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Kidney trajectory charts improve GP management of patients with reduced kidney function: a randomised controlled vignette study

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Abstract

Background
The stages of chronic kidney disease (CKD) and estimated glomerular filtration rate (eGFR) reference ranges are currently determined without considering age.

Aim

To determine whether a chart that graphs age with eGFR helps general practitioners (GPs) make better decisions about managing patients with declining eGFR.

Design and Setting

A randomised controlled vignette study amongst Australian GPs using a percentile chart plotting the trajectory of eGFR by age.

Method

373 GPs received two case studies of patients with declining renal function. They were randomised to receive the cases with the chart, or without the chart, and asked a series of questions about how they would manage the cases.

Results

In an older female case with stable but reduced kidney function, use of the chart was associated with GPs in the study recommending a longer follow up period, and longer time until repeat pathology testing. In a young male First Nations case with normal but decreasing kidney function, use of the chart was associated with GPs in the study recommending a shorter follow up period, shorter time to repeat pathology testing, increased management of blood pressure and lifestyle management and avoidance of nephrotoxic medications. This represents more appropriate care in both cases.

Conclusion

Having access to a chart of percentile eGFR by age was associated with more appropriate management review periods of patients with reduced kidney function, either by greater compliance with current guidelines, or greater awareness of a clinically relevant kidney problem.

Keywords-

Keywords: chronic kidney diseases, overdiagnosis, aging, general practice, primary health care

How this fits in.

What was previously known or believed

Age is not currently considered as a factor in the definition of patients with chronic kidney disease, and current guideline recommendations do not take age into account.

What this research adds
This research shows that considering age with a kidney trajectory chart can improve GP management recommendations for patients with declining renal function.

What is relevant to clinicians

A chart that plots eGFR with age may be a useful clinical tool to assist clinicians in their management of patients with declining renal function.

Introduction

Chronic kidney disease (CKD) is currently defined as a glomerular filtration rate (GFR) below 60 mL/min/1.73m² or GFR >60 mL/min/1.73m² with persistent albuminuria or other markers of kidney damage for at least 3 months.(1) Age is not considered as a factor in the stages of CKD, and GFR reference ranges are currently not age dependent,(1) despite the fact that kidney function declines with age as a natural process in the absence of disease (2,3). There is debate about whether age should be considered, given that 40% of people over the age of 70 years have a GFR that meets the definition of CKD,(4) and whether the early stages of CKD (particularly 3a and b) should be considered diseases.(4,5) There have been recommendations to lower the CKD threshold in people over the age of 65 years to a GFR of <45 mL/min/1.73m², (6,7), however current guidelines have not changed to incorporate this recommendation (8,9,10), the rationale being that older populations are still at risk of adverse outcomes with higher CKD stages (9). In the higher stages of CKD, guidelines recommend monitoring and medication to reduce cardiovascular risk.(1,8) However, it can be difficult to explain to patients what CKD means and when is appropriate to refer to a nephrologist.(5)

In younger people with a declining GFR, kidney disease may be under recognised if their GFR remains in the normal range. Younger adults can have adverse clinical outcomes with a modest reduction in GFR in the higher ranges.(11) There have been recommendations to change the threshold GFR to define CKD in younger people using percentiles or age-adapted staging, in order to recognise a clinically important decline at higher GFR values. (12) The current mode of reporting without an age reference may lead to under recognition of a clinically significant decline in younger people. (11)

There have been calls for the use of the concept of “kidney age” when GPs make decisions for patients about declining estimated glomerular filtration rate (eGFR).(13) The UK NICE Clinical Knowledge Summaries consider age as well as baseline GFR when giving clinical examples for the application of the guidelines (14). There have also been recommendations to utilise a kidney percentile chart when considering kidney function values. (12) We sought to investigate this concept by developing a percentile chart of kidney function with age (Supplementary file), and then testing it with GPs to see how they would use it to manage two hypothetical patient cases (clinical vignettes) (15). The concept of the kidney age trajectory chart, how it was developed, and testing its effect on GP diagnosis of CKD has been previously described, and showed the utility of the chart to help GPs recognise the clinical significance of eGFR results. (16) For the current study, we posed the question “Does a kidney age trajectory chart improve GP management of patients with declining kidney function?” We were interested to determine whether a chart helps GPs to recognise whether a patient’s kidney function is similar to patients of the same age and gender, and if this would help GPs make better decisions about
managing those patients. This paper describes the effect of the chart on GPs’ proposed management of the two patient cases.

**Method**

**Participants**

An electronic questionnaire using Qualtrics XM was sent by a third party database (AMPCo) to a stratified random sample of 9,500 Australian general practitioners asking them to participate in the study. The randomised vignette study presented two patient case studies and a percentile chart of kidney function with age.

The study occurred between August 2018 and November 2018. GPs were randomised 1:1 by the Qualtrics XM program to receive the case studies with the chart (immediate chart group), or without the chart (delayed chart group) and were asked a series of questions about how they would manage the cases. GPs who did not receive the chart immediately were subsequently given the chart and asked the same questions a second time. GPs with access to the chart were first asked to find the patient’s percentile kidney function on the chart before responding to the questions. The order of cases was allocated randomly.

**Case vignettes**

Case one was a 76 year old woman (no ethnicity specified) who had an eGFR in the CKD stage 3a range, which had been stable over a 12-month period. Her eGFR was 58 mL/min/1.73m² (just below the 50th percentile for her age) and she had no albuminuria. The woman was otherwise well and healthy, although was overweight and had a slightly elevated blood pressure (140/90 mmHg). Her lipid levels (and reference ranges in mmol/L) were: total cholesterol (TC) 5.4 (3.9-5.5), LDL 3.3 (0-4), HDL 1.81 (1.1-1.9), and fasting glucose 5.0 (3-6 mmol/L). Using the current Australian risk calculator, the woman’s absolute risk of CVD in the next 5 years was 5%, below the threshold currently recommended for lipid lowering therapy, although this information was not explicitly given in the vignette.(16)

Case two was a 45 year old First Nations man with an eGFR that was in the normal range, but had decreased by 5 mL/min/1.73m² over the preceding 12-month period. His eGFR was 65 mL/min/1.73m² (5th percentile for his age) with no albuminuria. The man was otherwise well and healthy, although was overweight and had a slightly elevated blood pressure (140/90 mmHg). He was also an ex-smoker (he quit 5 years previously), and had a strong family history of diabetes. His lipid levels (and reference ranges in mmol/L) were: total cholesterol 5.4 (3.9-5.5), LDL 3.3 (0-4), HDL 1.81 (1.1-1.9), and fasting glucose 5.0 (3-6 mmol/L). His estimated risk of CVD in the next 5 years was 2%, although it is recognised that the risk calculator will underestimate risk in First Nations people.(16)

For each case, participants were asked:

Question 1. When would you review the patient? (Options = 1 week, 3 months, 6 months, 12 months, only as required)
Question 2. When would you repeat the patient’s pathology tests? (Options as above)
Question 3. What is your management plan for this patient? (Options = No specific management, blood pressure reduction, lipid lowering treatment, lifestyle modification for weight management, avoidance of nephrotoxic medications, referral to a nephrologist for advice. More than one option could be selected.)

Statistical Analysis

Our primary comparison was between GPs who had access to the chart with the case (immediate chart group) and GPs who only had the cases (delayed chart group). A secondary comparison was between the responses of the GPs in the delayed chart group before and after seeing the chart.

Analysis was performed using SAS, Release 3.81. Multinomial logistic regression was used to estimate odds ratios, 95% confidence intervals and p-values for comparing the distribution of the five timing categories (as stated above) chosen for the next review and pathology testing between treatment groups. The reference group was 12 months for the older woman and 3 months for the young First Nations man. Binary logistic regression was used to estimate odds ratios, 95% confidence intervals and p-values for the comparison of probability of choosing each of the six individual management options (as stated above) between treatment groups. For the within-participants comparisons involving the delayed chart group only, McNemar’s test was used to compare the six management options before and after observing the chart. Bowker’s test of symmetry was used to compare the timing of the next review and pathology testing before and after observing the chart.

Results

We received 496 responses to the email invitation, of whom 390 participated in the randomised vignette study. Seventeen GPs did not complete all questions in the case studies, and so were excluded from the analysis after randomisation. A total of 373 responses were analysed (190 in the immediate chart group and 183 in the delayed chart group). (See Figure 1- CONSORT flow diagram.) See Table 1 for participant demographics.

Primary Analysis

Case 1: Older Woman

GPs in the immediate chart group chose longer intervals to review the patient compared to the delayed chart group. In the delayed chart group, 78% proposed that they would see her within 1 week to 6 months, compared to 67% who had the chart immediately. In the delayed chart group, 22% would review her at 12 months, compared to 33% with the chart immediately (p=0.015). (Figure 2a) Similar group differences were also reflected in the proposed time to repeat pathology testing. GPs in the immediate chart group were more likely to propose repeat pathology testing at 12 months compared to GPs in the delayed chart group (41% vs 29%, p=0.012).

The majority of GPs in both the immediate and delayed chart groups would treat the older woman’s blood pressure, advocate for lifestyle advice for the older woman, and would avoid nephrotoxic medications in this patient and would continue to manage the patient themselves (Figure 3, Table 2).
Access to the chart reduced the likelihood that GPs would prescribe lipid lowering therapy in the older woman (p=0.003) (Figure 3, Table 2).

Case 2: First Nations Man

GPs in the immediate chart group were more likely to choose earlier time intervals to review the First Nations man compared to the delayed chart group. Seventy-eight percent of GPs with the chart immediately would review him in 3 months or sooner, compared to only 50% in the delayed chart group (p<0.0001). (Figure 2b) Sixty percent of GPs with the chart immediately also chose to repeat pathology testing in 3 months or sooner compared to 39% in the delayed chart group (p<0.0001).

GPs in the immediate chart group were more likely to recommend blood pressure reduction for this patient case (p=0.046), more likely to recommend lifestyle intervention (p=0.012), and more likely to avoid nephrotoxic medications (p<0.0001) compared to the delayed chart group (Table 2, Figure 3).

Most GPs would not prescribe lipid lowering treatment for the First Nations man, and there was no difference between the groups (immediate and delayed chart) (p=0.15). Most GPs would not refer the First Nations man to a nephrologist, but access to the chart was associated with an increase in the proportion of GPs wanting to seek further advice (6% delayed chart vs 16% immediate chart, p=0.0015), (Table 2, Figure 3).

Secondary Before-After Comparison within the Delayed Chart Group

In the case of the older woman, after seeing the chart, GPs became more likely to choose to review the patient at a longer time period (p=0.014) and repeat her pathology testing at a longer time period (p=0.012). They were also more likely to not treat the older woman’s blood pressure (38%) compared to before they had seen the chart (31%, p=0.005). Before seeing the chart, the vast majority would not refer to a nephrologist (97%). However, after receiving the chart, an additional small minority (4%) of GPs would consider referring to a nephrologist for advice (p=0.04). Otherwise, access to the chart had no influence on whether the GPs would prescribe lipid lowering therapy, advise lifestyle management, or avoid nephrotoxic medications for this case.

With the First Nations male case, after seeing the chart, GPs were more likely to choose to review this patient in a shorter time period, compared to before they had the chart (p<0.0001) and to repeat the pathology tests sooner (p<0.0001). After seeing the chart, GPs were more likely to recommend blood pressure reduction therapy (87% vs 75% p=0.0003), more likely to commence lipid lowering therapy (45% vs 25% p<0.0001), more likely to avoid nephrotoxic medications (87% vs 65% p<0.0001) and more likely to refer the First Nations man to a nephrologist (31% vs 5% p<0.0001). Lifestyle management was unchanged by the chart, with the majority recommending this before and after the chart (p=1.0).

Discussion

Summary

This randomised case vignette study showed that having access to a chart that graphs percentile kidney function (eGFR) by age was associated with more appropriate management review periods for the patient cases with reduced kidney function. In the case of the older woman with stable but reduced
kidney function, use of the chart was associated with proposals for a longer follow up period, longer time until repeat pathology testing and less use of lipid lowering medication. In the young male First Nations patient case, use of the chart was associated with proposals for a shorter follow up period, shorter time to repeat pathology testing, increased management of blood pressure and lifestyle management and avoidance of nephrotoxic medications. Use of the chart reduced proposals for unnecessary pathology testing and unnecessary early follow up.

Strengths and limitations

This study was a case vignette study (15), with cases created for specific age, gender, ethnicity, biometric and blood test values. The patient cases had borderline hypertension and lipid values for which GPs might have differences in management based on a patient-centred approach. Therefore, results may not reflect how a GP would actually manage these cases in a real clinical setting. We did not ask the participating GPs any questions regarding their reasons for changing their proposed management, which should be further explored. The chart used in this study was based on cross-sectional data from an Australian population survey. (17) This may limit the generalisability of this chart to other population groups.

Comparison with existing literature

CKD guidelines do not currently use age as part of the treatment recommendation algorithm. The guidelines state: “An eGFR of <60 mL/min/1.73m^2 is common in older people but is nevertheless predictive of significantly increased risks of adverse clinical outcomes and should not be considered physiological or age-appropriate”. (8) There has been much debate about this, with reasons including that absolute cardiovascular risk increases with age, and therefore CKD diagnosis is an important requirement to manage CVD risk regardless of age. (9,18) People with a moderate or severe reduction in eGFR (<45 mL/min/1.73m^2) (Stage 4-5) are at the highest CVD risk. (18) However, there is still debate about older people in stage 3a as to how aggressively they need to be managed. An individual approach is required with older people, taking into account their co-morbidities, functional states and personal priorities.(8,19) A kidney trajectory chart can be a useful tool for GPs to help in a discussion with patients about their own functional status, likelihood of further decline in kidney function and other health priorities. (12)

The older woman case scenario had stable kidney function in the CKD stage 3a category. According to the CKD guidelines(8), management should include follow up every 12 months, with clinical assessment of blood pressure and weight, HbA1c and fasting lipids annually, as well as assessing absolute cardiovascular risk, and avoiding nephrotoxic medications. (8). Without the chart, GPs were more likely to review this woman earlier than 12 months. Only one quarter of GPs would prescribe lipid lowering therapy for the older woman, and GPs with the chart were less likely to prescribe this (13%). We did not give the GP participants the patient’s complete lipid values, only TC, HDL and LDL. CKD guidelines recommend use of statin therapy in older people with CKD regardless of their lipid levels (8,9,10). This woman had a five-year absolute cardiovascular risk of 5%, which puts her in the low-borderline-intermediate cardiovascular risk category depending on which guidelines and risk calculator is used (18, 20,21). We did not ask GPs any questions about why they changed their management plan for this patient. Reasons for this would be worth exploring, as there are some variations between guidelines, and recent changes to guidelines since this study was performed. (10,18,20,22)
With respect to the young male case scenario, his kidney function does not meet the definition of CKD according to the current guidelines. (8) However, with a loss of 5 mL/min/1.73m$^2$ in the previous year, there could be cause for concern that requires a shorter follow up period, given that a rapid loss of GFR in the normal range can be associated with an increased risk for end stage kidney disease, and increased cardiovascular risk. A recent study showed that, among young people, a modest reduction in kidney function at a higher baseline GFR is associated with adverse cardiovascular and renal outcomes, and that these patients are often not picked up in the clinical guidelines because they fall outside the current definitions of CKD. (11,23) Recognition that for the young male patient his eGFR was on the 5$^{th}$ percentile for age was associated with GPs in our study choosing to repeat his tests earlier. It was only with the chart that showed an age comparison that clearly showed that his eGFR might be problematic.

Implications for research

A trial of use of this chart in clinical practice would be important to see whether it improves the recognition and management of reduced kidney function overall and reduces overdiagnosis and concern in older people in the clinical environment. Our hypothesis would be that the chart improves GP patient management of CKD, improves timeliness of review and more appropriate referral to nephrologists for advice. Further qualitative research exploring GPs’ reasons for choosing management options would be useful to further understand how the chart might work in clinical practice. Charts based on longitudinal data from broader population groups relevant to the clinical population of interest should be considered and trialled.

Conclusion

Having access to a percentile chart that graphs kidney function with age was associated with more appropriate management review periods for patient case scenarios with reduced kidney function, either by greater compliance with current guidelines, or greater awareness of a clinically relevant problem. A trial of use of this chart in clinical practice would be useful to see whether it improves the recognition and management of reduced kidney function in the clinical setting.

Additional Information:

Funding

Funding for this project was received from Therapeutic Guidelines Ltd through a Royal Australian College of General Practitioners Foundation research grant. The funder did not play any role in the design, delivery or reporting of the study, and the researchers were independent from the funder.

Ethics approval

This study received ethics approval from the Bond University Human Research Ethics Committee, protocol number RO15987. Participants gave informed consent before taking part.

Competing interests
Dr Glasziou reports grants from the Australian National Health and Medical Research Council during the conduct of the study.

Dr. Shaw is supported by an Australian National Health and Medical Research Council Investigator Grant.

Dr Barr is supported by a Targeted Translation Research Accelerator (TTRA) Australian Stroke and Heart Research Accelerator Centre grant (TTRARC008)

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Ms Beller, Dr Jones, Dr Barr and Dr Doust have no interests to declare.

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Data availability statement

Data are available upon reasonable request. Data are anonymous participant questionnaire responses, and are available by contacting michelle.guppy@une.edu.au.

References


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Tables and Figures

Figure 1- Consort flow diagram.

1. **Enrollment**
   - Assessed for eligibility (n=9500)
   - Excluded (n=9110)
     - Did not respond to email (n=9031)
     - Did not attempt study questions (n=79)
   - Randomized (n=390)

2. **Allocation**
   - Allocated to delayed chart group (n=187)
     - Received allocated intervention (n=187)
   - Allocated to immediate chart group (n=203)
     - Received allocated intervention (n=203)

3. **Follow-Up**
   - Discontinued intervention (GP did not complete all questions) (n=4)
   - Discontinued intervention (GP did not complete all questions) (n=13)

4. **Analysis**
   - Analysed (n=183)
   - Analysed (n=190)
<table>
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<tr>
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<th>Delayed Chart</th>
<th>Immediate Chart</th>
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</thead>
<tbody>
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<td></td>
<td>((n=183*))</td>
<td>((n=190))</td>
</tr>
<tr>
<td><strong>n</strong></td>
<td>%</td>
<td>n</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>95  52.5</td>
<td>93  48.9</td>
</tr>
<tr>
<td>Male</td>
<td>86  47.5</td>
<td>97  51.1</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 20-29 years</td>
<td>6  3.3</td>
<td>9  4.7</td>
</tr>
<tr>
<td>30-39 years</td>
<td>46  25.4</td>
<td>56  29.5</td>
</tr>
<tr>
<td>40-49 years</td>
<td>50  27.6</td>
<td>41  21.6</td>
</tr>
<tr>
<td>50-59 years</td>
<td>39  21.5</td>
<td>41  21.6</td>
</tr>
<tr>
<td>60-69 years</td>
<td>29  16.0</td>
<td>35  18.4</td>
</tr>
<tr>
<td>70-79 years</td>
<td>11  6.1</td>
<td>8  4.2</td>
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<tr>
<td>Years of Experience</td>
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<td></td>
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<tr>
<td>GP Registrar</td>
<td>12  6.7</td>
<td>27  14.2</td>
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<tr>
<td>&lt;5 years</td>
<td>24  13.3</td>
<td>30  15.8</td>
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<tr>
<td>5-10 years</td>
<td>39  21.7</td>
<td>30  15.8</td>
</tr>
<tr>
<td>11-20 years</td>
<td>36  20.0</td>
<td>32  16.8</td>
</tr>
<tr>
<td>21-30 years</td>
<td>30  16.7</td>
<td>30  15.8</td>
</tr>
<tr>
<td>&gt;30 years</td>
<td>39  21.7</td>
<td>41  21.6</td>
</tr>
</tbody>
</table>

*some included participants did not specify all demographic values*
Figure 2a (Case of older woman) and 2b (Case of First Nations man)- Time period chosen by the GPs (cumulative %) for next review of the older woman and First Nations man before viewing the chart (delayed chart group) compared to viewing the chart at the time of seeing the case vignette (immediate chart group). Connecting lines highlight difference in cumulative proportion between groups.
Figure 3- GP management decisions for the cases of the older woman and First Nations man before viewing the chart (delayed chart group) compared to viewing the chart at the time of seeing the case vignette (immediate chart group).
Table 2: Proportion (%) of GPs without the chart (delayed= reference group) compared to GPs with the chart (immediate) who would recommend each management option.

<table>
<thead>
<tr>
<th>Management option recommended</th>
<th>Older Woman</th>
<th>OR (95% CI)</th>
<th>First Nations Man</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Delayed n=183</td>
<td>Immediate n=190</td>
<td></td>
<td>Delayed n=182</td>
</tr>
<tr>
<td>Blood pressure reduction</td>
<td>69%</td>
<td>64%</td>
<td>0.80 (0.52 to 1.20)</td>
<td>75%</td>
</tr>
<tr>
<td>Lipid management</td>
<td>25%</td>
<td>13%</td>
<td>0.44 (0.26 to 0.76)</td>
<td>25%</td>
</tr>
<tr>
<td>Lifestyle/ weight management</td>
<td>74%</td>
<td>73%</td>
<td>0.92 (0.58 to 1.47)</td>
<td>86%</td>
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<tr>
<td>Avoid nephrotoxic medication</td>
<td>77%</td>
<td>71%</td>
<td>0.71 (0.45 to 1.20)</td>
<td>65%</td>
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<tr>
<td>Nephrologist referral</td>
<td>3%</td>
<td>3%</td>
<td>1.20 (0.35 to 3.90)</td>
<td>6%</td>
</tr>
</tbody>
</table>
