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10 tips on performing economic evaluation in kidney disease

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ABSTRACT

Nephrology has benefited from a growing body of high-quality clinical evidence, including clinical trials of pharmacological therapies and health service research on alternative care approaches. Consequently, there is an increasing need to perform economic evaluations in kidney disease to inform reimbursement decisions and optimise healthcare spending, thereby improving patient care within budget constraints. Cost-effectiveness assesses if the additional health gains are worth any additional costs by estimating differences in the quality and quantity of life, and the costs, from the point of intervention over observed but also longer (even lifetime) timelines, capturing the entire patient pathway through healthcare, e.g. from early-stage chronic kidney disease (CKD) through to dialysis or transplantation. Working with stakeholders to define the decision problem, merging evidence from a range of sources, including clinical trials complicated by limited follow-up and non-generalisable participants, surrogacy studies to estimate the intervention's impact on longer-term kidney failure risk, quality of life data collected ideally using instruments sensitive to kidney disease progression and other real-world data are required to make extrapolations sufficiently far into the patient's lifetime to capture kidney failure. Consideration of disadvantaged populations and how interventions may operate differently in certain groups may be indicated. Failure to capture competing risks of cardiovascular disease and death will bias estimates of kidney failure. Application of our tips, combined with an understanding of how decision-makers use cost-effectiveness results and information about factors like rarity and disease severity maximises the likelihood of new kidney treatments and care approaches being adopted.

Keywords: cost-effectiveness, cost utility analysis, costs, decision-making, economic modelling

Nephrology has benefited from a growing body of high-quality clinical evidence, including randomized controlled trials (RCTs) of pharmacological therapies and health service research on alternative care approaches. Preventing kidney failure and thereby preventing the need for dialysis are cost-saving measures: globally the cost of chronic kidney disease (CKD) care increases by a factor of four from CKD stage G3a to G5, and CKD costs are projected to increase by ≈10% per year between 2022 and 2027 [1, 2]. To ensure that current practices are truly cost-effective and provide value for both patients and healthcare systems, all health benefits, potential harms (such as adverse side effects) and healthcare costs associated with kidney disease must be measured.

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Economic evaluations are employed to inform reimbursement decisions and optimise healthcare spending within and across disease areas, thereby improving patient care within budget constraints. In CKD economic evaluations, the journey through the CKD stages and kidney replacement modalities, the quality and quantity of time spent in these health states, the resource use and the associated cost incurred may all differ according to which CKD interventions or model of care a patient receives.

One approach to economic evaluation is to use a health economic model. These take evidence from a range of sources including RCTs with limited follow-up, surrogacy studies to estimate the impact on policy-relevant, longer-term outcomes, and other real-world data to make extrapolations where data are lacking. Economic models can estimate both the quality and quantity of life gained from the point of intervention over a longer (potentially even lifetime) horizon, capturing the entire patient pathway through healthcare, e.g. from early-stage CKD through to dialysis or transplantation. Models can estimate the impact in large, generalisable populations, such as all patients with CKD in a healthcare system, rather than just a subset limited by trial inclusion criteria. Finally, by drawing upon multiple evidence sources, economic models can account for important events not measured in specific clinical trials, such as hospital admissions for cardiovascular complications, dialysis catheter failures or the onset of anaemia [3–5]. However, it is important to note that not all health economic evaluations require models, and cost-effectiveness or cost-utility analyses can be performed using just clinical trial data when the duration of follow-up and outcomes captured are final [6].

Most healthcare regulatory authorities pay for CKD healthcare, even if it leads to greater total costs, because CKD healthcare adds more health, usually estimated as quality-adjusted life years (QALYs). The willingness to pay for more health varies by regulatory authority and the healthcare funding system: depending on the situation, the willingness to pay for one additional life year in full health (one QALY) can cost up to £30 000 in the UK and up to $150 000 in the USA [7]. Assessments of value can be sensitive to assumptions underlying the model and the choice of evidence sources for health benefits and costs, and economic evaluation within kidney disease has its own unique quirks and nuances. These top 10 tips have been selected to support those considering undertaking, designing, conducting or evaluating the results of heath economic evaluation in CKD, whether using modelling or non-modelling approaches.

1. WORK WITH STAKEHOLDERS WHO UNDERSTAND THE KIDNEY POPULATIONS, INTERVENTIONS AND COMPARATORS YOU ARE EVALUATING AND HOW THE INTERVENTION MAY ADD VALUE

Stakeholders such as doctors, nurses, people with kidney disease, healthcare providers and policymakers can help you clarify your population, intervention, comparator and outcomes (PICO). Projects needs to involve a wide profile of actors' voices to ensure that the evaluation captures accurately all parts of the disease, diagnostic and treatment pathways. These actors will differ depending on the intervention and nature of the kidney disease [8]. For example, if the intervention is a genomic test, geneticists in addition to nephrologists should be involved. If other diseases may be detected, the project may need to involve a wider clinical group, including urologists and oncologists. In terms of the extent of involvement, at a minimum, clinicians can be involved to consider the eligibility for people with kidney disease for a given intervention, help identify the highest-quality evidence sources for the model inputs, confirm the appropriateness of modelling assumptions, consider if guidelines have been appropriately reflected and check the face validity of the model results [9]. By focusing the model on key decision points and disease trajectories, clinician input can help to simplify the evaluation while also ensuring that findings inform practice and reach a wide audience of stakeholders. They can help decide if beyond-trial modelling is necessary.

There are other important stakeholders to involve in economic evaluation. People with kidney disease can provide insights into whether the proposed benefits align with their lived experiences and how relevant or significant these benefits feel to them. Epidemiologists provide important feedback on the appropriateness of epidemiological data used in the model and its interpretation. Early involvement of those with a decision-making perspective, e.g. by involving policymakers and members of regulatory agencies, can ensure you generate policy-relevant outputs. This includes, where appropriate, capturing wider benefits when assessing the cost-effectiveness of a treatment: increasing kidney transplantation or nocturnal dialysis in populations who are of reproductive or working age may lead to increased childbirth and/or societal financial value [10]. Improved mental well-being and sleep quality from reduced CKD-associated pruritus may reduce presenteeism and absenteeism in those of working age [11].

Working with stakeholders to establish the above can sound intimidating, but authoritative guidance on the conduct and reporting of such activities has been published by organisations such as the International Society for Pharmacoeconomics and Outcomes Research, who have also conceptualised the 'value flower', which outlines all the potential value domains that could be considered important to a wide range of stakeholders. It draws attention to quality and quantity of life as the most broadly accepted value that should be measured and monitored in economic evaluation [12, 13].

2. STRUCTURE YOUR EVALUATION TO MAXIMISE THE USE OF AVAILABLE HIGH-QUALITY EVIDENCE OR DATA AND AVOID RESEARCH WASTE

Economic evaluation requires appropriate data on the quality and quantity of life and the associated healthcare costs. The logistical barriers to collecting these data means that many evaluations choose to repurpose existing data. This data repurposing requires an understanding of whether the categorised stages of disease (e.g. CKD stages, lupus nephritis responses), the patient-reported outcome instruments [e.g. Kidney Disease Quality of Life (KDQOL) and EuroQol five-dimension (EQ-5D) measures] [14] and kidney function endpoints [e.g. estimated glomerular filtration rate (eGFR) slope or a 40% decrease in eGFR] [15] are relevant for the economic evaluation. Justifications and challenges include:

- **Limited follow-up:** The study duration required follow-up to meaningfully observe kidney failure, relative to common

study follow-up periods of roughly 2 years, makes kidney failure as an endpoint futile. This is highlighted by systematic reviews of kidney health economic models requiring a mean horizon of 14 years to capture kidney failure endpoints [16]. Therefore the use of published kidney function progression rates and surrogate relationships can relate short-term observed outcomes to long-term kidney failure events [17–20].

- **Limited sample sizes:** This issue not only effects kidney failure and patient survival outcomes, but the number of responses to quality-of-life instruments may be insufficient to credibly demonstrate differences between CKD stages or kidney replacement therapy modalities. To overcome this, evaluations can rely on other survey data that identify appropriate values for the population in which the treatment is being evaluated. Systematic reviews are often required by reimbursement agencies to demonstrate relevant evidence has been identified [21].
- **Laborious data collection:** Collecting information on resource use and costing it can be time-consuming. Stakeholders may find it acceptable to use values for CKD generally, and for your intervention, from existing literature [22], especially for later stages of CKD, which are rarely observed in trials of conventional duration.

3. RECOGNISE CLINICAL TRIAL POPULATIONS ARE DIFFERENT FROM THOSE SEEN IN CLINICAL PRACTICE AND UTILISE EXTERNAL REAL-WORLD EVIDENCE (RWE) TO ACCOUNT FOR THIS

While uncontrolled evaluations of interventions using observational data are prone to bias, there is growing recognition within and beyond kidney disease that RWE is essential to understand and evaluate how a treatment operates in clinical practice [23].

The following are recent examples from RCTs in kidney disease justifying the use of RWE. Acknowledging that trial populations are typically younger and have fewer comorbidities, the UK reimbursement authority was presented with the cost-effectiveness of dapagliflozin for CKD after substituting the trial population with data derived from Clinical Practice Research Datalink RWE. Two recent trials [EMPA-KIDNEY (NCT03594110) and DAPA-CKD (NCT03036150)] elicited the participants' health-related quality of life (QOL) at baseline using the five-level EQ-5D. QOL for people in CKD stages 2–4 where higher than values reported by the UK general population for the same mean age of 64 years, resulting in the use of EQ-5D data from a UK observational cohort [24].

The representativeness and generalisability of RWE is considered to be better than trials. For example, despite lupus nephritis occurring nine times more often in people of Black or Asian ethnicity than Whites, RCTs of lupus nephritis interventions recruited up to 88% White patients. Therefore, any potential health benefits demonstrated in RCTs of lupus nephritis may subsequently be undervalued, as data suggest these technologies may be more effective in pooled non-White populations [3, 25].

However, RWE is never absolutely representative of the CKD population. Ensuring these RWE sources exist and align with your PICO (tip 1), ensuring it aligns with your model structure (tip 2), is essential.

4. QUALITY OF LIFE DATA YOU COLLECT IN YOUR CLINICAL STUDY OR SOURCE FROM THE LITERATURE NEEDS TO BE RELEVANT TO YOUR POPULATION AND ECONOMIC EVALUATION

Health benefits in economic evaluation include both the quality and quantity of life, and therefore accurate and credible estimation of how both differ with a different healthcare intervention is required. Because decision-makers are often considering value in a range of disease areas, there is a preference for generic rather than disease-specific instruments for health-related QOL. When assessing treatments for reimbursement, most agencies recommend QOL is assessed using the EQ-5D, which asks respondents to score the five domains of pain, mobility, usual activities, self-care and depression and anxiety. These responses then have a value set applied that reports a utility value: where 1.0 is perfect health and 0.0 is death. Within kidney disease, this presents difficulties.

- **Use the correct (but insensitive) instrument or map another (sensitive) instrument to it:** Within kidney disease, one key difficulty is adequately capturing how the condition impacts patients' lives and the domains that matter most to them. Standardising Outcomes in Nephrology (SONG) recently identified fatigue and life participation as core outcome domains for haemodialysis (HD) and peritoneal dialysis (PD) patients, respectively [26, 27], while other targeted reviews have additionally identified sleep and skin problems such as pruritus [28]. Generic QOL measures do not necessarily directly reflect all the symptoms or broader QOL domains that are prevalent and have been identified as priorities for the kidney community. To demonstrate health-related QOL benefits in delaying the progression of CKD, measured health-related QOL would need to change with CKD progression. Systematic reviews and clinical trial cohorts reporting the EQ-5D show only small differences in utility by CKD stages [21] or dialysis modalities [29]. These small differences may be due to a lack of meaningful decline in QOL in early CKD in the domains assessed by the EQ-5D. Alternatively, it may reflect the absence of more salient domains in the EQ-5D instrument for people with kidney disease [28]. However, there are limitations with alternatives to the EQ-5D, such as instruments designed to capture the broad range of kidney-specific symptoms (e.g. IPOS-Renal, POS-Renal, KDQOL) or instruments measuring severity in conditions that specifically affect people with kidney disease such as CKD-associated pruritus (Worst Itch Numerical Rating Scale and 5-D itch). These can also be surprisingly insensitive to changes in earlier CKD stages [30] and currently do not have the associated preference-weighted value sets from which one can take an instrument response and calculate a credible utility value or score that ranges from 0 to 1. While value sets can be obtained from populations using a range of methods (time trade-offs, discrete choice experiments), it is a complex and difficult process, particularly when there are many questions within a given instrument [31]. One option is to instead use a mapping (a statistical regression or look-up table) to relate a kidney disease instrument to a measure that does have a value set [32, 33].
- **Use the right (often trial) data collected using these instruments at the right time:** Some decision-makers prefer or even require the use of utility instruments in studies such as phase 3 RCTs. There is specific guidance on how to do this

[34, 35]. Kidney trialists evaluating interventions that delay CKD progression are mainly focused on determining the effect of randomisation on outcomes including QOL. Health economic models usually just need a measure of QOL by CKD stage, irrespective of randomisation. This is because most interventions affect QOL through delaying CKD progression and the worse QOL reported in individuals with more advanced CKD, but the QOL for the same CKD stage, whether receiving intervention or control, should be similar.

5. DO NOT LIMIT YOUR ANALYSIS TO *QALYS*; WHERE POSSIBLE REPORT OTHER EVENTS LIKE KIDNEY FAILURE OR KIDNEY REPLACEMENT MODALITY THAT ARE RELEVANT TO KIDNEY STAKEHOLDERS

Although the cost per QALY may be the generic measure of economic value, appropriately specified health economic models can report health outcomes more relevant to a specific audience you are trying to convince (see tip 1). This could include numbers developing kidney failure, experiencing myocardial infarctions or admissions with heart failure, kidney transplants or flares of lupus [3]. If your evaluation is considering the persons' entire lifetime, these estimates will be numerically greater and therefore of greater relevance. Examples where more granular outcomes than just QALY differences have been reported include policy documents [36], evaluations of sodium–glucose cotransporter 2 inhibitors, individuals experiencing cardiovascular events and kidney failure [3], dialysis modalities (time receiving specific kidney replacement therapy modalities) and transplantation [4]. An important benefit of reporting these events in your evaluation is that findings can help assess the validity of your economic evaluation through comparison of those findings with existing real-world data sources like kidney disease registries.

6. THE COST OF KIDNEY CARE MAY VARY BY GEOGRAPHY BUT THE AMOUNT OF CARE DELIVERED MAY NOT

The cost of delivering healthcare, and therefore the financial value of reducing adverse health events, varies greatly across the globe [37]. This means the evaluator needs to consider the disease, the provider, the healthcare system and methodological conventions when transferring costs between geographies [38]. Illustrative examples include systematic reviews showing variations in the relative cost of HD versus PD of 2.25 to 0.22 by geography, with postulated differences including the relative difference of labour costs (HD) compared with goods import costs where local manufacturing is not available (PD) [39]. Economies of scale (where the unit cost decreases as the volume increases) have also been described in PD [40].

If total costs for a given treatment or disease are not available for your country, alternative approaches do exist. Well-conducted studies that adhere to reporting guidelines for economic models will present resource use and unit costs separately [3, 4, 41]. One common approach is to use event rates or resource use from other similar geographies, then apply individual costs (which could include tariffs or reimbursement costs) to these for the geography of interest. Transferability in the disease, the provider, the healthcare system and its capacity, human development index and methodological conventions between geographies should be recognised and/or established by the stakeholders you have involved in the evaluation (see tip 1).

7. IF ENDPOINTS LIKE KIDNEY FAILURE OR MORTALITY HAVE NOT BEEN OBSERVED IN YOUR STUDY, CONSIDER CHANGES IN SHORT-TERM ENDPOINTS AND THE STRENGTH, SIZE AND LIMITATION OF THE RELATIONSHIPS WITH THESE HARDER ENDPOINTS TO ESTIMATE THE LONG-TERM VALUE OF YOUR INTERVENTION

Within kidney disease, healthcare professionals often focus on absolute and relative changes in kidney function and proteinuria, but these are both considered surrogate outcomes by decision-makers [15]. The kidney community continues to generate evidence relating kidney function and proteinuria changes to kidney failure [42] and mortality [43] to support the significance of certain endpoints chosen in clinical trials and the endpoints and assumptions used in regulatory and reimbursement decisions. The need for evidence bridging surrogate outcomes with longer-term hard outcomes stems from difficulties in generating evidence on longer-term outcomes within trials, which include limited sizes of affected populations, the prolonged follow-up time required to demonstrate the key relationships and the associated cost.

An example of high-quality surrogacy evidence is when changes in the surrogate in the presence of an intervention lead to changes in the policy-relevant ('hard') endpoint. Relating eGFR and proteinuria at one timepoint with kidney failure, without considering if these surrogates had changed over time or in response to a therapy would represent a cross-sectional assessment and be classed as lower-quality evidence [44]. Accepted methods and surrogates for regulators and health technology assessment (HTA) agencies are available and represent an opportunity to learn from other disease areas [45, 46].

Possible kidney disease surrogate outcomes include eGFR slope, which has the advantage of informing progression through health states of a model [42]. In immunoglobulin A nephropathy, improvement in proteinuria within a given CKD stage has been associated with a reduction in risk of progressing into the next CKD stage [18]. Within lupus nephritis, the relationship between eGFR/urine protein definitions of complete and partial remission following intervention has been related to kidney failure and patient survival [19]. In oxaluria the sequential relationship between urinary oxalate, serum oxalate and organ damage has been used [47]. Within dialysis, the relationship between left ventricular mass and patient survival has been used to argue for the value of more intensive dialysis regimens despite conflicting surrogacy evidence [48].

8. CONSIDER THE COMPETING RISK OF CARDIOVASCULAR DEATH WHEN SEEKING VALUE FROM PREVENTING PEOPLE REQUIRING DIALYSIS

The kidney literature already covers the perils of failing to adequately consider competing risks and how this can lead to biased estimates of associations or effects [49]. As most health economic analyses are trying to estimate over time which health state (CKD stage, dialysis, transplant etc) a patient with kidney disease might occupy, estimating the risk of kidney failure without estimating the competing risk of death can lead to an overestimation of kidney failure events [50]. Therefore data that estimate the incidence of multiple relevant competing events are preferable. One approach is multistate models that

can estimate proportions in progressed kidney disease, kidney failure, cardiovascular events and death and have been applied for this purpose [51]. When interventions independently affect kidney disease progression and cardiovascular disease, it is essential to include cardiovascular disease, and therefore cardiovascular death, as a competing risk for kidney disease progression in health economic models. Comparing model outputs with clinical trial and real-world data sources is again critical to ensure the model and the data that informs it maintains face validity after competing risks are incorporated into the model (see tip 3). Competing events can also be of a type that is health enhancing. For example, keeping people on dialysis alive for longer may allow those who are suitable to be transplanted, which has large and sustained health benefits.

9. APPRECIATE HOW DECISION-MAKERS INTERPRET COST-EFFECTIVENESS CONSIDERING THE SEVERITY, RARITY AND COST OF SOME (KIDNEY) DISEASES

Most decision-makers globally have a defined amount they are willing to pay for a unit increase in health gain (QALYs) and treatments above this 'threshold' will not be paid for [7]. This threshold or other aspects of the evaluation can be altered in the presence of mitigating circumstances, many of which are specifically relevant to kidney disease and include innovation, rarity, end of life/proximity to death, curative potential, age, burden of illness and health inequalities.

HTA bodies in Europe, the USA and elsewhere previously or currently have had higher cost-effectiveness thresholds for medicines used to treat rarer diseases [52]. The definition of rare needs to be carefully considered: for instance, in the UK, the condition should have a prevalence of <1 in 50 000 people. Within kidney disease this would represent atypical haemolytic uraemic syndrome and primary hyperoxaluria type 1. It is notable that the general population appears indifferent to rarity as a reason for treatments to cost more [53]. Acknowledging the challenges associated with performing larger studies in smaller populations, the rarity of a disease also reduces the evidence available for an evaluation and therefore the flexibility around evidence decision-makers may demonstrate. An example includes surrogate relationships such as the use of eGFR slopes rather than a composite outcome including kidney failure and a 40% reduction in eGFR [15].

The public are generally more willing to give priority to a patient with more severe disease, and people receiving dialysis, who have historically had survival similar or worse than some solid organ malignancies, would seem like a cohort who would qualify [54]. However, some HTA agencies have a strict classification for what counts as a severe disease, e.g. if average life expectancy with the current standard of care was <2 years or compared to a healthy age-matched population your disease denies you >85% of your future QALYs [55]. In the UK, severity was not met in a recent appraisal of difelikefalin for the treatment of CKD-associated pruritus in people on dialysis, even when considering a population ineligible for kidney transplantation [56].

Although rarity and severity are powerful levers, mechanisms to account for the burden of dialysis within economic models may also be utilised. The inconvenient truth is that the annual cost of delivering HD exceeds what many decision-makers consider that health gain should cost. Therefore, without careful consideration, no proposed intervention, even if it was free, could be considered cost-effective [57]. Acknowledging this, mechanisms exist to make sure life extension on dialysis is preferred to no treatment. This includes subtracting expensive healthcare costs during the additional life years an individual on dialysis may gain from a treatment. This improves the cost-effectiveness of dialysis compared with no treatment and therefore also of interventions that improve the clinical efficacy of dialysis [58].

10. CAREFULLY CONSIDER HEALTH INEQUALITIES AND REPORTING OUTCOMES IN DISADVANTAGED KIDNEY POPULATIONS

It is increasingly recognised that among other populations, men have a higher risk of dialysis and acute kidney injury, South Asian adults develop CKD earlier and Black, Asian or mixed heritage individuals who are more likely to experience kidney failure than their White counterparts [59, 60] have inferior access to disease-modifying therapies and kidney transplantation and worse outcomes once kidney disease has developed. Therefore, interventions that potentially reduce inequalities may in some cases be assigned greater priority by decision-makers, depending on the characteristics of the health system. There are important considerations for health equity when considering the benefits of an intervention:

- Does your intervention impact (narrow or widen) health inequalities? Interventions may unintentionally exacerbate health inequalities due to factors such as communication barriers, technological literacy and access, service delivery challenges or differences in access to care. CKD educational interventions that rely on technology are good examples [61]. Economic evaluations should, at a minimum, acknowledge these potential issues, even if a full evaluation of their impact is not possible or desired by stakeholders.
- How does your evaluation capture changes to health inequalities? Kidney disease screening has been shown to be more cost-effective in high-risk ethnic populations [62], so you may wish to use methods that both capture the differences in health benefits and costs associated with disadvantaged populations and report outcomes in disadvantaged populations separately. Underlying societal preferences in reducing inequalities in decision-making can be reflected in economic evaluation [63]. These come with caveats and consequently are not yet often considered by decision-makers, leading to their very limited adoption in kidney disease economic evaluations to date.

CONCLUSION

As healthcare systems worldwide face growing pressure to provide effective and equitable care within constrained budgets, robust health economic analysis becomes critical for guiding decisions about which interventions offer the best value for patients and society. This set of top 10 tips is designed to offer practical, evidence-based guidance for researchers, clinicians, policymakers and all stakeholders involved in the design and interpretation of economic evaluations in kidney disease. By addressing methodological pitfalls, the limitations of available data, the nuances of QOL measurement, the need for inclusion of RWE and the importance of health equity, these recommendations aim to improve the relevance, credibility and transparency of economic evaluations in kidney disease. Importantly, while many of the principles outlined here are applicable across disease areas, CKD presents its own unique challenges and opportunities. We have

Table 1: Summary of tips, associated problems and solutions.

Tip	Problems and solutions
1. Work with stakeholders who understand kidney populations, interventions and comparators you are evaluating, and how the intervention may add value	**Problem:** Correct population, intervention, comparator and outcomes (PICO) and supporting data are essential for a successful economic evaluation **Solution:** Get support from stakeholders such as doctors, nurses, people with kidney disease, healthcare providers, and policymakers
2. Structure your evaluation to maximise the use of available high-quality evidence or data and avoid research waste	**Problem:** Data collection is resource-intensive and often requires large sample sizes and long follow-up durations **Solution:** Where appropriate, use published disease progression, surrogacy, health-related QoL surveys and costing data
3. Recognise clinical trial populations are different from those seen in clinical practice and utilise external RWE to account for this	**Problem:** Kidney trial populations are typically younger, have fewer comorbidities and are not demographically diverse **Solution:** Where appropriate, use RWE reflecting more generalisable populations for some evaluation inputs
4. Health-related QOL data you collect in your clinical study or source from the literature needs to be relevant to your population and economic evaluation	**Problem:** Generic health-related QOL instruments are insensitive to kidney disease progression but often mandated by decision-makers **Solution:** Map (associate) more sensitive measures to generic measures in addition to collecting generic measures at appropriate times
5. Do not limit your analysis to QALYs; where possible report other events like kidney failure or kidney replacement modality that are relevant to kidney stakeholders	**Problem:** Economic evaluations may not interest all stakeholders, are complex and are difficult to validate **Solution:** Report numbers of other events like kidney failure, myocardial infarctions, admissions with heart failure, kidney transplants and flares of lupus. Compare these to other data to validate your evaluation
6. The cost of kidney care may vary by geography but the amount of care delivered may not	**Problem:** Relevant resource use may not exist for your country and healthcare cost varies by country **Solution:** Find rates of events and resources consumed for a similar geography and apply costs for these items from your own geography
7. If endpoints like kidney failure or mortality have not been observed in your study, consider changes in short-term endpoints and the strength, size and limitation of the relationships with these harder endpoints to estimate the long-term value of your intervention	**Problem:** Studies that capture kidney failure and mortality require large sample sizes and long follow-up durations, which make them expensive. **Solution:** Use recognised surrogate relationships like change in proteinuria or eGFR slope that have been estimated in your specific population of interest
8. Consider the competing risk of cardiovascular death when seeking value from preventing people requiring dialysis	**Problem:** Failure to account for cardiovascular death inflates the risk of kidney failure **Solution:** Use data that can, for a given CKD stage, estimate the risks of progression, death and other relevant events independently
9. Appreciate how decision-makers interpret cost-effectiveness considering the severity, rarity and cost of some (kidney) diseases	**Problem:** Dialysis, the healthcare for people with rare kidney diseases and the development of treatments for them are expensive **Solution:** Know and utilise relevant reimbursement definitions of rarity and disease severity that allow treatments to cost more
10. Carefully consider health inequalities and reporting outcomes in disadvantaged kidney populations	**Problem:** Kidney disease disproportionately effects disadvantaged populations and some interventions can widen disadvantages **Solution:** Capture data on disadvantaged populations, reflect them in your modelling and report them separately

outlined established processes that will maximise the credibility of an evaluation. Ultimately, credible evaluation serves to not only to inform better resource allocation but also to accelerate access to interventions that make a real difference in the lives of people living with CKD (Table 1).

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