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Delta eGFR: An intuitive method of assessing progression and regression of chronic kidney disease (CKD)

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Poster Abstracts

How common is early CKD?

Reduced eGFR—does this mean CKD?

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Chronic kidney disease (CKD) is a growing public health concern. We aimed to establish with increased accuracy the prevalence of CKD in those with at least 1 creatinine $\geq 150 \mu\text{mol/l}$ (males) and $\geq 130 \mu\text{mol/l}$ (females) in a 6-month period in Grampian (population 500 000).

In a linked study (Poster Dr TZ Ali), 1918 patients could not be classified as having CKD as they did not fulfil our original criteria. 1405 of these have been analysed to date. All available creatinines were converted to eGFR (abbreviated MDRD formula) and patients were grouped according to their likelihood of having CKD. Unlikely $n=80$ (5%), Possible $n=245$ (17%), Probable $n=933$ (66%) and insufficient data $n=147$ (10%).

Those in the 'Probable' group were staged according to their index eGFR. Markers of kidney damage

determined from case note review allowed a further 61 patients to be staged (994 in total). Of these, 82% are in Stage 3, 17.7% Stage 4 and 0.3% in Stage 5. Hypertension and ischaemic heart disease were the most common comorbidities. Mortality in Stage 3 was 45% at 30–36 months.

131 patients in the 'Unlikely' group without markers were classed as having no definite evidence of CKD (5% of 1405). The remaining 336 patients had insufficient data for classification (25% of 1405).

70% (994) of patients in this study have evidence of CKD. A substantial minority (30%) have no conclusive evidence of CKD. These patients may have been included in other prevalence studies thus overestimating the prevalence of CKD.

Epidemiology of chronic kidney disease—a population-based study

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Chronic kidney disease (CKD) is a major public health problem. Most of the studies of prevalence are based on a single measure of renal function. We hypothesize that this may overestimate the prevalence of CKD.

In Grampian, we identified all patients with index serum creatinine concentrations $\geq 150 \mu\text{mol/l}$ (male) or $\geq 130 \mu\text{mol/l}$ (female) over a 6-month period between 1 January 2003 and 30 June 2003. CKD was defined as three elevated creatinine values (going back as far as

1996) each separated by at least 1 month with the rise sustained for 12 months. Patients were placed in stages 3–5 (KDOQI) after estimating GFR (MDRD equation). All case notes were studied.

25 275 elevated creatinines from 5321 patients were identified. 2315 (44%) were defined as having CKD. Eighty-three percent were ≥ 65 years old and 89% had two or more comorbid conditions: only 23% were known to renal physicians, 18% had died at 12 months. 324 patients were receiving RRT and

88 patients had acute on chronic renal failure. The prevalence of CKD in this 6-month period was 5454 pmp.

Of the remaining 2594, 474 had acute renal failure (ARF) according to the ADQI criteria, 202 were visitors to this area. 1918 (36%) were unclassified: many with

fluctuating levels of creatinine and it was unclear whether these had CKD.

CKD prevalence may be overestimated by using single elevated creatinine. Most patients are not known to renal physicians although the new Quality and Outcomes Framework (QOF) is changing this.

Prevalence of patients with chronic kidney disease attending the South East Essex Heart Failure Service

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Background. Patients with chronic heart failure (CHF) may have evidence of renal impairment, usually ascribed to a combination of poor cardiac output and the use of ACE-I, ARBs and diuretics.

We have audited the prevalence of renal impairment in patients under the care of the South East Essex Heart Failure Service (SEEHFS) during the latter part of 2005 and for 3 months in 2006 intending to develop pathways to manage chronic kidney disease (CKD).

Methods. Any patient with a serum creatinine $>12\mu\text{mol/l}$ during July–December 2005 had a retrospective eGFR (MDRD) calculated. Patients known to the renal service or with renal imaging were identified. Patients in July–September 2006 in whom eGFR was available were subject to a similar process with review of urinalysis.

Results. In 2005, 481 patients were on the SEEHFS register. 155 had a serum creatinine $>12\mu\text{mol/l}$; 99 Men CKD: stage 3 89; stage 4 3 and stage 5 1 (on HD); 56 women: stage 3 33, Stage 4 6 and Stage 5 1. Of the 149 patients in Stages 3–5, 63 were known to the renal service; and of these 34 had had no imaging (18 normal and 11 abnormal). In 2006, there were 700 patients. 193 had eGFR measured in Aug–Sept. 143 men: stage 3 82, stage 4 13 and stage 5 1; 50 women: stage 3 26, stage 4 5 and stage 5 1. Of the 20 in stage 4 or 5, 3 men and 1 woman were known to the renal service; urinalysis was available in 8.

Conclusions. The prevalence of CKD 4 and 5 is lower than we expected. We have recommended routine urinalysis on presentation, informal discussion of cases with a renal physician and use of CKD guidelines with primary care.

Prevalence of CKD in high-risk patients in an urban general practice—comparison of Cockcroft–Gault and MDRD formulae

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Background. Guidelines for the management of chronic kidney disease (CKD) based on eGFR (MDRD) were introduced in South East Essex on 1 June 2006. Reports suggest that eGFR may underestimate renal function. We have, therefore, compared the prevalence of CKD stage 3–5 by applying both Cockcroft–Gault (C–G) calculated creatinine clearance (CrCl) and eGFR to a high-risk group.

Methods. Patients with a diagnosis of ischaemic heart disease, cerebrovascular disease, diabetes, hypertension, heart failure, renal disease or cardiomyopathy were identified. Patients with an eGFR in the study period had a CrCl calculated. BMIs were recorded.

Results. A total of 1776 patients out of a practice population of 10472 were considered high risk. 523 had results available. MDRD eGFR $>60\text{ml/min}$

368 patients; Stage 3 147; Stage 4 11; Stage 5 1. C-G CrCl >60 ml/min 266; Stage 3 242; Stage 4 17; Stage 5 1. Of the 122 patients reclassified from CrCl in stage 3 to eGFR >60 ml/min, 54 had a body mass index <24, 43 BMI 25–29, 5 BMI 30+.

Conclusions. These results suggest that MDRD does not underestimate renal function if compared with C-G. There has been less reclassification in CKD stage 3 than expected. Low CrCl may be a reflection of BMI.

The impact of a cooked meat meal on creatinine, eGFR and the staging of chronic kidney disease

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Background. Recent national guidelines have recommended that biochemistry laboratories report estimated GFR (eGFR) to improve the diagnosis, staging and management of chronic kidney disease (CKD). The guidelines do not mention the possible effect of diet on serum creatinine concentration. Previous reports have suggested that intake of large amounts of cooked meat leads to a significant increase in serum creatinine concentration.

Methods. Measurement of serum creatinine (kinetic Jaffe method, enzymatic, IDMS) and cystatin-C, calculation of eGFR, and staging of CKD was carried out on 32 participants before and after a meal containing cooked meat and a meat-free meal. Post-prandial samples were taken after 1–2 and 3–4 h. Meat-containing meals included lamb, beef and chicken.

Results. Following intake of cooked meat, median serum creatinine concentration (kinetic Jaffe) increased from 80.5 µmol/l pre-prandially to

101.0 µmol/l 1–2 h post-prandially ($P < 0.0001$) and 99.0 µmol/l 3–4 h post-prandially ($P < 0.0001$). Median eGFR decreased from 84.0 ml/min/1.73 m² pre-prandially to 59.5 ml/min/1.73 m² 1–2 h post-prandially ($P < 0.0001$) and 64.0 ml/min/1.73 m² 3–4 h post-prandially ($P < 0.0001$). Consumption of non-meat-containing meals had little impact on serum creatinine concentration (kinetic Jaffe) and eGFR. CKD staging deteriorated in 12 cases after eating cooked meat. It changed from *better than CKD3* to CKD3 in 11 individuals and from CKD3 to CKD4 in one individual. Cystatin-C concentrations were unaffected by either meal.

Conclusions. Intake of cooked meat has a significant impact on serum creatinine concentration and eGFR, making misclassification of CKD likely. CKD staging must be based on samples taken in the appropriate conditions. National guidelines overlooking this factor should be revisited.

Is early CKD an important risk factor for cardiovascular disease?

Chronic kidney disease stage is a prognostic indicator in stroke patients both in the short-term and in the long-term

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Background. Renal dysfunction is an important, often forgotten prognostic indicator in acute stroke. The objective of this study was to investigate whether chronic kidney disease (CKD) stage using the 4-variable Modified Diet in

Renal Disease (4-v MDRD) study equation can predict short- and/or long-term survival after acute stroke.

Methods. Cohort study in a Scottish tertiary teaching hospital. Participants included 2042 unselected

consecutive stroke patients admitted to hospital within 48 h of stroke between 1988 and 1994. Main outcome measure was long-term survival (up to 7 years of follow-up) and short-term survival (30-day survival). Estimated glomerular filtration rate (eGFR), calculated using the 4-v MDRD study equation, was correlated with that calculated with the Cockcroft–Gault formula. We analysed eGFR to categorize into CKD stages and estimated relative risks of mortality (RR) with 95% confidence intervals (CI) using Cox proportional-hazard models.

Results. 1026 patients died during the follow-up period. The eGFR calculated with the 4-v MDRD

formula correlated significantly with that using the Cockcroft–Gault formula (Pearson 0.897, two-tailed $P < 0.0001$). CKD stage predicted survival to 30 days (log-rank test $P < 0.00001$) and overall survival (log-test $P < 0.00001$).

Conclusions. CKD stage at time of stroke predicts survival in the short-term (30 days) and in the long-term (to 7 years). CKD stages 4 and 5 with estimated GFR under 30 ml/min were associated with the poorest outcomes. The 4-v MDRD formula for eGFR and CKD stage assessment may be used to risk-stratify stroke patients on admission and target further treatments.

How does early CKD progress?

Managing nephrology outpatients—too many inappropriate referrals? Not enough nephrologists

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Background. Chronic kidney disease (CKD) is now recognized as a common condition and is associated with end-stage renal failure (ESRF) and premature cardiovascular death. The Renal Association have published referral guidelines for CKD re-emphasizing the importance of assessing patients with progressive CKD at Nephrology outpatients.

Methods. 2 892 340 routine blood samples collected in Northern Ireland between 1 January 2001 and 31 December 2002 were compared with an enriched Data Retrieval in General Practice (DRGP) data set and thereafter, applying the MDRD eGFR equation, a patient-level database of 75 434 with 307 663 results was produced. A three-point assessment of progression over the entire period was devised. Patients were then categorized depending on their change in eGFR in

relation to the threshold of 60 ml/min. eGFR slopes were categorized as stable, slow and rapid.

Results. 61 373 (81.4%) subjects had an eGFR > 60 and 14 061 (18.6%) had an eGFR < 60 at the end of the study. In total, 1167 were known to Nephrology. Of these, 29.2% had an eGFR > 60 over the 2 year period. Importantly 2699 (3.6%) subjects unknown to nephrology demonstrated a rapid decline from stage 1 or 2 CKD to stage 3 CKD.

Conclusion. Significant numbers of subjects attending nephrology services have no evidence of progressive decline in eGFR whilst the vast majority with CKD remain unseen. Although some of these patients may have important reasons for attending Nephrology services, this may be to the detriment of those with more progressive CKD.

Δ eGFR—an intuitive method of assessing progression and regression of chronic kidney disease (CKD)

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Background. The number of patients receiving renal replacement therapy in the UK is rising rapidly, costing over 2% of the total NHS budget. The Renal Association's CKD guidelines emphasize the importance of assessing patients with progressive disease based on eGFR.

Methods. In Northern Ireland, 2892340 creatinine samples from 1 January 2001 to 31 December 2002 were extracted from regional laboratories. Merging these to an enriched General Practice data set produced a cohort of 75434 subjects containing 307663 results. To capture progression over the 2-year period, a three-point assessment was devised. Progression and periods of regression were characterized by the gradients ΔA and ΔB . A cut-off level (eGFR 60 ml/min) was additionally used to categorize

the change in patient's eGFR. Progression was also categorized as stable, slow and rapid.

Results. 56356 (74.7%) subjects had 'all eGFR results' >60 throughout the entire period. 14061 (18.6%) had an eGFR <60 at the end of the study. 5017 (6.7%) subjects had a minimum eGFR measured <60 ml/min, and yet subsequently had a value >60 ml/min. Improvements in kidney function are common and in some patients are part of the natural history of CKD. **Conclusion.** Progression of CKD is often taught to be linear; this data indicates that alternative patterns of progression occur in the natural history of CKD, including improvement in function. This suggests, although further study is needed, that repeated sampling and the use of simple gradient functions are critical in monitoring CKD.

Can patients with stage 4 CKD be safely discharged to primary care?

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Background. Current guidelines recommend that all patients with stage 4 CKD be discussed with a nephrologist, however, as stage 4 CKD affects $\sim 0.5\%$ of the population, it would be impractical for nephrologists to manage all such patients. Many patients will be elderly with stable renal function; therefore, we sought to determine whether this subgroup could be safely discharged to primary care.

Methods. This was a retrospective, two-centre study that enrolled all patients with stage 4 CKD who were referred to the nephrology services of the Southern Health Board in Northern Ireland and the Lothian and Borders regions of Scotland between

1998 and 2002 inclusive. Patients were followed until end 2005 to determine factors conferring risk of renal replacement therapy (RRT) or death.

Results. We identified 424 patients with stage 4 CKD. After 5 years follow-up, 27.4% progressed to RRT, 49.7% died, while 34.4% remained alive without RRT. The risk of RRT increased with: younger age, male sex, higher baseline proteinuria and diastolic BP, lower baseline haemoglobin and eGFR and a more rapid early rate of deterioration in eGFR. During follow-up, 96 (23%) patients were discharged to primary care, five of whom were subsequently re-referred; however, none required

RRT. The median rate of change in renal function was $+0.41 \text{ ml/min/m}^2/\text{year}$ in patients following discharge, and $-2.04 \text{ ml/min/m}^2/\text{year}$ in those continuing in nephrological follow-up ($P < 0.0001$)

Conclusion. Baseline clinical parameters and historic rate of decline in renal function can be used to identify a group of patients with stage 4 CKD who can be safely discharged to primary care.

What are the best treatments for early CKD?

Slowing the progression of CVD and CKD—an audit of a DGH nephrology clinic

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Background. The two principle outcomes of chronic kidney disease (CKD) are the progressive loss of renal function, and the development and progression of cardiovascular disease (CVD). We undertook an audit of modifiable risk factors for both CKD and CVD progression in a district hospital nephrology clinic.

Findings. The average age of attending patients was 59.4 years, with 59% being male. Approximately 30% of patients attending the clinic were at each of CKD stages 3 and 4. Fifty-five percent were non-smokers. Twenty-eight percent had documented ischaemic heart disease. Diabetes was the cause of renal impairment in 21%, with glomerulonephritis forming 13% and renovascular disease 10% of cases. A target blood pressure was set in an average of 60% of cases, with this being attained in under 50%. Proteinuria was

quantified in about 40% of cases and renin-angiotensin blockers were used in a similar proportion. The HbA1c target was achieved in less than one-third of diabetic patients. Cholesterol targets were achieved in less than 15% of patients, with only 40% being prescribed a 'statin'.

Discussion. With the establishment of eGFR reporting, the expansion of the GP GMS contract into CKD and the development of CKD guidelines, it is important that nephrologists take this opportunity to reduce the burden not only of CKD progression but its attended burden of CVD. We have designed a management algorithm for CVD risk factors based around the current JBS2 guidelines. The plan is to close the audit loop at the beginning of 2007.

How do we re-design the treatment?

Supporting early chronic kidney disease (CKD) management in primary care—Walsall/Wolverhampton Collaboration

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Wolverhampton nephrologists provide weekly clinics in Walsall, supported by Walsall chemical pathologists. Referrals are often unsatisfactory: advanced nephropathy may present late; patients

with microalbuminuria but no other sign of renal disease are sometimes referred unnecessarily. After widespread consultation two flow-charts, based on national guidelines, were formulated to

help primary care with the renal management of diabetic and hypertensive patients. The assumption was that much primary care CKD management could be incorporated within their established mechanisms for the review of these underlying chronic conditions.

The charts were distributed electronically in November 2005. However, a subsequent survey showed that many GPs were unaware of these materials so a new approach was tried. Walsall conducts outreach education campaigns to primary care on prescribing issues. This vehicle was exploited to distribute hard-copy of the flow-charts during individual practice visits by trained pharmacists, often accompanied by a chemical pathologist. MDRD eGFR, CKD registers and the

flow-charts (which include aspects of treatment) were covered.

Audit of 500 diabetics aged 18–70 years assessed potential demand for nephrological advice arising from flow-chart recommendations. About 5% of patients on the basis of creatinine/eGFR results and/or significant urinary abnormalities warranted expert advice, albeit not necessarily clinic referral. Of these, only a third had been referred. Extrapolating to the entire local population, clinic capacity would be overwhelmed were all these patients referred. Minimal inappropriate referrals occurred in this cohort.

Optimizing CKD management outside conventional renal clinics, mainly in primary care, is essential; clinical biochemistry and practice pharmacists can help.

Efficient and educational—a consultant-provided renal e-mail helpline for primary care

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A hospital-based e-mail helpline was set up in June 2006 to help GPs deal with the introduction of CKD guidelines and eGFR measurements. The Middlesbrough renal unit serves a catchment population of 1 million, but the e-mail helpline was initially advertised only to practices serving less than half of that area.

By late October, there had been 43 e-mails to the helpline, 30 in the most recent 8 weeks. These contained 36 enquiries about specific patients and 10 general questions. Only one enquiry was inappropriate (paediatric) although three were largely urological. For the specific enquiries, patient age range was 14–98, median 77. The commonest reasons for enquiry were stable stage 4 chronic kidney disease ($n=12$), followed by recent worsening of already impaired renal function ($n=6$). Twenty-eight related to CKD. In only two cases was referral to renal OP clinic deemed necessary.

Six of the 10 general enquiries related to CKD and/or eGFR.

Twenty-nine replies were on the same day as receipt of the enquiry and 34 within 1 day. All replies were by consultant nephrologists, who aimed not only to give specific advice but also to explain the reasoning behind their decisions. Forty of the 46 enquiries could be dealt with in a single reply. One enquiry eventually involved two nephrologists and four GPs. Unsolicited compliments and thanks were received on eight occasions.

The introduction of CKD guidelines and eGFR measurement identifies high levels of CKD, especially in elderly patients with multiple comorbidities. An e-mail helpline allows GPs virtually instant access to consultant nephrologists to discuss these patients. Medical management of their CKD can be optimized whilst avoiding unnecessary hospital visits for patients, the majority of whom are over 75.

Managing CKD in the community—a successful model

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Since the inclusion of chronic kidney disease (CKD) into the Quality and Outcomes Framework (QOF) there has been significant increase in the number of patients being treated in general practice and the number referred to hospitals. Early identification of CKD in primary care is essential to manage the high risk of cardiovascular morbidity and mortality in these patients, to slow progression to end-stage kidney disease and to identify patients who will need dialysis at an early stage.

At the Heart of England Foundation Trust, we have been automatically reporting estimated eGFR since January 2004. GFR estimates are only reported when the serum creatinine concentration is above the laboratory assay's reference range (80 µm/l for women, 106 µm/l for men). We contend that estimates of GFR derived from creatinine values in the reference range do not add clinically useful information to the result and often cause unnecessary anxiety. We developed a simple flow chart for the management

of patients with CKD (http://www.heartofengland.nhs.uk/resources/clinical/docs/GFR_GP_algorithm.pdf). We have also run a series of CKD education sessions for GPs and practice nurses.

In the first year, referrals increased by 25% but the additional numbers of patients could be treated and monitored in primary care, as per the flow chart. Letters of advice specific for each patient were sent to the referring GP rather than a routine outpatient appointment being offered. We have also set up systems to help manage CKD in the community, including regular training sessions for practice nurses and the establishment of a community CKD nurse.

With a rational eGFR reporting system, a thorough education programme and true partnership between primary and secondary care, our local GPs have become more confident in managing CKD, the out-patient service is controlled and an improved service is being provided for patients.

Primary care-based disease management (DMP) improves outcomes and reduces resource utilization in patients with CKD

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Background. The prevalence of CKD 3–5 in the UK is 5%. There is evidence of historic under-diagnosis and referral.

Methods. A primary care-based disease management (DMP) for CKD commenced in West Lincolnshire UK in 2005 aiming to improve patient identification and outcomes. The programme relies on automated patient identification via eGFR (MDRD). Patients are risk-stratified and managed by a community-based nursing team to defined and audited outcome targets.

Results. In the first 18 months ~16 500 patients with CKD 3–5 were identified suggesting a prevalence of 8.4%. 989 patients had CKD 4/5 compared with 38 patients with CKD4/5 who had been referred to nephrology in the previous year. Around 84, 85, 57 and 20% of patients with CKD 2–5 respectively were identified in primary care (PC). Only 0.3, 2, 29 and 70%, respectively were identified from nephrology care; the remainder were followed up in non-nephrology secondary care. The latter were more likely to have a previous and future nephrology referral than those identified from PC ($P < 0.001$). In 2004/2005, 53 patients with CKD 4/5 presented to

nephrology. Eleven (20.8%) died within 12 months. Of the 989 patients identified in 2005/2006, 483 were enrolled in the DMP, 50 died (10.4%, $P < 0.05$). In 2004/2005, 38% of patients commenced dialysis with <3 months pre-dialysis care compared with 26% in 2005/2006.

Seventy-four patients had a decline in eGFR of >5 ml/min in the 9 months prior to joining the DMP. In 23 patients, the rate of decline reduced and in 20 patients renal function improved after joining the DMP. When compared with a cohort of patients with similar renal function the DMP patients experienced less A&E attendances, less inpatient stays, less days in hospital and less outpatient visits (24 vs 81; 25 vs 69; 227 vs 526/100 patient-years, and 3.3 vs 82/patient-years, respectively). The reduction in resource utilization and delay in start of dialysis correspond to a saving of in excess of £1 million per year.

Conclusion. These data confirm prior under diagnosis and referral and demonstrate that this DMP improves

patient identification and outcomes against clinical targets whilst reducing resource utilization.

Table 1 shows the percentage of patients achieving the defined biochemical targets.

Table 1. Percentage of patients achieving specified target

	6 months prior to DMP	At entry to DMP	9 months of DMP	Entry vs 9 months
Total cholesterol <5 mmol/l	67.3	64.4	75.0	$P < 0.001$
LDL cholesterol <3 mmol/l	72.3	69.1	81.9	$P < 0.05$
Triglycerides <2 mmol/l	65.3	64.9	70.9	$P < 0.05$
Systolic BP <130 mmHg	37.1	46.2	53.2	$P < 0.05$
Diastolic BP <80 mmHg	68.3	70.0	90.0	$P < 0.01$
Ferritin >150 g/l	79.5	49.5	68.1	$P < 0.01$