHS Vascular Checks Programme, introduced in 2009, includes screening for CKD (stage 3-5) in people aged 35-74 with newly identified type 2 diabetes or hypertension.[14] This study therefore aimed to compare the prevalence of CKD in the HSE 2003 with the combined HSE 2009/10 and to relate this to any changes in prevalence of risk factors for CKD, particularly obesity, diabetes and hypertension, over this period.

Methods

Full details of the conduct of the HSE, measurement of non-CKD variables and response rates are shown in the 2003 and 2009 Health Survey for England reports.[15,16] Survey participants within private households were selected using a multistage stratified random probability sample. Household response rates were 73% in HSE 2003 and 68%/66% in HSE 2009/2010. In co-operating households, 90% and 89%/86% of adults completed an interview questionnaire while 70% and 62%/57% respectively consented to a nurse visit, of whom 74%-76% provided a blood test. The HSE 2003 contained 18,533 individuals and data from HSE 2009 and HSE 2010 were combined to provide a sample size of 13,065 individuals. This totalled 31,598 individuals for the combined 2003, 2009 and 2010 HSEs. Eligible participants were individuals aged 16 years and older who had a valid serum creatinine value. This left 7,850 individuals from the 2003 HSE and 6,046 individuals from the combined 2009/10 HSEs, a total of 13,896 individuals for analysis.

Age was grouped into five categories: 16-34, 35-54, 55-64, 65-74 and 75+. There were four separate ethnic groupings: White, South Asian, Black and Other. Socio-economic factors included: i) occupation National Statistics Socio-Economic Classification (NS-SEC, divided into three categories: managerial and professional occupations; intermediate occupations and routine and manual occupations); ii) qualifications grouped as: degree or equivalent; below degree (other qualification) and none (no qualification); iii) household tenure (own vs renting); iv) access to motor vehicle (none vs. any).

Smoking status was defined as current, ex-smoker or never smoked. Hypertension was defined as doctor-diagnosed (pre-existing diagnosis), survey-defined (identified as having high blood pressure (BP, systolic ≥140mmHg and/or diastolic ≥90mmHg and/or taking medication for hypertension) at the survey examination), and 'total' (doctor + survey diagnosed). Survey-defined diabetes was glycated haemoglobin (HBA1c) ≥6.5% at nurse visit. Glycated haemoglobin data are presented for those with and without diagnosed diabetes. Body mass index (BMI) was defined as normal (<25kg/m^2), overweight (≥25, <30kg/m^2), and obese (≥30kg/m^2). Waist circumference was classified as: <94cm, 94–102cm (high), and >102cm (very high) for men, and <80cm, 80–88cm (high) and >88cm (very high) for women. For South Asian men, the waist circumference was classified as: <90cm, 90–102cm (high), and >102cm (very high). High density lipoprotein (HDL) cholesterol and total cholesterol were treated as continuous variables.

To investigate medication use, we examined the use of diuretics, ß-blockers, renin-angiotensin system (RAS) inhibitors (angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)), calcium channel blockers, and other anti-hypertensives in those with doctor diagnosed hypertension, doctor diagnosed diabetes and eGFR <60ml/min/1.73m^2, and use of lipid lowering drugs (the majority of which are statins) in the whole population. In 2003, 47% of respondents answered yes to whether they were taking any prescribed medication, and 50% in 2009/10.

Serum creatinine was assayed using an isotope dilution mass spectrometry (IDMS) traceable enzymatic assay in a single laboratory (Clinical Biochemistry Department at the Royal Victoria Infirmary (RVI), Newcastle-upon-Tyne). Both the Modified Diet in Renal Disease (MDRD) equation (in routine use in the UK) and the newer Chronic Kidney Disease Epidemiology Collaboration (CKDEPI) equation (which provides better risk prediction and is recommended for use in international guidelines) were used to define CKD.[2,17] eGFR values were derived using the standard equations.[18,19]

Details of laboratory analysis, internal quality control, and external quality assurance are provided in the HSE 2009/10 documentation, with these methods replicated in analysis of the 2003 HSE samples.[8]

Samples were assayed for serum creatinine over a 19 month time period with two different batches of tri-level Internal Quality Control (IQC) material. HSE 2009 and 2010 samples were analysed with Batch 1 or Batch 2 IQC, HSE 2003 samples were analysed with Batch 2 IQC. The creatinine assay was stable over time with IQC results very close to expected target values. Batch 1 IQC gave mean (SD) creatinine concentrations of 56(0.6),167(1.3) and 586(4.9) umol/L for levels 1,2 and 3 respectively compared with target means of 56, 167 and 588 umol/L. Batch 2 material gave mean(SD) creatinine concentrations of 51(1.1), 175(2.2) and 597(5.6)umol/L for levels 1,2 and 3 respectively compared with target means of 51, 175 and 599 umol/L.

The HSE 2003 samples had been stored, frozen at -40^{o}C, then thawed for measurement in 2010. Although such freezing is not thought to affect creatinine levels[20] we undertook a re-analysis in 2014 of a random sample of 500 serum creatinine samples taken from the 2009 HSE and subsequently frozen and stored under the same conditions as the HSE 2003 samples, stratified by quintile, to determine if there was a shift in measured creatinine on storage. We found mean serum creatinine increased on storage and was best predicted by a regression equation where the original 2009 serum creatinine value without storage equaled 0.303 plus 0.94 multiplied by the stored serum creatinine value. We assumed the same effect applied to the 2003 serum creatinine data which were analysed in 2009-10 and we applied the same adjustment. This decreased the 2003 serum creatinine values. eGFR was classified as below 60ml/min/1.73m^2 or equal to or greater than 60ml/min/1.73m^2. We compared the change in mean serum creatinine in people aged 20-39 without any diabetes or any hypertension as per Coresh at al.[9]

Statistics

Patient characteristics were compared between the 2003 and 2009/10 HSEs using chi-squared tests for categorical variables and Mann Whitney U tests for non-normally distributed continuous variables. eGFR<60ml/min/1.73m^2 prevalence in 2003 and 2009/10 was compared across age and sex groupings. BP levels were compared in all, in those with diagnosed hypertension and in those with eGFR<60ml/min/1.73m^2; glycated haemoglobin (HBA1c) was compared in all participants and in those with doctor-diagnosed diabetes. Binary logistic regression models were used to examine the relationships between eGFR<60ml/min/1.73m^2 and age, sex and socioeconomic and clinical factors to determine if there were significant differences between the two survey time periods. The dependent variable were CKDEPI and MDRD equation eGFR <60ml/min/1.73m^2 (indicative of stage 3-5 CKD). Four models were produced for each: 1) Age-sex adjusted; 2) model 1 plus socio-economic status and ethnicity; 3) model 2 plus behavioural, lipid levels (HDL and total cholesterol) and clinical variables except hypertension, 4) Model 3 plus doctor-diagnosed hypertension. Interactions between period and both diabetes and hypertension were tested.

Sensitivity analyses were performed by replacing doctor-diagnosed diabetes with HBA1c, replacing doctor-diagnosed hypertension with diastolic and systolic blood pressure and adjusting for lipid lowering agents in the full model. Non-response and blood sample weights were used in all analyses to address issues with missing individuals who did not have a blood sample taken and sent to laboratory for analysis to determine serum creatinine value. Full details on how the weights were obtained are provided in the final volume of the HSE report each year. The age, education and smoking status of those interviewed, having a nurse visit and having a blood test is similar once non-response is taken into account (data not shown). All analyses were performed using IBM SPSS Statistics version 20.

Results

The final sample for the study comprised of 13,896 individuals aged 16+ who had a valid serum creatinine value. Comparing the characteristics of these participants between the 2003 and 2009/10 surveys, the age structure, gender, NS-SEC and car ownership were similar while educational level improved and there was an increase in rented tenure (Table 1). Prevalence of diabetes however classified increased, as did obesity. In contrast, smoking and hypertension prevalence decreased.

There were significant increases in BMI, waist circumference and HBA1c in the population though no change in HBA1c in those with diagnosed diabetes (Table 2). Median BP levels (both systolic and diastolic) fell in all groups including those with diagnosed hypertension, doctor-diagnosed diabetes and with eGFR<60ml/min/1.73m^2. Median total and HDL cholesterol fell in both men and women.

The distribution of serum creatinine is similar for 2003 and 2009/10 (Figure 1). Median serum creatinine increased slightly, leading to a very small non-significant decrease in median eGFR using both MDRD and CKDEPI formulae (Table 2). Mean serum creatinine for those aged 20-39 without doctor diagnosed hypertension or diabetes increased slightly from 70.6µmol/L (SD 13.6) in 2003 to 71.4µmol/L (SD 14.3) in 2009/10 (p=0.09).

The proportion of individuals with MDRD eGFR<60ml/min/1.73m^2 decreased from 6.7% in 2003 to 6.0% in 2009/10 (p=0.13) and with eGFR <45ml/min/1.73m^2 from 1.9% to 1.4% (p=0.03). Corresponding figures for CKDEPI were 5.7% and 5.2% (p=0.26) and 1.8% and 1.4% (p=0.07). Prevalence of low eGFR fell in all age and gender groups and with either CKDEPI or MDRD equations, except for males aged 65-74 where there was a slight increase (Figure 2).

There was an increase in the mean number of anti-hypertensive agents taken in individuals with: doctor-diagnosed hypertension (1.19 in 2003 to 2.01 in 2009/10), doctor-diagnosed hypertension and doctor-diagnosed diabetes (1.47 to 2.57); MDRD eGFR <60ml/min/1.73m^2 (1.30 to 1.77); and CKDEPI eGFR < 60ml/min/1.73m^2 (1.35 to 1.93). The proportion taking RAS inhibitors in individuals with doctor-diagnosed diabetes, doctor-diagnosed hypertension, MDRD eGFR <60ml/min/1.73m^2 or CKDEPI eGFR < 60ml/min/1.73m^2 also increased, as did overall lipid lowering agent use (Appendix 1).

The age-sex adjusted odds ratio (OR) of having low eGFR (MDRD eGFR<60ml/min/1.73m^2) in 2009/10 compared with 2003 was 0.84 (95% confidence interval (CI) 0.72-0.98) and fully adjusted was 0.75 (0.61-0.92) (Table 3). The corresponding ORs for CKDEPI were 0.85 (0.72-1.00) and 0.73 (0.57-0.93) (Table 4).

Sensitivity analyses replacing doctor-diagnosed diabetes with HBA1c and doctor-diagnosed hypertension with diastolic and systolic BP made little difference to the adjusted ORs, as did the inclusion of lipid lowering agents. No interactions between period and diabetes or hypertension were identified.

Discussion

These analyses show that CKD prevalence in England estimated by serum creatinine based equations in England appeared to decrease from 2003 to 2009/10. This decrease was seen across all age groupings (except makes aged 65-74), for CKD defined by both MDRD and CKDEPI eGFR equations, was more pronounced for the MDRD equation and occurred despite increased prevalence of both diabetes and obesity.[21] Using the CKDEPI equation in place of MDRD to define CKD resulted in a lower prevalence of CKD. Whilst it reduced overall prevalence, the CKDEPI equation identified more individuals aged 75+ with CKD compared with the MDRD equation.[22,23]

The HSE 2003, 2009 and 2010 were nationally representative samples, with the 2009/10 data pooled over two years to increase numbers and precision of estimates. The age-sex characteristics of the different study periods sampled were similar. The surveys used standardised protocols for measurement by trained interviewers and nurses. All samples were tested in the same laboratory with standardised assays. The analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. We accounted for the shift in measured creatinine on storage in the 2003 HSE serum creatinine data by introduction of a correction factor derived from analysis of the effect of storage using 2009 data. Non-response weighting was undertaken in the HSE for both surveyed periods to reduce response bias and account for missing data for individuals who did not have blood sample taken and hence no serum creatinine value. We used both the HSE study design and the non-response weights to provide national prevalence estimates at each period and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences. The ethnic composition of the surveys changed over time with a small fall in the White population, but we adjusted for this change in the analysis.

The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. However the use of new, cross-sectional samples enables measurement of general population CKD prevalence at different time points. A single sample was tested for serum creatinine in each survey, and therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown. This is standard practice in national surveys such as NHANES, whereas studies based on routine testing can assess chronicity, such as the QICKD study. [24] Given the individual variation in kidney function, more extreme values will be averaged out on repeated testing (regression to the mean), reducing the prevalence of low eGFR.[25] The results may therefore slightly overestimate the prevalence of CKD. There were too few cases from the key minority ethnic groups to give robust data on ethnic differences in prevalence of CKD. South Asians and Black groups have higher rates of renal replacement but have been found to have lower prevalence of CKD than Caucasians.[26,27]

Prevalence of stage 4/5 CKD is likely to be underestimated as, whilst the HSE is able to adjust for non-response among the general population in private households, it may not fully account for some in whom more severe CKD (stage 4/5) will be more common. This includes people who were not able to give a blood or urine sample because of poor health and those who did not participate due to concurrent illness or hospitalisation, as well as those in residential care.

The absence of albuminuria data in the 2003 HSE is a major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of RAS inhibition).[3] We have therefore been unable to estimate

changes in prevalence of albuminuria per se, in all CKD (stages 1-5), and fully assess prevention and management.

The fall in low prevalence of eGFR could be due i) chance ii) artefact of differences in the serum creatinine measurement, iii) changes in serum creatinine production rather than excretion by the kidney, iv) residual confounding by differences in sample characteristics not adjusted for by sample weighting, v) true fall in eGFR. The two sets of samples were analysed in multiple analytical runs over a 19 month time period, which could lead to differences in results, however during this time period the internal quality control data indicates that the assay was accurate compared with assigned target values and stable. We found a storage artefact on serum creatinine measurement and accounted for this by introduction of a correction factor. A change in serum creatinine over time independent of kidney function could be due to less muscle mass (leading to lower serum creatinine production); there is no evidence for this and it seems unlikely to have occurred at the population level.

A decline in dietary protein consumption from cooked meat could also lead to change in serum creatinine. Statistics from the National Diet and Nutrition Survey show that meat consumption increased from 2001-02 to 2008-10 while protein intake remained virtually stable over the same period. [28] Mean consumption of meat and meat products increased from 154g per day in 2001-02 to 194g per day in 2008-10; protein intake contributing to food energy for adults aged 19+ increased slightly from 16-17% in 2001-02 to 17-18% in 2008-10; meat and meat products contributed to 37-38% of all protein intake for adults aged 19-64, with little change compared to 2008-10. Cooked meat consumption has been shown to increase serum creatinine in small case studies of volunteers and of patients with diabetic nephropathy and hence national guidance is to avoid eating cooked meat for 12 hours before a blood test for creatinine[29] but this was not done in HSE.

We used the HSE study design and non-response weights and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics differences is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences.

Key risk groups for developing CKD are people with hypertension and or diabetes especially if they have albuminuria. In this study there was evidence of modest reductions in the prevalence of hypertension, better control of hypertension in key groups, and greater use of RAS inhibitors which have anti-proteinuric as well as BP lowering effects, though the period changes in eGFR remained after correction for changes in hypertension prevalence. There is evidence from some studies using HSE, primary care databases and QOF data,[30-32] though not all,[33] of improved hypertension control in the last decade. However there are ethnic disparities with poorer control of BP in Black and South Asians who have higher risk of progression to need RRT.[34] Population salt consumption also fell during the last decade which is likely to have influenced population BP.[35,36] CKD prevalence could fall too if those identified with moderate CKD were treated more aggressively, especially those with hypertension and or albuminuria, leading to increased eGFR in some people to above 60ml/min/1.73m^2. The limited HSE data suggest better BP control and greater use of RAS inhibitors in those with eGFR <60ml/min/1.73m^2. Karunetatne et al examined BP control in those with and without CKD in a primary care population in Kent and showed that BP control had improved in CKD patients over time pre- and post the introduction of QOF and that it was greater than in non-CKD hypertensive patients. They also showed increased use of RAS inhibitors and other anti-hypertensive agents in CKD patients.[37]

There was evidence of increased lipid lowering agent use (indicative of increased statin use) and a small fall in population lipid levels. There is some evidence of reno-protective effects of statins in CKD patients; A lower rate of decline in GFR was found in patients with renal

disease who took antilipemic agents.[38] In the Heart Protection Study, the use of the hypolipidemic drug simvastatin reduced the rise in slightly elevated creatinine over time in both diabetic and non-diabetic CKD participants.[39] In the SHARP trial allocation of the lipid lowering ezetimibe plus simvastatin in participants not already on dialysis at randomisation reduced the outcome of end stage renal disease or a doubling of creatinine with an odds ratio of 0.93, though this was not statistically significant.[40] In the GREACE trial statin treatment prevented decline in renal function in people with high blood lipids and coronary heart disease; patients not treated with statins showed a 5.2% decrease in creatinine clearance, while patients treated with statins showed a 4.9% increase in creatinine clearance.[41] However our period changes were not altered by adjusting for statins (lipid lowering drugs) or lipid levels (HDL, total cholesterol).[37]

There are limited data from other countries with which to compare these findings. Coresh et al analysed the US NHANES surveys of 1988-1994 and 1999-2004, which both collected albuminuria and eGFR data. Both prevalence of albuminuria and MDRD eGFR <60ml/min/1.73m^2 increased, the latter from 5.6% to 8.1%.[8] The albuminuria increase was explained by changes in levels of obesity, diabetes and hypertension, whereas such adjustment only partly explained the fall in eGFR. Changes in population serum creatinine explained most of the remainder of the eGFR changes; this was analysed by comparing the mean serum creatinine in young people aged 20-39 without diabetes or hypertension and this had increased across the surveys.[9] The authors suggested that this rise in serum creatinine could be due to residual laboratory assay differences or to changes in dietary protein or muscle mass. Grams et al showed that prevalence of eGFR<60ml/min/1.73m^2 had also increased using the same survey data when eGFR was estimated using Cystatin C, a marker of kidney function that is independent of muscle mass, and this was not explained by changes in demography, hypertension, diabetes or obesity, suggesting a true increase in low eGFR.[41]

We can compare the estimated national CKD prevalence for HSE with QOF returns which record diagnosed CKD in primary care.[42] Prevalence has been increasing with improvements in detection and recording and in 2010 was 4.2%. The figures are not directly comparable as comparing a single screened value versus routine testing with presumed allowance for chronicity, but this may suggest some under-diagnosis of CKD.

If this change in prevalence in England is true, then based on the HSE 2003 age-sex-specific estimates and 2001 and 2011 Census data, the estimated number of CKD cases (for those aged 16 and over) would be 2.62 million based on the MDRD equation, falling by 0.03 million for 2009/10. Equivalent figures for CKDEPI eGFR <60ml/min/1.73m^2 are 2.23 million and 0.02 million increase respectively. The impact of such changes would be twofold: a consistent pool of patients at risk of progressing to need RRT; and a contribution to consistent cardiovascular incidence and mortality. The former is supported by stabilised acceptance rates onto RRT in England.[4]

Conclusions

The prevalence of a low eGFR appears to have decreased in England from 2003 to 2009/10, despite increases in obesity and diabetes. It is unclear why this has occurred and it is difficult to infer directly that this is due to current policies to improve prevention of CKD and the identification and management of people with CKD. There is a need for repeated national prevalence estimates to further assess CKD patterns over time, including measures of albuminuria and of Cystatin C, both of which were available in HSE 2009 and 2010.

What is already known on this topic • eGFR and albuminuria are strong independent risk factors for progression to end-stage renal disease (ESRD), which may require costly renal replacement therapy (RRT) • Prevalence of low eGFR has increased over time in countries such as the US**,** even after adjustment for adverse trends in CKD risk factors • Little is known about CKD prevalence trends in England
What this study adds • Prevalence of a low eGFR derived from serum creatinine and indicative of CKD in England has decreased from 2003 to 2009/10, despite increasing prevalence of diabetes and obesity • This pattern of prevalence of low eGFR was maintained even after adjustment for potential mediating and confounding factors • A future need for repeated national prevalence estimates, that includes measures of albuminuria and Cystatin C, is required to further assess CKD patterns over time.

Contributors: GA was involved in the analysis and interpretation of the data. PR drafted the paper. GA, PR, SF and GM made substantial contributions to the study conception and design. JM co-ordinated the Health Surveys for England. DO provided background information on CKD policy. JD conducted the laboratory analyses. All authors critically reviewed the paper and were involved in the drafting and approval of the manuscript. GA is the guarantor.
Acknowledgements: Scott Harris contributed to the production of the regression equation that was applied to the 2003 serum creatinine samples as a correction factor.
Funding: Kidney function testing in the Health Surveys for England was funded by NHS Kidney Care. GA is funded by a University of Southampton PhD scholarship.
Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.
Ethical approval: Approval was obtained from the London Multi-Centre Research Ethnics Committee for the 2003 survey (HSE 2003 ref MREC/02/2/72) and approval was obtained from the Oxford B Research Ethics Committee for both 2009 and 2010 surveys (HSE 2009 ref 08/H0605/103, HSE 2010 ref 09/H0605/73).
Transparency: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
Data sharing: The HSE 2003, 2009 and 2010 are archived with the UK Data Service. Technical Appendix, statistical code and dataset available from corresponding author Grant Aitken at G.Aitken@soton.ac.uk. Creatinine measurements for the HSE 2003 undertaken for this study will be archived in due course.

Figure Legends

Figure 1. Distribution of serum creatinine (μmol/L) for 2003 and 2009/10 survey data. Serum creatinine categories are grouped in bands of 5 μmol/L from 40μmol/L to 130μmol/L. Serum creatinine values <40 μmol/L and those >130μmol/L are grouped together.

Figure 2. Comparison of low eGFR (<60ml/min/1.73m^2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender

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Table 1. Comparison of prevalence of categorical measures in 2003 and 2009/10[1]

Variable	Category	2003		2009-10		Chi-squared test
		Number	%	Number	%	p-value
All	Aged 16+	7850[2]	100.0	6046[2]	100.0	-
Age	16-34	2425	31.0	1847	30.6	p = 0.44
	34-54	2790	35.7	2129	35.3	
	55-64	1126	14.4	886	14.7	
	65-74	813	10.4	639	10.6	
	75+	662	8.5	539	8.9	
	Missing	0	-	0	-	
Ethnicity	White	7226	92.5	5244	90.7	**p < 0.001**
	South Asian	332	4.3	243	4.2	
	Black	144	1.8	154	2.7	
	Other	108	1.4	139	2.4	
	Missing	0	-	0	-	
Sex	Male	3795	48.6	2961	49.0	p = 0.80
	Female	4020	51.4	3080	51.0	
	Missing	0	-	0	-	
Qualification	Degree	1375	17.6	1295	22.5	**p < 0.001**
	Below degree	4551	58.3	3296	57.0	
	None	1874	24.0	1191	20.6	
	Missing	11	-	3	-	
NSSEC	Highest	2514	33.7	1894	34.8	p = 0.43
	Middle	1674	22.4	1203	22.1	
	Lowest	3273	43.9	2343	43.1	
	Missing	350	-	345	-	
Car Ownership	Yes	6460	82.7	4728	81.7	p = 0.17
	No	1348	17.3	1056	18.3	
	Missing	2	-	1	-	
Tenure	Own	5878	75.4	3955	68.5	**p < 0.001**
	Rent	1914	24.6	1817	31.5	
	Missing	11	-	13	-	
Smoking	Current	1960	25.2	1210	21.0	**p < 0.001**
	Ex	1877	24.1	1429	24.8	
	Never	3951	50.7	3126	54.2	
	Missing	22	-	20	-	
Body mass index	Normal /underweight (<25kg/m^2)	2867	39.2	1956	36.8	**p < 0.001**
	Overweight (25-30 kg/m^2)	2868	39.2	2047	38.5	
	Obese (>30kg/m^2)	1587	21.7	1314	24.7	
	Missing	489	-	469	-	
Waist Circumference	Low (<94cm male, <80cm female)	3060	39.8	2120	37.1	**p < 0.001**
	High (94-102cm male, 80-88cm female)	1929	25.1	1347	23.6	
	Very High	2703	35.1	2242	39.3	

	(>102cm male, >88cm female)					
	Missing	118	-	77	-	
Doctor diagnosed Diabetes	Yes	305	3.9	322	5.3	**p < 0.001**
	No	7504	96.1	5715	94.7	
	Missing	6	-	2	-	
Survey diagnosed Diabetes	Yes (HBA1c ≥6.5%)	296	3.8	316	5.5	**p < 0.001**
	No (HBA1c <6.5%)	7401	96.2	5417	94.5	
	Missing	113	-	52	-	
Total Diabetes	Yes	406	5.2	446	7.4	**p < 0.001**
	No	7405	94.8	5585	92.6	
	Missing	0	-	0	-	
Doctor diagnosed Hypertension	Yes	2118	27.2	1501	25.0	**p = 0.003**
	No	5662	72.8	4527	75.0	
	Missing	36	-	10	-	
Survey diagnosed Hypertension	Yes	2065	31.5	1545	29.2	**p = 0.02**
	No	4499	68.5	3744	70.8	
	Missing	1246	-	496	-	
Total Hypertension	Yes	2866	36.7	2062	34.2	**p = 0.004**
	No	4933	63.3	3968	65.8	
	Missing	12	-	0	-	
eGFR CKDEPI	<45 (ml/min/1.73m^2)	142	1.8	81	1.4	p = 0.07
	<60 (ml/min/1.73m^2)	444	5.7	303	5.2	p = 0.26
	Missing	0	-	0	-	
eGFR MDRD	<45 (ml/min/1.73m^2)	146	1.9	80	1.4	**p = 0.03**
	<60 (ml/min/1.73m^2)	521	6.7	349	6.0	p = 0.13
	Missing	0	-	0	-	

[1] Weighted for non-response (unless stated otherwise)
[2] Not weighted

Table 2. Weighed Comparison of continuous measures in 2003 and 2009-10

Variable	Category	2003	2009-10	Mann Whitney U test
		Median value (IQR)	Median value (IQR)	p value
Serum Creatinine (µmol/L)	Median value	71.7 (62.3 to 82.1)	72.0 (62.0 to 83.0)	p=0.66
eGFR (ml/min/1.73m^2)	MDRD	90.5 (77.2 to 105.4)	90.3 (77.1 to 104.7)	p=0.62
	CKDEPI	99.3 (84.1 to 113.9)	98.6 (84.0. to 112.5)	p=0.11
BMI (kg/m^2)	All	26.2 (23.3 to 29.4)	26.6 (23.5 to 30.0)	**p<0.001**
	Male	26.6 (24.0 to 29.4)	27.0 (24.2 to 29.9)	**p=0.001**
	Female	25.7 (22.7 to 29.5)	26.1 (23.1 to 30.0)	**p<0.001**
Waist circumference (cm)	All	90.6 (81.1 to 100.0)	92.0 (81.6 to 101.7)	**p<0.001**
	Male	95.8 (88.0 to 104.0)	96.7 (88.2 to 105.0)	p=0.05
	Female	84.6 (76.4 to 94.0)	86.3 (77.3 to 96.7)	**p<0.001**
Systolic BP (mmHg)	All	125.5 (115.5 to 138.0)	124.5 (114.0 to 136.0)	**p<0.001**
	Dr-diagnosed HT	135.5 (124.0 to 149.5)	134.0 (122.2 to 145.5)	**p<0.001**
	Dr-diagnosed DM	134.5 (122.5 to 148.0)	131.8 (120.0 to 143.5)	**p<0.001**
	eGFR<60 (CKDEPI)	140.2 (126.0 to 156.0)	131.8 (119.0 to 143.5)	**p<0.001**
	eGFR<60 (MDRD)	137.5 (124.0 to 153.7)	129.2 (118.0 to 142.5)	**p<0.001**
Diastolic BP (mmHg)	All	73.0 (65.5 to 80.5)	72.5 (65.5 to 80.)	**p<0.001**
	Dr-diagnosed HT	77.5 (70.0 to 85.5)	76.0 (68.0 to 83.5)	**p<0.001**
	Dr-diagnosed DM	72.0 (64.5 to 80.5)	71.50 (64.5 to 78.5)	**p<0.001**
	eGFR<60 (CKDEPI)	71.5 (62.9 to 80.5)	68.5 (60.5 to 76.0)	**p<0.001**
	eGFR<60 (MDRD)	72.5 (64.0 to 81.5)	69.0 (61.5 to 76.8)	**p<0.001**
Glycated Hb (%)	All	5.20 (5.00 to 5.50)	5.30 (5.10 to 5.70)	**p<0.001**
	Dr-diagnosed DM	6.90 (5.90 to 8.20)	6.90 (5.90 to 8.30)	p=0.85
HDL Cholesterol (mmol/L)	All	1.50 (1.20 to 1.70)	1.40 (1.20 to 1.70)	**p<0.001**
	Male	1.30 (1.20 to 1.60)	1.30 (1.10 to 1.50)	**p<0.001**
	Female	1.60 (1.40 to 1.90)	1.60 (1.30 to 1.90)	**p=0.046**
Total Cholesterol (mmol/L)	All	5.40 (4.70 to 6.20)	5.20 (4.40 to 5.90)	**p<0.001**
	Male	5.40 (4.70 to 6.20)	5.10 (4.30 to 5.90)	**p<0.001**
	Female	5.40 (4.70 to 6.20)	5.20 (4.50 to 6.00)	**p=0.001**

Table 3. Prevalence and associations of low eGFR (<60ml/min/1.73m^2) by MDRD equation with adjustment for socio-demographic and clinical factors

Variable		MDRD				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	6.7	1	1	1	1
	2009-10	6.0	**0.84 (0.72 – 0.98)***	**0.84 (0.73 – 0.99)***	**0.75 (0.61 – 0.92)****	**0.75 (0.61 – 0.92)****
Age	16-34	0.2	1	1	1	1
	35-54	2.1	**10.8 (5.3 – 22.0)****	**11.1 (5.5 –22.8)****	**10.8 (5.0 – 23.4)****	**10.7 (4.9 – 23.2)****
	55-64	6.8	**37 (18 – 75)****	**36 (18 – 73)****	**33 (15 – 72)****	**32 (14 – 69)****
	65-74	14.5	**87 (43 – 175)****	**82 (40 – 167)****	**65 (30 – 143)****	**62 (28 – 135)****
	75+	35.6	**276 (138 – 555)****	**247 (122 – 501)****	**216 (99 – 470)****	**202 (93 – 440)****
Sex	Male	5.0	1	1	1	1
	Female	7.7	**1.42 (1.22 – 1.65)****	**1.37 (1.17 – 1.60)****	**1.69 (1.36 – 2.10)****	**1.66 (1.34 – 2.06)****
Ethnic	White	6.8	-	1	1	1
	South Asian	1.7	-	0.83 (0.43 – 1.59)	0.73 (0.33 – 1.60)	0.71 (0.32 – 1.56)
	Black	1.7	-	0.38 (0.15 – 1.00)	0.33 (0.09 – 1.19)	0.32 (0.09 – 1.16)
	Other	1.6	-	0.81 (0.29 – 2.30)	0.64 (0.17 – 2.46)	0.64 (0.17 – 2.44)
Tenure	Own	6.3	-	1	1	1
	Rent	6.6	-	**1.34 (1.11 – 1.60)****	1.23 (0.97 – 1.57)	1.23 (0.96 – 1.56)
Education	Degree Level	2.4	-	1	1	1
	Below degree	4.4	-	1.31 (0.99 – 1.74)	1.15 (0.83 – 1.60)	1.20 (0.84 – 1.70)
	None	14.9	-	**1.52 (1.13 – 2.04)****	1.20 (0.84 – 1.70)	1.23 (0.96 – 1.57)
Smoking	Never	6.1	-	-	1	1
	Ex-Smoker	10.1	-	-	1.17 (0.91 – 1.49)	1.15 (0.85 – 1.54)
	Current Smoker	3.2	-	-	1.02 (0.75 – 1.38)	1.04 (0.80 – 1.40)
BMI (kg/m^2)	Normal (<25)	3.4	-	-	1	1
	Overweight (25-30)	6.6	-	-	1.16 (0.91 – 1.49)	1.15 (0.90 – 1.47)
	Obese (>30)	8.4	-	-	1.31 (0.99 – 1.71)	1.26 (0.96 – 1.65)
HDL Cholesterol	Continuous	-	-	-	**0.51 (0.38 – 0.67)****	**0.51 (0.38 – 0.68)****
Total Cholesterol	Continuous	-	-	-	0.91 (0.84 – 1.00)	0.92 (0.84 – 1.00)
Doctor diagnosed Diabetes	No	5.9	-	-	1	1
	Yes	17.3	-	-	1.42 (0.92 – 2.22)	1.36 (0.87 – 2.11)
Doctor diagnosed Hypertension	No	4.0	-	-	-	1
	Yes	13.3	-	-	-	**1.27 (1.03 – 1.55)***

[1]Prevalence for combined 2003 and 2009-10 HSE
[2]Adjusted for age and sex

[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Table 4. Prevalence and associations of low eGFR (<60) by CKDEPI equation with adjustment for socio-demographic and clinical factors

Variable		CKDEPI				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	5.7	1	1	1	1
	2009-10	5.2	0.85 (0.72 – 1.00)	0.86 (0.72 – 1.01)	**0.73 (0.57 – 0.93)***	**0.73 (0.57 – 0.93)***
Age	16-34	0.1	1	1	1	1
	35-54	1.0	**15.1 (4.5 – 51.4)****	**16.1 (4.7 – 55.0)****	**13.8 (4.0 – 47.2)****	**13.5 (3.9 – 46.5)****
	55-64	4.2	**67 (20 – 225)****	**67 (20 – 227)****	**55 (16 – 190)****	**52 (15 – 177)****
	65-74	12.5	**219 (66 – 725)****	**219 (65 – 731)****	**162 (47 – 553)****	**151 (44 – 517)****
	75+	36.8	**890 (269 – 2938)****	**844 (253 – 2808)****	**754 (222 – 2559)****	**693 (203 – 2355)****
Sex	Male	4.6	1	1	1	1
	Female	6.3	1.15 (0.97 – 1.36)	1.11 (0.93 – 1.31)	**1.31 (1.01 – 1.68)***	**1.28 (1.00 – 1.65)***
Ethnic	White	5.8	-	1	1	1
	South Asian	1.4	-	0.93 (0.43 – 2.00)	0.89 (0.35 – 2.42)	0.85 (0.34 – 2.16)
	Black	2.0	-	0.56 (0.23 – 1.39)	0.55 (0.16 – 1.82)	0.53 (0.16 – 1.77)
	Other	1.6	-	1.19 (0.40 – 3.56)	1.13 (0.29 – 4.41)	1.13 (0.29 – 4.41)
Tenure	Own	5.3	-	1	1	1
	Rent	6.0	-	**1.44 (1.19 – 1.75)****	1.29 (0.98 – 1.69)	1.28 (0.97 – 1.69)
Education	Degree Level	1.8	-	1	1	1
	Below degree	3.6	-	1.36 (0.97 – 1.90)	1.05 (0.69 – 1.58)	1.04 (0.69 – 1.58)
	None	13.6	-	**1.51 (1.08 – 2.13)***	1.12 (0.76 – 1.66)	1.11 (0.75 – 1.65)
Smoking	Never	5.2	-	-	1	1
	Ex-Smoker	9.0	-	-	1.09 (0.77 – 1.55)	1.07 (0.75 – 1.52)
	Current Smoker	2.6	-	-	0.80 (0.70 – 1.41)	0.79 (0.54 – 1.14)
BMI (kg/m^2)	Normal (<25)	2.7	-	-	1	1
	Overweight (25-30)	5.5	-	-	1.14 (0.86 – 1.51)	1.12 (0.85 – 1.49)
	Obese (>30)	7.2	-	-	1.31 (0.96 – 1.80)	1.25 (0.91 – 1.72)
HDL Cholesterol	Continuous	-	-	-	**0.40 (0.29 – 0.56)****	**0.40 (0.29 – 0.57)****
Total Cholesterol	Continuous	-	-	-	0.93 (0.84 – 1.04)	0.94 (0.86 – 1.04)
Doctor diagnosed Diabetes	No	5.0	-	-	1	1
	Yes	16.3	-	-	1.55 (0.96 – 2.48)	1.46 (0.91 – 2.35)
Doctor diagnosed Hypertension	No	3.1	-	-	-	1
	Yes	12.3	-	-	-	**1.33 (1.05 – 1.67)****

[1]Prevalence for combined 2003 and 2009-10 HSE

[2]Adjusted for age and sex
[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010
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Abstract

Objectives
To determine whether the prevalence of CKD in England has changed over time.
Design
Cross-sectional analysis of nationally representative Health Survey for England (HSE) random samples.
Setting
England 2003 and 2009/2010.
Survey participants
13,896 Adults aged 16+ participating in HSE, adjusted for sampling and non-response, 2009/10 surveys combined.
Main outcome measure
Change in prevalence of eGFR <60ml/min/1.73m^2 (as proxy for stage 3-5 chronic kidney disease [CKD]), from 2003 to 2009/10 based on a single serum creatinine measure using IDMS traceable enzymatic assay in a single laboratory; eGFR derived using MDRD and CKDEPI eGFR formulae.
Analysis
Multivariate logistic regression modelling to adjust time changes for socio-demographic and clinical factors (body mass index, hypertension, diabetes, lipids). A correction factor was applied to the 2003 HSE serum creatinine to account for a storage effect.
Results
~~National prevalence of low eGFR (<60) decreased from 9.6% to 6.0% using MDRD (P<0.001) and from 7.6% in 2003 to 5.2% in 2009/10 using CKDEPI (p<0.001).~~ National p~~P~~revalence of low eGFR (<60) decreased within each age and gender group for both formulae except males aged 65-74. Prevalence of both obesity and diabetes increased in this period, there was a decrease in hypertension. Adjustment for demographic and clinical factors led to a significant decrease in CKD between the surveyed periods. The fully adjusted odds ratio for eGFR<60ml/min/1.73m^2 was ~~0.49 (0.42 0.57)~~ 0.75 (0.61-0.92) comparing 2009/10 with 2003 using the MDRD equation, and was similar using the CKDEPI equation 0.73 (0.57-0.93).
Conclusion
The prevalence of a low eGFR indicative of CKD in England has decreased over this seven year period, despite rising prevalence of obesity and diabetes, two key causes of CKD. Hypertension prevalence declined and blood pressure control improved but this did not appear to explain the fall. Periodic assessment of eGFR and albuminuria in future HSEs is needed to evaluate trends in CKD.

Article Summary

Strengths & Limitations of this study

- This study uses of nationally representative samples, with later HSEs pooled over two years to increase numbers and precision of estimates. The surveys used standardised protocols for measurement by trained interviewers and nurses, with all samples were tested in the same laboratory with standardised assays.
- Another strength of the study is that the analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. Weighting was introduced for both surveyed periods to reduce response bias and account for missing data. A correction factor was applied to 2003 HSE data to adjust for the shift in measured creatinine due to sample storage.
- The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. The study was also limited by a single sample was tested for serum creatinine in each survey,

therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown.

- ~~Another weakness is that~~ The prevalence of stage 4/5 CKD is likely to be underestimated as the HSE may not fully account for some in whom more severe CKD (stage 4/5) will be more common.
- The absence of albuminuria data in the 2003 HSE is another major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management ~~(e.g. use of RAS inhibition).~~ (e.g. use of renin-angiotensin system (RAS) inhibition).

Total word count n=~~3225~~ 3,844

Introduction

Chronic kidney disease (CKD) is recognised as a global public health problem.[1] CKD is defined and staged using the estimated glomerular filtration rate (eGFR) and markers of kidney damage, mainly albuminuria.[2] Both eGFR and albuminuria are strong independent risk factors for all-cause and cardiovascular disease (CVD) mortality, and progression to end-stage renal disease (ESRD), which may require renal replacement therapy (RRT) by dialysis or transplantation.[3] In England in 2010 the prevalence of RRT was 832 per million population, a 3% increase from 2009; NHS costs of RRT were estimated at £780 million for 2009/10, and the total cost at £1.45 billion, a nearly threefold increase on estimated costs for 2002.[4,5]

The population prevalence of CKD in England was reported for the first time using data on eGFR and albuminuria in the nationally-representative Health Surveys for England (HSE) 2009 and 2010, though there had previously been estimates based on routine testing using primary care data.[6,7] In the combined 2009/2010 HSE, 6% of men and 7% of women had eGFR <60ml/min/1.73m^2 (equivalent to CKD stage 3-5 if chronic) with a strong age gradient.[8] The prevalence of low eGFR increased in the US, based on National Health and Nutrition Examination (NHANES) surveys between 1988-2004, even after adjusting for adverse trends in risk factors (obesity, diabetes, hypertension), but little is known about CKD prevalence trends in England.[9,10,11]

Information on prevalence change is needed to assess the impact of trends in underlying determinants, and of strategies to prevent and manage CKD. Several policy initiatives have been introduced in England that have had an impact on prevention, detection and management of CKD. The National Service Framework for Renal Services 2004/05 led to national reporting of eGFR by clinical biochemistry laboratories from 2006,[12] the General Practice pay for performance Quality Outcomes Framework (QOF) included targets for CKD management from 2006/07,[13] and the NHS Vascular Checks Programme, introduced in 2009, includes screening for CKD (stage 3-5) in people aged 35-74 with newly identified type 2 diabetes or hypertension.[14] This study therefore aimed to compare the prevalence of CKD in the HSE 2003 with the combined HSE 2009-10 and to relate this to any changes in prevalence of risk factors for CKD, particularly obesity, diabetes and hypertension, over this period.

Methods

Full details of the conduct of the HSE, measurement of non-CKD variables and response rates are shown in the 2003, 2009 and 2010 Health Survey for England reports.[15,16] Survey participants within private households were selected using a multistage stratified random probability sample. Household response rates were 73% in HSE2003 and 68%/66% in HSE 2009/2010. In co-operating households, 90% and 89%/86% of adults completed an interview questionnaire while 70% and 62%/57% respectively consented to a nurse visit, of whom 74%-76% provided a blood test. The HSE 2003 contained 18,533 individuals and data from HSE 2009 and HSE 2010 were combined to provide a larger sample size of 13,065 individuals. This totalled 31,598 individuals for the combined 2003, 2009 and 2010 HSEs. Eligible participants were individuals aged 16 years and older who had a valid serum creatinine value. This left 7,850 individuals from the 2003 HSE and 6,046 individuals from the combined 2009/10 HSEs, leaving a total of 13,896 individuals for analysis.

Age was grouped into five categories: 16-34, 35-54, 55-64, 65-74 and 75+. There were four separate ethnic groupings: White, South Asian, Black and Other. Socio-economic factors included: i) occupation National Statistics Socio-Economic Classification (NS-SEC, divided into three categories: managerial and professional occupations; intermediate occupations and routine and manual occupations); ii) qualifications grouped as: degree or equivalent; below degree (other qualification) and none (no qualification); iii) household tenure (own vs renting); iv) access to motor vehicle (none vs. any).

Smoking status was defined as current, ex-smoker or never smoked. Hypertension was defined as doctor-diagnosed (pre-existing diagnosis), survey-defined (identified as having high blood pressure (BP, systolic ≥140mmHg and/or diastolic ≥90mmHg and/or taking medication for hypertension) at the survey examination), and 'total' (doctor + survey diagnosed). Survey-defined diabetes was glycated haemoglobin (HBA1c) ≥6.5% at nurse visit. Glycated haemoglobin data are presented for those with and without diagnosed diabetes. Body mass index (BMI) was defined as normal (<25kg/m^2), overweight (≥25, <30kg/m^2), and obese (≥30kg/m^2). Waist circumference was classified as: <94cm, 94–102cm (high), and >102cm (very high) for men, and <80cm, 80–88cm (high) and >88cm (very high) for women. For South Asian men, the waist circumference was classified as: <90cm, 90–102cm (high), and >102cm (very high). High density lipoprotein (HDL) cholesterol and total cholesterol were treated as continuous variables.

To investigate medication use, we examined the use of diuretics, ß-blockers, renin-angiotensin system (RAS) inhibitors (angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)), calcium channel blockers, and other anti-hypertensives in those with doctor diagnosed hypertension, doctor diagnosed diabetes and eGFR <60ml/min/1.73m^2, and use of lipid lowering agents (the majority of which are statins) in the whole population. In 2003, 47% of respondents answered yes to whether they were taking any prescribed medication, and 50% in 2009/10.

Serum creatinine was assayed using an isotope dilution mass spectrometry (IDMS) traceable enzymatic assay in a single laboratory (Clinical Biochemistry Department at the Royal Victoria Infirmary (RVI), Newcastle-upon-Tyne). Both the Modified Diet in Renal Disease (MDRD) equation (in routine use in the UK) and the newer Chronic Kidney Disease Epidemiology Collaboration (CKDEPI) equation (which provides better risk prediction and is

recommended for use in international guidelines) were used to define CKD.[2,17] eGFR values were derived using the standard equations.[18,19]

Samples were assayed for serum creatinine over a 19 month time period with two different batches of tri-level Internal Quality Control (IQC) material. HSE 2009 and 2010 samples were analysed with Batch 1 or Batch 2 IQC, HSE 2003 samples were analysed with Batch 2 IQC. The creatinine assay was stable over time with IQC results very close to expected target values. Batch 1 IQC gave mean (SD) creatinine concentrations of 56(0.6),167(1.3) and 586(4.9) umol/L for levels 1,2 and 3 respectively compared with target means of 56, 167 and 588 umol/L. Batch 2 material gave mean(SD) creatinine concentrations of 51(1.1), 175(2.2) and 597(5.6)umol/L for levels 1,2 and 3 respectively compared with target means of 51, 175 and 599 umol/L.

Details of laboratory analysis, internal quality control, and external quality assurance are provided in the HSE 2009/10 documentation, with these methods replicated in the 2003 HSE.[8] ~~The HSE 2003 samples had been stored, frozen at -40°C, then thawed for measurement in 2012. Such freezing does not affect creatinine levels.~~[20] The HSE 2003 samples had been stored, frozen at -40°C, then thawed for measurement in 2010. Although such freezing is not thought to affect creatinine levels[20] we undertook a re-analysis in 2014 of a random sample of 500 serum creatinine samples taken from the 2009 HSE and subsequently frozen and stored under the same conditions as the HSE 2003 samples, stratified by quintile, to determine if there was a shift in measured creatinine on storage. We found mean serum creatinine increased on storage and was best predicted by a regression equation where the original 2009 serum creatinine value without storage equaled 0.303 plus 0.94 multiplied by the stored serum creatinine value. We assumed the same effect applied to the 2003 serum creatinine data which were analysed in 2009-10 and we applied the same adjustment. This decreased the 2003 serum creatinine values. eGFR was classified as below 60ml/min/1.73m^2 or equal to or greater than 60ml/min/1.73m^2.

~~Samples were assayed for serum creatinine over a 19 month time period with two different batches of tri-level Internal Quality Control (IQC) material. HSE 2009 and 2010 samples were analysed with Batch 1 or Batch 2 IQC, HSE 2003 samples were analysed with Batch 2 IQC. The creatinine assay was stable over time with IQC results very close to expected target values. Batch 1 IQC gave mean (SD) creatinine concentrations of 56(0.6),167(1.3) and 586(4.9) umol/L for levels 1,2 and 3 respectively compared with target means of 56, 167 and 588 umol/L. Batch 2 material gave mean(SD) creatinine concentrations of 51(1.1),175(2.2) and 597(5.6)umol/L for levels 1,2 and 3 respectively compared with target means of 51, 175 and 599 umol/L.~~ We compared the change in mean serum creatinine in people aged 20-39 without any diabetes or any hypertension as per Coresh at al.[9]

Statistics

Patient characteristics were compared between the 2003 and 2009/10 HSEs using chi-squared tests for categorical variables and Mann Whitney U tests for non-normally distributed continuous variables. eGFR<60ml/min/1.73m^2 prevalence in 2003 and 2009/10 was compared across age and sex groupings. BP levels were compared in all, in those with diagnosed hypertension and in those with eGFR<60ml/min/1.73m^2; glycated haemoglobin (HBA1c) was compared in all participants and in those with doctor-diagnosed diabetes. Binary logistic regression models were used to examine the relationships between eGFR<60ml/min/1.73m^2 and age, sex and socioeconomic and clinical factors to determine if there were significant differences between the two survey time periods. The dependent variable were CKDEPI and MDRD equation eGFR <60ml/min/1.73m^2 (indicative of stage 3-5 CKD). Four models were produced for each: 1) Age-sex adjusted; 2) model 1 plus socio-economic status and ethnicity; 3) model 2 plus behavioural, lipid levels (HDL and total

cholesterol) and clinical variables except hypertension, 4) Model 3 plus doctor-diagnosed hypertension. Interactions between period and both diabetes and hypertension were tested.

Sensitivity analyses were performed by replacing doctor-diagnosed diabetes with HBA1c and replacing doctor-diagnosed hypertension with diastolic and systolic blood pressure and adjusting for lipid lowering agents in the full model. Non-response and blood sample weights were used in all analyses to address issues with missing ~~data~~ individuals who did not have a blood sample taken and sent to laboratory for analysis to determine serum creatinine value. Full details on how the weights were obtained are provided in the final volume of the HSE report each year. The age, education and smoking status of those interviewed, having a nurse visit and having a blood test is similar once non-response is taken into account (data not shown). All analyses were performed using IBM SPSS Statistics version 20.

Results

The final sample for the study comprised of 13,896 individuals aged 16+ who had a valid serum creatinine value. Comparing the characteristics of these participants between the 2003 and 2009/10 surveys, the age structure, gender, NS-SEC and car ownership were similar while educational level improved and there was an increase in rented tenure (Table 1). Prevalence of diabetes however classified increased, as did obesity. In contrast, smoking and hypertension prevalence decreased.

There were significant increases in BMI, waist circumference and HBA1c in the population though no change in HBA1c in those with diagnosed diabetes (Table 2). Median BP levels (both systolic and diastolic) fell in all groups including those with diagnosed hypertension, doctor-diagnosed diabetes and with eGFR<60ml/min/1.73m^2. Median total and HDL cholesterol fell in both men and women.

The distribution of serum creatinine ~~was shifted to the left in 2009/10; 1.7% values were greater than 130µmol/L in 2003, but only 0.1% in 2009/10~~ is similar for 2003 and 2009/10 (Figure 1). ~~Mean serum creatinine decreased, leading to an increase in mean eGFR using both MDRD and CKDEPI formulae~~ Median serum creatinine increased slightly, leading to a very small non-significant decrease in median eGFR using both MDRD and CKDEPI formulae (Table 2). Mean serum creatinine for those aged 20-39 without doctor diagnosed hypertension or diabetes ~~fell significantly from 74.8µmol/L (SD 14.8) in 2003 to 71.4µmol/L (SD 14.3) in 2009/10 (p<0.001)~~ increased slightly from 70.6µmol/L (SD 13.6) in 2003 to 71.4µmol/L (SD 14.3) in 2009/10 (p=0.09).~~.~~

The proportion of individuals with MDRD eGFR<60ml/min/1.73m^2 decreased from ~~9.66~~6.7% in 2003 to 6.0% in 2009/10 (~~p<0.001~~p=0.13) and with eGFR <45ml/min/1.73m^2 from ~~2.4~~1.9% to 1.4% (p~~<0.001~~=0.03). Corresponding figures for CKDEPI were ~~7.65~~7% and 5.2% (p~~<0.001~~=0.26) and ~~2.2~~1.8% and 1.4% (p=0.0~~01~~7). Prevalence of low eGFR fell in all age and gender groups and with either CKDEPI or MDRD equations, except for males aged 65-74 where there was a slight increase (Figure 2).

There was an increase in the mean number of anti-hypertensive agents taken in individuals with: doctor-diagnosed hypertension (1.19 in 2003 to 2.01 in 2009-10), doctor-diagnosed hypertension and doctor-diagnosed diabetes (1.47 to 2.57); MDRD eGFR <60ml/min/1.73m^2 (1.~~26~~30 to 1.77); and CKDEPI eGFR < 60ml/min/1.73m^2 (1.~~29~~35 to 1.93). The proportion taking RAS inhibitors in individuals with doctor-diagnosed diabetes, doctor-diagnosed hypertension, MDRD eGFR <60ml/min/1.73m^2 or CKDEPI eGFR < 60ml/min/1.73m^2 also increased, as did overall lipid lowering agent use (Appendix 1).

The age-sex adjusted odds ratio (OR) of having low eGFR (MDRD eGFR<60ml/min/1.73m^2) in 2009/10 compared with 2003 was 0.~~52~~84 (95% confidence interval (CI) 0.~~45~~72-0.98~~60~~) and fully adjusted was 0.75 (0.61-0.92) (Table 3). ~~This pattern was maintained on further adjustment for potential confounding factors (Table 3) and when using CKDEPI eGFR (Table 4).~~ The corresponding ORs for CKDEPI were 0.85 (0.72-1.00) and 0.73 (0.57-0.93) (Table 4).

Sensitivity analyses replacing doctor-diagnosed diabetes with HBA1c and doctor-diagnosed hypertension with diastolic and systolic BP made little difference to the adjusted ORs as did the inclusion of lipid lowering agents. No interactions between period and diabetes or hypertension were identified.

Discussion

These analyses show that CKD prevalence in England estimated by serum creatinine based equations in England decreased from 2003 to 2009/10. This decrease was seen across all age groupings (except makes aged 65-74), for CKD defined by both MDRD and CKDEPI eGFR equations ~~(though more pronounced for the MDRD equation), and despite~~ was more pronounced for the MDRD equation and occurred despite increased prevalence of both diabetes and obesity.[21] Using the CKDEPI equation in place of MDRD to define CKD resulted in a lower prevalence of CKD. Whilst it reduces overall prevalence, the CKDEPI equation identifies more individuals aged 75+ with CKD compared with the MDRD equation.[22,23]

The HSE 2003, 2009 and 2010 were nationally representative samples, with the 2009/10 data pooled over two years to increase numbers and precision of estimates. The age-sex characteristics of the different study periods sampled were similar. The surveys used standardised protocols for measurement by trained interviewers and nurses. All samples were tested in the same laboratory with standardised assays. The analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the

application and comparison of the two equations to derive eGFR. ~~Weighting was introduced for both surveyed periods to reduce response bias and account for missing data.~~ We accounted for the shift in measured creatinine on storage in the 2003 HSE serum creatinine data by introduction of a correction factor derived from analysis of the effect of storage using 2009 data. Non-response weighting was undertaken in the HSE for both surveyed periods to reduce response bias and account for missing data for individuals who did not have blood sample taken and hence no serum creatinine value. We used both the HSE study design and the non-response weights to provide national prevalence estimates at each period and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences. The ethnic composition of the surveys changed over time with a small fall in the White population, but we adjusted for this change in the analysis.

The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. However the use of new, cross-sectional samples enables measurement of general population CKD prevalence at different time points. A single sample was tested for serum creatinine in each survey, and therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown. This is standard practice in national surveys such as NHANES, whereas studies based on routine testing can assess chronicity, such as the QICKD study. [24] Given the individual variation in kidney function, more extreme values will be averaged out on repeated testing (regression to the mean), reducing the prevalence of low eGFR.[24] The results may therefore slightly overestimate the prevalence of CKD. ~~Despite high numbers of participants,~~ There were too few cases from the key minority ethnic groups to give robust data on ethnic differences in prevalence of CKD~~, over 90% of the participants for both survey periods were white (data not shown).~~ South Asians and Black groups have higher rates of renal replacement but have been found to have lower prevalence of CKD than Caucasians.[25,26]

Prevalence of stage 4/5 CKD is likely to be underestimated as, whilst the HSE is able to adjust for non-response among the general population in private households, it may not fully account for some in whom more severe CKD (stage 4/5) will be more common. This includes people who were not able to give a blood or urine sample because of poor health and those who did not participate due to concurrent illness or hospitalisation, as well as those in residential care.

The absence of albuminuria data in the 2003 HSE is a major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of RAS inhibition).[3] We have therefore been unable to estimate changes in prevalence of albuminuria per se, in all CKD (stages1-5), and fully assess prevention and management.

The fall in low prevalence of eGFR could be due i) chance ii) artefact of differences in the serum creatinine measurement, iii) changes in serum creatinine production rather than excretion by the kidney, iv) residual confounding by differences in sample characteristics not adjusted for by sample weighting, v) true fall in eGFR. ~~The period effects were highly statistically significant making chance unlikely. The 2003 assay results data were from stored sera, however this should be stable for creatinine even after long storage.[20] Moreover, if the 2003 serum creatinine had been underestimated this would have reduced any fall over the period.~~ The two sets of samples were analysed in multiple analytical runs over a 19 month time period, which could lead to differences in results, however during this time period the internal quality control data indicates that the assay was accurate compared with assigned target values and stable~~, with no indication of assay drift with time~~. ~~Artefact due to serum creatinine measurement changes does not seem to be the explanation. A fall in serum creatinine over time independent of kidney function could be due to less muscle~~

~~mass (leading to lower serum creatinine production); there is no evidence for this and it seems unlikely to have occurred at the population level. A fall in dietary protein consumption from cooked meat could also lead to fall in serum creatinine. Cooked meat consumption has been shown to increase serum creatinine in small case studies of volunteers and of patients with diabetic nephropathy and hence national guidance is to avoid eating cooked meat for 12 hours before a blood test for creatinine[27] but this was not done in HSE. We used the HSE study design and non response weights and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics differences is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences.~~

A change in serum creatinine over time independent of kidney function could be due to less muscle mass (leading to lower serum creatinine production); there is no evidence for this and it seems unlikely to have occurred at the population level.

A decline in dietary protein consumption from cooked meat could also lead to change in serum creatinine. Statistics from the National Diet and Nutrition Survey show that meat consumption increased from 2001-02 to 2008-10 while protein intake remained virtually stable over the same period. [28] Mean consumption of meat and meat products increased from 154g per day in 2001-02 to 194g per day in 2008-10; protein intake contributing to food energy for adults aged 19+ increased slightly from 16-17% in 2001-02 to 17-18% in 2008-10; meat and meat products contributed to 37-38% of all protein intake for adults aged 19-64, with little change compared to 2008-10. Cooked meat consumption has been shown to increase serum creatinine in small case studies of volunteers and of patients with diabetic nephropathy and hence national guidance is to avoid eating cooked meat for 12 hours before a blood test for creatinine[29] but this was not done in HSE.

We used the HSE study design and non-response weights and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics differences is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences.

Key risk groups for developing CKD are those with hypertension and or diabetes especially if they have albuminuria. In this study there was evidence of modest reductions in the prevalence of hypertension, better control of hypertension in key groups, and greater use of RAS inhibitors which have anti-proteinuric as well as BP lowering effects, though the period changes in eGFR remained after correction for changes in hypertension prevalence. There is evidence from some studies using HSE, primary care databases and QOF data,[28-30] though not all,[31] of improved hypertension control in the last decade. However there are ethnic disparities with poorer control of BP in Black and South Asians who have higher risk of progression to need RRT.[32] Population salt consumption also fell during the last decade which is likely to have influenced population BP.[33,34] CKD prevalence could fall too if those identified with moderate CKD were treated more aggressively, especially those with hypertension and or albuminuria, leading to increased eGFR in some people to above 60ml/min/1.73m^2. The limited HSE data suggest better BP control and greater use of RAS inhibitors in those with eGFR <60ml/min/1.73m^2. Karunetatne et al examined BP control in those with and without CKD in a primary care population in Kent and showed that BP control had improved in CKD patients over time pre- and post the introduction of QOF and that it was greater than in non-CKD hypertensive patients. They also showed increased use of RAS inhibitors and other anti-hypertensive agents in CKD patients.[35] ~~Whilst there was a small fall in population lipid levels and some evidence of increased statin use, this would not be expected to lead to a reduced incidence of CKD, and our period changes were not altered by adjusting for lipid levels.[36]~~

There was evidence of increased lipid lowering agent use (indicative of increased statin use) and a small fall in population lipid levels. There is some evidence of reno-protective effects of statins in CKD patients; A lower rate of decline in GFR was found in patients with renal disease who took antilipemic agents.[38] In the Heart Protection Study, the use of the hypolipidemic drug simvastatin reduced the rise in slightly elevated creatinine over time in both diabetic and non-diabetic CKD participants.[39] In the SHARP trial allocation of the lipid lowering ezetimibe plus simvastatin in participants not already on dialysis at randomisation reduced the outcome of end stage renal disease or a doubling of creatinine with an odds ratio of 0.93, though this was not statistically significant.[40] In the GREACE trial statin treatment prevented decline in renal function in people with high blood lipids and coronary heart disease; patients not treated with statins showed a 5.2% decrease in creatinine clearance, while patients treated with statins showed a 4.9% increase in creatinine clearance.[41] However our period changes were not altered by adjusting for statins (lipid lowering drugs) or lipid levels (HDL, total cholesterol).[37]

There are limited data from other countries with which to compare these findings. Coresh et al analysed the US NHANES surveys of 1988-1994 and 1999-2004, which both collected albuminuria and eGFR data. Both prevalence of albuminuria and MDRD eGFR <60ml/min/1.73m^2 increased, the latter from 5.6% to 8.1%.[8] The albuminuria increase was explained by changes in levels of obesity, diabetes and hypertension, whereas this adjustment only partly explained eGFR falls. Changes in population serum creatinine explained most of the remainder of the eGFR changes; this was analysed by comparing the mean serum creatinine in young people aged 20-39 without diabetes or hypertension and this had increased across the surveys.[9] The authors suggested that this rise in serum creatinine could be due to residual laboratory assay differences or to changes in dietary protein or muscle mass. Grams et al showed that prevalence of eGFR<60ml/min/1.73m^2 had also increased using the same survey data when eGFR was estimated using Cystatin C, a marker of kidney function that is independent of muscle mass, and this was not explained by changes in demography, hypertension, diabetes or obesity, suggesting a true increase in low eGFR.[37]

We can compare the estimated national CKD prevalence for HSE with QOF returns which record diagnosed CKD in primary care.[43] Prevalence has been increasing with improvements in detection and recording and in 2010 was 4.2%. The figures are not directly comparable as comparing a single screened value versus routine testing with presumed allowance for chronicity, but this may suggest some under-diagnosis of CKD.

If this change in prevalence in England is true, then based on the HSE 2003 age-sex-specific estimates and 2001 and 2011 Census data, the estimated number of CKD cases (for those aged 16 and over) would be 2.62 million based on the MDRD equation, falling by 0.03 million for 2009/10. Equivalent figures for CKDEPI eGFR <60ml/min/1.73m^2 are 2.23 million and 0.02 million increase respectively. The impact of such changes would be twofold: a consistent pool of patients at risk of progressing to need RRT; and a contribution to consistent cardiovascular incidence and mortality. The former is supported by stabilised acceptance rates onto RRT in England.[4]

~~If this change in prevalence in England is true, then based on the HSE 2003 age-sex-specific estimates and 2001 and 2011 Census data, the estimated number of CKD cases (for those aged 16 and over) would be 3.77 million based on the MDRD equation, falling by 1.18 million for 2009/10. Equivalent figures for CKDEPI eGFR <60ml/min/1.73m^2 are 2.98 million and 0.75 million respectively. The impact of such changes would be twofold: a reduced pool of patients at risk of progressing to need RRT; and a contribution to falling~~

~~cardiovascular incidence and mortality. The former is supported by stabilised acceptance rates onto RRT in England.[4]~~

Conclusions

The prevalence of a low eGFR appears to have decreased in England from 2003 to 2009/10, despite increases in obesity and diabetes. It is unclear why this has occurred and it is difficult to infer directly that this is due to current policies to improve prevention of CKD and the identification and management of people with CKD. There is a need for repeated national prevalence estimates to further assess CKD patterns over time, including measures of albuminuria and of Cystatin C, both of which were available in HSE 2009 and 2010.

What is already known on this topic

- eGFR and albuminuria are strong independent risk factors for progression to end-

stage renal disease (ESRD), which may require costly renal replacement therapy (RRT)
- Prevalence of low eGFR has increased over time in countries such as the US, even after adjustment for adverse trends in CKD risk factors
- Little is known about CKD prevalence trends in England

What this study adds
- Prevalence of a low eGFR derived from serum creatinine and indicative of CKD in England has decreased from 2003 to 2009/10, despite increasing prevalence of diabetes and obesity
- This pattern of prevalence of low eGFR was maintained even after adjustment for potential mediating and confounding factors
- A future need for repeated national prevalence estimates, that includes measures of albuminuria and Cystatin C, is required to further assess CKD patterns over time.

Contributors: GA was involved in the analysis and interpretation of the data. PR drafted the paper. GA, PR, SF and GM made substantial contributions to the study conception and

design. JM co-ordinated the Health Surveys for England. DO provided background information on CKD policy. JD conducted the laboratory analyses. All authors critically reviewed the paper and were involved in the drafting and approval of the manuscript. GA is the guarantor.

Acknowledgements: Scott Harris contributed to the production of the regression equation that was applied to the 2003 serum creatinine samples as a correction factor.

Funding: Kidney function testing in the Health Surveys for England was funded by NHS Kidney Care. GA is funded by a University of Southampton PhD scholarship.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Approval was obtained from the London Multi-Centre Research Ethnics Committee for the 2003 survey (HSE 2003 ref MREC/02/2/72) and approval was obtained from the Oxford B Research Ethics Committee for both 2009 and 2010 surveys (HSE 2009 ref 08/H0605/103, HSE 2010 ref 09/H0605/73).

Transparency: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: The HSE 2003, 2009 and 2010 are archived with the UK Data Service. Creatinine measurements for the HSE 2003 undertaken for this study will be archived in due course.

Figure Legends

Figure 1. Distribution of serum creatinine (µmol/L) for 2003 and 2009/10 survey data. Serum creatinine categories are grouped in bands of 5 µmol/L from 40µmol/L to 130µmol/L. Serum creatinine values <40 µmol/L and those >130µmol/L are grouped together.

Figure 2. Comparison of low eGFR (<60ml/min/1.73m^2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender

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Table 1. Comparison of prevalence of categorical measures in 2003 and 2009/10[1]

Variable	Category	2003		2009-10		Chi-squared test
		Number	%	Number	%	p-value
All	Aged 16+	7850[2]	100.0	6046[2]	100.0	-
Age	16-34	2425	31.0	1847	30.6	p = 0.441
	34-54	2790	35.7	2129	35.3	
	55-64	1126	14.4	886	14.7	
	65-74	813	10.4	639	10.6	
	75+	662	8.5	539	8.9	
	Missing	0	-	0	-	
Ethnicity	White	7226	92.5	5244	90.7	**p < 0.001**
	South Asian	332	4.3	243	4.2	
	Black	144	1.8	154	2.7	
	Other	108	1.4	139	2.4	
	Missing	0	-	0	-	
Sex	Male	3795	48.6	2961	49.0	p = 0.803
	Female	4020	51.4	3080	51.0	
	Missing	0	-	0	-	
Qualification	Degree	1375	17.6	1295	22.5	**p < 0.001**
	Below degree	4551	58.3	3296	57.0	
	None	1874	24.0	1191	20.6	
	Missing	11	-	3	-	
NSSEC	Highest	2514	33.7	1894	34.8	p = 0.434
	Middle	1674	22.4	1203	22.1	
	Lowest	3273	43.9	2343	43.1	
	Missing	350	-	345	-	
Car Ownership	Yes	6460	82.7	4728	81.7	p = 0.1768
	No	1348	17.3	1056	18.3	
	Missing	2	-	1	-	
Tenure	Own	5878	75.4	3955	68.5	**p < 0.001**
	Rent	1914	24.6	1817	31.5	
	Missing	11	-	13	-	
Smoking	Current	1960	25.2	1210	21.0	**p < 0.001**
	Ex	1877	24.1	1429	24.8	
	Never	3951	50.7	3126	54.2	
	Missing	22	-	20	-	
Body mass index	Normal /underweight (<25kg/m^2)	2867	39.2	1956	36.8	**p < 0.001**
	Overweight (25-30 kg/m^2)	2868	39.2	2047	38.5	
	Obese (>30kg/m^2)	1587	21.7	1314	24.7	
	Missing	489	-	469	-	
Waist Circumference	Low (<94cm male, <80cm female)	3060	39.8	2120	37.1	**p < 0.001**
	High (94-102cm male, 80-88cm female)	1929	25.1	1347	23.6	

	Very High (>102cm male, >88cm female)	2703	35.1	2242	39.3	
	Missing	118	-	77	-	
Doctor diagnosed Diabetes	Yes	305	3.9	322	5.3	**p < 0.001**
	No	7504	96.1	5715	94.7	
	Missing	6	-	2	-	
Survey diagnosed Diabetes	Yes (HBA1c ≥6.5%)	296	3.8	316	5.5	**p < 0.001**
	No (HBA1c <6.5%)	7401	96.2	5417	94.5	
	Missing	113	-	52	-	
Total Diabetes	Yes	406	5.2	446	7.4	**p < 0.001**
	No	7405	94.8	5585	92.6	
	Missing	0	-	0	-	
Doctor diagnosed Hypertension	Yes	2118	27.2	1501	25.0	**p = 0.003**
	No	5662	72.8	4527	75.0	
	Missing	36	-	10	-	
Survey diagnosed Hypertension	Yes	2065	31.5	1545	29.2	**p = 0.0219**
	No	4499	68.5	3744	70.8	
	Missing	1246	-	496	-	
Total Hypertension	Yes	2866	36.7	2062	34.2	**p = 0.004**
	No	4933	63.3	3968	65.8	
	Missing	12	-	0	-	
eGFR CKDEPI	<45 (ml/min/1.73m^2)	142176	1.82.2	8181	1.41.4	p = 0.07**p = 0.001**
	<60 (ml/min/1.73m^2)	444594	5.77.6	303303	5.25.2	p = 0.26**p < 0.001**
	Missing	00	--	00	--	
eGFR MDRD	<45 (ml/min/1.73m^2)	146186	1.92.4	8080	1.41.4	**p = 0.03p < 0.001**
	<60 (ml/min/1.73m^2)	521751	6.79.6	349349	6.06.0	p = 0.13**p < 0.001**
	Missing	0	-	0	-	

[1] Weighted for non-response (unless stated otherwise)
[2] Not weighted

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Table 2. Weighed Comparison of continuous measures in 2003 and 2009-10

Variable	Category	2003	2009-10	Mann Whitney U test
		Median value (IQR)	Median value (IQR)	p value
Serum Creatinine (µmol/L)	Median value	71.7 (62.3 to 82.1)~~76.0 (66.0 to 87.0)~~	72.0 (62.0 to 83.0)~~72.0 (62.0 to 83.0)~~	p=0.66~~**p<0.001**~~
eGFR (ml/min/1.73m^2)	MDRD	90.5 (77.2 to 105.4)~~84.7 (72.2 to 98.7)~~	90.3 (77.1 to 104.7)~~90.3(77.1 to 104.7)~~	p=0.62~~**p<0.001**~~
	CKDEPI	99.3 (84.1 to 113.9)~~94.3 (78.6 to 109.7)~~	98.6 (84.0. to 112.5)~~98.6 (84.0. to 112.5)~~	p=0.11~~**p<0.001**~~
BMI (kg/m^2)	All	26.2 (23.3 to 29.4)	26.6 (23.5 to 30.0)	**p<0.001**
	Male	26.6 (24.0 to 29.4)	27.0 (24.2 to 29.9)	**p=0.001**
	Female	25.7 (22.7 to 29.5)	26.1 (23.1 to 30.0)	**p<0.001**
Waist circumference (cm)	All	90.6 (81.1 to 100.0)	92.0 (81.6 to 101.7)	**p<0.001**
	Male	95.8 (88.0 to 104.0)	96.7 (88.2 to 105.0)	p=0.052
	Female	84.6 (76.4 to 94.0)	86.3 (77.3 to 96.7)	**p<0.001**
Systolic BP (mmHg)	All	125.5 (115.5 to 138.0)	124.5 (114.0 to 136.0)	**p<0.001**
	Dr-diagnosed HT	135.5 (124.0 to 149.5)	134.0 (122.2 to 145.5)	**p<0.001**
	Dr-diagnosed DM	134.5 (122.5 to 148.0)	131.8 (120.0 to 143.5)	**p<0.001**
	CKD (CKDEPI)	139.5 (126.0 to 154.5)	131.8 (119.0 to 143.5)	**p<0.001**
	CKD (MDRD)	137.0 (123.0 to 151.0)	129.2 (118.0 to 142.5)	**p<0.001**
Diastolic BP (mmHg)	All	73.0 (65.5 to 80.5)	72.5 (65.5 to 80.)	**p<0.001**
	Dr-diagnosed HT	77.5 (70.0 to 85.5)	76.0 (68.0 to 83.5)	**p<0.001**
	Dr-diagnosed DM	72.0 (64.5 to 80.5)	71.50 (64.5 to 78.5)	**p<0.001**
	eGFR<60 (CKDEPI)	72.0 (64.5 to 80.5)	68.5 (60.5 to 76.0)	**p<0.001**
	eGFR<60 (MDRD)	73.0 (65.5 to 81.5)	69.0 (61.5 to 76.8)	**p<0.001**
Glycated Hb (%)	All	5.20 (5.00 to 5.50)	5.30 (5.10 to 5.70)	**p<0.001**
	Dr-diagnosed DM	6.90 (5.90 to 8.20)	6.90 (5.90 to 8.30)	p=0.8546
HDL Cholesterol (mmol/L)	All	1.50 (1.20 to 1.70)	1.40 (1.20 to 1.70)	**p<0.001**
	Male	1.30 (1.20 to 1.60)	1.30 (1.10 to 1.50)	**p<0.001**
	Female	1.60 (1.40 to 1.90)	1.60 (1.30 to 1.90)	**p=0.0546**
Total Cholesterol (mmol/L)	All	5.40 (4.70 to 6.20)	5.20 (4.40 to 5.90)	**p<0.001**
	Male	5.40 (4.70 to 6.20)	5.10 (4.30 to 5.90)	**p<0.001**

	Female	5.40 (4.70 to 6.20)	5.20 (4.50 to 6.00)	**p=0.001**

~~**Figure 1. Distribution of serum creatinine (μmol/L) for 2003 and 2009/10 survey data. Serum creatinine categories are grouped in bands of 5 μmol/L from 40μmol/L to 130μmol/L. Serum creatinine values <40 μmol/L and those >130μmol/L are grouped together.**~~

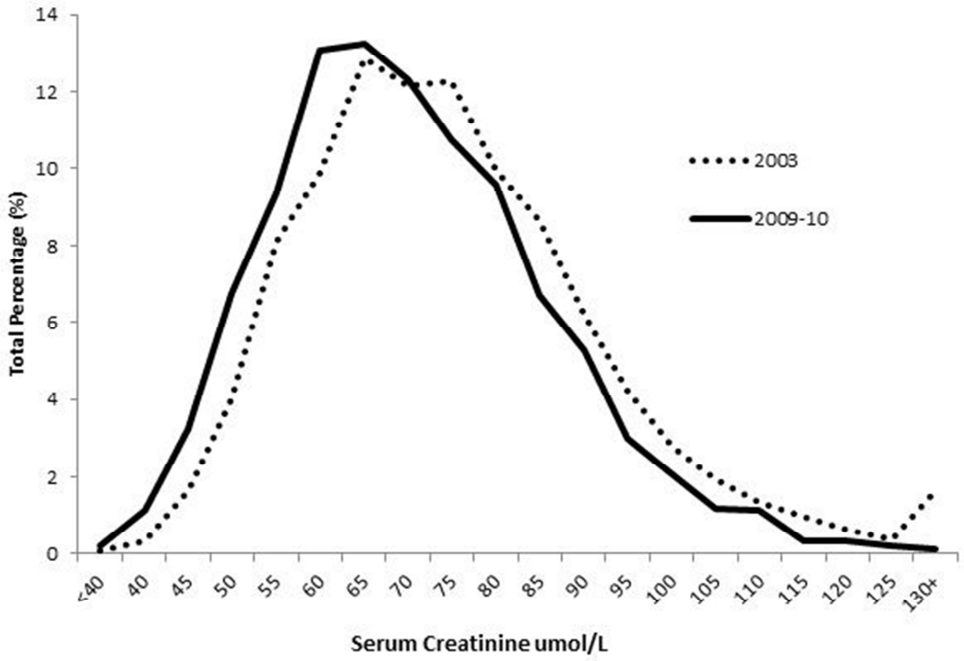

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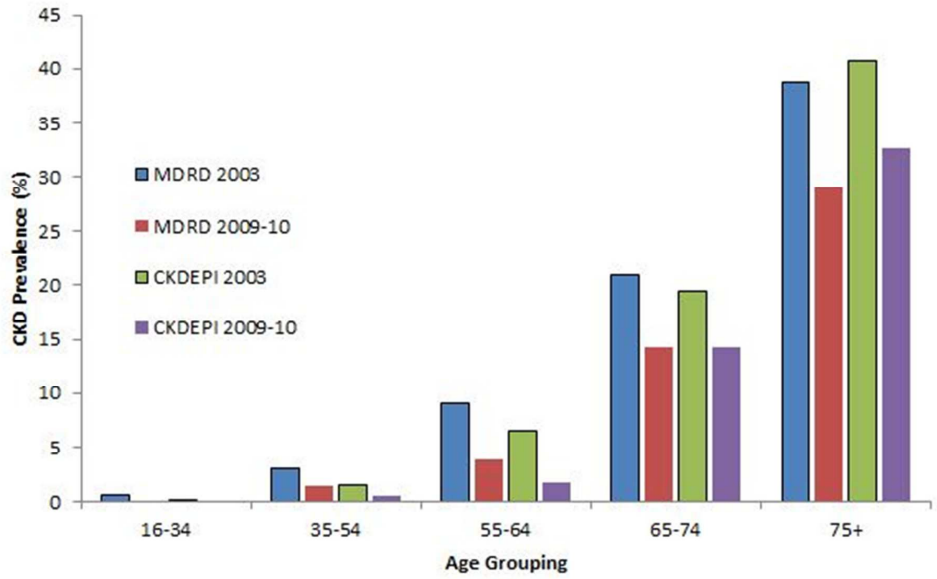
Figure 2. Comparison of low eGFR (<60ml/min/1.73m^2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender

Male



Female

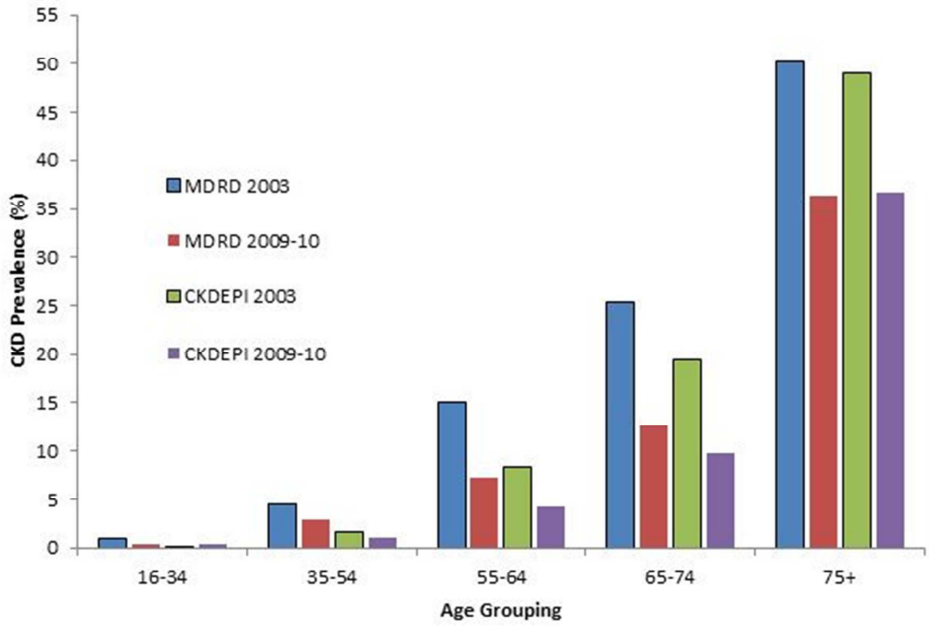


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Table 3. Prevalence and associations of low eGFR (<60ml/min/1.73m^2) by MDRD equation with adjustment for socio-demographic and clinical factors

Variable		MDRD				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	6.7~~9.6~~	1	1	1	1
	2009-10	6.0~~6.0~~	**0.84 (0.72 – 0.98)*~~0.52 (0.45 – 0.60)**~~**	**0.84 (0.73 – 0.99)*~~0.53 (0.44 – 0.62)**~~**	**0.75 (0.61 – 0.92)**~~0.48 (0.41 – 0.57)**~~**	**0.75 (0.61 – 0.92)**~~0.49 (0.42 – 0.57)**~~**
Age	16-34	0.2~~0.6~~	1	1	1	1
	35-54	2.1~~3.0~~	**10.8 (5.3 – 22.0)**~~5.8 (3.7-9.0)**~~**	**11.1 (5.5 – 22.8)**~~5.7 (3.5-9.1)**~~**	**10.8 (5.0 – 23.4)**~~5.2 (3.3 – 8.2)**~~**	**10.7 (4.9 – 23.2)**~~5.0 (3.2 – 7.9)**~~**
	55-64	6.8~~9.2~~	**37 (18 – 75)**~~19 (12 – 30)**~~**	**36 (18 – 73)**~~17 (11 – 28)**~~**	**33 (15 – 72)**~~14 (9 – 23)**~~**	**32 (14 – 69)**~~13 (8 – 20)**~~**
	65-74	14.5~~19.0~~	**87 (43 – 175)**~~44 (28 – 68)**~~**	**82 (40 – 167)**~~39 (24 – 63)**~~**	**65 (30 – 143)**~~31 (20 – 50)**~~**	**62 (28 – 135)**~~28 (17 – 44)**~~**
	75+	35.6~~40.3~~	**276 (138 – 555)**~~127 (83 – 196)**~~**	**247 (122 – 501)**~~109 (69 – 175)**~~**	**216 (99 – 470)**~~88 (55 – 140)**~~**	**202 (93 – 440)**~~76 (48 – 122)**~~**
Sex	Male	5.0~~6.3~~	1	1	1	1
	Female	7.7~~9.8~~	**1.42 (1.22 – 1.65)**~~1.45 (1.26 – 1.68)**~~**	**1.37 (1.17 – 1.60)**~~1.39 (1.19 – 1.62)**~~**	**1.69 (1.36 – 2.10)**~~1.45 (1.23 – 1.70)**~~**	**1.66 (1.34 – 2.06)**~~1.43 (1.22 – 1.67)**~~**
Ethnic	White	6.8~~8.6~~	-	1	1	1
	South Asian	1.7~~2.3~~	-	0.83 (0.43 – 1.59)~~0.63 (0.32 – 1.26)~~	0.73 (0.33 – 1.60)~~0.74 (0.41 – 1.34)~~	0.71 (0.32 – 1.56)~~0.72 (0.40 – 1.32)~~
	Black	1.7~~2.7~~	-	0.38 (0.15 – 1.00)~~0.73 (0.32 – 1.69)~~	0.33 (0.09 – 1.19)~~0.41 (0.17 – 1.02)~~	0.32 (0.09 – 1.16)~~0.40 (0.16 – 1.01)~~
	Other	1.6~~2.4~~	-	0.81 (0.29 – 2.30)~~1.19 (0.46 – 3.08)~~	0.64 (0.17 – 2.46)~~0.92 (0.36 – 2.30)~~	0.64 (0.17 – 2.44)~~0.93 (0.37 – 2.34)~~
Tenure	Own	6.3~~8.3~~	-	1	1	1
	Rent	6.6~~7.6~~	-	**1.34 (1.11 – 1.60)**~~1.13 (0.93 –~~	1.23 (0.97 – 1.57)~~1.11 (0.92 –~~	1.23 (0.96 – 1.56)~~1.10 (0.91 –~~

				1.36)	1.34)	1.33)
Education	Degree Level	2.43.1	-	1	1	1
	Below degree	4.45.9	-	1.31 (0.99 – 1.74)1.29 (0.98 – 1.70)	1.15 (0.83 – 1.60)**1.34 (1.03 – 1.74)***	1.20 (0.84 – 1.70)**1.33 (1.02 – 1.74)***
	None	14.918.2	-	**1.52 (1.13 – 2.04)****1.43 (1.06 – 1.93)***	1.20 (0.84 – 1.70)**1.50 (1.14 – 1.99)****	1.23 (0.96 – 1.57)**1.50 (1.13 – 1.98)****
Smoking	Never	6.17.7	-	-	1	1
	Ex-Smoker	10.112.8	-	-	1.17 (0.91 – 1.49)1.23 (0.97 – 1.55)	1.15 (0.85 – 1.54)1.20 (0.94 – 1.53)
	Current Smoker	3.24.3	-	-	1.02 (0.75 – 1.38)1.22 (0.96 – 1.57)	1.04 (0.80 – 1.40)1.19 (0.94 – 1.51)
BMI (kg/m^2)	Normal (<25)	3.44.3	-	-	1	1
	Overweight (25-30)	6.68.8	-	-	1.16 (0.91 – 1.49)**1.57 (1.30 – 1.90)****	1.15 (0.90 – 1.47)**1.51 (1.25 – 1.83)****
	Obese (>30)	8.410.6	-	-	1.31 (0.99 – 1.71)**1.80 (1.47 – 2.21)****	1.26 (0.96 – 1.65)**1.65 (1.33 – 2.03)****
HDL Cholesterol	Continuous	--	-	-	**0.51 (0.38 – 0.67)****0.53 (0.41 – 0.68)****	**0.51 (0.38 – 0.68)****0.54 (0.43 – 0.69)****
Total Cholesterol	Continuous	--	-	-	0.91 (0.84 – 1.00)0.95 (0.88 – 1.11)	0.92 (0.84 – 1.00)0.96 (0.90 – 1.12)
Doctor diagnosed Diabetes	No	5.97.5	-	-	1	1
	Yes	17.319.9	-	-	1.42 (0.92 – 2.22)1.42 (0.95 – 2.12)	1.36 (0.87 – 2.11)1.31 (0.88 – 1.97)
Doctor diagnosed Hypertension	No	4.05.1	-	-	-	1
	Yes	13.316.5	-	-	-	**1.27 (1.03 – 1.55)***1.47 (1.23 – 1.75)****

[1]Prevalence for combined 2003 and 2009-10 HSE
[2]Adjusted for age and sex

[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Table 4. Prevalence and associations of low eGFR (<60) by CKDEPI equation with adjustment for socio-demographic and clinical factors

Variable		CKDEPI				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	5.7~~7.6~~	1	1	1	1
	2009-10	5.2~~5.2~~	0.85 (0.72 – 1.00)~~0.57 (0.48-0.67)**~~	0.86 (0.72 – 1.01)~~0.59 (0.49 – 0.71)**~~	**0.73 (0.57 – 0.93)*~~0.52 (0.43 – 0.63)**~~	**0.73 (0.57 – 0.93)*~~0.52 (0.43 – 0.62)**~~
Age	16-34	0.1~~0.1~~	1	1	1	1
	35-54	1.0~~1.3~~	**15.1 (4.5 – 51.4)**~~8.4 (3.7 – 19.2)**~~	**16.1 (4.7 – 55.0)**~~7.5 (3.3 – 17.1)**~~	**13.8 (4.0 – 47.2)**~~9.1 (3.7 – 22.1)**~~	**13.5 (3.9 – 46.5)**~~8.7 (3.6 – 21.2)**~~
	55-64	4.2~~5.6~~	**67 (20 – 225)**~~38 (17.4 – 86.0)**~~	**67 (20 – 227)**~~31 (14 – 69)**~~	**55 (16 – 190)**~~38 (16 – 91)**~~	**52 (15 – 177)**~~33 (14 – 81)**~~
	65-74	12.5~~16.3~~	**219 (66 – 725)**~~128 (58 – 292)**~~	**219 (65 – 731)**~~104 (47 – 231)**~~	**162 (47 – 553)**~~119 (50 – 269)**~~	**151 (44 – 517)**~~103 (43 – 247)**~~
	75+	36.8~~41.0~~	**890 (269 – 2938)**~~465 (212 – 1019)**~~	**844 (253 – 2808)**~~356 (160 – 790)**~~	**754 (222 – 2559)**~~420 (175 – 1003)**~~	**693 (203 – 2355)**~~357 (149 – 857)**~~
Sex	Male	4.6~~5.6~~	1	1	1	1
	Female	6.3~~7.6~~	1.15 (0.97 – 1.36)~~1.17 (1.01 – 1.37)*~~	1.11 (0.93 – 1.31)~~1.11 (0.93 – 1.32)~~	**1.31 (1.01 – 1.68)*~~1.37 (1.09 – 1.70)**~~	**1.28 (1.00 – 1.65)*~~1.36 (1.09 – 1.67)**~~
Ethnic	White	5.8~~7.0~~	-	1	1	1
	South Asian	1.4~~1.7~~	-	0.93 (0.43 – 2.00)~~0.80 (0.36 – 1.79)~~	0.89 (0.35 – 2.42)~~0.66 (0.30 – 1.99)~~	0.85 (0.34 – 2.16)~~0.63 (0.29 – 1.97)~~
	Black	2.0~~2.3~~	-	0.56 (0.23 – 1.39)~~0.90 (0.35 – 2.34)~~	0.55 (0.16 – 1.82)~~0.47 (0.16 – 1.87)~~	0.53 (0.16 – 1.77)~~0.44 (0.14 – 1.56)~~
	Other	1.6~~1.6~~	-	1.19 (0.40 – 3.56)~~1.13 (0.33 – 3.88)~~	1.13 (0.29 – 4.41)~~1.42 (0.22 – 2.89)~~	1.13 (0.29 – 4.41)~~1.44 (0.24 – 3.03)~~
Tenure	Own	5.3~~6.5~~	-	1	1	1
	Rent	6.0~~6.8~~	-	**1.44 (1.19 –**	1.29 (0.98 –	1.28 (0.97 –

				1.75)**1.31 (1.07 – 1.62)*	1.69)1.30 (1.04 – 1.59)*	1.69)1.29 (1.05 – 1.59)*
Education	Degree Level	1.82.1	-	1	1	1
	Below degree	3.64.4	-	1.36 (0.97 – 1.90)1.32 (0.94 – 1.84)	1.05 (0.69 – 1.58)1.23 (0.87 – 1.79)	1.04 (0.69 – 1.58)1.24 (0.86 – 1.81)
	None	13.616.2	-	**1.51 (1.08 – 2.13)***1.42 (0.99 – 2.02)	1.12 (0.76 – 1.66)1.32 (0.95 – 1.85)	1.11 (0.75 – 1.65)1.33 (0.97 – 1.86)
Smoking	Never	5.26.2	-	-	1	1
	Ex-Smoker	9.010.7	-	-	1.09 (0.77 – 1.55)1.20 (0.90 – 1.59)	1.07 (0.75 – 1.52)1.17 (0.81 – 1.44)
	Current Smoker	2.63.1	-	-	0.80 (0.70 – 1.41)0.99 (0.70 – 1.41)	0.79 (0.54 – 1.14)0.96 (0.68 – 1.45)
BMI (kg/m^2)	Normal (<25)	2.73.4	-	-	1	1
	Overweight (25-30)	5.56.8	-	-	1.14 (0.86 – 1.51)1.43 (1.15 – 1.78)**	1.12 (0.85 – 1.49)1.36 (1.09 – 1.70)**
	Obese (>30)	7.28.6	-	-	1.31 (0.96 – 1.80)1.78 (1.40 – 2.25)**	1.25 (0.91 – 1.72)1.72 (1.27 – 2.04)**
HDL Cholesterol	Continuous	--	-	-	**0.40 (0.29 – 0.56)****0.49 (0.37 – 0.66)**	**0.40 (0.29 – 0.57)****0.49 (0.37 – 0.65)**
Total Cholesterol	Continuous	--	-	-	0.93 (0.84 – 1.04)0.95 (0.89 – 1.03)	0.94 (0.86 – 1.04)0.97 (0.90 – 1.04)
Doctor diagnosed Diabetes	No	5.06.0	-	-	1	1
	Yes	16.318.4	-	-	1.55 (0.96 – 2.48)1.59 (1.02 – 2.48)*	1.46 (0.91 – 2.35)1.49 (0.96 – 2.33)
Doctor diagnosed Hypertension	No	3.13.8	-	-	-	1
	Yes	12.314.5	-	-	-	**1.33 (1.05 – 1.67)****1.40 (1.14 – 1.72)**

[1]Prevalence for combined 2003 and 2009-10 HSE

[2]Adjusted for age and sex
[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Appendix 1: Medication use in key subgroups who reported yes to taking doctor prescribed medication

		2003				2009-10		
Group	**Drug type**	**Number**	**Yes (%)**	**No (%)**		**Number**	**Yes (%)**	**No (%)**
Any Doctor-diagnosed hypertension	**Diuretics**	2118	523 (24.7%)	1595 (75.3%)		1501	378 (25.2%)	1123 (74.8%)
	ß-Blockers		419 (19.8%)	1699 (80.2%)			249 (16.6%)	1252 (83.4%)
	Calcium channel blockers		324 (15.3%)	1794 (84.7%)			357 (23.8%)	1144 (76.2%)
	RAS inhibitors		1027 (48.5%)	1091 (52.5%)			932 (62.1%)	569 (37.9%)
Any Doctor-diagnosed diabetes	**RAS inhibitors**	305	172 (56.4%)	133 (43.6%)		322	199 (61.8%)	123 (38.2%)
eGFR <60ml/min/1.73m^2 MDRD	**RAS inhibitors**	751	386 (51.4%)	365 (48.6%)		349	205 (58.7%)	144 (41.3%)
eGFR <60ml/min/1.73m^2 CKDEPI	**RAS inhibitors**	594	351(59.1%)	243 (40.9%)		303	199 (65.7%)	104 (34.3%)
All	**Lipid lowering**	7810	484 (6.2%)	7326 (93.8%)		5786	770 (13.3%)	5016 (86.7%)

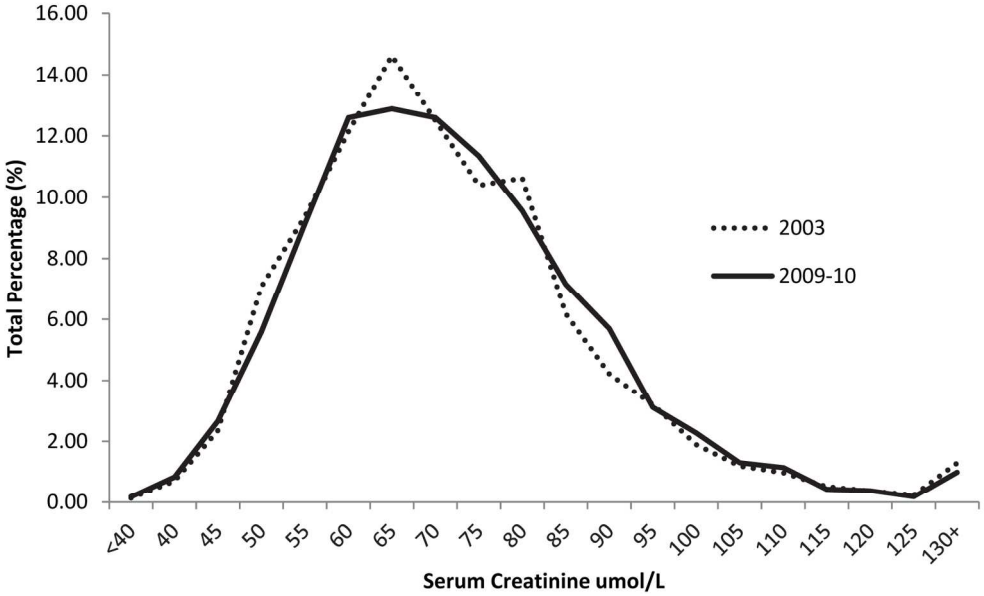

Figure 1. Distribution of serum creatinine (μmol/L) for 2003 and 2009/10 survey data.
Serum creatinine categories are grouped in bands of 5 μmol/L from 40μmol/L to 130μmol/L. Serum creatinine values <40 μmol/L and those >130μmol/L are grouped together.

156x93mm (300 x 300 DPI)

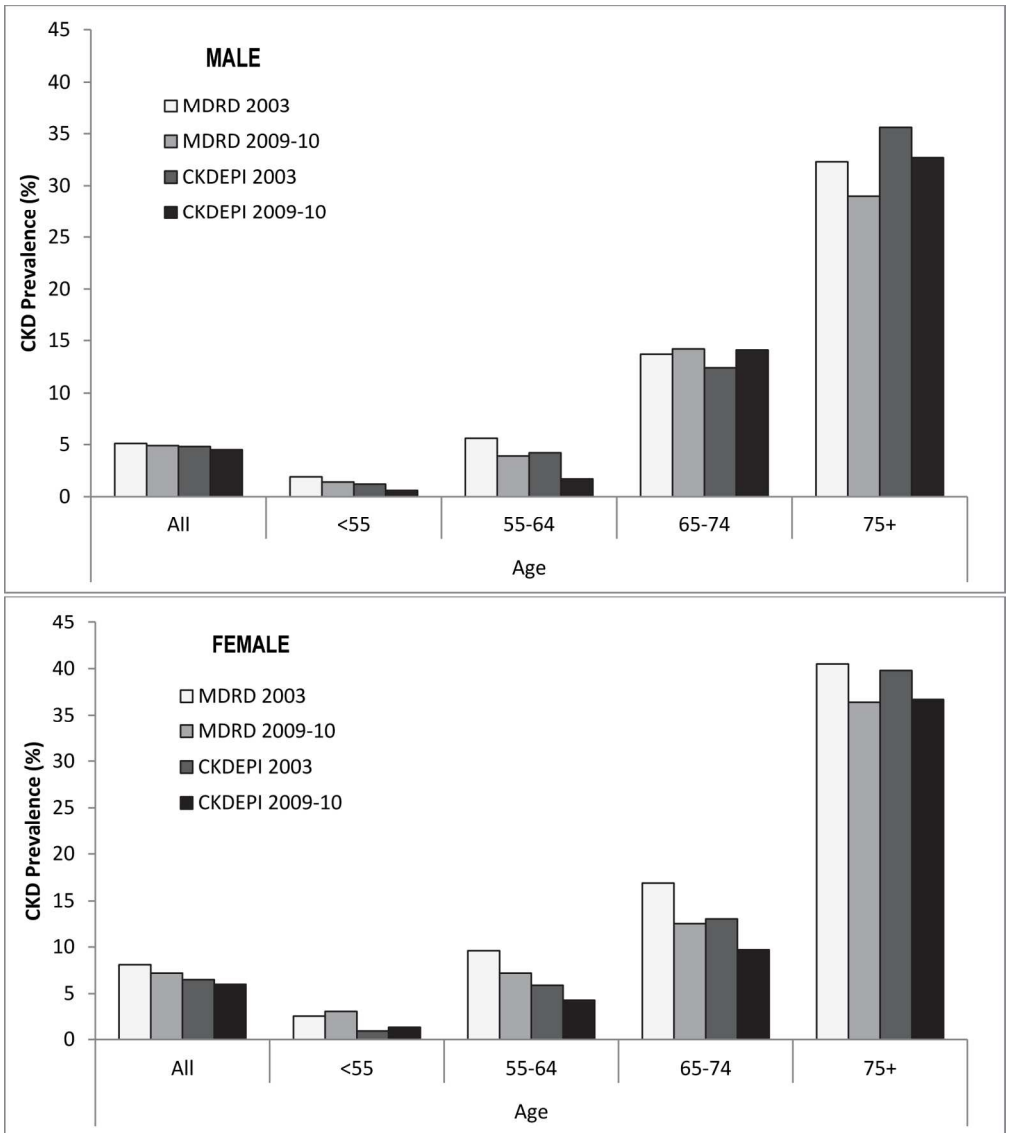

Figure 2. Comparison of low eGFR (<60ml/min/1.73m2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender
159x179mm (300 x 300 DPI)

Appendix 1: Medication use in key subgroups who reported yes to taking doctor prescribed medication

		2003				2009-10		
Group	**Drug type**	**Number**	**Yes (%)**	**No (%)**		**Number**	**Yes (%)**	**No (%)**
Any Doctor-diagnosed hypertension	**Diuretics**	2118	523 (24.7%)	1595 (75.3%)		1501	378 (25.2%)	1123 (74.8%)
	ß-Blockers		419 (19.8%)	1699 (80.2%)			249 (16.6%)	1252 (83.4%)
	Calcium channel blockers		324 (15.3%)	1794 (84.7%)			357 (23.8%)	1144 (76.2%)
	RAS inhibitors		1027 (48.5%)	1091 (52.5%)			932 (62.1%)	569 (37.9%)
Any Doctor-diagnosed diabetes	**RAS inhibitors**	305	172 (56.4%)	133 (43.6%)		322	199 (61.8%)	123 (38.2%)
eGFR <60ml/min/1.73m^2 MDRD	**RAS inhibitors**	521	279 (53.6%)	242 (46.4%)		349	205 (58.7%)	144 (41.3%)
eGFR <60ml/min/1.73m^2 CKDEPI	**RAS inhibitors**	444	273 (61.5%)	171 (38.5%)		303	199 (65.7%)	104 (34.3%)
All	**Lipid lowering**	7810	484 (6.2%)	7326 (93.8%)		5786	770 (13.3%)	5016 (86.7%)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	4,5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, 16
		(b) Indicate number of participants with missing data for each variable of interest	16
Outcome data	15*	Report numbers of outcome events or summary measures	16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	21,22,23
		(*b*) Report category boundaries when continuous variables were categorized	16,17
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8,9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2014-005480.R2
Article Type:	Research
Date Submitted by the Author:	05-Sep-2014
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Primary Subject Heading:	Epidemiology
Secondary Subject Heading:	Renal medicine, Health policy, Epidemiology
Keywords:	EPIDEMIOLOGY, Chronic renal failure < NEPHROLOGY, End stage renal failure < NEPHROLOGY, PUBLIC HEALTH

Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010

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Abstract

Objectives
To determine whether the prevalence of CKD in England has changed over time.

Design
Cross-sectional analysis of nationally representative Health Survey for England (HSE) random samples.

Setting
England 2003 and 2009/2010.

Survey participants
13,896 Adults aged 16+ participating in HSE, adjusted for sampling and non-response, 2009/10 surveys combined.

Main outcome measure
Change in prevalence of eGFR <60ml/min/1.73m^2 (as proxy for stage 3-5 chronic kidney disease [CKD]), from 2003 to 2009/10 based on a single serum creatinine measure using IDMS traceable enzymatic assay in a single laboratory; eGFR derived using MDRD and CKDEPI eGFR formulae.

Analysis
Multivariate logistic regression modelling to adjust time changes for socio-demographic and clinical factors (body mass index, hypertension, diabetes, lipids). A correction factor was applied to the 2003 HSE serum creatinine to account for a storage effect.

Results
National prevalence of low eGFR (<60) decreased within each age and gender group for both formulae except males aged 65-74. Prevalence of both obesity and diabetes increased in this period, there was a decrease in hypertension. Adjustment for demographic and clinical factors led to a significant decrease in CKD between the surveyed periods. The fully adjusted odds ratio for eGFR<60ml/min/1.73m^2 was 0.75 (0.61-0.92) comparing 2009/10 with 2003 using the MDRD equation, and was similar using the CKDEPI equation 0.73 (0.57-0.93).

Conclusion
The prevalence of a low eGFR indicative of CKD in England appeared to decrease over this seven year period, despite rising prevalence of obesity and diabetes, two key causes of CKD. Hypertension prevalence declined and blood pressure control improved but this did not appear to explain the fall. Periodic assessment of eGFR and albuminuria in future HSEs is needed to evaluate trends in CKD.

Article Summary

Strengths & Limitations of this study

- This study used nationally representative samples, with later HSEs pooled over two years to increase numbers and precision of estimates. The surveys used standardised protocols for measurement by trained interviewers and nurses, with all samples tested in the same laboratory with standardised assays.
- Another strength of the study is that the analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. Weighting was introduced for both surveyed periods to reduce response bias and account for missing data. A correction factor was applied to 2003 HSE data to adjust for the shift in measured creatinine due to sample storage.
- The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. The study was also limited by use of a single sample to test for serum creatinine in each survey, therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown.
- The prevalence of stage 4/5 CKD is likely to be underestimated as the HSE may not fully account for some people in whom more severe CKD (stage 4/5) will be more common.
- The absence of albuminuria data in the 2003 HSE is another major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of renin-angiotensin system (RAS) inhibition).

Total word count n=3,844

Introduction

Chronic kidney disease (CKD) is recognised as a global public health problem.[1] CKD is defined and staged using the estimated glomerular filtration rate (eGFR) and markers of kidney damage, mainly albuminuria.[2] Both eGFR and albuminuria are strong independent risk factors for all-cause and cardiovascular disease (CVD) mortality, and progression to end-stage renal disease (ESRD), which may require renal replacement therapy (RRT) by dialysis or transplantation.[3] In England in 2010 the prevalence of RRT was 832 per million population, a 3% increase from 2009; NHS costs of RRT were estimated at £780 million for 2009/10, and the total cost at £1.45 billion, a nearly threefold increase on estimated costs for 2002.[4,5]

The population prevalence of CKD in England was reported for the first time using data on eGFR and albuminuria in the nationally-representative Health Surveys for England (HSE) 2009 and 2010, though there had previously been estimates based on routine testing using primary care data.[6,7] In the combined 2009/2010 HSE, 6% of men and 7% of women had eGFR <60ml/min/1.73m^2 (equivalent to CKD stage 3-5 if chronic) with a strong age gradient.[8] The prevalence of low eGFR increased in the US, based on National Health and Nutrition Examination (NHANES) surveys between 1988-2004, even after adjusting for adverse trends in risk factors (obesity, diabetes, hypertension), but little is known about CKD prevalence trends in England.[9,10,11]

Information on prevalence change is needed to assess the impact of trends in underlying determinants, and of strategies to prevent and manage CKD. Several policy initiatives have been introduced in England that have had an impact on prevention, detection and management of CKD. The National Service Framework for Renal Services 2004/05 led to national reporting of eGFR by clinical biochemistry laboratories from 2006,[12] the General Practice pay for performance Quality Outcomes Framework (QOF) included targets for CKD management from 2006/07,[13] and the NHS Vascular Checks Programme, introduced in 2009, includes screening for CKD (stage 3-5) in people aged 35-74 with newly identified type 2 diabetes or hypertension.[14] This study therefore aimed to compare the prevalence of CKD in the HSE 2003 with the combined HSE 2009/10 and to relate this to any changes in prevalence of risk factors for CKD, particularly obesity, diabetes and hypertension, over this period.

Methods

Full details of the conduct of the HSE, measurement of non-CKD variables and response rates are shown in the 2003 and 2009 Health Survey for England reports.[15,16] Survey participants within private households were selected using a multistage stratified random probability sample. Household response rates were 73% in HSE 2003 and 68%/66% in HSE 2009/2010. In co-operating households, 90% and 89%/86% of adults completed an interview questionnaire while 70% and 62%/57% respectively consented to a nurse visit, of whom 74%-76% provided a blood test. The HSE 2003 contained 18,533 individuals and data from HSE 2009 and HSE 2010 were combined to provide a sample size of 13,065 individuals. This totalled 31,598 individuals for the combined 2003, 2009 and 2010 HSEs. Eligible participants were individuals aged 16 years and older who had a valid serum creatinine value. This left 7,850 individuals from the 2003 HSE and 6,046 individuals from the combined 2009/10 HSEs, a total of 13,896 individuals for analysis.

Age was grouped into five categories: 16-34, 35-54, 55-64, 65-74 and 75+. There were four separate ethnic groupings: White, South Asian, Black and Other. Socio-economic factors included: i) occupation National Statistics Socio-Economic Classification (NS-SEC, divided into three categories: managerial and professional occupations; intermediate occupations and routine and manual occupations); ii) qualifications grouped as: degree or equivalent; below degree (other qualification) and none (no qualification); iii) household tenure (own vs renting); iv) access to motor vehicle (none vs. any).

Smoking status was defined as current, ex-smoker or never smoked. Hypertension was defined as doctor-diagnosed (pre-existing diagnosis), survey-defined (identified as having high blood pressure (BP, systolic ≥140mmHg and/or diastolic ≥90mmHg and/or taking medication for hypertension) at the survey examination), and 'total' (doctor + survey diagnosed). Survey-defined diabetes was glycated haemoglobin (HBA1c) ≥6.5% at nurse visit. Glycated haemoglobin data are presented for those with and without diagnosed diabetes. Body mass index (BMI) was defined as normal (<25kg/m^2), overweight (≥25, <30kg/m^2), and obese (≥30kg/m^2). Waist circumference was classified as: <94cm, 94–102cm (high), and >102cm (very high) for men, and <80cm, 80–88cm (high) and >88cm (very high) for women. For South Asian men, the waist circumference was classified as: <90cm, 90–102cm (high), and >102cm (very high). High density lipoprotein (HDL) cholesterol and total cholesterol were treated as continuous variables.

To investigate medication use, we examined the use of diuretics, ß-blockers, renin-angiotensin system (RAS) inhibitors (angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)), calcium channel blockers, and other anti-hypertensives in those with doctor diagnosed hypertension, doctor diagnosed diabetes and eGFR <60ml/min/1.73m^2, and use of lipid lowering drugs (the majority of which are statins) in the whole population. In 2003, 47% of respondents answered yes to whether they were taking any prescribed medication, and 50% in 2009/10.

Serum creatinine was assayed using an isotope dilution mass spectrometry (IDMS) traceable enzymatic assay in a single laboratory (Clinical Biochemistry Department at the Royal Victoria Infirmary (RVI), Newcastle-upon-Tyne). Both the Modified Diet in Renal Disease (MDRD) equation (in routine use in the UK) and the newer Chronic Kidney Disease Epidemiology Collaboration (CKDEPI) equation (which provides better risk prediction and is recommended for use in international guidelines) were used to define CKD.[2,17] eGFR values were derived using the standard equations.[18,19]

Details of laboratory analysis, internal quality control, and external quality assurance are provided in the HSE 2009/10 documentation, with these methods replicated in analysis of the 2003 HSE samples.[8]

Samples were assayed for serum creatinine over a 19 month time period with two different batches of tri-level Internal Quality Control (IQC) material. HSE 2009 and 2010 samples were analysed with Batch 1 or Batch 2 IQC, HSE 2003 samples were analysed with Batch 2 IQC. The creatinine assay was stable over time with IQC results very close to expected target values. Batch 1 IQC gave mean (SD) creatinine concentrations of 56(0.6),167(1.3) and 586(4.9) umol/L for levels 1,2 and 3 respectively compared with target means of 56, 167 and 588 umol/L. Batch 2 material gave mean(SD) creatinine concentrations of 51(1.1), 175(2.2) and 597(5.6)umol/L for levels 1,2 and 3 respectively compared with target means of 51, 175 and 599 umol/L.

The HSE 2003 samples had been stored, frozen at -40^{o}C, then thawed for measurement in 2010. Although such freezing is not thought to affect creatinine levels[20] we undertook a re-analysis in 2014 of a random sample of 500 serum creatinine samples taken from the 2009 HSE and subsequently frozen and stored under the same conditions as the HSE 2003 samples, stratified by quintile, to determine if there was a shift in measured creatinine on storage. We found mean serum creatinine increased on storage and was best predicted by a regression equation where the original 2009 serum creatinine value without storage equaled 0.303 plus 0.94 multiplied by the stored serum creatinine value. We assumed the same effect applied to the 2003 serum creatinine data which were analysed in 2009-10 and we applied the same adjustment. This decreased the 2003 serum creatinine values. eGFR was classified as below 60ml/min/1.73m^2 or equal to or greater than 60ml/min/1.73m^2. We compared the change in mean serum creatinine in people aged 20-39 without any diabetes or any hypertension as per Coresh at al.[9]

Statistics

Patient characteristics were compared between the 2003 and 2009/10 HSEs using chi-squared tests for categorical variables and Mann Whitney U tests for non-normally distributed continuous variables. eGFR<60ml/min/1.73m^2 prevalence in 2003 and 2009/10 was compared across age and sex groupings. BP levels were compared in all, in those with diagnosed hypertension and in those with eGFR<60ml/min/1.73m^2; glycated haemoglobin (HBA1c) was compared in all participants and in those with doctor-diagnosed diabetes. Binary logistic regression models were used to examine the relationships between eGFR<60ml/min/1.73m^2 and age, sex and socioeconomic and clinical factors to determine if there were significant differences between the two survey time periods. The dependent variable were CKDEPI and MDRD equation eGFR <60ml/min/1.73m^2 (indicative of stage 3-5 CKD). Four models were produced for each: 1) Age-sex adjusted; 2) model 1 plus socio-economic status and ethnicity; 3) model 2 plus behavioural, lipid levels (HDL and total cholesterol) and clinical variables except hypertension, 4) Model 3 plus doctor-diagnosed hypertension. Interactions between period and both diabetes and hypertension were tested.

Sensitivity analyses were performed by replacing doctor-diagnosed diabetes with HBA1c, replacing doctor-diagnosed hypertension with diastolic and systolic blood pressure and adjusting for lipid lowering agents in the full model. Non-response and blood sample weights were used in all analyses to address issues with missing individuals who did not have a blood sample taken and sent to laboratory for analysis to determine serum creatinine value. Full details on how the weights were obtained are provided in the final volume of the HSE report each year. The age, education and smoking status of those interviewed, having a nurse visit and having a blood test is similar once non-response is taken into account (data not shown). All analyses were performed using IBM SPSS Statistics version 20.

Results

The final sample for the study comprised of 13,896 individuals aged 16+ who had a valid serum creatinine value. Comparing the characteristics of these participants between the 2003 and 2009/10 surveys, the age structure, gender, NS-SEC and car ownership were similar while educational level improved and there was an increase in rented tenure (Table 1). Prevalence of diabetes however classified increased, as did obesity. In contrast, smoking and hypertension prevalence decreased.

There were significant increases in BMI, waist circumference and HBA1c in the population though no change in HBA1c in those with diagnosed diabetes (Table 2). Median BP levels (both systolic and diastolic) fell in all groups including those with diagnosed hypertension, doctor-diagnosed diabetes and with eGFR<60ml/min/1.73m^2. Median total and HDL cholesterol fell in both men and women.

The distribution of serum creatinine is similar for 2003 and 2009/10 (Figure 1). Median serum creatinine increased slightly, leading to a very small non-significant decrease in median eGFR using both MDRD and CKDEPI formulae (Table 2). Mean serum creatinine for those aged 20-39 without doctor diagnosed hypertension or diabetes increased slightly from 70.6µmol/L (SD 13.6) in 2003 to 71.4µmol/L (SD 14.3) in 2009/10 (p=0.09).

The proportion of individuals with MDRD eGFR<60ml/min/1.73m^2 decreased from 6.7% in 2003 to 6.0% in 2009/10 (p=0.13) and with eGFR <45ml/min/1.73m^2 from 1.9% to 1.4% (p=0.03). Corresponding figures for CKDEPI were 5.7% and 5.2% (p=0.26) and 1.8% and 1.4% (p=0.07). Prevalence of low eGFR fell in all age and gender groups and with either CKDEPI or MDRD equations, except for males aged 65-74 where there was a slight increase (Figure 2).

There was an increase in the mean number of anti-hypertensive agents taken in individuals with: doctor-diagnosed hypertension (1.19 in 2003 to 2.01 in 2009/10), doctor-diagnosed hypertension and doctor-diagnosed diabetes (1.47 to 2.57); MDRD eGFR <60ml/min/1.73m^2 (1.30 to 1.77); and CKDEPI eGFR < 60ml/min/1.73m^2 (1.35 to 1.93). The proportion taking RAS inhibitors in individuals with doctor-diagnosed diabetes, doctor-diagnosed hypertension, MDRD eGFR <60ml/min/1.73m^2 or CKDEPI eGFR < 60ml/min/1.73m^2 also increased, as did overall lipid lowering agent use (Appendix 1).

The age-sex adjusted odds ratio (OR) of having low eGFR (MDRD eGFR<60ml/min/1.73m^2) in 2009/10 compared with 2003 was 0.84 (95% confidence interval (CI) 0.72-0.98) and fully adjusted was 0.75 (0.61-0.92) (Table 3). The corresponding ORs for CKDEPI were 0.85 (0.72-1.00) and 0.73 (0.57-0.93) (Table 4).

Sensitivity analyses replacing doctor-diagnosed diabetes with HBA1c and doctor-diagnosed hypertension with diastolic and systolic BP made little difference to the adjusted ORs, as did the inclusion of lipid lowering agents. No interactions between period and diabetes or hypertension were identified.

Discussion

These analyses show that CKD prevalence in England estimated by serum creatinine based equations in England appeared to decrease from 2003 to 2009/10. This decrease was seen across all age groupings (except males aged 65-74), for CKD defined by both MDRD and CKDEPI eGFR equations, was more pronounced for the MDRD equation and occurred despite increased prevalence of both diabetes and obesity.[21] Using the CKDEPI equation in place of MDRD to define CKD resulted in a lower prevalence of CKD. Whilst it reduced overall prevalence, the CKDEPI equation identified more individuals aged 75+ with CKD compared with the MDRD equation.[22,23]

The HSE 2003, 2009 and 2010 were nationally representative samples, with the 2009/10 data pooled over two years to increase numbers and precision of estimates. The age-sex characteristics of the different study periods sampled were similar. The surveys used standardised protocols for measurement by trained interviewers and nurses. All samples were tested in the same laboratory with standardised assays. The analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. We accounted for the shift in measured creatinine on storage in the 2003 HSE serum creatinine data by introduction of a correction factor derived from analysis of the effect of storage using 2009 data. Non-response weighting was undertaken in the HSE for both surveyed periods to reduce response bias and account for missing data for individuals who did not have blood sample taken and hence no serum creatinine value. We used both the HSE study design and the non-response weights to provide national prevalence estimates at each period and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences. The ethnic composition of the surveys changed over time with a small fall in the White population, but we adjusted for this change in the analysis.

The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. However the use of new, cross-sectional samples enables measurement of general population CKD prevalence at different time points. A single sample was tested for serum creatinine in each survey, and therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown. This is standard practice in national surveys such as NHANES, whereas studies based on routine testing can assess chronicity, such as the QICKD study. [24] Given the individual variation in kidney function, more extreme values will be averaged out on repeated testing (regression to the mean), reducing the prevalence of low eGFR.[25] The results may therefore slightly overestimate the prevalence of CKD. There were too few cases from the key minority ethnic groups to give robust data on ethnic differences in prevalence of CKD. South Asians and Black groups have higher rates of renal replacement but have been found to have lower prevalence of CKD than Caucasians.[26,27]

Prevalence of stage 4/5 CKD is likely to be underestimated as, whilst the HSE is able to adjust for non-response among the general population in private households, it may not fully account for some in whom more severe CKD (stage 4/5) will be more common. This includes people who were not able to give a blood or urine sample because of poor health and those who did not participate due to concurrent illness or hospitalisation, as well as those in residential care.

The absence of albuminuria data in the 2003 HSE is a major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of RAS inhibition).[3] We have therefore been unable to estimate

changes in prevalence of albuminuria per se, in all CKD (stages 1-5), and fully assess prevention and management.

The fall in low prevalence of eGFR could be due i) chance ii) artefact of differences in the serum creatinine measurement, iii) changes in serum creatinine production rather than excretion by the kidney, iv) residual confounding by differences in sample characteristics not adjusted for by sample weighting, v) true fall in eGFR. The two sets of samples were analysed in multiple analytical runs over a 19 month time period, which could lead to differences in results, however during this time period the internal quality control data indicates that the assay was accurate compared with assigned target values and stable. We found a storage artefact on serum creatinine measurement and accounted for this by introduction of a correction factor. A change in serum creatinine over time independent of kidney function could be due to less muscle mass (leading to lower serum creatinine production); there is no evidence for this and it seems unlikely to have occurred at the population level.

A decline in dietary protein consumption from cooked meat could also lead to change in serum creatinine. Statistics from the National Diet and Nutrition Survey show that meat consumption increased from 2001-02 to 2008-10 while protein intake remained virtually stable over the same period. [28] Mean consumption of meat and meat products increased from 154g per day in 2001-02 to 194g per day in 2008-10; protein intake contributing to food energy for adults aged 19+ increased slightly from 16-17% in 2001-02 to 17-18% in 2008-10; meat and meat products contributed to 37-38% of all protein intake for adults aged 19-64, with little change compared to 2008-10. Cooked meat consumption has been shown to increase serum creatinine in small case studies of volunteers and of patients with diabetic nephropathy and hence national guidance is to avoid eating cooked meat for 12 hours before a blood test for creatinine[29] but this was not done in HSE.

We used the HSE study design and non-response weights and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics differences is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences.

Key risk groups for developing CKD are people with hypertension and or diabetes especially if they have albuminuria. In this study there was evidence of modest reductions in the prevalence of hypertension, better control of hypertension in key groups, and greater use of RAS inhibitors which have anti-proteinuric as well as BP lowering effects, though the period changes in eGFR remained after correction for changes in hypertension prevalence. There is evidence from some studies using HSE, primary care databases and QOF data,[30-32] though not all,[33] of improved hypertension control in the last decade. However there are ethnic disparities with poorer control of BP in Black and South Asians who have higher risk of progression to need RRT.[34] Population salt consumption also fell during the last decade which is likely to have influenced population BP.[35,36] CKD prevalence could fall too if those identified with moderate CKD were treated more aggressively, especially those with hypertension and or albuminuria, leading to increased eGFR in some people to above 60ml/min/1.73m^2. The limited HSE data suggest better BP control and greater use of RAS inhibitors in those with eGFR <60ml/min/1.73m^2. Karunaratne et al examined BP control in those with and without CKD in a primary care population in Kent and showed that BP control had improved in CKD patients over time pre- and post the introduction of QOF and that it was greater than in non-CKD hypertensive patients. They also showed increased use of RAS inhibitors and other anti-hypertensive agents in CKD patients.[37]

There was evidence of increased lipid lowering agent use (indicative of increased statin use) and a small fall in population lipid levels. There is some evidence of reno-protective effects of statins in CKD patients; A lower rate of decline in GFR was found in patients with renal

disease who took antilipemic agents.[38] In the Heart Protection Study, the use of the hypolipidemic drug simvastatin reduced the rise in slightly elevated creatinine over time in both diabetic and non-diabetic CKD participants.[39] In the SHARP trial allocation of the lipid lowering ezetimibe plus simvastatin in participants not already on dialysis at randomisation reduced the outcome of end stage renal disease or a doubling of creatinine with an odds ratio of 0.93, though this was not statistically significant.[40] In the GREACE trial statin treatment prevented decline in renal function in people with high blood lipids and coronary heart disease; patients not treated with statins showed a 5.2% decrease in creatinine clearance, while patients treated with statins showed a 4.9% increase in creatinine clearance.[41] However our period changes were not altered by adjusting for statins (lipid lowering drugs) or lipid levels (HDL, total cholesterol).[37]

There are limited data from other countries with which to compare these findings. Coresh et al analysed the US NHANES surveys of 1988-1994 and 1999-2004, which both collected albuminuria and eGFR data. Both prevalence of albuminuria and MDRD eGFR <60ml/min/1.73m^2 increased, the latter from 5.6% to 8.1%.[8] The albuminuria increase was explained by changes in levels of obesity, diabetes and hypertension, whereas such adjustment only partly explained the fall in eGFR. Changes in population serum creatinine explained most of the remainder of the eGFR changes; this was analysed by comparing the mean serum creatinine in young people aged 20-39 without diabetes or hypertension and this had increased across the surveys.[9] The authors suggested that this rise in serum creatinine could be due to residual laboratory assay differences or to changes in dietary protein or muscle mass. Grams et al showed that prevalence of eGFR<60ml/min/1.73m^2 had also increased using the same survey data when eGFR was estimated using Cystatin C, a marker of kidney function that is independent of muscle mass, and this was not explained by changes in demography, hypertension, diabetes or obesity, suggesting a true increase in low eGFR.[41]

We can compare the estimated national CKD prevalence for HSE with QOF returns which record diagnosed CKD in primary care.[42] Prevalence has been increasing with improvements in detection and recording and in 2010 was 4.2%. The figures are not directly comparable as comparing a single screened value versus routine testing with presumed allowance for chronicity, but this may suggest some under-diagnosis of CKD.

If this change in prevalence in England is true, then based on the HSE 2003 age-sex-specific estimates and 2001 and 2011 Census data, the estimated number of CKD cases (for those aged 16 and over) would be 2.62 million based on the MDRD equation, falling by 0.03 million for 2009/10. Equivalent figures for CKDEPI eGFR <60ml/min/1.73m^2 are 2.23 million and 0.02 million increase respectively. The impact of such changes would be twofold: a consistent pool of patients at risk of progressing to need RRT; and a contribution to consistent cardiovascular incidence and mortality. The former is supported by stabilised acceptance rates onto RRT in England.[4]

Conclusions

The prevalence of a low eGFR appears to have decreased in England from 2003 to 2009/10, despite increases in obesity and diabetes. It is unclear why this has occurred and it is difficult to infer directly that this is due to current policies to improve prevention of CKD and the identification and management of people with CKD. There is a need for repeated national prevalence estimates to further assess CKD patterns over time, including measures of albuminuria and of Cystatin C, both of which were available in HSE 2009 and 2010.

What is already known on this topic • eGFR and albuminuria are strong independent risk factors for progression to end-stage renal disease (ESRD), which may require costly renal replacement therapy (RRT) • Prevalence of low eGFR has increased over time in countries such as the US**,** even after adjustment for adverse trends in CKD risk factors • Little is known about CKD prevalence trends in England
What this study adds • Prevalence of a low eGFR derived from serum creatinine and indicative of CKD in England has decreased from 2003 to 2009/10, despite increasing prevalence of diabetes and obesity • This pattern of prevalence of low eGFR was maintained even after adjustment for potential mediating and confounding factors • A future need for repeated national prevalence estimates, that includes measures of albuminuria and Cystatin C, is required to further assess CKD patterns over time.

Contributors: GA was involved in the analysis and interpretation of the data. PR drafted the paper. GA, PR, SF and GM made substantial contributions to the study conception and design. JM co-ordinated the Health Surveys for England. DO provided background information on CKD policy. JD conducted the laboratory analyses. All authors critically reviewed the paper and were involved in the drafting and approval of the manuscript. GA is the guarantor.
Acknowledgements: Scott Harris contributed to the production of the regression equation that was applied to the 2003 serum creatinine samples as a correction factor.
Funding: Kidney function testing in the Health Surveys for England was funded by NHS Kidney Care. GA is funded by a University of Southampton PhD scholarship.
Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.
Ethical approval: Approval was obtained from the London Multi-Centre Research Ethnics Committee for the 2003 survey (HSE 2003 ref MREC/02/2/72) and approval was obtained from the Oxford B Research Ethics Committee for both 2009 and 2010 surveys (HSE 2009 ref 08/H0605/103, HSE 2010 ref 09/H0605/73).
Transparency: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.
Data sharing: The HSE 2003, 2009 and 2010 are archived with the UK Data Service. Technical Appendix, statistical code and dataset available from corresponding author Grant Aitken at G.Aitken@soton.ac.uk. Creatinine measurements for the HSE 2003 undertaken for this study will be archived in due course.

Figure Legends

Figure 1. Distribution of serum creatinine (μmol/L) for 2003 and 2009/10 survey data. Serum creatinine categories are grouped in bands of 5 μmol/L from 40μmol/L to 130μmol/L. Serum creatinine values <40 μmol/L and those >130μmol/L are grouped together.

Figure 2. Comparison of low eGFR (<60ml/min/1.73m^2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender

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Table 1. Comparison of prevalence of categorical measures in 2003 and 2009/10[1]

Variable	Category	2003		2009-10		Chi-squared test
		Number	%	Number	%	p-value
All	Aged 16+	7850[2]	100.0	6046[2]	100.0	-
Age	16-34	2425	31.0	1847	30.6	p = 0.44
	34-54	2790	35.7	2129	35.3	
	55-64	1126	14.4	886	14.7	
	65-74	813	10.4	639	10.6	
	75+	662	8.5	539	8.9	
	Missing	0	-	0	-	
Ethnicity	White	7226	92.5	5244	90.7	**p < 0.001**
	South Asian	332	4.3	243	4.2	
	Black	144	1.8	154	2.7	
	Other	108	1.4	139	2.4	
	Missing	0	-	0	-	
Sex	Male	3795	48.6	2961	49.0	p = 0.80
	Female	4020	51.4	3080	51.0	
	Missing	0	-	0	-	
Qualification	Degree	1375	17.6	1295	22.5	**p < 0.001**
	Below degree	4551	58.3	3296	57.0	
	None	1874	24.0	1191	20.6	
	Missing	11	-	3	-	
NSSEC	Highest	2514	33.7	1894	34.8	p = 0.43
	Middle	1674	22.4	1203	22.1	
	Lowest	3273	43.9	2343	43.1	
	Missing	350	-	345	-	
Car Ownership	Yes	6460	82.7	4728	81.7	p = 0.17
	No	1348	17.3	1056	18.3	
	Missing	2	-	1	-	
Tenure	Own	5878	75.4	3955	68.5	**p < 0.001**
	Rent	1914	24.6	1817	31.5	
	Missing	11	-	13	-	
Smoking	Current	1960	25.2	1210	21.0	**p < 0.001**
	Ex	1877	24.1	1429	24.8	
	Never	3951	50.7	3126	54.2	
	Missing	22	-	20	-	
Body mass index	Normal /underweight (<25kg/m^2)	2867	39.2	1956	36.8	**p < 0.001**
	Overweight (25-30 kg/m^2)	2868	39.2	2047	38.5	
	Obese (>30kg/m^2)	1587	21.7	1314	24.7	
	Missing	489	-	469	-	
Waist Circumference	Low (<94cm male, <80cm female)	3060	39.8	2120	37.1	**p < 0.001**
	High (94-102cm male, 80-88cm female)	1929	25.1	1347	23.6	
	Very High	2703	35.1	2242	39.3	

	(>102cm male, >88cm female)					
	Missing	118	-	77	-	
Doctor diagnosed Diabetes	Yes	305	3.9	322	5.3	**p < 0.001**
	No	7504	96.1	5715	94.7	
	Missing	6	-	2	-	
Survey diagnosed Diabetes	Yes (HBA1c ≥6.5%)	296	3.8	316	5.5	**p < 0.001**
	No (HBA1c <6.5%)	7401	96.2	5417	94.5	
	Missing	113	-	52	-	
Total Diabetes	Yes	406	5.2	446	7.4	**p < 0.001**
	No	7405	94.8	5585	92.6	
	Missing	0	-	0	-	
Doctor diagnosed Hypertension	Yes	2118	27.2	1501	25.0	**p = 0.003**
	No	5662	72.8	4527	75.0	
	Missing	36	-	10	-	
Survey diagnosed Hypertension	Yes	2065	31.5	1545	29.2	**p = 0.02**
	No	4499	68.5	3744	70.8	
	Missing	1246	-	496	-	
Total Hypertension	Yes	2866	36.7	2062	34.2	**p = 0.004**
	No	4933	63.3	3968	65.8	
	Missing	12	-	0	-	
eGFR CKDEPI	<45 (ml/min/1.73m^2)	142	1.8	81	1.4	p = 0.07
	<60 (ml/min/1.73m^2)	444	5.7	303	5.2	p = 0.26
	Missing	0	-	0	-	
eGFR MDRD	<45 (ml/min/1.73m^2)	146	1.9	80	1.4	**p = 0.03**
	<60 (ml/min/1.73m^2)	521	6.7	349	6.0	p = 0.13
	Missing	0	-	0	-	

[1] Weighted for non-response (unless stated otherwise)
[2] Not weighted

Table 2. Weighed Comparison of continuous measures in 2003 and 2009-10

Variable	Category	2003	2009-10	Mann Whitney U test
		Median value (IQR)	Median value (IQR)	p value
Serum Creatinine (µmol/L)	Median value	71.7 (62.3 to 82.1)	72.0 (62.0 to 83.0)	p=0.66
eGFR (ml/min/1.73m^2)	MDRD	90.5 (77.2 to 105.4)	90.3 (77.1 to 104.7)	p=0.62
	CKDEPI	99.3 (84.1 to 113.9)	98.6 (84.0. to 112.5)	p=0.11
BMI (kg/m^2)	All	26.2 (23.3 to 29.4)	26.6 (23.5 to 30.0)	**p<0.001**
	Male	26.6 (24.0 to 29.4)	27.0 (24.2 to 29.9)	**p=0.001**
	Female	25.7 (22.7 to 29.5)	26.1 (23.1 to 30.0)	**p<0.001**
Waist circumference (cm)	All	90.6 (81.1 to 100.0)	92.0 (81.6 to 101.7)	**p<0.001**
	Male	95.8 (88.0 to 104.0)	96.7 (88.2 to 105.0)	p=0.05
	Female	84.6 (76.4 to 94.0)	86.3 (77.3 to 96.7)	**p<0.001**
Systolic BP (mmHg)	All	125.5 (115.5 to 138.0)	124.5 (114.0 to 136.0)	**p<0.001**
	Dr-diagnosed HT	135.5 (124.0 to 149.5)	134.0 (122.2 to 145.5)	**p<0.001**
	Dr-diagnosed DM	134.5 (122.5 to 148.0)	131.8 (120.0 to 143.5)	**p<0.001**
	eGFR<60 (CKDEPI)	140.2 (126.0 to 156.0)	131.8 (119.0 to 143.5)	**p<0.001**
	eGFR<60 (MDRD)	137.5 (124.0 to 153.7)	129.2 (118.0 to 142.5)	**p<0.001**
Diastolic BP (mmHg)	All	73.0 (65.5 to 80.5)	72.5 (65.5 to 80.)	**p<0.001**
	Dr-diagnosed HT	77.5 (70.0 to 85.5)	76.0 (68.0 to 83.5)	**p<0.001**
	Dr-diagnosed DM	72.0 (64.5 to 80.5)	71.50 (64.5 to 78.5)	**p<0.001**
	eGFR<60 (CKDEPI)	71.5 (62.9 to 80.5)	68.5 (60.5 to 76.0)	**p<0.001**
	eGFR<60 (MDRD)	72.5 (64.0 to 81.5)	69.0 (61.5 to 76.8)	**p<0.001**
Glycated Hb (%)	All	5.20 (5.00 to 5.50)	5.30 (5.10 to 5.70)	**p<0.001**
	Dr-diagnosed DM	6.90 (5.90 to 8.20)	6.90 (5.90 to 8.30)	p=0.85
HDL Cholesterol (mmol/L)	All	1.50 (1.20 to 1.70)	1.40 (1.20 to 1.70)	**p<0.001**
	Male	1.30 (1.20 to 1.60)	1.30 (1.10 to 1.50)	**p<0.001**
	Female	1.60 (1.40 to 1.90)	1.60 (1.30 to 1.90)	**p=0.046**
Total Cholesterol (mmol/L)	All	5.40 (4.70 to 6.20)	5.20 (4.40 to 5.90)	**p<0.001**
	Male	5.40 (4.70 to 6.20)	5.10 (4.30 to 5.90)	**p<0.001**
	Female	5.40 (4.70 to 6.20)	5.20 (4.50 to 6.00)	**p=0.001**

Table 3. Prevalence and associations of low eGFR (<60ml/min/1.73m^2) by MDRD equation with adjustment for socio-demographic and clinical factors

Variable		MDRD				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	6.7	1	1	1	1
	2009-10	6.0	**0.84 (0.72 – 0.98)***	**0.84 (0.73 – 0.99)***	**0.75 (0.61 – 0.92)****	**0.75 (0.61 – 0.92)****
Age	16-34	0.2	1	1	1	1
	35-54	2.1	**10.8 (5.3 – 22.0)****	**11.1 (5.5 –22.8)****	**10.8 (5.0 – 23.4)****	**10.7 (4.9 – 23.2)****
	55-64	6.8	**37 (18 – 75)****	**36 (18 – 73)****	**33 (15 – 72)****	**32 (14 – 69)****
	65-74	14.5	**87 (43 – 175)****	**82 (40 – 167)****	**65 (30 – 143)****	**62 (28 – 135)****
	75+	35.6	**276 (138 – 555)****	**247 (122 – 501)****	**216 (99 – 470)****	**202 (93 – 440)****
Sex	Male	5.0	1	1	1	1
	Female	7.7	**1.42 (1.22 – 1.65)****	**1.37 (1.17 – 1.60)****	**1.69 (1.36 – 2.10)****	**1.66 (1.34 – 2.06)****
Ethnic	White	6.8	-	1	1	1
	South Asian	1.7	-	0.83 (0.43 – 1.59)	0.73 (0.33 – 1.60)	0.71 (0.32 – 1.56)
	Black	1.7	-	0.38 (0.15 – 1.00)	0.33 (0.09 – 1.19)	0.32 (0.09 – 1.16)
	Other	1.6	-	0.81 (0.29 – 2.30)	0.64 (0.17 – 2.46)	0.64 (0.17 – 2.44)
Tenure	Own	6.3	-	1	1	1
	Rent	6.6	-	**1.34 (1.11 – 1.60)****	1.23 (0.97 – 1.57)	1.23 (0.96 – 1.56)
Education	Degree Level	2.4	-	1	1	1
	Below degree	4.4	-	1.31 (0.99 – 1.74)	1.15 (0.83 – 1.60)	1.20 (0.84 – 1.70)
	None	14.9	-	**1.52 (1.13 – 2.04)****	1.20 (0.84 – 1.70)	1.23 (0.96 – 1.57)
Smoking	Never	6.1	-	-	1	1
	Ex-Smoker	10.1	-	-	1.17 (0.91 – 1.49)	1.15 (0.85 – 1.54)
	Current Smoker	3.2	-	-	1.02 (0.75 – 1.38)	1.04 (0.80 – 1.40)
BMI (kg/m^2)	Normal (<25)	3.4	-	-	1	1
	Overweight (25-30)	6.6	-	-	1.16 (0.91 – 1.49)	1.15 (0.90 – 1.47)
	Obese (>30)	8.4	-	-	1.31 (0.99 – 1.71)	1.26 (0.96 – 1.65)
HDL Cholesterol	Continuous	-	-	-	**0.51 (0.38 – 0.67)****	**0.51 (0.38 – 0.68)****
Total Cholesterol	Continuous	-	-	-	0.91 (0.84 – 1.00)	0.92 (0.84 – 1.00)
Doctor diagnosed Diabetes	No	5.9	-	-	1	1
	Yes	17.3	-	-	1.42 (0.92 – 2.22)	1.36 (0.87 – 2.11)
Doctor diagnosed Hypertension	No	4.0	-	-	-	1
	Yes	13.3	-	-	-	**1.27 (1.03 – 1.55)***

[1]Prevalence for combined 2003 and 2009-10 HSE
[2]Adjusted for age and sex

[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Table 4. Prevalence and associations of low eGFR (<60) by CKDEPI equation with adjustment for socio-demographic and clinical factors

Variable		CKDEPI				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	5.7	1	1	1	1
	2009-10	5.2	0.85 (0.72 – 1.00)	0.86 (0.72 – 1.01)	**0.73 (0.57 – 0.93)***	**0.73 (0.57 – 0.93)***
Age	16-34	0.1	1	1	1	1
	35-54	1.0	**15.1 (4.5 – 51.4)****	**16.1 (4.7 – 55.0)****	**13.8 (4.0 – 47.2)****	**13.5 (3.9 – 46.5)****
	55-64	4.2	**67 (20 – 225)****	**67 (20 – 227)****	**55 (16 – 190)****	**52 (15 – 177)****
	65-74	12.5	**219 (66 – 725)****	**219 (65 – 731)****	**162 (47 – 553)****	**151 (44 – 517)****
	75+	36.8	**890 (269 – 2938)****	**844 (253 – 2808)****	**754 (222 – 2559)****	**693 (203 – 2355)****
Sex	Male	4.6	1	1	1	1
	Female	6.3	1.15 (0.97 – 1.36)	1.11 (0.93 – 1.31)	**1.31 (1.01 – 1.68)***	**1.28 (1.00 – 1.65)***
Ethnic	White	5.8	-	1	1	1
	South Asian	1.4	-	0.93 (0.43 – 2.00)	0.89 (0.35 – 2.42)	0.85 (0.34 – 2.16)
	Black	2.0	-	0.56 (0.23 – 1.39)	0.55 (0.16 – 1.82)	0.53 (0.16 – 1.77)
	Other	1.6	-	1.19 (0.40 – 3.56)	1.13 (0.29 – 4.41)	1.13 (0.29 – 4.41)
Tenure	Own	5.3	-	1	1	1
	Rent	6.0	-	**1.44 (1.19 – 1.75)****	1.29 (0.98 – 1.69)	1.28 (0.97 – 1.69)
Education	Degree Level	1.8	-	1	1	1
	Below degree	3.6	-	1.36 (0.97 – 1.90)	1.05 (0.69 – 1.58)	1.04 (0.69 – 1.58)
	None	13.6	-	**1.51 (1.08 – 2.13)***	1.12 (0.76 – 1.66)	1.11 (0.75 – 1.65)
Smoking	Never	5.2	-	-	1	1
	Ex-Smoker	9.0	-	-	1.09 (0.77 – 1.55)	1.07 (0.75 – 1.52)
	Current Smoker	2.6	-	-	0.80 (0.70 – 1.41)	0.79 (0.54 – 1.14)
BMI (kg/m^2)	Normal (<25)	2.7	-	-	1	1
	Overweight (25-30)	5.5	-	-	1.14 (0.86 – 1.51)	1.12 (0.85 – 1.49)
	Obese (>30)	7.2	-	-	1.31 (0.96 – 1.80)	1.25 (0.91 – 1.72)
HDL Cholesterol	Continuous	-	-	-	**0.40 (0.29 – 0.56)****	**0.40 (0.29 – 0.57)****
Total Cholesterol	Continuous	-	-	-	0.93 (0.84 – 1.04)	0.94 (0.86 – 1.04)
Doctor diagnosed Diabetes	No	5.0	-	-	1	1
	Yes	16.3	-	-	1.55 (0.96 – 2.48)	1.46 (0.91 – 2.35)
Doctor diagnosed Hypertension	No	3.1	-	-	-	1
	Yes	12.3	-	-	-	**1.33 (1.05 – 1.67)****

[1]Prevalence for combined 2003 and 2009-10 HSE

[2]Adjusted for age and sex
[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Change in prevalence of Chronic Kidney Disease in England over time: comparison of nationally representative cross-sectional surveys from 2003 to 2010
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Abstract

Objectives
To determine whether the prevalence of CKD in England has changed over time.
Design
Cross-sectional analysis of nationally representative Health Survey for England (HSE) random samples.
Setting
England 2003 and 2009/2010.
Survey participants
13,896 Adults aged 16+ participating in HSE, adjusted for sampling and non-response, 2009/10 surveys combined.
Main outcome measure
Change in prevalence of eGFR <60ml/min/1.73m^2 (as proxy for stage 3-5 chronic kidney disease [CKD]), from 2003 to 2009/10 based on a single serum creatinine measure using IDMS traceable enzymatic assay in a single laboratory; eGFR derived using MDRD and CKDEPI eGFR formulae.
Analysis
Multivariate logistic regression modelling to adjust time changes for socio-demographic and clinical factors (body mass index, hypertension, diabetes, lipids). A correction factor was applied to the 2003 HSE serum creatinine to account for a storage effect.
Results
~~National prevalence of low eGFR (<60) decreased from 9.6% to 6.0% using MDRD (P<0.001) and from 7.6% in 2003 to 5.2% in 2009/10 using CKDEPI (p<0.001).~~ National p~~P~~revalence of low eGFR (<60) decreased within each age and gender group for both formulae except males aged 65-74. Prevalence of both obesity and diabetes increased in this period, there was a decrease in hypertension. Adjustment for demographic and clinical factors led to a significant decrease in CKD between the surveyed periods. The fully adjusted odds ratio for eGFR<60ml/min/1.73m^2 was ~~0.49 (0.42 0.57)~~ 0.75 (0.61-0.92) comparing 2009/10 with 2003 using the MDRD equation, and was similar using the CKDEPI equation 0.73 (0.57-0.93).
Conclusion
The prevalence of a low eGFR indicative of CKD in England has decreased over this seven year period, despite rising prevalence of obesity and diabetes, two key causes of CKD. Hypertension prevalence declined and blood pressure control improved but this did not appear to explain the fall. Periodic assessment of eGFR and albuminuria in future HSEs is needed to evaluate trends in CKD.

Article Summary

Strengths & Limitations of this study

- This study uses of nationally representative samples, with later HSEs pooled over two years to increase numbers and precision of estimates. The surveys used standardised protocols for measurement by trained interviewers and nurses, with all samples were tested in the same laboratory with standardised assays.
- Another strength of the study is that the analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the application and comparison of the two equations to derive eGFR. Weighting was introduced for both surveyed periods to reduce response bias and account for missing data. A correction factor was applied to 2003 HSE data to adjust for the shift in measured creatinine due to sample storage.
- The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. The study was also limited by a single sample was tested for serum creatinine in each survey,

therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown.

- ~~Another weakness is that~~ The prevalence of stage 4/5 CKD is likely to be underestimated as the HSE may not fully account for some in whom more severe CKD (stage 4/5) will be more common.
- The absence of albuminuria data in the 2003 HSE is another major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management ~~(e.g. use of RAS inhibition).~~ (e.g. use of renin-angiotensin system (RAS) inhibition).

Total word count n=~~3225~~ 3,844

Introduction

Chronic kidney disease (CKD) is recognised as a global public health problem.[1] CKD is defined and staged using the estimated glomerular filtration rate (eGFR) and markers of kidney damage, mainly albuminuria.[2] Both eGFR and albuminuria are strong independent risk factors for all-cause and cardiovascular disease (CVD) mortality, and progression to end-stage renal disease (ESRD), which may require renal replacement therapy (RRT) by dialysis or transplantation.[3] In England in 2010 the prevalence of RRT was 832 per million population, a 3% increase from 2009; NHS costs of RRT were estimated at £780 million for 2009/10, and the total cost at £1.45 billion, a nearly threefold increase on estimated costs for 2002.[4,5]

The population prevalence of CKD in England was reported for the first time using data on eGFR and albuminuria in the nationally-representative Health Surveys for England (HSE) 2009 and 2010, though there had previously been estimates based on routine testing using primary care data.[6,7] In the combined 2009/2010 HSE, 6% of men and 7% of women had eGFR <60ml/min/1.73m^2 (equivalent to CKD stage 3-5 if chronic) with a strong age gradient.[8] The prevalence of low eGFR increased in the US, based on National Health and Nutrition Examination (NHANES) surveys between 1988-2004, even after adjusting for adverse trends in risk factors (obesity, diabetes, hypertension), but little is known about CKD prevalence trends in England.[9,10,11]

Information on prevalence change is needed to assess the impact of trends in underlying determinants, and of strategies to prevent and manage CKD. Several policy initiatives have been introduced in England that have had an impact on prevention, detection and management of CKD. The National Service Framework for Renal Services 2004/05 led to national reporting of eGFR by clinical biochemistry laboratories from 2006,[12] the General Practice pay for performance Quality Outcomes Framework (QOF) included targets for CKD management from 2006/07,[13] and the NHS Vascular Checks Programme, introduced in 2009, includes screening for CKD (stage 3-5) in people aged 35-74 with newly identified type 2 diabetes or hypertension.[14] This study therefore aimed to compare the prevalence of CKD in the HSE 2003 with the combined HSE 2009-10 and to relate this to any changes in prevalence of risk factors for CKD, particularly obesity, diabetes and hypertension, over this period.

Methods

Full details of the conduct of the HSE, measurement of non-CKD variables and response rates are shown in the 2003, 2009 and 2010 Health Survey for England reports.[15,16] Survey participants within private households were selected using a multistage stratified random probability sample. Household response rates were 73% in HSE2003 and 68%/66% in HSE 2009/2010. In co-operating households, 90% and 89%/86% of adults completed an interview questionnaire while 70% and 62%/57% respectively consented to a nurse visit, of whom 74%-76% provided a blood test. The HSE 2003 contained 18,533 individuals and data from HSE 2009 and HSE 2010 were combined to provide a larger sample size of 13,065 individuals. This totalled 31,598 individuals for the combined 2003, 2009 and 2010 HSEs. Eligible participants were individuals aged 16 years and older who had a valid serum creatinine value. This left 7,850 individuals from the 2003 HSE and 6,046 individuals from the combined 2009/10 HSEs, leaving a total of 13,896 individuals for analysis.

Age was grouped into five categories: 16-34, 35-54, 55-64, 65-74 and 75+. There were four separate ethnic groupings: White, South Asian, Black and Other. Socio-economic factors included: i) occupation National Statistics Socio-Economic Classification (NS-SEC, divided into three categories: managerial and professional occupations; intermediate occupations and routine and manual occupations); ii) qualifications grouped as: degree or equivalent; below degree (other qualification) and none (no qualification); iii) household tenure (own vs renting); iv) access to motor vehicle (none vs. any).

Smoking status was defined as current, ex-smoker or never smoked. Hypertension was defined as doctor-diagnosed (pre-existing diagnosis), survey-defined (identified as having high blood pressure (BP, systolic ≥140mmHg and/or diastolic ≥90mmHg and/or taking medication for hypertension) at the survey examination), and 'total' (doctor + survey diagnosed). Survey-defined diabetes was glycated haemoglobin (HBA1c) ≥6.5% at nurse visit. Glycated haemoglobin data are presented for those with and without diagnosed diabetes. Body mass index (BMI) was defined as normal (<25kg/m^2), overweight (≥25, <30kg/m^2), and obese (≥30kg/m^2). Waist circumference was classified as: <94cm, 94–102cm (high), and >102cm (very high) for men, and <80cm, 80–88cm (high) and >88cm (very high) for women. For South Asian men, the waist circumference was classified as: <90cm, 90–102cm (high), and >102cm (very high). High density lipoprotein (HDL) cholesterol and total cholesterol were treated as continuous variables.

To investigate medication use, we examined the use of diuretics, ß-blockers, renin-angiotensin system (RAS) inhibitors (angiotensin-converting-enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs)), calcium channel blockers, and other anti-hypertensives in those with doctor diagnosed hypertension, doctor diagnosed diabetes and eGFR <60ml/min/1.73m^2, and use of lipid lowering agents (the majority of which are statins) in the whole population. In 2003, 47% of respondents answered yes to whether they were taking any prescribed medication, and 50% in 2009/10.

Serum creatinine was assayed using an isotope dilution mass spectrometry (IDMS) traceable enzymatic assay in a single laboratory (Clinical Biochemistry Department at the Royal Victoria Infirmary (RVI), Newcastle-upon-Tyne). Both the Modified Diet in Renal Disease (MDRD) equation (in routine use in the UK) and the newer Chronic Kidney Disease Epidemiology Collaboration (CKDEPI) equation (which provides better risk prediction and is

recommended for use in international guidelines) were used to define CKD.[2,17] eGFR values were derived using the standard equations.[18,19]

Samples were assayed for serum creatinine over a 19 month time period with two different batches of tri-level Internal Quality Control (IQC) material. HSE 2009 and 2010 samples were analysed with Batch 1 or Batch 2 IQC, HSE 2003 samples were analysed with Batch 2 IQC. The creatinine assay was stable over time with IQC results very close to expected target values. Batch 1 IQC gave mean (SD) creatinine concentrations of 56(0.6),167(1.3) and 586(4.9) umol/L for levels 1,2 and 3 respectively compared with target means of 56, 167 and 588 umol/L. Batch 2 material gave mean(SD) creatinine concentrations of 51(1.1), 175(2.2) and 597(5.6)umol/L for levels 1,2 and 3 respectively compared with target means of 51, 175 and 599 umol/L.

Details of laboratory analysis, internal quality control, and external quality assurance are provided in the HSE 2009/10 documentation, with these methods replicated in the 2003 HSE.[8] ~~The HSE 2003 samples had been stored, frozen at -40°C, then thawed for measurement in 2012. Such freezing does not affect creatinine levels.~~[20] The HSE 2003 samples had been stored, frozen at -40°C, then thawed for measurement in 2010. Although such freezing is not thought to affect creatinine levels[20] we undertook a re-analysis in 2014 of a random sample of 500 serum creatinine samples taken from the 2009 HSE and subsequently frozen and stored under the same conditions as the HSE 2003 samples, stratified by quintile, to determine if there was a shift in measured creatinine on storage. We found mean serum creatinine increased on storage and was best predicted by a regression equation where the original 2009 serum creatinine value without storage equaled 0.303 plus 0.94 multiplied by the stored serum creatinine value. We assumed the same effect applied to the 2003 serum creatinine data which were analysed in 2009-10 and we applied the same adjustment. This decreased the 2003 serum creatinine values. eGFR was classified as below 60ml/min/1.73m^2 or equal to or greater than 60ml/min/1.73m^2.

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Statistics

Patient characteristics were compared between the 2003 and 2009/10 HSEs using chi-squared tests for categorical variables and Mann Whitney U tests for non-normally distributed continuous variables. eGFR<60ml/min/1.73m^2 prevalence in 2003 and 2009/10 was compared across age and sex groupings. BP levels were compared in all, in those with diagnosed hypertension and in those with eGFR<60ml/min/1.73m^2; glycated haemoglobin (HBA1c) was compared in all participants and in those with doctor-diagnosed diabetes. Binary logistic regression models were used to examine the relationships between eGFR<60ml/min/1.73m^2 and age, sex and socioeconomic and clinical factors to determine if there were significant differences between the two survey time periods. The dependent variable were CKDEPI and MDRD equation eGFR <60ml/min/1.73m^2 (indicative of stage 3-5 CKD). Four models were produced for each: 1) Age-sex adjusted; 2) model 1 plus socio-economic status and ethnicity; 3) model 2 plus behavioural, lipid levels (HDL and total

cholesterol) and clinical variables except hypertension, 4) Model 3 plus doctor-diagnosed hypertension. Interactions between period and both diabetes and hypertension were tested.

Sensitivity analyses were performed by replacing doctor-diagnosed diabetes with HBA1c and replacing doctor-diagnosed hypertension with diastolic and systolic blood pressure and adjusting for lipid lowering agents in the full model. Non-response and blood sample weights were used in all analyses to address issues with missing ~~data~~ individuals who did not have a blood sample taken and sent to laboratory for analysis to determine serum creatinine value. Full details on how the weights were obtained are provided in the final volume of the HSE report each year. The age, education and smoking status of those interviewed, having a nurse visit and having a blood test is similar once non-response is taken into account (data not shown). All analyses were performed using IBM SPSS Statistics version 20.

Results

The final sample for the study comprised of 13,896 individuals aged 16+ who had a valid serum creatinine value. Comparing the characteristics of these participants between the 2003 and 2009/10 surveys, the age structure, gender, NS-SEC and car ownership were similar while educational level improved and there was an increase in rented tenure (Table 1). Prevalence of diabetes however classified increased, as did obesity. In contrast, smoking and hypertension prevalence decreased.

There were significant increases in BMI, waist circumference and HBA1c in the population though no change in HBA1c in those with diagnosed diabetes (Table 2). Median BP levels (both systolic and diastolic) fell in all groups including those with diagnosed hypertension, doctor-diagnosed diabetes and with eGFR<60ml/min/1.73m^2. Median total and HDL cholesterol fell in both men and women.

The distribution of serum creatinine ~~was shifted to the left in 2009/10; 1.7% values were greater than 130µmol/L in 2003, but only 0.1% in 2009/10~~ is similar for 2003 and 2009/10 (Figure 1). ~~Mean serum creatinine decreased, leading to an increase in mean eGFR using both MDRD and CKDEPI formulae~~ Median serum creatinine increased slightly, leading to a very small non-significant decrease in median eGFR using both MDRD and CKDEPI formulae (Table 2). Mean serum creatinine for those aged 20-39 without doctor diagnosed hypertension or diabetes ~~fell significantly from 74.8µmol/L (SD 14.8) in 2003 to 71.4µmol/L (SD 14.3) in 2009/10 (p<0.001)~~ increased slightly from 70.6µmol/L (SD 13.6) in 2003 to 71.4µmol/L (SD 14.3) in 2009/10 (p=0.09).~~.~~

The proportion of individuals with MDRD eGFR<60ml/min/1.73m^2 decreased from ~~9.66~~6.7% in 2003 to 6.0% in 2009/10 (~~p<0.001~~p=0.13) and with eGFR <45ml/min/1.73m^2 from ~~2.4~~1.9% to 1.4% (p~~<0.001~~=0.03). Corresponding figures for CKDEPI were ~~7.65~~7% and 5.2% (p~~<0.001~~=0.26) and ~~2.2~~1.8% and 1.4% (p=0.0~~01~~7). Prevalence of low eGFR fell in all age and gender groups and with either CKDEPI or MDRD equations, except for males aged 65-74 where there was a slight increase (Figure 2).

There was an increase in the mean number of anti-hypertensive agents taken in individuals with: doctor-diagnosed hypertension (1.19 in 2003 to 2.01 in 2009-10), doctor-diagnosed hypertension and doctor-diagnosed diabetes (1.47 to 2.57); MDRD eGFR <60ml/min/1.73m^2 (1.~~26~~30 to 1.77); and CKDEPI eGFR < 60ml/min/1.73m^2 (1.~~29~~35 to 1.93). The proportion taking RAS inhibitors in individuals with doctor-diagnosed diabetes, doctor-diagnosed hypertension, MDRD eGFR <60ml/min/1.73m^2 or CKDEPI eGFR < 60ml/min/1.73m^2 also increased, as did overall lipid lowering agent use (Appendix 1).

The age-sex adjusted odds ratio (OR) of having low eGFR (MDRD eGFR<60ml/min/1.73m^2) in 2009/10 compared with 2003 was 0.~~52~~84 (95% confidence interval (CI) 0.~~45~~72-0.98~~60~~) and fully adjusted was 0.75 (0.61-0.92) (Table 3). ~~This pattern was maintained on further adjustment for potential confounding factors (Table 3) and when using CKDEPI eGFR (Table 4).~~ The corresponding ORs for CKDEPI were 0.85 (0.72-1.00) and 0.73 (0.57-0.93) (Table 4).

Sensitivity analyses replacing doctor-diagnosed diabetes with HBA1c and doctor-diagnosed hypertension with diastolic and systolic BP made little difference to the adjusted ORs as did the inclusion of lipid lowering agents. No interactions between period and diabetes or hypertension were identified.

Discussion

These analyses show that CKD prevalence in England estimated by serum creatinine based equations in England decreased from 2003 to 2009/10. This decrease was seen across all age groupings (except makes aged 65-74), for CKD defined by both MDRD and CKDEPI eGFR equations ~~(though more pronounced for the MDRD equation), and despite~~ was more pronounced for the MDRD equation and occurred despite increased prevalence of both diabetes and obesity.[21] Using the CKDEPI equation in place of MDRD to define CKD resulted in a lower prevalence of CKD. Whilst it reduces overall prevalence, the CKDEPI equation identifies more individuals aged 75+ with CKD compared with the MDRD equation.[22,23]

The HSE 2003, 2009 and 2010 were nationally representative samples, with the 2009/10 data pooled over two years to increase numbers and precision of estimates. The age-sex characteristics of the different study periods sampled were similar. The surveys used standardised protocols for measurement by trained interviewers and nurses. All samples were tested in the same laboratory with standardised assays. The analyses enable a longitudinal comparison of CKD estimates across different age-sex groupings and the

application and comparison of the two equations to derive eGFR. ~~Weighting was introduced for both surveyed periods to reduce response bias and account for missing data.~~ We accounted for the shift in measured creatinine on storage in the 2003 HSE serum creatinine data by introduction of a correction factor derived from analysis of the effect of storage using 2009 data. Non-response weighting was undertaken in the HSE for both surveyed periods to reduce response bias and account for missing data for individuals who did not have blood sample taken and hence no serum creatinine value. We used both the HSE study design and the non-response weights to provide national prevalence estimates at each period and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences. The ethnic composition of the surveys changed over time with a small fall in the White population, but we adjusted for this change in the analysis.

The study was limited by the cross-sectional nature of the HSE, which restricts the ability to infer causal relationships from the associations identified. However the use of new, cross-sectional samples enables measurement of general population CKD prevalence at different time points. A single sample was tested for serum creatinine in each survey, and therefore the persistence of reduced eGFR levels to confirm chronicity cannot be shown. This is standard practice in national surveys such as NHANES, whereas studies based on routine testing can assess chronicity, such as the QICKD study. [24] Given the individual variation in kidney function, more extreme values will be averaged out on repeated testing (regression to the mean), reducing the prevalence of low eGFR.[24] The results may therefore slightly overestimate the prevalence of CKD. ~~Despite high numbers of participants,~~ There were too few cases from the key minority ethnic groups to give robust data on ethnic differences in prevalence of CKD~~, over 90% of the participants for both survey periods were white (data not shown).~~ South Asians and Black groups have higher rates of renal replacement but have been found to have lower prevalence of CKD than Caucasians.[25,26]

Prevalence of stage 4/5 CKD is likely to be underestimated as, whilst the HSE is able to adjust for non-response among the general population in private households, it may not fully account for some in whom more severe CKD (stage 4/5) will be more common. This includes people who were not able to give a blood or urine sample because of poor health and those who did not participate due to concurrent illness or hospitalisation, as well as those in residential care.

The absence of albuminuria data in the 2003 HSE is a major limitation, given its strong independent association with adverse outcomes and its use to stratify risk for prevention and management (e.g. use of RAS inhibition).[3] We have therefore been unable to estimate changes in prevalence of albuminuria per se, in all CKD (stages1-5), and fully assess prevention and management.

The fall in low prevalence of eGFR could be due i) chance ii) artefact of differences in the serum creatinine measurement, iii) changes in serum creatinine production rather than excretion by the kidney, iv) residual confounding by differences in sample characteristics not adjusted for by sample weighting, v) true fall in eGFR. ~~The period effects were highly statistically significant making chance unlikely. The 2003 assay results data were from stored sera, however this should be stable for creatinine even after long storage.[20] Moreover, if the 2003 serum creatinine had been underestimated this would have reduced any fall over the period.~~ The two sets of samples were analysed in multiple analytical runs over a 19 month time period, which could lead to differences in results, however during this time period the internal quality control data indicates that the assay was accurate compared with assigned target values and stable~~, with no indication of assay drift with time~~. ~~Artefact due to serum creatinine measurement changes does not seem to be the explanation. A fall in serum creatinine over time independent of kidney function could be due to less muscle~~

~~mass (leading to lower serum creatinine production); there is no evidence for this and it seems unlikely to have occurred at the population level. A fall in dietary protein consumption from cooked meat could also lead to fall in serum creatinine. Cooked meat consumption has been shown to increase serum creatinine in small case studies of volunteers and of patients with diabetic nephropathy and hence national guidance is to avoid eating cooked meat for 12 hours before a blood test for creatinine[27] but this was not done in HSE. We used the HSE study design and non response weights and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics differences is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences.~~

A change in serum creatinine over time independent of kidney function could be due to less muscle mass (leading to lower serum creatinine production); there is no evidence for this and it seems unlikely to have occurred at the population level.

A decline in dietary protein consumption from cooked meat could also lead to change in serum creatinine. Statistics from the National Diet and Nutrition Survey show that meat consumption increased from 2001-02 to 2008-10 while protein intake remained virtually stable over the same period. [28] Mean consumption of meat and meat products increased from 154g per day in 2001-02 to 194g per day in 2008-10; protein intake contributing to food energy for adults aged 19+ increased slightly from 16-17% in 2001-02 to 17-18% in 2008-10; meat and meat products contributed to 37-38% of all protein intake for adults aged 19-64, with little change compared to 2008-10. Cooked meat consumption has been shown to increase serum creatinine in small case studies of volunteers and of patients with diabetic nephropathy and hence national guidance is to avoid eating cooked meat for 12 hours before a blood test for creatinine[29] but this was not done in HSE.

We used the HSE study design and non-response weights and adjusted for a wide range of socio-demographic factors so residual confounding due to differences in sample characteristics differences is less likely. Moreover, the distribution of age groupings was similar for both periods, so does not explain the observed eGFR differences.

Key risk groups for developing CKD are those with hypertension and or diabetes especially if they have albuminuria. In this study there was evidence of modest reductions in the prevalence of hypertension, better control of hypertension in key groups, and greater use of RAS inhibitors which have anti-proteinuric as well as BP lowering effects, though the period changes in eGFR remained after correction for changes in hypertension prevalence. There is evidence from some studies using HSE, primary care databases and QOF data,[28-30] though not all,[31] of improved hypertension control in the last decade. However there are ethnic disparities with poorer control of BP in Black and South Asians who have higher risk of progression to need RRT.[32] Population salt consumption also fell during the last decade which is likely to have influenced population BP.[33,34] CKD prevalence could fall too if those identified with moderate CKD were treated more aggressively, especially those with hypertension and or albuminuria, leading to increased eGFR in some people to above 60ml/min/1.73m^2. The limited HSE data suggest better BP control and greater use of RAS inhibitors in those with eGFR <60ml/min/1.73m^2. Karunetatne et al examined BP control in those with and without CKD in a primary care population in Kent and showed that BP control had improved in CKD patients over time pre- and post the introduction of QOF and that it was greater than in non-CKD hypertensive patients. They also showed increased use of RAS inhibitors and other anti-hypertensive agents in CKD patients.[35] ~~Whilst there was a small fall in population lipid levels and some evidence of increased statin use, this would not be expected to lead to a reduced incidence of CKD, and our period changes were not altered by adjusting for lipid levels.[36]~~

There was evidence of increased lipid lowering agent use (indicative of increased statin use) and a small fall in population lipid levels. There is some evidence of reno-protective effects of statins in CKD patients; A lower rate of decline in GFR was found in patients with renal disease who took antilipemic agents.[38] In the Heart Protection Study, the use of the hypolipidemic drug simvastatin reduced the rise in slightly elevated creatinine over time in both diabetic and non-diabetic CKD participants.[39] In the SHARP trial allocation of the lipid lowering ezetimibe plus simvastatin in participants not already on dialysis at randomisation reduced the outcome of end stage renal disease or a doubling of creatinine with an odds ratio of 0.93, though this was not statistically significant.[40] In the GREACE trial statin treatment prevented decline in renal function in people with high blood lipids and coronary heart disease; patients not treated with statins showed a 5.2% decrease in creatinine clearance, while patients treated with statins showed a 4.9% increase in creatinine clearance.[41] However our period changes were not altered by adjusting for statins (lipid lowering drugs) or lipid levels (HDL, total cholesterol).[37]

There are limited data from other countries with which to compare these findings. Coresh et al analysed the US NHANES surveys of 1988-1994 and 1999-2004, which both collected albuminuria and eGFR data. Both prevalence of albuminuria and MDRD eGFR <60ml/min/1.73m^2 increased, the latter from 5.6% to 8.1%.[8] The albuminuria increase was explained by changes in levels of obesity, diabetes and hypertension, whereas this adjustment only partly explained eGFR falls. Changes in population serum creatinine explained most of the remainder of the eGFR changes; this was analysed by comparing the mean serum creatinine in young people aged 20-39 without diabetes or hypertension and this had increased across the surveys.[9] The authors suggested that this rise in serum creatinine could be due to residual laboratory assay differences or to changes in dietary protein or muscle mass. Grams et al showed that prevalence of eGFR<60ml/min/1.73m^2 had also increased using the same survey data when eGFR was estimated using Cystatin C, a marker of kidney function that is independent of muscle mass, and this was not explained by changes in demography, hypertension, diabetes or obesity, suggesting a true increase in low eGFR.[37]

We can compare the estimated national CKD prevalence for HSE with QOF returns which record diagnosed CKD in primary care.[43] Prevalence has been increasing with improvements in detection and recording and in 2010 was 4.2%. The figures are not directly comparable as comparing a single screened value versus routine testing with presumed allowance for chronicity, but this may suggest some under-diagnosis of CKD.

If this change in prevalence in England is true, then based on the HSE 2003 age-sex-specific estimates and 2001 and 2011 Census data, the estimated number of CKD cases (for those aged 16 and over) would be 2.62 million based on the MDRD equation, falling by 0.03 million for 2009/10. Equivalent figures for CKDEPI eGFR <60ml/min/1.73m^2 are 2.23 million and 0.02 million increase respectively. The impact of such changes would be twofold: a consistent pool of patients at risk of progressing to need RRT; and a contribution to consistent cardiovascular incidence and mortality. The former is supported by stabilised acceptance rates onto RRT in England.[4]

~~If this change in prevalence in England is true, then based on the HSE 2003 age-sex-specific estimates and 2001 and 2011 Census data, the estimated number of CKD cases (for those aged 16 and over) would be 3.77 million based on the MDRD equation, falling by 1.18 million for 2009/10. Equivalent figures for CKDEPI eGFR <60ml/min/1.73m^2 are 2.98 million and 0.75 million respectively. The impact of such changes would be twofold: a reduced pool of patients at risk of progressing to need RRT; and a contribution to falling~~

~~cardiovascular incidence and mortality. The former is supported by stabilised acceptance rates onto RRT in England.[4]~~

Conclusions

The prevalence of a low eGFR appears to have decreased in England from 2003 to 2009/10, despite increases in obesity and diabetes. It is unclear why this has occurred and it is difficult to infer directly that this is due to current policies to improve prevention of CKD and the identification and management of people with CKD. There is a need for repeated national prevalence estimates to further assess CKD patterns over time, including measures of albuminuria and of Cystatin C, both of which were available in HSE 2009 and 2010.

What is already known on this topic

- eGFR and albuminuria are strong independent risk factors for progression to end-

stage renal disease (ESRD), which may require costly renal replacement therapy (RRT)
- Prevalence of low eGFR has increased over time in countries such as the US, even after adjustment for adverse trends in CKD risk factors
- Little is known about CKD prevalence trends in England

What this study adds
- Prevalence of a low eGFR derived from serum creatinine and indicative of CKD in England has decreased from 2003 to 2009/10, despite increasing prevalence of diabetes and obesity
- This pattern of prevalence of low eGFR was maintained even after adjustment for potential mediating and confounding factors
- A future need for repeated national prevalence estimates, that includes measures of albuminuria and Cystatin C, is required to further assess CKD patterns over time.

Contributors: GA was involved in the analysis and interpretation of the data. PR drafted the paper. GA, PR, SF and GM made substantial contributions to the study conception and

design. JM co-ordinated the Health Surveys for England. DO provided background information on CKD policy. JD conducted the laboratory analyses. All authors critically reviewed the paper and were involved in the drafting and approval of the manuscript. GA is the guarantor.

Acknowledgements: Scott Harris contributed to the production of the regression equation that was applied to the 2003 serum creatinine samples as a correction factor.

Funding: Kidney function testing in the Health Surveys for England was funded by NHS Kidney Care. GA is funded by a University of Southampton PhD scholarship.

Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

Ethical approval: Approval was obtained from the London Multi-Centre Research Ethnics Committee for the 2003 survey (HSE 2003 ref MREC/02/2/72) and approval was obtained from the Oxford B Research Ethics Committee for both 2009 and 2010 surveys (HSE 2009 ref 08/H0605/103, HSE 2010 ref 09/H0605/73).

Transparency: The lead author (the manuscript's guarantor) affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data sharing: The HSE 2003, 2009 and 2010 are archived with the UK Data Service. Creatinine measurements for the HSE 2003 undertaken for this study will be archived in due course.

Figure Legends

Figure 1. Distribution of serum creatinine (µmol/L) for 2003 and 2009/10 survey data. Serum creatinine categories are grouped in bands of 5 µmol/L from 40µmol/L to 130µmol/L. Serum creatinine values <40 µmol/L and those >130µmol/L are grouped together.

Figure 2. Comparison of low eGFR (<60ml/min/1.73m^2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender

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Table 1. Comparison of prevalence of categorical measures in 2003 and 2009/10[1]

Variable	Category	2003		2009-10		Chi-squared test
		Number	%	Number	%	p-value
All	Aged 16+	7850[2]	100.0	6046[2]	100.0	-
Age	16-34	2425	31.0	1847	30.6	p = 0.441
	34-54	2790	35.7	2129	35.3	
	55-64	1126	14.4	886	14.7	
	65-74	813	10.4	639	10.6	
	75+	662	8.5	539	8.9	
	Missing	0	-	0	-	
Ethnicity	White	7226	92.5	5244	90.7	**p < 0.001**
	South Asian	332	4.3	243	4.2	
	Black	144	1.8	154	2.7	
	Other	108	1.4	139	2.4	
	Missing	0	-	0	-	
Sex	Male	3795	48.6	2961	49.0	p = 0.803
	Female	4020	51.4	3080	51.0	
	Missing	0	-	0	-	
Qualification	Degree	1375	17.6	1295	22.5	**p < 0.001**
	Below degree	4551	58.3	3296	57.0	
	None	1874	24.0	1191	20.6	
	Missing	11	-	3	-	
NSSEC	Highest	2514	33.7	1894	34.8	p = 0.434
	Middle	1674	22.4	1203	22.1	
	Lowest	3273	43.9	2343	43.1	
	Missing	350	-	345	-	
Car Ownership	Yes	6460	82.7	4728	81.7	p = 0.1768
	No	1348	17.3	1056	18.3	
	Missing	2	-	1	-	
Tenure	Own	5878	75.4	3955	68.5	**p < 0.001**
	Rent	1914	24.6	1817	31.5	
	Missing	11	-	13	-	
Smoking	Current	1960	25.2	1210	21.0	**p < 0.001**
	Ex	1877	24.1	1429	24.8	
	Never	3951	50.7	3126	54.2	
	Missing	22	-	20	-	
Body mass index	Normal /underweight (<25kg/m^2)	2867	39.2	1956	36.8	**p < 0.001**
	Overweight (25-30 kg/m^2)	2868	39.2	2047	38.5	
	Obese (>30kg/m^2)	1587	21.7	1314	24.7	
	Missing	489	-	469	-	
Waist Circumference	Low (<94cm male, <80cm female)	3060	39.8	2120	37.1	**p < 0.001**
	High (94-102cm male, 80-88cm female)	1929	25.1	1347	23.6	

	Very High (>102cm male, >88cm female)	2703	35.1	2242	39.3	
	Missing	118	-	77	-	
Doctor diagnosed Diabetes	Yes	305	3.9	322	5.3	**p < 0.001**
	No	7504	96.1	5715	94.7	
	Missing	6	-	2	-	
Survey diagnosed Diabetes	Yes (HBA1c ≥6.5%)	296	3.8	316	5.5	**p < 0.001**
	No (HBA1c <6.5%)	7401	96.2	5417	94.5	
	Missing	113	-	52	-	
Total Diabetes	Yes	406	5.2	446	7.4	**p < 0.001**
	No	7405	94.8	5585	92.6	
	Missing	0	-	0	-	
Doctor diagnosed Hypertension	Yes	2118	27.2	1501	25.0	**p = 0.003**
	No	5662	72.8	4527	75.0	
	Missing	36	-	10	-	
Survey diagnosed Hypertension	Yes	2065	31.5	1545	29.2	**p = 0.0219**
	No	4499	68.5	3744	70.8	
	Missing	1246	-	496	-	
Total Hypertension	Yes	2866	36.7	2062	34.2	**p = 0.004**
	No	4933	63.3	3968	65.8	
	Missing	12	-	0	-	
eGFR CKDEPI	<45 (ml/min/1.73m^2)	142176	1.82.2	8181	1.41.4	p = 0.07**p = 0.001**
	<60 (ml/min/1.73m^2)	444594	5.77.6	303303	5.25.2	p = 0.26**p < 0.001**
	Missing	00	--	00	--	
eGFR MDRD	<45 (ml/min/1.73m^2)	146186	1.92.4	8080	1.41.4	**p = 0.03p < 0.001**
	<60 (ml/min/1.73m^2)	521751	6.79.6	349349	6.06.0	p = 0.13**p < 0.001**
	Missing	0	-	0	-	

[1] Weighted for non-response (unless stated otherwise)
[2] Not weighted

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Table 2. Weighed Comparison of continuous measures in 2003 and 2009-10

Variable	Category	2003	2009-10	Mann Whitney U test
		Median value (IQR)	Median value (IQR)	p value
Serum Creatinine (µmol/L)	Median value	71.7 (62.3 to 82.1)~~76.0 (66.0 to 87.0)~~	72.0 (62.0 to 83.0)~~72.0 (62.0 to 83.0)~~	p=0.66~~**p<0.001**~~
eGFR (ml/min/1.73m^2)	MDRD	90.5 (77.2 to 105.4)~~84.7 (72.2 to 98.7)~~	90.3 (77.1 to 104.7)~~90.3(77.1 to 104.7)~~	p=0.62~~**p<0.001**~~
	CKDEPI	99.3 (84.1 to 113.9)~~94.3 (78.6 to 109.7)~~	98.6 (84.0. to 112.5)~~98.6 (84.0. to 112.5)~~	p=0.11~~**p<0.001**~~
BMI (kg/m^2)	All	26.2 (23.3 to 29.4)	26.6 (23.5 to 30.0)	**p<0.001**
	Male	26.6 (24.0 to 29.4)	27.0 (24.2 to 29.9)	**p=0.001**
	Female	25.7 (22.7 to 29.5)	26.1 (23.1 to 30.0)	**p<0.001**
Waist circumference (cm)	All	90.6 (81.1 to 100.0)	92.0 (81.6 to 101.7)	**p<0.001**
	Male	95.8 (88.0 to 104.0)	96.7 (88.2 to 105.0)	p=0.052
	Female	84.6 (76.4 to 94.0)	86.3 (77.3 to 96.7)	**p<0.001**
Systolic BP (mmHg)	All	125.5 (115.5 to 138.0)	124.5 (114.0 to 136.0)	**p<0.001**
	Dr-diagnosed HT	135.5 (124.0 to 149.5)	134.0 (122.2 to 145.5)	**p<0.001**
	Dr-diagnosed DM	134.5 (122.5 to 148.0)	131.8 (120.0 to 143.5)	**p<0.001**
	CKD (CKDEPI)	139.5 (126.0 to 154.5)	131.8 (119.0 to 143.5)	**p<0.001**
	CKD (MDRD)	137.0 (123.0 to 151.0)	129.2 (118.0 to 142.5)	**p<0.001**
Diastolic BP (mmHg)	All	73.0 (65.5 to 80.5)	72.5 (65.5 to 80.)	**p<0.001**
	Dr-diagnosed HT	77.5 (70.0 to 85.5)	76.0 (68.0 to 83.5)	**p<0.001**
	Dr-diagnosed DM	72.0 (64.5 to 80.5)	71.50 (64.5 to 78.5)	**p<0.001**
	eGFR<60 (CKDEPI)	72.0 (64.5 to 80.5)	68.5 (60.5 to 76.0)	**p<0.001**
	eGFR<60 (MDRD)	73.0 (65.5 to 81.5)	69.0 (61.5 to 76.8)	**p<0.001**
Glycated Hb (%)	All	5.20 (5.00 to 5.50)	5.30 (5.10 to 5.70)	**p<0.001**
	Dr-diagnosed DM	6.90 (5.90 to 8.20)	6.90 (5.90 to 8.30)	p=0.8546
HDL Cholesterol (mmol/L)	All	1.50 (1.20 to 1.70)	1.40 (1.20 to 1.70)	**p<0.001**
	Male	1.30 (1.20 to 1.60)	1.30 (1.10 to 1.50)	**p<0.001**
	Female	1.60 (1.40 to 1.90)	1.60 (1.30 to 1.90)	**p=0.0546**
Total Cholesterol (mmol/L)	All	5.40 (4.70 to 6.20)	5.20 (4.40 to 5.90)	**p<0.001**
	Male	5.40 (4.70 to 6.20)	5.10 (4.30 to 5.90)	**p<0.001**

	Female	5.40 (4.70 to 6.20)	5.20 (4.50 to 6.00)	**p=0.001**

~~**Figure 1. Distribution of serum creatinine (μmol/L) for 2003 and 2009/10 survey data. Serum creatinine categories are grouped in bands of 5 μmol/L from 40μmol/L to 130μmol/L. Serum creatinine values <40 μmol/L and those >130μmol/L are grouped together.**~~

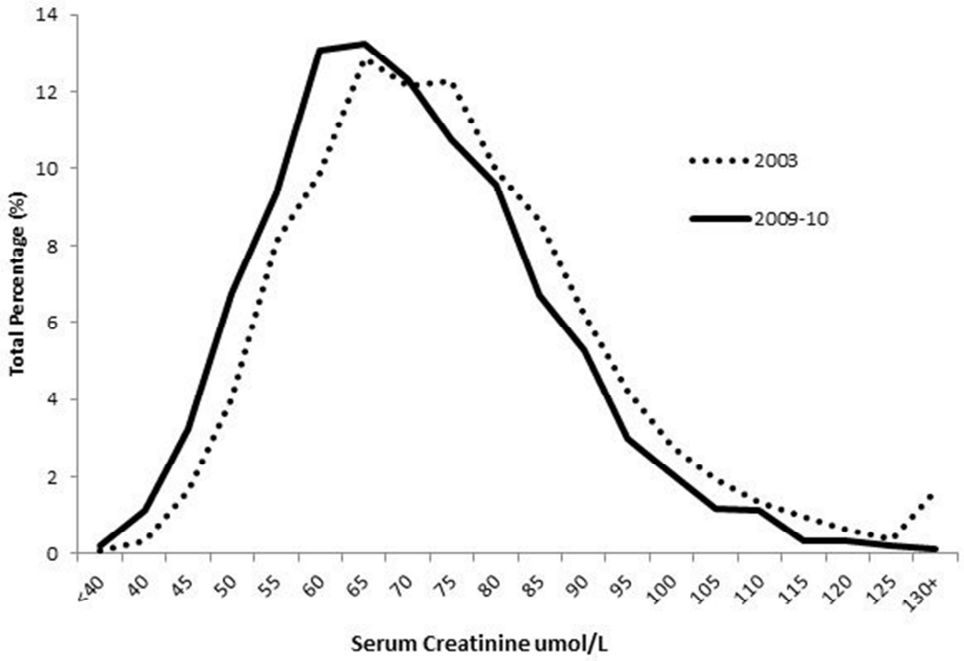

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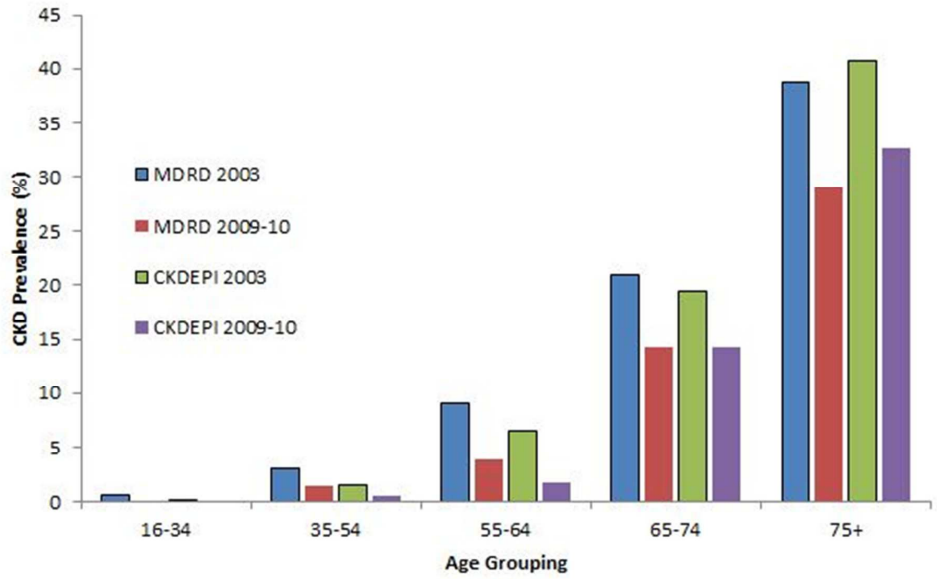
Figure 2. Comparison of low eGFR (<60ml/min/1.73m^2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender

Male



Female

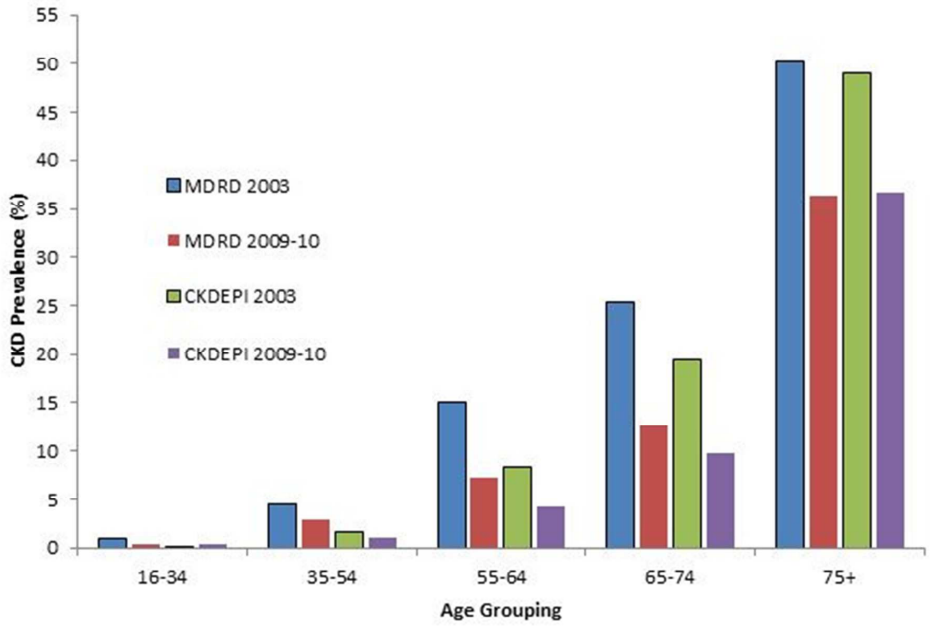


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Table 3. Prevalence and associations of low eGFR (<60ml/min/1.73m^2) by MDRD equation with adjustment for socio-demographic and clinical factors

Variable		MDRD				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	6.7~~9.6~~	1	1	1	1
	2009-10	6.0~~6.0~~	**0.84 (0.72 – 0.98)*~~0.52 (0.45 – 0.60)**~~**	**0.84 (0.73 – 0.99)*~~0.53 (0.44 – 0.62)**~~**	**0.75 (0.61 – 0.92)**~~0.48 (0.41 – 0.57)**~~**	**0.75 (0.61 – 0.92)**~~0.49 (0.42 – 0.57)**~~**
Age	16-34	0.2~~0.6~~	1	1	1	1
	35-54	2.1~~3.0~~	**10.8 (5.3 – 22.0)**~~5.8 (3.7-9.0)**~~**	**11.1 (5.5 – 22.8)**~~5.7 (3.5-9.1)**~~**	**10.8 (5.0 – 23.4)**~~5.2 (3.3 – 8.2)**~~**	**10.7 (4.9 – 23.2)**~~5.0 (3.2 – 7.9)**~~**
	55-64	6.8~~9.2~~	**37 (18 – 75)**~~19 (12 – 30)**~~**	**36 (18 – 73)**~~17 (11 – 28)**~~**	**33 (15 – 72)**~~14 (9 – 23)**~~**	**32 (14 – 69)**~~13 (8 – 20)**~~**
	65-74	14.5~~19.0~~	**87 (43 – 175)**~~44 (28 – 68)**~~**	**82 (40 – 167)**~~39 (24 – 63)**~~**	**65 (30 – 143)**~~31 (20 – 50)**~~**	**62 (28 – 135)**~~28 (17 – 44)**~~**
	75+	35.6~~40.3~~	**276 (138 – 555)**~~127 (83 – 196)**~~**	**247 (122 – 501)**~~109 (69 – 175)**~~**	**216 (99 – 470)**~~88 (55 – 140)**~~**	**202 (93 – 440)**~~76 (48 – 122)**~~**
Sex	Male	5.0~~6.3~~	1	1	1	1
	Female	7.7~~9.8~~	**1.42 (1.22 – 1.65)**~~1.45 (1.26 – 1.68)**~~**	**1.37 (1.17 – 1.60)**~~1.39 (1.19 – 1.62)**~~**	**1.69 (1.36 – 2.10)**~~1.45 (1.23 – 1.70)**~~**	**1.66 (1.34 – 2.06)**~~1.43 (1.22 – 1.67)**~~**
Ethnic	White	6.8~~8.6~~	-	1	1	1
	South Asian	1.7~~2.3~~	-	0.83 (0.43 – 1.59)~~0.63 (0.32 – 1.26)~~	0.73 (0.33 – 1.60)~~0.74 (0.41 – 1.34)~~	0.71 (0.32 – 1.56)~~0.72 (0.40 – 1.32)~~
	Black	1.7~~2.7~~	-	0.38 (0.15 – 1.00)~~0.73 (0.32 – 1.69)~~	0.33 (0.09 – 1.19)~~0.41 (0.17 – 1.02)~~	0.32 (0.09 – 1.16)~~0.40 (0.16 – 1.01)~~
	Other	1.6~~2.4~~	-	0.81 (0.29 – 2.30)~~1.19 (0.46 – 3.08)~~	0.64 (0.17 – 2.46)~~0.92 (0.36 – 2.30)~~	0.64 (0.17 – 2.44)~~0.93 (0.37 – 2.34)~~
Tenure	Own	6.3~~8.3~~	-	1	1	1
	Rent	6.6~~7.6~~	-	**1.34 (1.11 – 1.60)**~~1.13 (0.93 –~~	1.23 (0.97 – 1.57)~~1.11 (0.92 –~~	1.23 (0.96 – 1.56)~~1.10 (0.91 –~~

				1.36)	1.34)	1.33)
Education	Degree Level	2.43.1	-	1	1	1
	Below degree	4.45.9	-	1.31 (0.99 – 1.74)1.29 (0.98 – 1.70)	1.15 (0.83 – 1.60)**1.34 (1.03 – 1.74)***	1.20 (0.84 – 1.70)**1.33 (1.02 – 1.74)***
	None	14.918.2	-	**1.52 (1.13 – 2.04)****1.43 (1.06 – 1.93)***	1.20 (0.84 – 1.70)**1.50 (1.14 – 1.99)****	1.23 (0.96 – 1.57)**1.50 (1.13 – 1.98)****
Smoking	Never	6.17.7	-	-	1	1
	Ex-Smoker	10.112.8	-	-	1.17 (0.91 – 1.49)1.23 (0.97 – 1.55)	1.15 (0.85 – 1.54)1.20 (0.94 – 1.53)
	Current Smoker	3.24.3	-	-	1.02 (0.75 – 1.38)1.22 (0.96 – 1.57)	1.04 (0.80 – 1.40)1.19 (0.94 – 1.51)
BMI (kg/m^2)	Normal (<25)	3.44.3	-	-	1	1
	Overweight (25-30)	6.68.8	-	-	1.16 (0.91 – 1.49)**1.57 (1.30 – 1.90)****	1.15 (0.90 – 1.47)**1.51 (1.25 – 1.83)****
	Obese (>30)	8.410.6	-	-	1.31 (0.99 – 1.71)**1.80 (1.47 – 2.21)****	1.26 (0.96 – 1.65)**1.65 (1.33 – 2.03)****
HDL Cholesterol	Continuous	--	-	-	**0.51 (0.38 – 0.67)****0.53 (0.41 – 0.68)****	**0.51 (0.38 – 0.68)****0.54 (0.43 – 0.69)****
Total Cholesterol	Continuous	--	-	-	0.91 (0.84 – 1.00)0.95 (0.88 – 1.11)	0.92 (0.84 – 1.00)0.96 (0.90 – 1.12)
Doctor diagnosed Diabetes	No	5.97.5	-	-	1	1
	Yes	17.319.9	-	-	1.42 (0.92 – 2.22)1.42 (0.95 – 2.12)	1.36 (0.87 – 2.11)1.31 (0.88 – 1.97)
Doctor diagnosed Hypertension	No	4.05.1	-	-	-	1
	Yes	13.316.5	-	-	-	**1.27 (1.03 – 1.55)***1.47 (1.23 – 1.75)****

[1]Prevalence for combined 2003 and 2009-10 HSE
[2]Adjusted for age and sex

[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Table 4. Prevalence and associations of low eGFR (<60) by CKDEPI equation with adjustment for socio-demographic and clinical factors

Variable		CKDEPI				
		Prevalence of CKD (%)[1]	OR (95% CI)[2]	OR (95% CI)[3]	OR (95% CI)[4]	OR (95% CI)[5]
HSE Year	2003	5.7~~7.6~~	1	1	1	1
	2009-10	5.2~~5.2~~	0.85 (0.72 – 1.00)~~0.57 (0.48-0.67)**~~	0.86 (0.72 – 1.01)~~0.59 (0.49 – 0.71)**~~	**0.73 (0.57 – 0.93)*~~0.52 (0.43 – 0.63)**~~	**0.73 (0.57 – 0.93)*~~0.52 (0.43 – 0.62)**~~
Age	16-34	0.1~~0.1~~	1	1	1	1
	35-54	1.0~~1.3~~	**15.1 (4.5 – 51.4)**~~8.4 (3.7 – 19.2)**~~	**16.1 (4.7 – 55.0)**~~7.5 (3.3 – 17.1)**~~	**13.8 (4.0 – 47.2)**~~9.1 (3.7 – 22.1)**~~	**13.5 (3.9 – 46.5)**~~8.7 (3.6 – 21.2)**~~
	55-64	4.2~~5.6~~	**67 (20 – 225)**~~38 (17.4 – 86.0)**~~	**67 (20 – 227)**~~31 (14 – 69)**~~	**55 (16 – 190)**~~38 (16 – 91)**~~	**52 (15 – 177)**~~33 (14 – 81)**~~
	65-74	12.5~~16.3~~	**219 (66 – 725)**~~128 (58 – 292)**~~	**219 (65 – 731)**~~104 (47 – 231)**~~	**162 (47 – 553)**~~119 (50 – 269)**~~	**151 (44 – 517)**~~103 (43 – 247)**~~
	75+	36.8~~41.0~~	**890 (269 – 2938)**~~465 (212 – 1019)**~~	**844 (253 – 2808)**~~356 (160 – 790)**~~	**754 (222 – 2559)**~~420 (175 – 1003)**~~	**693 (203 – 2355)**~~357 (149 – 857)**~~
Sex	Male	4.6~~5.6~~	1	1	1	1
	Female	6.3~~7.6~~	1.15 (0.97 – 1.36)~~1.17 (1.01 – 1.37)*~~	1.11 (0.93 – 1.31)~~1.11 (0.93 – 1.32)~~	**1.31 (1.01 – 1.68)*~~1.37 (1.09 – 1.70)**~~	**1.28 (1.00 – 1.65)*~~1.36 (1.09 – 1.67)**~~
Ethnic	White	5.8~~7.0~~	-	1	1	1
	South Asian	1.4~~1.7~~	-	0.93 (0.43 – 2.00)~~0.80 (0.36 – 1.79)~~	0.89 (0.35 – 2.42)~~0.66 (0.30 – 1.99)~~	0.85 (0.34 – 2.16)~~0.63 (0.29 – 1.97)~~
	Black	2.0~~2.3~~	-	0.56 (0.23 – 1.39)~~0.90 (0.35 – 2.34)~~	0.55 (0.16 – 1.82)~~0.47 (0.16 – 1.87)~~	0.53 (0.16 – 1.77)~~0.44 (0.14 – 1.56)~~
	Other	1.6~~1.6~~	-	1.19 (0.40 – 3.56)~~1.13 (0.33 – 3.88)~~	1.13 (0.29 – 4.41)~~1.42 (0.22 – 2.89)~~	1.13 (0.29 – 4.41)~~1.44 (0.24 – 3.03)~~
Tenure	Own	5.3~~6.5~~	-	1	1	1
	Rent	6.0~~6.8~~	-	**1.44 (1.19 –**	1.29 (0.98 –	1.28 (0.97 –

				1.75)**1.31 (1.07 – 1.62)*	1.69)1.30 (1.04 – 1.59)*	1.69)1.29 (1.05 – 1.59)*
Education	Degree Level	1.82.1	-	1	1	1
	Below degree	3.64.4	-	1.36 (0.97 – 1.90)1.32 (0.94 – 1.84)	1.05 (0.69 – 1.58)1.23 (0.87 – 1.79)	1.04 (0.69 – 1.58)1.24 (0.86 – 1.81)
	None	13.616.2	-	**1.51 (1.08 – 2.13)***1.42 (0.99 – 2.02)	1.12 (0.76 – 1.66)1.32 (0.95 – 1.85)	1.11 (0.75 – 1.65)1.33 (0.97 – 1.86)
Smoking	Never	5.26.2	-	-	1	1
	Ex-Smoker	9.010.7	-	-	1.09 (0.77 – 1.55)1.20 (0.90 – 1.59)	1.07 (0.75 – 1.52)1.17 (0.81 – 1.44)
	Current Smoker	2.63.1	-	-	0.80 (0.70 – 1.41)0.99 (0.70 – 1.41)	0.79 (0.54 – 1.14)0.96 (0.68 – 1.45)
BMI (kg/m^2)	Normal (<25)	2.73.4	-	-	1	1
	Overweight (25-30)	5.56.8	-	-	1.14 (0.86 – 1.51)1.43 (1.15 – 1.78)**	1.12 (0.85 – 1.49)1.36 (1.09 – 1.70)**
	Obese (>30)	7.28.6	-	-	1.31 (0.96 – 1.80)1.78 (1.40 – 2.25)**	1.25 (0.91 – 1.72)1.72 (1.27 – 2.04)**
HDL Cholesterol	Continuous	--	-	-	**0.40 (0.29 – 0.56)****0.49 (0.37 – 0.66)**	**0.40 (0.29 – 0.57)****0.49 (0.37 – 0.65)**
Total Cholesterol	Continuous	--	-	-	0.93 (0.84 – 1.04)0.95 (0.89 – 1.03)	0.94 (0.86 – 1.04)0.97 (0.90 – 1.04)
Doctor diagnosed Diabetes	No	5.06.0	-	-	1	1
	Yes	16.318.4	-	-	1.55 (0.96 – 2.48)1.59 (1.02 – 2.48)*	1.46 (0.91 – 2.35)1.49 (0.96 – 2.33)
Doctor diagnosed Hypertension	No	3.13.8	-	-	-	1
	Yes	12.314.5	-	-	-	**1.33 (1.05 – 1.67)****1.40 (1.14 – 1.72)**

[1]Prevalence for combined 2003 and 2009-10 HSE

[2]Adjusted for age and sex
[3]Adjusted for age, sex, ethnicity, tenure and education
[4]Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol and doctor diagnosed diabetes
[5] Adjusted for age, sex, ethnicity, tenure, education, smoking, BMI, HDL cholesterol, total cholesterol, doctor diagnosed diabetes and doctor diagnosed hypertension
* p<0.05 **p<0.01

Appendix 1: Medication use in key subgroups who reported yes to taking doctor prescribed medication

		2003				2009-10		
Group	**Drug type**	**Number**	**Yes (%)**	**No (%)**		**Number**	**Yes (%)**	**No (%)**
Any Doctor-diagnosed hypertension	**Diuretics**	2118	523 (24.7%)	1595 (75.3%)		1501	378 (25.2%)	1123 (74.8%)
	ß-Blockers		419 (19.8%)	1699 (80.2%)			249 (16.6%)	1252 (83.4%)
	Calcium channel blockers		324 (15.3%)	1794 (84.7%)			357 (23.8%)	1144 (76.2%)
	RAS inhibitors		1027 (48.5%)	1091 (52.5%)			932 (62.1%)	569 (37.9%)
Any Doctor-diagnosed diabetes	**RAS inhibitors**	305	172 (56.4%)	133 (43.6%)		322	199 (61.8%)	123 (38.2%)
eGFR <60ml/min/1.73m^2 MDRD	**RAS inhibitors**	751	386 (51.4%)	365 (48.6%)		349	205 (58.7%)	144 (41.3%)
eGFR <60ml/min/1.73m^2 CKDEPI	**RAS inhibitors**	594	351(59.1%)	243 (40.9%)		303	199 (65.7%)	104 (34.3%)
All	**Lipid lowering**	7810	484 (6.2%)	7326 (93.8%)		5786	770 (13.3%)	5016 (86.7%)

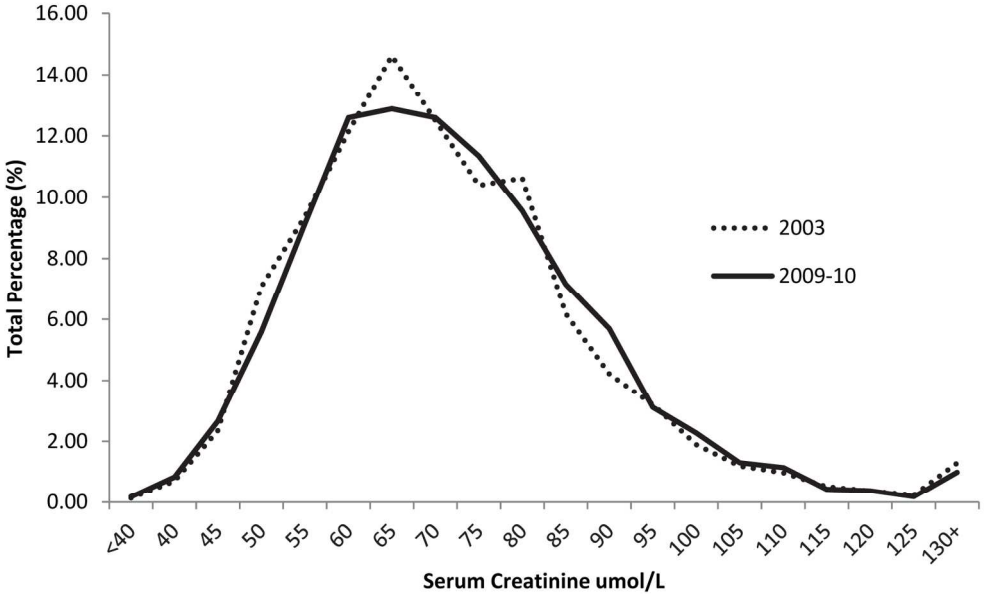

Figure 1. Distribution of serum creatinine (μmol/L) for 2003 and 2009/10 survey data.
Serum creatinine categories are grouped in bands of 5 μmol/L from 40μmol/L to 130μmol/L. Serum creatinine values <40 μmol/L and those >130μmol/L are grouped together.

156x93mm (300 x 300 DPI)

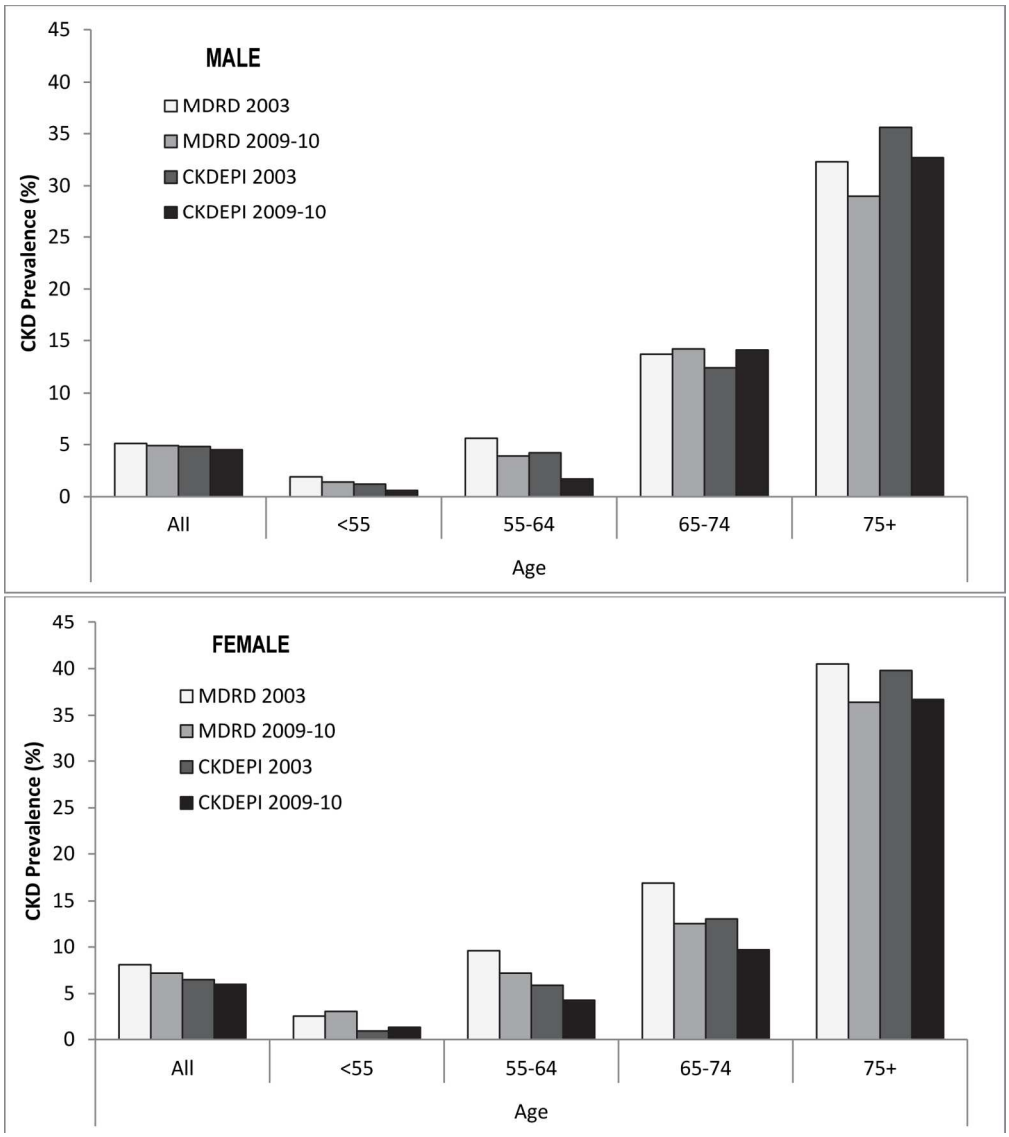

Figure 2. Comparison of low eGFR (<60ml/min/1.73m2) prevalence difference for MDRD and CKDEPI equations between the 2003 and 2009/10 HSE for each age group by gender
159x179mm (300 x 300 DPI)

Appendix 1: Medication use in key subgroups who reported yes to taking doctor prescribed medication

		2003				2009-10		
Group	**Drug type**	**Number**	**Yes (%)**	**No (%)**		**Number**	**Yes (%)**	**No (%)**
Any Doctor-diagnosed hypertension	**Diuretics**	2118	523 (24.7%)	1595 (75.3%)		1501	378 (25.2%)	1123 (74.8%)
	ß-Blockers		419 (19.8%)	1699 (80.2%)			249 (16.6%)	1252 (83.4%)
	Calcium channel blockers		324 (15.3%)	1794 (84.7%)			357 (23.8%)	1144 (76.2%)
	RAS inhibitors		1027 (48.5%)	1091 (52.5%)			932 (62.1%)	569 (37.9%)
Any Doctor-diagnosed diabetes	**RAS inhibitors**	305	172 (56.4%)	133 (43.6%)		322	199 (61.8%)	123 (38.2%)
eGFR <60ml/min/1.73m^2 MDRD	**RAS inhibitors**	521	279 (53.6%)	242 (46.4%)		349	205 (58.7%)	144 (41.3%)
eGFR <60ml/min/1.73m^2 CKDEPI	**RAS inhibitors**	444	273 (61.5%)	171 (38.5%)		303	199 (65.7%)	104 (34.3%)
All	**Lipid lowering**	7810	484 (6.2%)	7326 (93.8%)		5786	770 (13.3%)	5016 (86.7%)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	2,3
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	4
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	4
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4,5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4,5
Bias	9	Describe any efforts to address potential sources of bias	4,5
Study size	10	Explain how the study size was arrived at	4
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	4,5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	5
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	6, 16
		(b) Indicate number of participants with missing data for each variable of interest	16
Outcome data	15*	Report numbers of outcome events or summary measures	16
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	21,22,23
		(*b*) Report category boundaries when continuous variables were categorized	16,17
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	n/a
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	6
Discussion			
Key results	18	Summarise key results with reference to study objectives	7
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	7
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	7,8
Generalisability	21	Discuss the generalisability (external validity) of the study results	8,9
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.