Helping people to live well with chronic kidney disease

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Introduction

In this paper we will be considering some of the implications of having chronic kidney disease (CKD), discussing what we know of the experience of the condition from the patient perspective, and, based on these issues, addressing how we as clinicians can best help people to 'live well' when they have the diagnosis.

In the last decade CKD has courted a degree of controversy. It has been included in debates on 'too much medicine' with concerns about over-labelling individuals with a 'disease' and the resulting burden and costs of clinical assessment, investigations, and 'unnecessary' treatment for both patients and health services (Moynihan et al. 2013). On the other hand, it is clearly a condition with a wide spectrum of severity, from a minor degree of reduced kidney function, often identified as an incidental finding, to life-changing end stage kidney disease (ESKD) requiring complex decisions about kidney replacement therapy (KRT, dialysis or transplantation) or conservative care. And it is not just ESKD that presents clinical challenges – there is now incontrovertible evidence that any degree of kidney dysfunction or damage is strongly associated with poor outcomes for patients. Large, international meta-analyses of both high risk and general population cohort studies have shown that any degree of low estimated glomerular filtration rate (eGFR) and albuminuria are both independent risk factors for poor outcomes including all-cause and cardiovascular mortality (CKD Prognosis Consortium 2010 and van der Velde et al. 2011), cardiovascular disease (Matsushita et al. 2015), progression of CKD, hospitalisation, and acute kidney injury (AKI) (Gansevoort et al. 2011; Astor et al. 2011; Grams et al. 2015).

This has understandably left some clinicians with uncertainty about how best to approach management, particularly in early or moderate CKD. Should the condition be played down as 'not that important' and possibly not even disclosed to patients as it may cause unnecessary distress? Or should its identification be prioritised with a view to early intervention to allow the best possible opportunity for the prevention of progression to end stage disease or other complications?

We hope that this paper will unpick some of these issues and provide some useful strategies with practical clinical application while keeping the person with CKD at the centre of the discussion.

Classification and epidemiology of CKD

The Kidney Disease Improving Global Outcomes (KDIGO) risk classification of CKD includes both reduced excretory function (by estimated glomerular filtration rate (eGFR)) and kidney damage (by presence of albuminuria) (KDIGO 2013). eGFR is categorised into six stages – G1 ($\geq$90ml/min/1.73m^2) to G5 (eGFR <15 ml/min/1.73m^2), and albuminuria into three groups (A1 reflecting urine albumin to creatinine ratio (uACR)<3 mg/mmol to A3 indicating uACR$\geq$30 mg per mmol) (KDIGO 2013).

CKD is common; prevalence in England is estimated at between 12 and 13% of the population, based on the nationally-representative Health Survey for England (and including both eGFR and uACR), rising to over 30% among people over 75 years (Fraser et al. 2014). While it is important to note that this was based on a single eGFR measure, and studies basing their CKD definition on two values of eGFR at least 90 days apart, as per KDIGO guidelines, have found lower prevalence, prevalence of eGFR

<60ml/min/1.73m^2 was still 16% among people aged over 60 in the Oxford Renal Cohort Study (Hirst et al. 2018). Future incidence and prevalence is likely to reflect a balance between the growing, ageing population, and increasing prevalence of obesity and type two diabetes, against improving hypertension control and falling smoking prevalence (Hounkpatin et al. 2020). As these population demographics and risk factors change over time, it is also likely that patients who have CKD as one of their health problems are increasingly complex and multimorbid (Fraser et al. 2015; Fraser et al. 2016; Tonelli et al. 2018). Given this context, the main focus of this paper will be on how we as clinicians can help people with CKD generally, rather than on the specific context of people on KRT, which has its own unique challenges and requires specialist input. The overall aim is to understand how we can offer the most holistic care to people with the condition.

What do we mean by 'living well'?

Before we continue it is worth considering what we mean by living well. Arguably, clinical interventions in any chronic condition could be considered as having one of two broad aims:

1. To reduce the risk of adverse events occurring *in the future*, and
2. To enhancing quality of life *now*.

The first might include things like prescribing statins for secondary prevention of cardiovascular disease, or inhaled steroids to prevent acute exacerbations of asthma. The second may focus on trying to alleviate unpleasant symptoms, such as addressing pain or breathlessness, providing rehabilitation to improve function, or adjusting medications that are causing side effects. We will use this framework to consider how, within the specific context of CKD, we can advise patients on living well by reducing the risk of various adverse future events and optimising quality of life. In order to do this we must understand the implications of having CKD

Living with CKD – the patients' perspective

Awareness of kidney function and CKD

In understanding patients' experiences of living with CKD, it is worth bearing in mind the public understanding of kidneys and their function. In 2014, as part of the UK 'Think Kidneys' programme, over 2000 UK residents were surveyed on their knowledge and understanding of kidneys, with results weighted for key demographic characteristics. This survey found that only 51% of people knew that kidneys make urine (the figure was 59% among graduates), 60% knew that the kidneys help remove waste, 12% knew that kidneys have a role in processing medicines, only 1% thought that smoking endangers kidney health and more than 60% thought alcohol endangers kidney health (Slevin and Talor 2015).[15]

It is also worth remembering that a significant proportion of people with mild or moderate CKD may be unaware that they have the condition. In the Renal Risk in Derby study, a cohort of about 1700 people with CKD stage 3 recruited from primary care, 41% were unaware of their CKD diagnosis at baseline (McIntyre et al. 2012).

Patients' experience of living with CKD

A systematic review and meta-ethnography of ten qualitative studies involving a total of 596 patients with non-KRT requiring CKD identified seven themes that express the experience of being diagnosed and living with the condition (Teasdale et al. 2017). These are summarised in Table 1 and show that many patients find receiving the diagnosis difficult, worry about its causation and have important concerns about future risk. They are often concerned about the way in which CKD will limit their life and feel that they have insufficient information with which to address these concerns. A further level of complexity in identifying the best ways of supporting patients is the relatively high prevalence of low health literacy, particularly among some more vulnerable groups of people with CKD (Taylor et al. 2017).

Table 1. Summary findings of a meta-ethnography of the experience of being diagnosed with and living with CKD

Theme	Summary aspects of the theme
A challenging diagnosis	– feeling well and asymptomatic when first diagnosed – feelings of shock and incomprehension about the diagnosis – uncertainty about CKD permanence
Diverse beliefs about causation	– believing CKD was a result of their own actions e.g. poor eating habits and alcohol or long-term medication use. – attributing CKD to external factors such as heredity or as the result of having other conditions such as diabetes
Anticipated concerns about progression	– concerns about future treatment – anticipated social and financial burden – being unable to continue working and/or inability to care for significant others
Delaying disease progression	– making adjustments to daily life to try and delay disease progression e.g. lifestyle changes
Unmet informational needs	– common viewpoint: participants believed they had received insufficient information about CKD and its progression from health professionals. – some perceived this as a deliberate attempt to withhold information
Psychosocial impact	– loss of freedom / restricted choices (particularly in people with CKD 5) due to treatment regimens, fatigue, dietary restrictions and/or dependence on others
Adjustment to life with CKD	– greater involvement with decision making – importance of community/social support – trying to live life to the full, ‘carry on as normal’, be positive

(Table data taken from: Teasdale et al 2017)

It is important to be mindful of this patient perspective when considering the more clinical implications of having CKD.

What are the implications of having CKD?

CKD and future risk

It is beyond the scope of this paper to discuss all of the measures used to assess and quantify each of the following risks, attributes and outcomes but it is helpful for all health carers to have a basic understanding (Kazmi et al. 2018).

Mortality and end stage kidney disease

As mentioned above, the two most important risk factors for mortality associated with CKD are reduced GFR and albuminuria, though the risk varies with age (see Table 2). The relative risk of mortality for people with reduced GFR remains statistically significantly higher than for their peers with better renal function, although it decreases with increasing age. However, the absolute risk associated with having reduced GFR increases considerably. There is a similar picture for albuminuria.

Table 2. Variation in relative and absolute mortality risk by age for people with CKD

Age	**Reduced GFR:** eGFR 45 mL/min/1.73 m^2 vs. 80 mL/min/1.73 m^2		**Albuminuria:** uACR of 300 mg/g vs. 10 mg/g	
	Relative (adjusted HR (95%CI))	**Absolute (excess deaths per 1000 person-years (95%CI))**	**Relative (adjusted HR (95%CI))**	**Absolute (excess deaths per 1000 person-years (95%CI))**
18-54	3.50 (2.55-4.81)	9.0 (6.0-12.8)	2.53 (2.13-3.03)	7.5 (4.3-11.9)
55-64	2.21 (2.02-2.41)	12.2 (10.3-14.3)	2.30 (1.84-2.88)	12.2 (7.9-17.6)
65-74	1.59 (1.42-1.77)	13.3 (9.0-18.6)	2.10 (1.83-2.44)	22.7 (15.3-31.6)
≥75	1.35 (1.23-1.48)	27.2 (13.5-45.5)	1.73 (1.45-2.05)	34.3 (19.5-52.4)

(Table data taken from: Hallan et al. 2012)

For any outcome in CKD, there are issues of competing risks. For example, if assessing the risk of progression to ESKD, account needs to be taken of the competing risk of death (i.e. that individuals die before they 'have the opportunity' to experience the outcome of ESKD). Bansal et al. (2015) developed a score to predict risk of mortality among older patients with CKD. The model includes age, sex, race, eGFR, urine albumin-to-creatinine ratio, smoking, diabetes mellitus, and history of heart failure and stroke. Similarly, Tangri et al. (2011) developed a kidney failure risk equation for prediction of progression to ESKD. Adoption of these risk scores to evaluate the relative risks of death versus ESKD has been proposed by the European Renal Best Practice Group as part of a Clinical Practice Guideline on the management of older patients with chronic kidney disease stage 3b or higher (Farrington et al 2017).

Cardiovascular disease and cardiovascular death

For the majority of people with CKD, risk of cardiovascular disease is substantially higher than risk of ESKD (Chronic Kidney Disease Prognosis Consortium 2010; van der Velde et al. 2011; Matsushita et al. 2015). Following evidence that they improve prediction accuracy, eGFR and urinary albumin to creatinine ratio (uACR) are recommended to be included in cardiovascular risk prediction models (Matsushita et al. 2015). The CKD Prognosis Consortium has developed a risk scoring tool that simultaneously estimates the risk of death, cardiovascular events and ESKD, though this is applicable only to persons with CKD category G4 (Grams et al. 2011).

Hospitalisation

A large UK study showed that among 15,336 participants aged 75 years and older from 53 UK general practices, dipstick-positive proteinuria and/or eGFR<30ml/min/1.73m^2 was associated with an increased risk of single and multiple hospitalization after adjustment for age, sex and cardiovascular risk factors (Nitsch et al. 2011). After full adjustment the hazard ratio for hospitalisations during less than six months of follow-up was 1.66 (95% CI, 1.21-2.27) for eGFR <30mL/min/1.73 m^2 compared with eGFR of 60-74 mL/min/1.73 m^2. Dipstick-positive proteinuria was also associated with an increased hazard ratio for admission (HR, 1.29 [95% CI, 1.11-1.49]) (Nitsch et al. 2011).

Acute kidney injury

A further CKD Prognosis Consortium study involving eight general-population cohorts (1,285,049 participants) and five chronic kidney disease (CKD) cohorts (79,519 participants), showed that lower eGFR and higher uACR were both strongly and independently associated with AKI (Grams et al. 2015). Compared with eGFR of 80mL/min/1.73m^2, the adjusted hazard ratio of AKI at eGFR of 45mL/min/1.73m^2 was 3.35 (95% CI, 2.75-4.07) and compared with a uACR of 5mg/g, the risk of AKI at uACR of 300mg/g was 2.73 (95% CI, 2.18-3.43).Older age was also associated with higher risk of AKI (Grams et al. 2015).

Inequalities

Age represents one of the key inequalities in CKD. It is beyond the remit of this paper to describe all aspects of CKD inequality, but they include greater prevalence in lower socioeconomic groups, variation in prevalence and progression by ethnicity and sex. More women have kidney disease, but more men start dialysis and people from South Asian and Black backgrounds are more likely to start dialysis than people from White backgrounds (Caskey and Dreyer 2019).

Comorbidities

As suggested above, comorbidities are common in people with CKD and are associated with polypharmacy (Fraser et al. 2015). They are an important determinant of adverse outcomes and this is true not only for the 'usual suspects' that we expect in the context of CKD – diabetes and cardiovascular conditions – but also for conditions that have been considered 'discordant', such as dementia and cancer (Tonelli et al. 2015).

Some specific comorbidities and other attributes are considered below.

Quality of life

Quality of life tends to be poorer for people with CKD than their general population peers (Perlman et al. 2005). Quality of life scores also tend to decline with decreasing GFR (Perlman et al. 2005 and Mujais et al. 2009). In a large North American cohort study of people with CKD 3-5, other associations of poor quality of life included being female and having comorbidities (particularly diabetes and cardiovascular disease, including heart failure) (Mujais et al. 2009). It is notable that physical functioning scores also declined progressively with more advanced stages of CKD in this cohort and that lower quality of life was associated with anaemia and beta blocker use (Mujais et al. 2009). Decline in functional capacity, often linked to the presence of comorbidities, is also associated with worsening renal function (Chin et al 2014).

Pain

The prevalence of chronic pain in people with CKD stages 1- 4 has been estimated at about 70% in two US studies, with musculoskeletal the most common cause (Davison et al. 2014). However, there is wide variation in prevalence estimates, potentially dependent on population studied and definition of pain. In the UK, a cohort study using repeat pain medication to define pain among people with CKD stage 3 identified a prevalence of about 30% (Fraser et al. 2015). In the Tonelli et al. (2015) large database study from Canada (n=530,771 with CKD), where 'chronic pain' was based on clinical codes, the prevalence of painful condition was nearer to 10%.

Depression

Depression is also common among people with CKD. In a review of eight studies of people with CKD stage 2-5 (total n=11,501), depression prevalence varied between 21 and 47% (Shirazian et al. 2017). Outcomes associated with depression in these studies included hospitalization, ESKD, AKI, worse QoL, faster / greater decline in GFR and mortality (Shirazian et al. 2017). The Tonelli et al (2015) study, where again depression was based on ICD codes, identified a depression prevalence of 11.3% and in the Renal Risk in Derby study, where depression was based on antidepressant medication prescription, it was even lower at about 5% (Fraser et al. 2015). These latter studies with more restricted definitions, almost certainly represent an under-estimation of the true prevalence. The prevalence reported in the eight-study review is not dissimilar to estimated prevalence in the England general population, reported to be about 27% among people aged over 65 years (Feng at al. 2015).

Functional limitation

CKD seems to be associated with an adverse impact on Activities of Daily Living (ADL). For example, a Korean cohort of 984 people with varying degree of renal function impairment followed for five years found that the incidence of ADL/ instrumental activities of daily living (IADL – activities that support independent living) decline was 13%, 12.5% and 29.5% in participants who showed improvement, no change, and decline in GFR respectively (p = 0.01) (Chin et al. 2014). An Alabama cohort exploring the impact on IADL and basic activities of daily living (BADL – self care tasks) conducted over two years had similar findings, with adjusted odds ratios for CKD vs. non-CKD IADL and BADL decline of 1.83 (95% confidence intervals (CI) 1.06-3.17, p =0.03) and 2.46 (1.19-5.12, p =0.02), respectively (Bowling et al. 2011).

Frailty

Frailty may be more common among people with CKD than people without. Among 5808 adults in a cross sectional US study, prevalence of frailty was 15% in people with CKD versus 6% in those without (p < 0.001). After multivariable adjustment for comorbidity, CKD remained significantly associated with frailty (odds ratio 1.76; 95%CI 1.28 to 2.41) (Shlipak et al. 2004). More work is needed on the relationship between CKD and frailty to explore the direction of causality.

Fatigue

Fatigue is common – particularly among people with advanced CKD (Artom et al. 2014). Prevalence estimates vary between about 40% and 90% depending on stage of CKD, measurement instruments used and treatment modality (for those on dialysis).

Treatment burden and polypharmacy

Treatment burden can be defined as the workload of healthcare, or the 'work of being a patient', and its impact on patient functioning and wellbeing (Shippee et al. 2012 and Sav et al. 2015). Activities such as taking and managing multiple medications, organising and attending healthcare appointments, monitoring health, performing self-care, and modifying lifestyle behaviours all contribute to this workload. This includes polypharmacy, but goes beyond it to consider issues which can be very burdensome for patients, such as making dietary modifications and attending multiple appointments with different specialists. While by no means unique, such things are very common among the mostly older population of people with CKD, who are frequently managing multiple conditions (Fraser et al. 2015; Fraser et al. 2016; Tonelli et al. 2018).

Living *well* with CKD

What can we do as clinicians?

Awareness of the patient perspective and using clear communication

Given the potential for a low level of understanding of kidneys and kidney disease, it is vital that we understand something of the patient perspective described above. We can use this knowledge to inform both *what* we say and *how* we approach clinical interactions. It is important to ask ourselves questions such as:

- 'Is this patient aware of their CKD diagnosis?'
- 'What do they understand about their condition?'
- 'What is the patient's main concern?'

- ‘What might they need to know?
- ‘How can I enhance health literacy here?’ (rather than ‘how can I dumb this down so that people understand?’)
- ‘Have I checked back that they understand?’

Having our own uncertainties about CKD as a condition risks adding further to patients’ concerns.[15]

Advice for patients

There are important things we can advise our patients. These are summarised in Table 3, categorised according to reducing future risk and enhancing quality of life. Some aspects, such as encouraging physical activity, appear in both categories.

Table 3. Things that people with chronic kidney disease and clinicians can do to support ‘living well’ with the condition

	Patients	**Clinicians**
Reducing future risk	Undertake monitoring, particularly of their own blood pressure	Regular monitoring, particularly albuminuria, eGFR and blood pressure
	Lifestyle measures: dietary sodium restriction, weight loss, exercise	Cardiovascular risk assessment (including use of risk prediction tools) and management: smoking cessation, blood pressure control, use of statins, diabetes control, proteinuria control
	Enquiring about progression and other risks - enhancing health literacy	Careful assessment of CKD progression risk relative to other risks e.g. kidney failure risk equation (Tangri et al. 2011).
	Understanding purpose of medicines and avoiding nephrotoxic medicines - enhancing health literacy, discuss treatment burden with clinicians	Careful medicines management including appropriate dose adjustments and minimisation of polypharmacy
	Understanding need for and engaging with activity - enhancing health literacy	Encouraging (and potentially referring for) exercise to improve mobility and strength
	Fluid management, avoiding nephrotoxic medicines, flu vaccination, medication adherence, potentially temporary avoidance of certain medications when sick (though caution in heart failure)	Good clinical care to reduce acute kidney injury risk e.g. fluids, sepsis management, avoiding nephrotoxic medications
Enhancing quality of life	Understanding CKD – enhancing health literacy through asking about the diagnosis	Careful explanation of the CKD diagnosis and its likely causality
	Enquiring about progression and other risks - enhancing health literacy	Careful explanation of progression risk relative to other risks (CVE, death before ESKD). Most people with CKD are at low risk of progressing to ESKD. Adapt information provided according to the dominant risk.

	Understanding purpose of medicines, monitoring and appointments and querying unnecessary visits. Developing strategies / routines to manage treatment burden	Assessing overall treatment burden (consider using a validated measure)
	Enhancing patient activation balanced with burden Consider the importance of peer support either ‘formal’ (e.g. via kidney care networks) or informal e.g. social networks.	Supporting self-management without overloading the patient
	Understanding purpose of medicines - enhancing health literacy	Careful medicines management including appropriate dose adjustments and minimisation of polypharmacy
	Understanding need for and engaging with activity - enhancing health literacy	Encouraging (and potentially referring for) exercise to improve mobility and strength
	Inform clinicians about pain. Consider non-pharmacological solutions for pain	Adequately address pain. Consider non-pharmacological solutions for pain

Conclusions

CKD is a condition with both specific and general health risks. The population of people with CKD tends to have more challenges across a number of domains than their peers. Helping people with the condition to live well includes considering ways of reducing future risk and enhancing quality of life. Patients can, and should, be actively engaged in this in order to enhance their capacity to manage the condition and reduce the burden both of the disease and its treatment.

Five to eight key points which summarize the major themes of your article:

1. Key issues reported by patients with CKD include being shocked by the diagnosis, being uncertain about the cause, worry about progression and concerns about future treatment and its anticipated social and financial burden.

2. Helping people to live well with a chronic condition like CKD should include efforts to reduce the risk of adverse events occurring *in the future*, and consider what can be done to enhance quality of life *now*.

3. As clinicians we can help people live well with CKD by being aware of their perspective and communicating clearly, including checking their understanding, particularly of the CKD diagnosis, its likely causality and the risk of progression.

4. People with CKD commonly suffer from multiple comorbidities and lower quality of life, often experiencing chronic pain, depression, functional limitation, frailty, fatigue and high treatment burden.

5. Assessing overall treatment burden is an important component of management.

6. Reduced glomerular filtration rate and presence of albuminuria are both associated with increased risk of several poor outcomes including cardiovascular disease, hospitalisation, acute kidney injury and death.

7. Interventions to reduce future risk in CKD include regular monitoring (particularly albuminuria, eGFR and blood pressure), careful assessment of CKD progression risk relative to other risks, and careful medicines management.

8. Non-pharmacological interventions that may improve mobility, strength and pain should be considered.

Conflicts

The authors declare no conflicts of interest

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