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Original Article

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The impact of population-based identification of chronic kidney disease using estimated glomerular filtration rate (eGFR) reporting

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Abstract

Background. The object of this study was to determine the impact of estimated glomerular filtration rate (eGFR) reporting, as part of a disease management programme (DMP), and clarify the prevalence of chronic kidney disease (CKD) and the level of un-met need in a UK Primary Care Trust.

Methods. Our approach was to prospectively identify patients with an eGFR <60 ml/min/1.73 m^2 using the four-variable MDRD equation in all patients from West Lincolnshire PCT (population 185 434 over the age of 15 years) having a routine estimation of serum creatinine.

Results. During the first 12 months of the programme 25.4% of the population had an eGFR reported. The likelihood of having an eGFR reported increased markedly with age. The prevalence of CKD stages 3–5 within primary care was 7.3%. Only 3.7% of patients with CKD stages 3–5 were under nephrology care compared to 13.7% in non-nephrology secondary care and 82.6% in primary care. There were marked differences in the male to female ratio between primary care and nephrology care, 1:1.9 versus 0.6:1, respectively ($P < 0.001$). The incidence of newly identified patients with CKD stages 4 and 5 was 0.16%. Initially there was a marked (up to 7-fold month on month) rise in nephrology referrals following institution of eGFR reporting which was reversed by the introduction of a referral management service as part of the DMP. Only 33% of patients with CKD stage 4 or 5, identified from within primary care, went on to have a nephrology referral in the subsequent 12 months compared with 44% and 78% respectively identified from non-nephrology secondary care ($P < 0.001$).

Conclusions. The reporting of the eGFR in association with this DMP effectively identified patients with CKD. A referral assessment programme can effectively ensure appropriate nephrology referral and avoids exceeding the capacity of nephrology services. The vast majority of patients with CKD stages 3–5 are cared for within primary care. There are marked gender differences in the prevalence of CKD stages 3–5 that are not reflected by referral patterns to nephrology services. There are significant differences in referral practices between primary and secondary care. In a steady state the burden of incident patients with CKD stages 4–5 should not exceed the capacity of the local nephrology service.

Keywords CKD; disease management; eGFR; prevalence

Introduction

The prevalence of chronic kidney disease stages 3–5 in the United Kingdom is estimated to be between 5% and 8.5% [1,2], which is comparable to the figure of 4.7% [3] in the USA. Despite this, the acceptance rate to dialysis of new patients in the United Kingdom is approximately two-thirds of that of Western Europe and one-third of that in the USA [3]. Between 22% and 67% of patients commencing dialysis in the United Kingdom do so with <3 months' predialysis care, which is associated with significantly higher morbidity and mortality than those with >12 months' predialysis care [5]. This alone should be a reason to pursue earlier diagnosis. Furthermore, early identification of patients with CKD offers the potential to delay progression and reduce the high cardiovascular morbidity and mortality of this group of patients [6].

The burden of CKD is increasing and has been likened to an epidemic [7]. The number of patients with end-stage renal disease, in Europe and the USA, has doubled in the last two decades due to the ageing population and the epidemic of type 2 diabetes. It is estimated that the number will not plateau for the next two decades [7]. CKD carries with it not only the risk of progression to end-stage renal disease but also increased morbidity and mortality from cardiovascular disease [8–10]. Indeed, it is more likely that a patient with CKD stages 3–5 will die of cardiovascular disease than progress to dialysis [11]. CKD does not affect all sectors of the population equally, with higher prevalence in the elderly, patients of South Asian and Afro Caribbean

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origin and the socially disadvantaged [12]. There is evidence that upstream preventative strategies could significantly reduce the burden of disease [13] and there is evidence that such strategies are not in place. Thus, CKD fulfils the four criteria required for being a public health issue [14].

The four-variable MDRD equation, although not without its shortcomings, provides an accessible and pragmatic way of estimating a patient's glomerular filtration rate (eGFR). It is generally accepted as a better tool for estimating renal function than serum creatinine alone. The automated reporting of the eGFR was widely introduced throughout the NHS in April 2006 following recommendations of part II of the National Service Framework for Renal Disease [15] and the Joint Royal College guidelines on the identification, management and referral of patients with chronic kidney disease [16]. This paper describes the impact of eGFR reporting, as part of a disease management programme, in West Lincolnshire Primary Care Trust on the identification and referral of patients with CKD stages 3–5 from April 2005, 1 year prior to the national role out of eGFR reporting.

Subjects and methods

West Lincolnshire Primary Care Trust (WLPCT) has a population of 185 434 aged $\geq$15 years, covers an area of 750 square miles and has 109 general practitioners in 40 practices, 31 of whom agreed to take part in the programme. There is one whole time equivalent nephrologist in the local district general hospital. Optimal Renal Care UK (ORC UK) commenced a primary care-based disease management programme (DMP) for patients with CKD in April 2005 in WLPCT. The database was closed to new patients in November 2006. The programme was guideline- and algorithm-based, derived from an established DMP in the USA and the draft UK guidelines at that time for the identification, management and referral of patients with CKD [15]. The programme relied on automated patient identification using the eGFR generated from all routine serum creatinine (measured using an Olympus AU640, rate Jaffe method) samples received in the Lincolnshire pathology computer system. The programme specifically did not set out to screen the population and did not offer guidance on which patients should be tested, relying instead on those patients who were tested as part of their routine care. The eGFR was calculated automatically using the four-variable MDRD formula [16] with results being reported to the requesting clinician and to ORC UK. Estimated GFR reporting was introduced 2 weeks prior to the commencement of the DMP. Blood samples received from inpatients were not considered in this analysis. The DMP guidance stated that an initial eGFR $<$60ml/min/1.73 m^2 should be repeated within a week to confirm the original result and exclude acute renal injury. In retrospect, this was unrealistic. All the results reported were repeated, 82.4% at $>$90 days following the original. Patients were designated as primary care, secondary care (non-nephrology) or nephrology care dependent upon the site of origin of the first eGFR received during the course of the programme. Patients with CKD stage 3, 4 or 5 originating in primary care or secondary care (non-nephrology) were tracked prospectively for 12 months looking for an eGFR originating from within nephrology care. Patients were considered not to be under active nephrology care if they did not have an eGFR result originating from within nephrology in the 12 months preceding their identification by the DMP.

The DMP was primary care based but spanned both primary and secondary care. The programme was based around a bespoke IT solution and delivered by community nurses, dietician and social worker. This team of individuals provided a resource for the patients, primary care and secondary care. Care was delivered face to face and by the phone. The main objectives of the programme were automated identification, change in referral practice to ensure appropriate referrals, patient education leading to patient empowerment and management to defined and continuously audited outcome targets. Patient education was based around CKD and its implications, life style change, medicines management and dietary modification where appropriate. Patients had access to a named individual they could contact for information without a prior appointment at times to suite them. Patients were risk stratified to determine the frequency of planned contact with the care team.

Differences between proportions were assessed by chi-square tests, differences between mean by Student's *t*-tests, with $P < 0.05$ being taken as significant. Values were calculated using Sigma Stat 3.0 San Jose CA, USA.

Results

Patients identified

In the first 12 months of the programme, an eGFR was reported from blood samples originating in primary care, from 47 119 patients (males 21 446, females 25 673) representing 25.4% (males 23.8%, females 26.9%) of the population aged $\geq$15 years. The proportion of the population tested increased markedly with age (Table 1). Twenty-nine percent (males 22.1%, females 34.6%) of eGFR results were in the CKD stage 3–5 range, giving an estimated prevalence of CKD stages 3–5 of 7.3% within primary care (males 5.3%, females 9.3%, $P < 0.001$) with a male to female ratio of 1:1.86 based on the initial eGFR result.

Over the course of the first 6 weeks the number of eGFR requests increased by 9.7% from a mean of 2893 $\pm$ 130 per week to 3204 $\pm$ 31 per week over the subsequent 30 weeks ($P < 0.002$).

The total number of patients identified by CKD stage, sex and site are shown in Table 2. In total, only 3.7% of patients with CKD stages 3–5 were under active nephrology care compared with 13.7% in non-nephrology secondary care and 82.6% in primary care (Table 2). Only in patients with CKD stage 5 were the majority under nephrology care. In contrast to primary care, there were significantly fewer women than men under nephrology care (0.57:1, $P < 0.001$). The patients identified were elderly (Table 3) with 65%, 81% and 49% being over the age of 70 in CKD stages 3, 4 and 5 respectively. The estimate of prevalence of CKD 3–5 from all sources is 8.8%, which is markedly age related (Table 4).

Table 1. Numbers and percentage of the population with an eGFR recorded between 1 April 2005 and 31 March 2006 by age, derived from an estimate of serum creatinine originating in primary care

Age (years)	Males tested	% population	Females tested	% population	Total tested	% population
15–19	212	2.8	476	6.4	688	4.6
20–29	610	4.4	1379	9.7	1989	7.1
30–39	1176	8.0	1983	13.0	3159	10.5
40–49	2459	15.6	3007	19.0	5466	17.3
50–59	4227	29.0	4234	28.9	8461	28.9
60–69	5602	47.0	5303	44.1	10 905	45.5
70–79	4761	60.5	5303	57.8	10 064	59.1
≥80	2399	63.1	3988	59.5	6387	60.8
Total	21 446	23.8	25 673	26.9	47 119	25.4

Table 2. Total number of patients identified by sex, site and CKD stage and the percentage of patients by site of identification, based on their initial eGFR recorded by the DMP

	Primary care		Secondary care		Nephrology care		
	Females no. (%)	Males no. (%)	Females no. (%)	Males no. (%)	Females no. (%)	Males no. (%)	Total
CKD 3	8486 (55.3)	4496 (29.3)	1319 (8.6)	805 (5.2)	77 (0.5)	162 (1.0)	15 354
CKD 4	346 (38.5)	217 (24.2)	59 (6.6)	50 (5.6)	96 (10.7)	129 (14.4)	897
CKD 5	39 (16.5)	32 (13.5)	8 (3.4)	13 (5.5)	48 (20.2)	97 (40.9)	237

Table 3. Age distribution by CKD stage expressed as percentage

Age	CKD 3	CKD 4	CKD 5
<20	0.0	0.1	0.0
20–29	0.2	0.5	2.9
30–39	0.9	1.4	6.8
40–49	2.9	2.4	9.2
50–59	9.3	4.2	11.6
60–69	21.9	10.6	20.8
70–79	33.8	30.6	27.1
>80	31.1	50.0	21.7

Table 4. Prevalence, of CKD stages 3–5, expressed as patients per million of the population

Age	CKD 3	CKD 4	CKD 5
<20	96	48	0
20–29	750	111	168
30–39	3 199	268	341
40–49	10 442	440	440
50–59	35 529	826	601
60–69	102 579	2 536	1314
70–79	222 429	10 270	2406
>80	332 393	271 182	3136

Subsequent nephrology referral

Of 779 patients with CKD stage 4 identified from primary care and not previously known to the nephrologists, 256 (33%) went on to have a subsequent nephrology outpatient appointment compared to 215 of 486 (44%) patients identified from non-nephrology secondary care ($P < 0.001$). Of 52 patients with CKD 5 identified from primary care, not previously known to the nephrologists, 17 (33%) had a subsequent nephrology outpatient referral compared to 114 of 147 patients identified from secondary care (78%) ($P < 0.001$).

Historic referrals

In 2004–2005, 53 patients with CKD stage 4–5 were referred to the nephrology services from all sources from WLPCT; 11 (20.8%) died within 12 months. In 2005–2006 the ORC UK DMP enrolled 483 patients with CKD stage 4 or 5; 50 (10.4%) died within 12 months ($P < 0.05$). This suggests that the programme was having a significant impact in terms of earlier referral relative to previous clinical practice.

Impact of eGFR reporting on nephrology referrals

There was an initial increase in referrals following introduction of eGFR reporting. This reflects the increased identification of patients not previously suspected of having CKD, which is an expected consequence. Expressed as a 3-month rolling average, the number of referrals rose to 2.7 times compared to their level during the 11 months prior to commencement of the DMP (Figure 1).

Following the introduction of a referral assessment service in October 2005, as part of the DMP, there was a month on month decline in referrals with a reduction of 42% from the peak after 9 months. The referral rate remained elevated at 1.5 times greater than the 11 months prior to introduction of the eGFR reporting, but the patients referred were more appropriate for a specialist service: those approaching dialysis, those with a significant fall of eGFR or those with systemic symptoms and/or significant proteinuria (PCR >100).

The introduction of the referral assessment service demonstrated that 40% of referrals did not follow the referral guidelines and could be returned to the referring

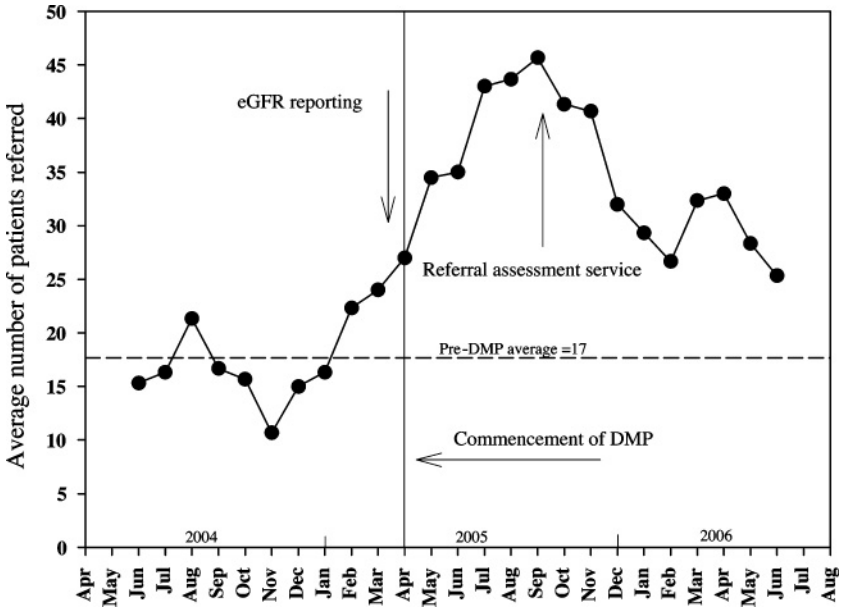

Fig. 1. Monthly nephrology referrals, prior to and following introduction of eGFR reporting, commencement of the disease management programme (DMP) and the referral assessment service, expressed as a 3-month rolling average.

clinician with additional guidance. The proportion of referrals where guidelines had not been adequately followed remained at about 40% throughout.

Guidance within the ORC UK DMP suggested that all patients with CKD stage 4 or 5 should be referred for a nephrology opinion. Clearly, this raises issues of capacity within secondary care nephrology services. Examining patient identification week on week there was an initial surge in patient identification (as those previously unrecognized were identified), with a peak of 95 at Week 2. This tailed off rapidly such that a steady state developed after about 6 months with an average of five new CKD stage 4 or 5 patients being identified each week thereafter, equivalent of an incidence of 0.16%, which is within the capacity of the local nephrology service (Figure 2).

Discussion

These data, from the ORC UK DMP, confirm that CKD is common, that there is evidence of historic under diagnosis and under referral and that an overwhelming majority of patients are currently cared for in primary care. There is now good evidence that preventative strategies exist, mainly targeted at reduction of cardiovascular risk, which will reduce morbidity and mortality and progression to end-stage renal disease in these patients [13]. Whilst the burden of disease in terms of CKD stages 3–5 is high (8.8% in this population), it is comparable to that described by Stevens *et al.* [2]. When CKD stages 4 and 5 are considered, the incidence is much lower (0.16% in this population). It is these patients who are most likely to benefit from the specialist intervention of a secondary care-based nephrology service. After the initial surge in patient identification has passed (about 6 months following introduction of eGFR reporting) the number of new cases is such that broadly they may be dealt with within current nephrology service resources. However, experience from the referral assessment service suggested that neither the local nor national guidance on diagnosis, referral and management was being followed. As such, nephrology services can be readily overwhelmed unless eGFR reporting is introduced along side a referral assessment service to ensure that the guidelines are adhered to. The increase in referral numbers is clearly important; however, possibly of greater importance is the change of referral type due to enforced adherence to the referral guidelines through the referral management process. The result of this is that the nephrologists are now seeing appropriate patients to whose management they are likely to add value, thus improving the utilisation of this scarce resource.

Whilst the DMP did not undertake population screening and did not offer guidance as to which patients should be tested it is likely that there has been a degree of ascertainment bias. The people tested would not represent the general population, and the fact that the number of eGFR requests increased significantly following the introduction of eGFR reporting and commencement of the DMP would serve to support this notion. It has not been possible to ascertain whether the increase in eGFR requests and number of referrals was related to the introduction of eGFR reporting, the commencement of the programme or a combination of the two. Figure 2 suggests that the number of referrals was increasing prior to both eGFR reporting and commencement of DMP. This is almost certainly related to an awareness of the programme within the PCT.

The MDRD equation provides a pragmatic method for estimating GFR, that is superior to creatinine alone, but it is not without its limitations. In particular, it may not be valid in certain racial groups (for example Asian populations) and

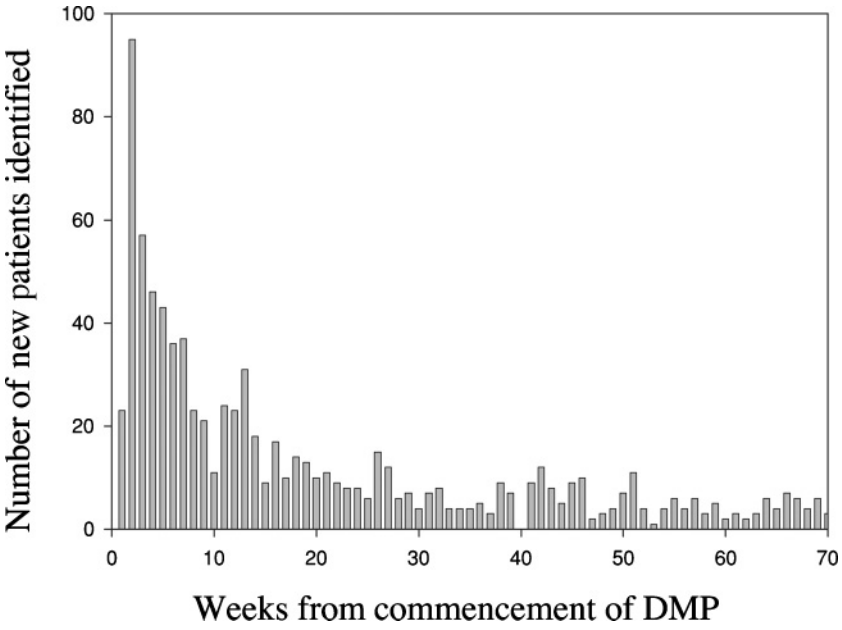

Fig. 2. Number of new patients identified each week with CKD stage 4 or 5.

it relies on the estimation of serum creatinine, which may be confounded by other factors (e.g. extremes of body size, exceptional dietary protein intake, liver disease). Based on the 2001 census, the population of Lincolnshire is 98.64% White, 0.17% Black and 0.49% Asian, so race is unlikely to be a significant factor. Patients were not given instructions to fast prior to test nor was a dietary history taken from each patient, as quite clearly this is practically impossible in the context of the routine treatment programme. In view of this, it is possible that some patients will have had either an inappropriately high or low eGFR.

When undertaking risk assessment in patients with CKD, an important factor to take into account is the presence or otherwise of significant proteinuria. The guidance in the DMP suggested that urinalysis for protein should be undertaken in all patients with an eGFR of <9;90 ml/min/1.73 m^2. This guidance did not take into account that urine testing is not routinely undertaken in primary care due to a combination of cost and logistics. As a result of this, insufficient data were obtained to be of any value.

For patients with CKD stage 4 or 5 there are obvious differences in subsequent referral to a nephrology service between primary and secondary (non-nephrology) care. These differences may be related to case mix with frailer more elderly patients in primary care or may be related to clinical practice with secondary care patients being more actively managed.

These data suggest that women are approximately 2-fold more likely to have CKD stages 3–5 than men but are much less likely to be referred to a nephrology service. Whilst this is not related to the severity of the CKD, it may be related to age and the level of comorbidity and bias introduced by the greater longevity of women. In addition, the detection of CKD based on serum creatinine may have resulted in an under recognition of the severity of CKD (and hence lower referral rates) in women due to their reduced muscle mass. A number of previous studies have noted similar gender difference as described above. Clause *et al*. [17] used four equations to assess renal function in a large community-based, non-diabetic population who participated in NHANES III describing higher prevalence of CKD in women using both the MDRD and Cockcroft–Gault equations. Coresh *et al*. [18] also examined the NHANES data and described a 50% greater prevalence rate in women than men using the simplified MDRD equation. Similar findings were also reported by Viktorsdottir *et al.* [19] in Iceland, and John *et al.* [19] and Stevens *et al.* [2] in the United Kingdom. However, Chadban *et al.* [21], using the Cockcroft–Gault equation, did not report significant gender differences in Australians. These findings are interesting as they fly in the face of ERSD statistics where men are disproportionably represented [22]. Whilst there are a number of possible explanations for this discrepancy, it also remains possible that both the Cockcroft–Gault and simplified MDRD equations may underestimate GFR in women although other explanations are possible.

In summary, these data demonstrate that eGFR reporting effectively identifies patients with significant renal disease (CKD stages 3–5) permitting appropriate referral of those patients most likely to benefit from a nephrology service whilst allowing the majority to remain in primary care. There is a risk that local nephrology services may be overwhelmed by eGFR reporting in the absence of referral management systems to ensure that the referral guidelines are appropriately interpreted and adhered to. In the long term, eGFR reporting should allow the early identification of patients with CKD to ensure that measures can be put into place to delay progression and improve cardiovascular outcomes. In addition, it should ensure that acceptance rates to dialysis appropriately reflect the demand from those who might benefit from treatment, whilst reducing the number of patients who present with ESRF and commence dialysis

with <3 months' pre-dialysis care. The gender differences in prevalence of CKD and referral patterns require further examination.

Conflict of interest statement. The results presented in this paper have not been published in whole or part except in abstract format. Dr N.T. Richards is an employee of Fresenius Medical Care Renal Services UK Ltd. Dr D. Marcelli is an employee of Fresenius Medical Care Ag and Co KaGA. All other authors declare that they have no conflict of interest to declare.

(See related article by Nick Richards *et al*. Primary care-based disease management of chronic kidney disease (CKD), based on estimated glomerular filtration rate (eGFR) reporting, improves patient outcomes. *Nephrol Dial Transplant* 2008; 23: 549–555.)

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