Chronic Kidney Disease Referrals from General Practitioners Pre and Post National Institute for Clinical Excellence Guidance 2014

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Introduction:

Mortality from chronic kidney disease (CKD) is increasing Worldwide and is currently ranked 14th commonest cause of death¹. Most patients die from cardiovascular disease and management of cardiovascular risk is the key to prevent both death and decline of renal function to the point of end stage renal disease (ESRD). In the UK 14% of men and 13% women have CKD, the majority being managed in primary care. In 2014, National Institute for Clinical Excellence (NICE) introduced guidance to help General Practitioners (GP) manage patients with CKD, focussing on cardiovascular risk and prevention of late referral of patients likely to require renal replacement therapy²

This study examined the management of cardiovascular risk and timeliness of referral in all new GP referrals to the renal clinic in 2012, and again in 2016, two years after the introduction of NICE CKD guidance in 2014. The study was aimed at determining the impact of the updated CKD guidance on CKD/cardiovascular risks optimisation and the timeliness of referral from the primary care

Methods:

All new GP referrals to the Regional Renal Service in 2012 and 2016 were analyzed. Data were collected on patient age, CKD stage and estimated Glomerular Filtration Rate at referral (eGFR), renal imaging pre-referral, blood pressure (BP), smoking, body mass index (BMI), glycated haemoglobin (HbA1C) (in diabetic patients), and lipid assessment.

Chi-square analyses were performed using IBM SPSS Statistics version 24. A p value of less than 0.05 was considered significant.

Results:

A total of 486 new GP referrals were received in 2012, compared to 574 in 2016. Data completion was 100% for renal imaging pre-referral; blood pressure; BMI; diabetic status; and, lipid assessment at referral. The distribution of eGFR of the referred patients is shown in Figure 2. 2 patients in both cohorts did not have eGFR/renal stage assessments due to age (< 18 years), and 1 patient in the 2016 cohort refused blood testing.

Nearly one third of referrals in 2012 (29.01%) and one fourth in 2016 (24.39%) were aged >80years (see Figure 1). 27.8% in 2012 and 30.7% in 2016 of referrals were diabetic. Of the patients with diabetes, 60/134 (44.8%) in 2012, and 82/176 (46.6%) in 2016 had HbA1c of greater than 58 mmol/mol. With 11/134 (8.2%) of diabetic patients in 2012, and 13/176 (7.4%) diabetic patients in

2016 having HbA1c greater than 86 mmol/mol. HbA1c was not measured in 1 of the 2012 diabetic patients.

In 2012, 167 patients had a systolic blood pressure (SBP) less than 140mmHg compared to 245 in 2016. 402/486 (82.7%) patients referred in 2012 and 509/573 (88.8%) patients referred in 2016 had cholesterol levels checked. Of those tested, 14.9% patients in 2012, and 15.9% in 2016 had a serum total cholesterol of 6.3 mmol/L or greater.

The proportion of obese patients referred shown in Figure 3. 11.7% (2012) and 12.6% (2016) of referred patients were current smokers at the time of referral. Pre-referral, Renal Ultrasound was done only in 206 of 438 patients in 2012 and 252 of 529 patients in 2016. 48 in 2012 and 45 in 2016 did not require Renal imaging.

The change in the proportion of cardiovascular risk factors post NICE guidelines is shown in Table 1. Post NICE guidelines there has been an 18% increase in GP referrals. Although the number of smokers and obese patients in the referred population have not improved. BP control has significantly improved post-NICE (p 0.006 for SBP control) and significantly more patients have had cholesterol levels checked (p 0.004). Post NICE guidelines, although significantly fewer Stage 4 and 5 CKD patients are being referred (p<0.001), there is no statistically significant improvement in late CKD referrals (eGFR <20ml/min/1.73m2, p=0.272)

Discussion:

Chronic kidney disease is associated with an increased risk of cardiovascular disease and related mortality ^{3,4,5}. Impaired kidney function and raised concentrations of albumin in urine also increase the risk of cardiovascular disease by two to four times⁶ and are independent predictors of mortality risk⁴. Stroke risk also increases linearly and additively with declining GFR and increasing albuminuria⁸.

The prevalence of CKD stages 3-5 increases with age especially in those above 80 years of age⁹. Among patients of all ages, there was an inverse association between eGFR and the proportion of deaths from a cardiovascular cause^{6,8}. However, among those with comparable levels of eGFR, older patients are more likely to die than reaching ESRD requiring renal replacement therapy¹⁰.

High BMI is a common, strong, potentially modifiable and an independent risk factor for CKD progression and death^{11,12}. A meta-analysis concluded from smaller, short-duration studies in patients with CKD that, nonsurgical weight loss interventions reduce proteinuria and BP and seem to prevent further decline in renal function¹³.

Poorly controlled diabetes is associated with greater risk of microvascular complications in both Type1 and Type2 diabetics^{14,15}. Diabetes is now the most common cause of ESRD in developed countries and diabetic patients are more likely to require dialysis and less likely to be transplanted¹⁶.

Hypertension is a well-established risk factor for cardiovascular disease (CVD) and a major promoter of CKD progression in both diabetic and nondiabetic kidney disease ^{17,18}. The reduction in BP significantly reduces the risk of death and cardiovascular disease in general population ¹⁹⁻²² and is

markedly reno-protective in CKD population, regardless of the type of drug administered²³⁻²⁶. NICE recommends aiming a systolic BP of less than 140mmHg in CKD patients and less than 130mmHg in CKD patients with diabetes and or proteinuria.

Reduction of LDL, cholesterol with medications safely reduced the incidence of major atherosclerotic events in patients with less advanced chronic kidney disease²⁷.

Risk of death is higher in renal failure patients who are current smokers compared to non-smokers and the risk increases with increase in number of daily cigarettes²⁸.

Conclusion:

GPs are better in optimising Blood pressure control and screening for hyperlipidaemia in the CKD population. Management of other cardiovascular risk factors in CKD patients need further optimisation pre-referral with attention to diabetes management and life style modifications such as smoking cessation and weight reduction. Early referrals to Nephrology should be considered for patients, who meets referral criteria as per NICE CKD guidelines for better patient prognosis and late CKD referrals to be avoided where possible.

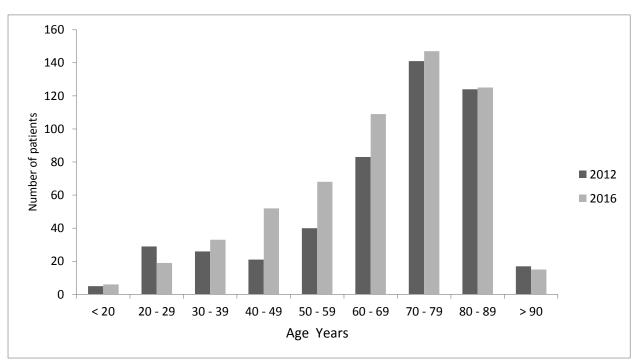


Figure 1: Distribution of new patients referred to renal clinic from GPs based on age before (n = 486) and after (n=574) the introduction of NICE guidelines (CG182)

Table 1: Comparison of cardiovascular risk factors in GP referred patients pre- (n= 486) and post-NICE (n=574) guidelines (CG182)

Change in proportion of:	Pre- NICE (% yes)	Post NICE (% yes)	Chi square	p-value
stage 4 & 5 patients	33.9	23.5	14.024	< 0.001
eGFR < 20	7.9	6.1	1.206	0.272
Ultrasound pre referral	47.0	47.5	0.025	0.875
SBP > 140	65.6	57.4	7.483	0.006
DBP > 90	26.3	19.0	8.100	0.004
Cholesterol tested	82.7	88.8	8.178	0.004
High BMI	34.8	40.8	4.102	0.043
Diabetic	27.8	30.7	1.094	0.296
Smoker	11.7	12.6	0.172	0.678

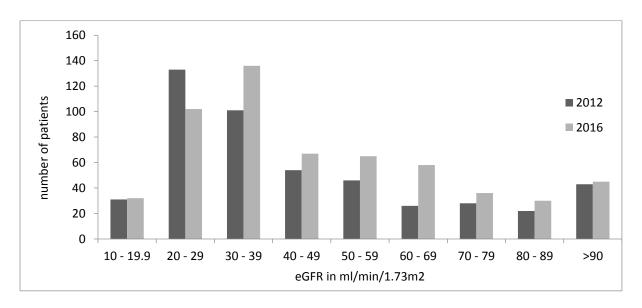


Figure 2: Distribution of referred patients based on eGFR (ml/min/1.73m²) at the time of referral before and after the introduction of NICE guidelines (CG182)

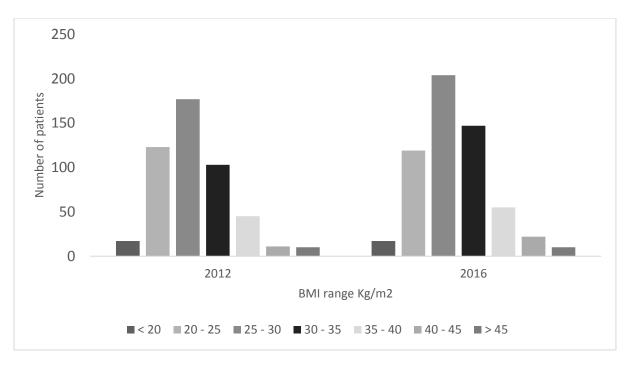


Figure 3: Distribution of patients based on Body mass index (kg/m²) before and after the introduction of NICE guidelines (CG182)

References:

- 1. Webster AC, Nagler EV, Morton RL et al. Chronic Kidney Disease. WHO data, Lancet 2017; 389: 1238 52.
- 2. NICE Chronic kidney disease in adults: assessment and management 2015; available online at https://www.nice.org.uk/guidance/CG182/
- 3. Association of estimated glomerular filtration rate and albuminuria with all-cause and cardiovascular mortality in general population cohorts: a collaborative meta-analysis. Chronic kidney disease prognosis consortium. Volume 375, ISSUE 9731, P2073-2081, June 12, 2010. The Lancet
- 4. Foley RN, Parfrey PS, Sarnak MJ. Clinical epidemiology of cardiovascular disease in chronic renal disease. Am J Kidney Dis 1998; 32 (suppl 3): S112–19
- 5. Clinical epidemiology of cardiovascular disease in chronic renal disease. Foley, American Journal of Kidney diseases, Nov 1998;32: S112-S119
- 6. Cause of Death in Patients with Reduced Kidney Function. Stephanie Thompson, Matthew James, Natasha Wiebe, Brenda Hemmelgarn, Braden Manns, Scott Klarenbach, and Marcello Tonelli for the Alberta Kidney Disease Network; J Am Soc Nephrol26: 2504–2511, 2015
- 7. Chronic kidney disease and cardiovascular risk: epidemiology, mechanisms, and prevention. Dr Ron T Gansevoort et al. Lancet Volume 382, No. 9889, p339–352, 27 July 2013
- 8. Chronic kidney disease and the risk of stroke: a systematic review and meta-analysis. Philip Masson1, Angela C. Webster, Martin Hong, Robin Turner, Richard I. Lindley and Jonathan C. Craig; Nephrol Dial Transplant 2015; 30: 1162 1169
- 9. Health survey for England. Adult CKD prevalence.

- 10. Age Affects Outcomes in Chronic Kidney Disease. Ann M. O'Hare et al. J Am Soc Nephrol 18: 2758–2765, 2007
- 11. Adiposity and risk of decline in glomerular filtration rate: meta-analysis of individual participant data in a global consortium. BMJ 2019; 364 (Published 10 January 2019)
- 12. Body mass index and risk for end-stage renal disease. Hsu CY1, McCulloch CE, Iribarren C, Darbinian J, Go AS. Ann Intern Med. 2006 Jan 3;144(1):21-8.
- 13. Weight loss interventions in chronic kidney disease: a systematic review and meta-analysis. Navaneethan SD1, Yehnert H, Moustarah F, Schreiber MJ, Schauer PR, Beddhu S. Clin J Am Soc Nephrol. 2009 Oct;4(10):1565-74. doi: 10.2215/CJN.02250409. Epub 2009 Sep 17.
- 14. T Alder Al, Stevens RJ, manley SE et al. Development and progression of nephropathy in type 2 diabetes: The United Kingdom prospective diabetes study (UKPDS 64). Kid Int 2003; 63:225-232.
- 15. The Renal association. UK Renal Registry- The seventeenth annual report, Bristol: The Renal association, 2014,
- 16. Jacobsen P, Rossing K, Tarnow L, Rossing P, Mallet C, Poirier O, Cambien F, Parving HH: Progression of diabetic nephropathy in normotensive type 1 diabetic patients. Kidney Int Suppl 71: S101 –S105, 1999
- 17. Klahr S, Levey AS, Beck GJ, Caggiula AW, Hunsicker L, Kusek JW, Striker G: The effects of dietary protein restriction and blood pressure control on the progression of chronic renal disease. N Engl J Med 330: 877 –884, 1994
- 18. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Dena Ettehad, Connor A Emdin, Amit Kiran, Simon G Anderson, Thomas Callender, Jonathan Emberson, John Chalmers, Anthony Rodgers, Kazem Rahimi. The Lancet Volume 387, ISSUE 10022, P957-967, March 05, 2016
- 19. Effects of intensive blood pressure lowering on cardiovascular and renal outcomes: updated systematic review and meta-analysis. Xinfang Xie, Emily Atkins, Jicheng Lv, Alexander Bennett, Bruce Neal, Toshiharu Ninomiya. Volume 387, ISSUE 10017, P435-443, January 30, 2016. The Lancet
- 20. Effects of Intensive BP Control in CKD. Alfred K. Cheung. J Am Soc Nephrol 28: ccc-ccc, 2017
- 21. A Randomized Trial of Intensive versus Standard Blood-Pressure Control. The SPRINT Research Group. N Engl J Med 2015; 373:2103-2116
- 22. Importance of Blood Pressure Control in Chronic Kidney Disease. Maura Ravera, Michela Re, Luca Deferrari, Simone Vettoretti and Giacomo Deferrari. JASN April 2006, 17 (4 suppl 2) S98-S103; DOI: https://doi.org/10.1681/ASN.2005121319
- 23. Jafar TH, Stark PC, Schmid CH, Landa M, Maschio G, de Jong PE, de Zeeuw D, Shahinfar S, Toto R, Levey AS; AIPRD Study Group: Progression of chronic kidney disease: The role of blood pressure control, proteinuria, and angiotensin-converting enzyme inhibition: A patient-level meta-analysis. Ann Intern Med 139: 244 –252, 2003CrossRefPubMedGoogle Scholar
- 24. Lewis JB, Berl T, Bain RP, Rohde RD, Lewis EJ: Effect of intensive blood pressure control on the course of type 1 diabetic nephropathy. Collaborative Study Group. Am J Kidney Dis 34: 809 –817, 1999CrossRefPubMedGoogle Scholar

- 25. CKD and Diabetes: What Can We Learn from Their Similarities and Differences? Andrew S. Levey, MD Tufts Medical Center Boston, Massachusetts Rudy Bilous, MD, FRCP Newcastle University Newcastle upon Tyne, United Kingdom Michael G. Shlipak, MD, MPH San Francisco Veterans Affairs Medical Centre University of California San Francisco, California.
- 26. Deferrari G, Ravera M, Berruti V: Treatment of diabetic nephropathy in its early stages. Diabetes Metab Res Rev 19: 101 –114, 2003CrossRefPubMedGoogle Scholar
- 27. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebocontrolled trial. Colin Baigent et al. Lancet 2011; 377: 2181–92
- 28. Smoking and Mortality Beyond Established Causes. Brian D. Carter, M.P.H., Christian C. Abnet, Ph.D., Diane Feskanich, Sc.D., Neal D. Freedman, Ph.D., Patricia Hartge, Sc.D., Cora E. Lewis, M.D., Judith K. Ockene, Ph.D., Ross L. Prentice, Ph.D., Frank E. Speizer, M.D., Michael J. Thun, M.D., and Eric J. Jacobs, Ph.D. N Engl J Med 2015;372:631-40