The potential of kidney transplantation to reduce mortality from chronic kidney disease: a global, cross-sectional, modelling study

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Summary

Background Globally, the burden of chronic kidney disease and ensuing need for kidney replacement therapy (KRT)—dialysis or kidney transplantation—are increasing. Despite the mortality benefit of transplantation over dialysis, dialysis services are expanding more rapidly than access to transplantation. We aimed to cross-sectionally assess the association between country-level KRT rates and chronic kidney disease mortality to facilitate evidence-based prioritisation of KRT modalities.

Methods For all countries with publicly available data, we collected income level and gross domestic product per capita (GDP-PC) from the World Bank (data from 2022), age-standardised chronic kidney disease prevalence and mortality from the Global Burden of Diseases, Injuries, and Risk Factors Study (GBD; data from 2021), and dialysis prevalence and kidney transplantation incidence from the International Society of Nephrology–Global Kidney Health Atlas (ISN-GKHA) and Global Observatory on Donation and Transplantation (data from 2022). To account for varying chronic kidney disease prevalence among countries, we divided each of the latter three variables by the chronic kidney disease prevalence to obtain national dialysis rates, kidney transplantation rates, and the mortality–prevalence ratio, respectively. We modelled mortality–prevalence ratio as a multivariable function of GDP-PC and KRT rates. We used this model to estimate how increased kidney transplantation rates might affect chronic kidney disease mortality.

Findings Among 203 countries and territories with epidemiological data available from both the GBD and ISN-GKHA, median age-standardised chronic kidney disease prevalence was 7·78% (IQR 6·54–9·48%). Data availability was associated with income level (p<0·0001). Higher GDP-PC was associated with higher KRT rates (p<0·0001 for both dialysis and kidney transplantation) and lower mortality–prevalence ratio (p<0·0001). On multivariable analysis, decreases in mortality–prevalence ratio were independently associated with GDP-PC (coefficient –0·258; 95% CI –0·413 to –0·103; p=0·0031) and kidney transplantation rates (–574; –1090 to –43·5; p=0·039), but not dialysis rates (10·8; –29·5 to –6·27; p=0·22). Conservative increases in kidney transplantation rates could avert 290 000 chronic kidney disease deaths annually.

Interpretation We provide, to our knowledge, the first compilation of evidence that countries with higher kidney transplantation rates have lower mortality–prevalence ratio, regardless of GDP-PC; dialysis does not have a similar association. GDP-PC-based disparities in data availability, kidney transplantation rates, and mortality–prevalence ratio are expected to worsen with anticipated increases in prevalence of chronic kidney disease. To mitigate this risk, policy makers should leverage international guidelines and partnerships to increase access to safe and ethical transplantation.

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Introduction

From 1990 to 2021, chronic kidney disease rose from the 16th to the ninth leading cause of death worldwide.[1] For individuals who develop kidney failure (an estimated 14·5 million people in 2030), kidney replacement therapy (KRT)—dialysis or kidney transplantation—is the only life-sustaining treatment, but access to KRT is affected by large disparities both within and between countries.[2] Increasing risk factors for chronic kidney disease, particularly in low-income countries (LICs),[3,4] underscore the urgency of providing equitable access to KRT.

For most patients, kidney transplantation is the optimal form of KRT. Compared with dialysis, kidney transplantation improves survival and quality of life, and—in high-income and middle-income settings—is more cost-effective.[5] Globally, however, kidney transplantation accounts for only 22% of KRT, and

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Research in context

Evidence before this study

The global burden of kidney failure is increasing, and access to the only life-sustaining treatment, kidney replacement therapy (KRT)—dialysis or kidney transplantation—is marred by inequities across income levels. Data from middle-income countries and high-income countries indicate that kidney transplantation is more cost-effective and substantially improves survival and increases quality of life relative to dialysis. Nevertheless, globally, dialysis services are expanding while access to kidney transplantation is decreasing. Although this situation might reflect challenges in developing and maintaining kidney transplantation programmes, it also reveals an evidence gap regarding the effect of KRT rates on national mortality and disability from chronic kidney disease.

Between Oct 25, 2023, and Dec 6, 2024, we searched PubMed and Google Scholar for reports of multinational chronic kidney disease mortality rates using the search string "kidney AND (disease OR failure) AND (mortality OR death OR dialysis OR transplantation) AND (global OR country-level OR national OR population-level)" without restrictions on language or publication date. We found no peer-reviewed articles examining the relationship between country-level chronic kidney disease mortality and KRT rates. Existing studies use inconsistent metrics of clinical variables, including crude number of deaths and number of deaths per national population. We therefore aimed to assess the relationship between country-level KRT rates (number of people on maintenance dialysis and number of people undergoing kidney transplantation, as proportions of chronic kidney disease prevalence) and chronic kidney disease mortality (measured as the number of deaths from chronic kidney disease divided by chronic kidney disease prevalence) in countries of all income levels.

Added value of this study

To our knowledge, we provide the first evidence that—regardless of gross domestic product per capita—countries with greater proportions of patients with chronic kidney disease undergoing kidney transplantation have lower chronic kidney disease mortality; dialysis does not share this association. On multivariable modelling, we estimate that an annual 290 000 lives could be saved and 7 810 000 disability-adjusted life-years averted with conservative increases in kidney transplantation rates. Income-based inequities affect data availability, KRT rates, and chronic kidney disease mortality. Throughout our analysis, we use consistent metrics that facilitate international comparisons.

Implications of all the available evidence

The increasing global burden of chronic kidney disease and the concomitant income-based disparities in KRT rates underscore the importance of evidence-based policy for KRT expansion, especially in lower-income settings. The opportunity cost of increasing dialysis services without concomitant expansion of kidney transplantation services should prompt national policy makers and philanthropic donors to shift their focus towards transplantation, leveraging international partnerships and existing frameworks for ethics and safety. Researchers can further support policy makers with country-specific cost–utility analyses comparing kidney transplantation with dialysis.

kidney transplantation rates have been decreasing while dialysis rates continue to rise, a discrepancy that is largely driven by insufficient public funding for kidney transplantation.[6] This discrepancy shows a gap in the evidence to guide policy making: there are no published data quantifying the relative benefits of increasing kidney transplantation versus dialysis rates on a country level.[7–10]

We therefore aimed to identify the relationship between country-level KRT rates and chronic kidney disease mortality. For each country, we modelled the relationships among gross domestic product (GDP) per capita, KRT rates, and the burden of death and disability from chronic kidney disease. We hypothesised that higher GDP per capita would be positively associated with KRT rates and negatively associated with chronic kidney disease mortality and disability, and kidney transplantation rates would be negatively associated with chronic kidney disease mortality.

Methods

Study design

This cross-sectional study of global chronic kidney disease epidemiology and treatment is reported according to the STROBE guidelines (appendix p 2).[11] We (AZ-L) searched four global databases (accessed between November, 2023 and November, 2024), and assembled the most recent, publicly available, country-level data (appendix p 4).

See **Online** for appendix

First, we obtained data on chronic kidney disease prevalence, mortality, and disability from all countries included in the 2021 iteration of the Global Burden of Disease, Injuries, and Risk Factors Study (GBD; Jan 1 to Dec 31, 2021 data), an initiative of the Institute for Health Metrics and Evaluation (Seattle, WA, USA).[1] GBD combines a systematic review of published and unpublished data with modelling to derive country-level estimates of epidemiological and outcomes data for more than 300 diseases.[1,3] Although we acknowledge the limitations of modelling on the global scale, these estimates represent a synthesis of the best-available epidemiological data on chronic kidney disease.

Second, we obtained basic population and financial data on member countries of the International Monetary Fund from the World Bank Development Data Group (July 1, 2022, and Jan 1 to Dec 31, 2022 data, respectively).[12] Data are provided by members' statistical systems, with support as needed from the World Bank to maintain professional standards.

Third, to measure KRT access, we used the March, 2023, iteration of the International Society of Nephrology–Global Kidney Health Atlas (ISN–GKHA) to obtain country-level dialysis prevalence and kidney transplantation incidence (Jan 1 to Dec 31, 2022 data).[13] The ISN–GKHA combines literature review and key stakeholder surveys to evaluate assess to care across all countries and regions.[14]

Finally, we used the Global Observatory on Donation and Transplantation (GODT) to obtain kidney transplantation rates that were not available in the 2023 ISN–GKHA (Jan 1 to Dec 31, 2022 data). GODT, a joint effort between WHO and the Spanish Ministry of Health, distributes an annual questionnaire to the 194 WHO member states to collect data on organisational structure, legislation, and transplantation activity.[15]

As an analysis of publicly available, unidentifiable data, this study was exempt from ethical review requirements. No individual-level data were assessed. We use the term country to refer to countries and territories defined individually within the GBD. We make no claim regarding the legal status of any country or territory mentioned in this manuscript.

Definitions of epidemiological variables

We used age-standardised metrics of prevalence and mortality to account for varying age distributions among countries. In the GBD, chronic kidney disease is defined by estimated glomerular filtration rate, albumin–creatinine ratio, or both, and includes stages 1–5.[3] Age-standardisation uses a world population age standard derived from the non-weighted mean of the age-specific proportional distributions for countries with populations of more than 5 million. Disability weights are based on a multinational, survey-based study specifically performed for the GBD and validated across heterogeneous settings.[16]

We assessed chronic kidney disease mortality using the mortality–prevalence ratio (MPR, appendix pp 3–5). To create this variable, we divided each country's age-standardised number of deaths from chronic kidney disease by the age-standardised chronic kidney disease prevalence. We similarly computed chronic kidney disease-specific, age-standardised, disability-adjusted life-years (DALYs) to estimate the number of healthy years of life lost per person with chronic kidney disease (1 DALY represents 1 year of healthy life lost).

We used ISN–GKHA and GODT data to obtain dialysis prevalence and kidney transplantation incidence per million people. As with the mortality variable, we divided national dialysis prevalence and kidney transplantation incidence by age-standardised chronic kidney disease prevalence to compute the dialysis rate and kidney transplantation rate: the proportion of people with chronic kidney disease who were on dialysis and who underwent kidney transplantation, respectively (appendix p 4). We obtained kidney transplantation incidence from the GODT for four countries with missing kidney transplantation incidence data in ISN–GKHA (Afghanistan, Barbados, Jamaica, and Moldova).

Henceforth, in this Article, dialysis rate, kidney transplantation rate, MPR, and chronic kidney disease DALYs all refer to metrics computed as proportions of national chronic kidney disease prevalence, rather than of the total national population. Although existing literature reports these values as proportions of the national population, we reported them as proportions of national chronic kidney disease prevalence to assess the morbidity and treatment of chronic kidney disease in relation to the age-standardised burden of chronic kidney disease, which varies substantially by country (appendix pp 3, 7).

Eligibility criteria

We included all countries with chronic kidney disease prevalence and mortality data in the GBD. We excluded countries with more than 50% missing data to maximise the reliability of our multivariable models.

Statistical analysis

For the descriptive analysis, we grouped countries by World Bank income level—LICs, lower-middle-income countries (LMICs), upper-middle-income countries (UMICs), and high-income countries (HICs)—to facilitate baseline comparisons with published literature. We reported within-group and overall medians for each variable. We summarised data missingness as the percent of missing values, averaged across all variables examined. For inferential statistics, we used GDP per capita adjusted for purchasing power parity (GDP-PC) instead of income level to maximise model precision and avoid the bias introduced by categorising a continuous variable.

For hypothesis testing, we modelled prespecified clinical variables (KRT rates, MPR, and chronic kidney disease DALYs) as functions of log-transformed GDP-PC. Separately, we modelled MPR and DALYs as functions of GDP-PC and KRT rates. We ruled out collinearity among the predictors by examining both variance inflation factors (all <2) and a Pearson correlation matrix (all correlations <0·7). Given that KRT rates, MPR, and chronic kidney disease DALYs were defined as proportions of chronic kidney disease prevalence, we did not include prevalence as a covariate in the multivariable model. Because most published studies report these variables as proportions of the total national population, we performed a sensitivity analysis, replacing chronic kidney disease prevalence with national population as the denominator.

Given the positively skewed distribution of the principal outcome variables (MPR and chronic kidney disease DALYs), we used generalised linear models (GLMs) with a gamma distribution and a log-link function for regression analyses. Due to its exponential relationship with both outcomes, we log-transformed the GDP-PC variable for

	Overall (n=203)	Low-income countries (n=29)	Lower-middle-income countries (n=54)	Upper-middle-income countries (n=53)	High-income countries (n=67)
Gross domestic product per capita	$15 900 (5880–41 000)	$1990 (1670–2670)	$6410 (4410–10 200)	$17 800 (14 300–23 000)	$52 500 (41 700–68 800)
Age-standardised chronic kidney disease prevalence	7·78% (6·54–9·48)	7·33% (6·02–7·76)	9·19% (7·96–9·91)	9·08% (7·16–9·88)	6·95% (6·22–8·74)
Dialysis rate	0·508% (0·124–0·954)	0·007% (0·004–0·027)	0·056% (0·017–0·317)	0·494% (0·207–0·893)	0·882% (0·574–1·361)
Kidney transplantation rate	0·013% (0·003–0·035)	0·003% (0·003–0·007)	0·002% (0·001–0·006)	0·007% (0·003–0·012)	0·039% (0·020–0·061)
Mortality–prevalence ratio	0·346% (0·183–0·551)	0·571% (0·463–0·635)	0·392% (0·239–0·568)	0·319% (0·226–0·549)	0·200% (0·143–0·349)
Chronic kidney disease disability-adjusted life-years	8·07 (4·74–14·2)	14·10 (11·71–15·69)	10·64 (6·91–14·44)	8·01 (6·29–14·42)	4·63 (3·53–7·85)
Data missingness*	9·50%	18·81%	11·83%	8·84%	5·97%

Data are median (IQR) unless otherwise stated. Gross domestic product per capital in 2022, in US$, adjusted for purchasing power parity. *For each variable included in the study, we identified the percentage of countries with missing data, then computed the mean of those percentages across all variables to obtain a summary estimate of missingness.

Table 1: **Chronic kidney disease burden and kidney replacement therapy rates by income level**

	Coefficient (95% CI)	p value
Dialysis rate	1·077 (0·884 to 1·265)	<0·0001
Kidney transplantation rate	0·934 (0·741 to 1·116)	<0·0001
Mortality–prevalence ratio	−0·252 (−0·319 to −0·185)	<0·0001
Chronic kidney disease DALYs	−0·274 (−0·338 to −0·210)	<0·0001

DALYs=disability-adjusted life-years.

Table 2: **Univariable modelling of relationships between log-transformed gross domestic product per capita, adjusted for purchasing power parity, and clinical variables**

analysis. The other two predictor variables (dialysis and kidney transplantation rates) did not have an unambiguously linear relationship with the outcomes (appendix p 6). We therefore compared three multivariable models using linear, spline, and log-transformed terms for dialysis and kidney transplantation rates to identify the optimal fit. Model performance was similar on the basis of the Akaike information criterion, deviance explained, and predictive error on ten-fold cross-validation (appendix p 6). Because linear terms maximise model interpretability, we used the simpler GLM with log-transformed GDP per capita and untransformed dialysis and kidney transplantation rates in the multivariable analysis. We set the threshold of statistical significance at $\alpha=0 \cdot 05$ and only performed complete case analyses. All analyses were performed using R (version 4.3.1); the source code is publicly accessible and available upon request.

Mediation testing and estimation of avertable deaths and DALYs

We used the aforementioned GLM framework to formally test whether KRT rates could mediate the perceived effect of GDP-PC on MPR.

On the basis of the negative observed association between MPR and kidney transplantation rate, we used predictive modelling to estimate deaths and DALYs that could be averted by increasing national kidney transplantation rates (appendix p 9). We generated two counterfactual scenarios: a conservative scenario in which countries match the highest kidney transplantation rate within their income level, and an optimistic scenario in which countries match the highest kidney transplantation rate overall. This approach is similar to previous studies modelling the potential lives saved by increasing access to surgical care.[17,18] In both scenarios, to maintain consistent KRT rates, we mirrored each unit increase in national kidney transplantation rate with a unit decrease in that country's dialysis rate.

We then used these counterfactual KRT rates in our multivariable model to estimate avertable deaths and DALYs for each country, calculating the difference between: (A) the deaths and DALYs modelled based on observed KRT rates, and (B) the deaths and DALYs modelled on the basis of counterfactual KRT rates. We reported potential reductions in deaths and DALYs (in absolute terms) for both the conservative and optimistic scenarios.

Role of the funding source

There was no funding source for this study.

Results

After excluding eight countries or territories with >50% missing data (British Virgin Islands, Cayman Islands, Hong Kong, Kosovo, Liechtenstein, Macao, New Caledonia, and Turks and Caicos Islands), 203 countries or territories (appendix p 4) were included in the analysis: 29 (14·3%) LICs, 54 (26·6%) LMICs, 53 (26·1%) UMICs, and 67 (33·0%) HICs (table 1). In 2021, the most recent year of reporting for epidemiological data, the median global age-standardised chronic kidney disease prevalence was 7·78% (IQR 6·54–9·48%), with an MPR of 0·346%

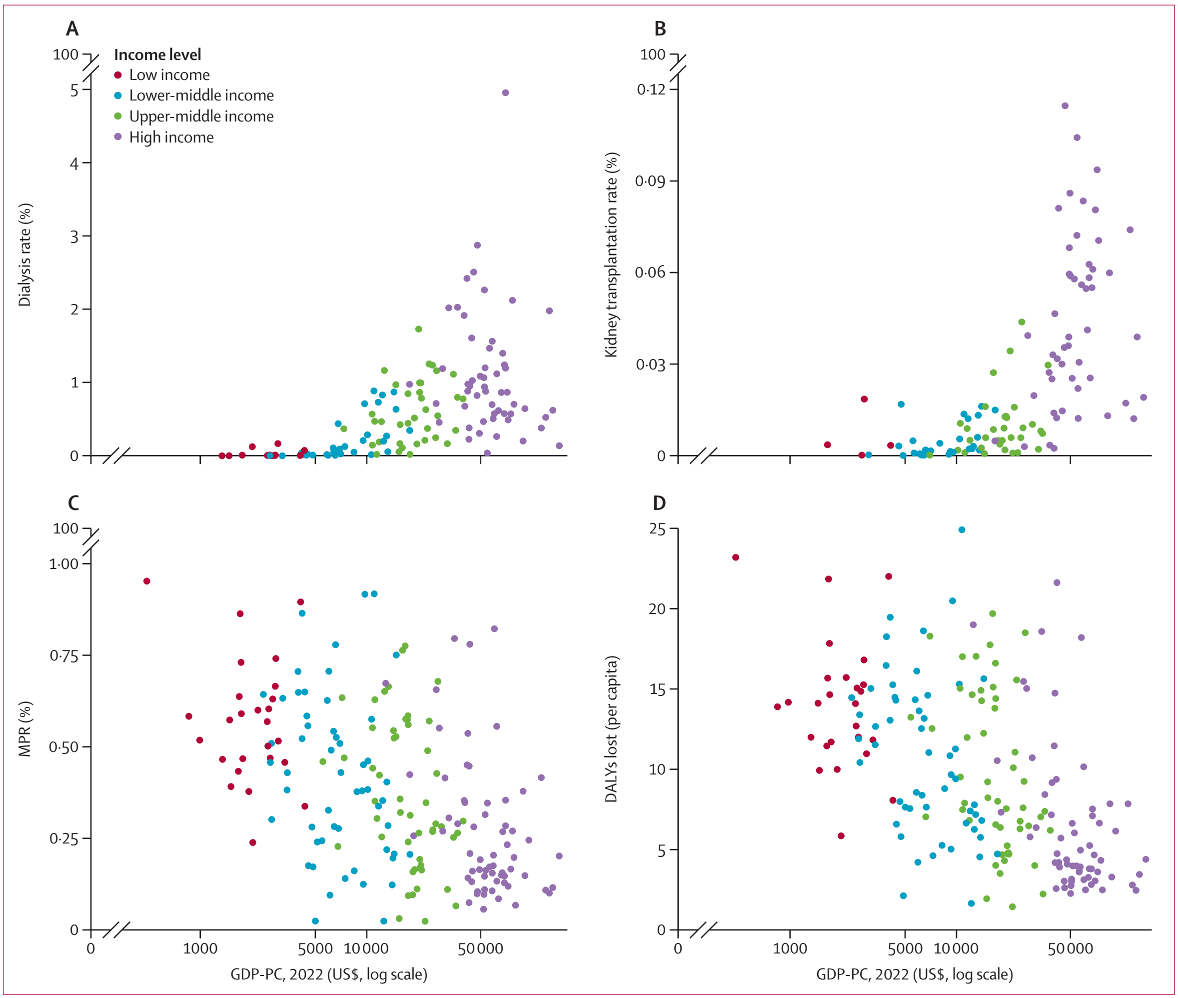

***Figure 1:* Relationship between log-transformed GDP-PC and dialysis rate (A), kidney transplantation rate (B), mortality–prevalence ratio (C), and chronic kidney disease disability-adjusted life-years (D)**

GDP-PC in 2022, in US$, adjusted for purchasing power parity. GDP-PC=gross domestic product per capita. MPR=mortality–prevalence ratio.

(0·183–0·551%). In 2023, the most recent year of reporting for KRT data, 0·508% (0·124–0·954%) of people with chronic kidney disease were on dialysis and 0·013% (0·003–0·035%) underwent kidney transplantation. Each unit increase in income level was associated with a decrease in missingness of 8·69% (95% CI –11·8% to –5·61%; p<0·0001; appendix p 6).

We performed univariable generalised linear modelling of each epidemiological variable as a function of log-transformed GDP-PC (table 2). Each 1% increase in GDP-PC was associated with a 1·077% (95% CI 0·884–1·265) increase in dialysis rates and a 0·934% (0·741–1·116) increase in kidney transplantation rates, and a decrease of 0·252% (0·185–0·319) in MPR and 0·274% (0·210–0·338) in DALYs (all p<0·0001). The associations between GDP-PC and KRT rates, DALYs, and MPR are shown graphically in figure 1.

We used univariable modelling to test for associations between MPR and prespecified country-level predictors: GDP-PC, dialysis rate, and kidney transplantation rate. MPR and chronic kidney disease DALYs were negatively associated with all three predictors (all p≤0·0044, table 3).

In a multivariable model with log-transformed GDP-PC, dialysis rate, and kidney transplantation rate as predictors (table 3), dialysis rate was no longer significantly associated with MPR (p=0·22) or DALYs (p=0·16). By contrast, the kidney transplantation rate remained negatively associated with both MPR and DALYs (table 3). In other words, an increase in kidney transplantation rate by 0·013% (the current global median) was associated with an adjusted MPR decrease of 1–exp(–574×0·013%) or 7·19%, and an adjusted DALY decrease of 1–exp(–1090×0·013%) or 13·2%. These findings were consistent in a sensitivity analysis in which MPR and KRT rates were measured per national population rather than per number of people with chronic kidney disease (appendix p 7).

	Outcome: mortality–prevalence ratio		Outcome: chronic kidney disease disability-adjusted life-years	
	Coefficient (95% CI)	p value	Coefficient (95% CI)	p value
Univariable analysis				
GDP-PC	−0·252 (−0·319 to −0·185)	<0·0001	−0·274 (−0·338 to −0·210)	<0·0001
Dialysis rate	−20·54 (−32·23 to −7·77)	0·0044	−21·30 (−32·53 to −9·07)	0·0023
Kidney transplantation rate	−947 (−1330 to −537)	<0·0001	−1090 (−1430 to −728)	<0·0001
Multivariable analysis				
GDP-PC	−0·258 (−0·413 to −0·103)	0·0031	−0·276 (−0·419 to −0·133)	0·0004
Dialysis rate	10·76 (−6·27 to 29·51)	0·22	10·88 (−4·37 to 27·53)	0·16
Kidney transplantation rate	−574 (−1090 to −43·5)	0·039	−662 (−1120 to −190)	0·0079

GDP-PC in 2022, in US$, log-transformed, adjusted for purchasing power parity. Dialysis rate is annual prevalence of dialysis divided by prevalence of chronic kidney disease, and kidney transplantation rate is annual incidence of kidney transplantation divided by prevalence of chronic kidney disease. GDP-PC=gross domestic product per capita.

Table 3: **Univariable and multivariable generalised linear models of mortality–prevalence ratio and chronic kidney disease disability-adjusted life-years, with log-transformed GDP-PC and country-level clinical variables as predictors**

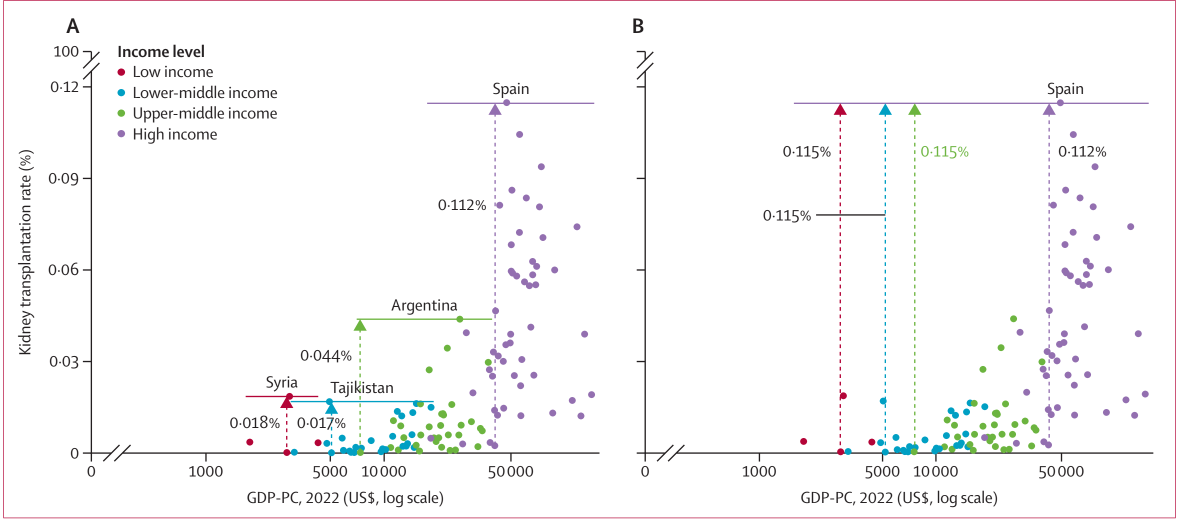

Figure 2: **Counterfactual scenarios depicting conservative and optimistic increases in national kidney transplantation rates**
Symbolic representation of counterfactual scenarios: conservative (A) and optimistic (B) increases in national kidney transplantation rates. (A) Each country increases its kidney transplantation rate to match the highest rate in its income level (low-income countries to match Syria, lower-middle-income countries to match Tajikistan, upper-middle-income countries to match Argentina, and high-income countries to match Spain). (B) Each country increases its kidney transplantation rate to match the highest rate overall (observed in Spain). GDP-PC in 2022, in US$, adjusted for purchasing power parity. GDP-PC=gross domestic product per capita.

Mediation testing showed a significant (p=0·036) but small indirect effect of GDP-PC on MPR via the kidney transplantation rate, which accounted for 0·005% of the total effect. The direct effect of GDP on MPR remained significant. By contrast, dialysis rate did not mediate this relationship (p=0·81).

Given the robust negative association between kidney transplantation rate and both MPR and DALYs, we performed a modelling analysis to quantify the potential benefit of increases in kidney transplantation rates (figure 2). For the conservative counterfactual scenario, we modelled the expected change in mortality and DALYs if each country were to increase its kidney transplantation rate to match the highest rate within its income level. In order of increasing income levels, the highest kidney transplantation rates were seen in Syria, Tajikistan, Argentina, and Spain (figure 2A). For the optimistic counterfactual scenario, we modelled the effect of all countries performing kidney transplantation at the highest rate worldwide, which was seen in Spain (figure 2B). Our predictive model, ranging from conservative to optimistic, estimated that shifting resources from dialysis to kidney transplantation could avert 290 000–1 020 000 deaths and 7 810 000–27 200 000 DALYs annually (appendix p 8).

Discussion

This cross-sectional analysis of 2021 and 2022 data on chronic kidney disease from 203 countries provides three key findings. First, GDP-PC is associated with national KRT rates, MPR, and data availability. Second, independent of GDP-PC, countries with higher kidney transplantation rates have lower MPR and DALYs, but higher dialysis rates are not associated with the same benefit. Third, conservative increases in kidney transplantation rates could save hundreds of thousands of lives and avert millions of DALYs each year.

Two concerning observations reveal an urgent need for the global health community to prioritise kidney care, particularly in lower-income settings. First, we show that countries with higher GDP-PC have lower chronic kidney disease MPR, regardless of access to treatment. This relationship reflects the dependence of kidney care on broad, GDP-related social and health-care system factors, including distance to nearest hospital, national clinician density, and access to reliable diagnostic tools and essential medications.[19] The WHO framework for health system strengthening offers development strategies for these factors.[20] Second, the global disease burden is shifting towards non-communicable diseases,[1] in part due to global investments in infectious disease prevention and treatment.[1] Looking ahead, an ageing global population and increasing prevalence of climate-related and diet-related risk factors for chronic kidney disease, particularly in LICs and LMICs, portend a growing chronic kidney disease burden and potentially a doubling of KRT use between 2015 and 2030.[3,21] The need will be greatest in lower-income settings, in which already strained health-care systems have little resilience to these rapidly changing factors.[22]

Despite this grim outlook, our principal finding indicates that, regardless of GDP, countries with better kidney transplantation access have lower MPR, a pattern not observed with access to dialysis. This finding does not demonstrate causality, but it provides an important addition of population-level evidence to what is well known at the individual level. For an individual patient with kidney failure, dialysis prolongs survival, and kidney transplantation further improves both survival and quality of life.[5] To our knowledge, however, the KRT access–mortality relationship has not been examined on a national level. If this observed relationship is causal, our models estimate that feasible increases in kidney transplantation access could avert more than 290 000 deaths due to chronic kidney disease annually. Although we adjust for GDP-PC (a proxy for overall financial resources) and dialysis rates (a proxy for national commitment to kidney care), our model did not explicitly account for ancillary medical services (eg, pathology and immunology) and infrastructure—prerequisites for kidney disease programmes that could confound the kidney transplantation rate–mortality relationship. Importantly, these prerequisites also represent the potential of kidney transplantation programmes to catalyse multidisciplinary health system improvements that extend beyond chronic kidney disease. For countries seeking to expand KRT access, establishing dialysis centres could require fewer upfront investments, but the opportunity costs measured in both mortality and positive externalities make it a worse long-term investment.

Although we have not seen previous reports of the relationship between national KRT rates and MPR, analogous modelling strategies have guided policy making for other major diseases. For example, AIDS and tuberculosis researchers modelled disease-specific mortality as a function of antiretroviral and anti-tuberculosis medication availability.[23,24] Like these earlier studies, we measured treatment and mortality rates relative to disease burden (in this case, age-standardised chronic kidney disease prevalence), not relative to the national population. This approach allowed us to account for varying age distributions and chronic kidney disease prevalence, which ranges from 4·8% to 12·1% among the 203 countries.

Our findings contribute crucial evidence to the global call on policy makers to expand kidney transplantation access. Beginning in 2010 with the *WHO guiding principles on human cell, tissue and organ transplantation*,[25] the international transplant community has published multiple documents to guide the safe, ethical, and equitable expansion of kidney transplantation services. These documents include a consensus statement defining kidney transplantation as part of universal health coverage for chronic kidney disease[26] and a framework for governments to develop comprehensive care for kidney failure.[7] To date, these documents have not resulted in sufficient change: globally, dialysis remains the dominant mode of KRT, and access to dialysis is increasing while kidney transplantation access is decreasing, with grave inequities within and among countries.[2,6] South Africa provides a stark example, in which public sector rationing of maintenance dialysis restricts the service to patients who would be fit for transplant; as a result, 39·8% of all patients with kidney failure in the country have undergone kidney transplantation. In contrast, in South Africa's private sector, which has ten-times higher health expenditure per capita, this proportion is only 11·3%.[27] We acknowledge that the need for dialysis typically exceeds the need for kidney transplantation; not all patients with kidney failure are eligible for kidney transplantation, and some patients with acute kidney failure regain kidney function after temporary support on dialysis. We also acknowledge that kidney transplantation programme development can be challenging due to infrastructural limitations, workforce shortages, and high startup costs (eg, from establishing immunology services and supplying immunosuppressive medications).[19] But patients on dialysis can have catastrophic health expenditures,[20] and, as we show, national dialysis availability might not translate to reductions in MPR. Conversely, kidney transplantation expansion could allow countries to reduce death and disability from chronic kidney disease and yield positive externalities that transcend disease states. We believe these benefits will, in most cases, outweigh the costs of programme setup and maintenance.

Translating this evidence into implementation requires several important considerations. First, kidney transplantation expansion should be grounded in ethics and equity. For example, strict legislation and enforcement mechanisms are prerequisite guardrails for safe declaration of death in deceased donation and protection against coercion in living donation. These protections are particularly important for economically disadvantaged and socially vulnerable populations.[28] Second, across the income level spectrum, we acknowledge that countries have varying public health priorities and costs of human resources and medications. One way to compare kidney transplantation against competing public health interests is through cost–utility analyses, which, to date, have only been done in middle-income and high-income settings.[5] To further assist policy makers in adequately prioritising KRT for their context, future work should include country-specific cost–utility analyses of kidney transplantation and dialysis, including the option of pre-emptive kidney transplantation. Third, even countries that consider kidney transplantation expansion a priority might lack the necessary supporting infrastructure. They could leverage international partnerships to provide clinical training,[8] increase medication availability,[29] and develop and maintain health information systems.[30] In our own data, the correlation between income level and data availability underscores the need for chronic kidney disease health information systems in lower-income settings. Fewer than 18% of LICs have KRT registries,[30] which are essential for monitoring disease burden, measuring effectiveness of interventions, and allocating resources. We commend efforts by the African Association of Nephrology and the International Society of Nephrology to bridge this gap through international partnerships, but progress is challenged by onerous maintenance costs. International kidney registries could be a prime target for philanthropic seed funding: not only would the impact extend across borders, but an expected 7:1 return on investment (from reduced dialysis and transplant complications) could allow participating countries to achieve independent sustainability.[29]

The main limitations of this study stem from the nature of global databases. First, chronic kidney disease is largely asymptomatic and underdiagnosed, requiring modelling to estimate disease prevalence and mortality in data-poor settings; the GBD has previously explained these limitations.[3] By measuring key epidemiological variables (ie, national KRT rates and mortality) as a proportion of chronic kidney disease prevalence, we improve upon the current metrics, which report KRT and mortality rates as a proportion of the national population without accounting for variations in prevalence. However, we still fall short of the ideal metric, which would use the incidence of kidney failure as the denominator; unfortunately this metric is currently unavailable outside of high-resource settings (due to underdiagnosis and undertreatment, and lack of registries or registry maintenance in some countries) and therefore too limiting for a global study such as this one. Future work should examine the robustness of the chronic kidney disease epidemiology estimates and facilitate access to data disaggregated by chronic kidney disease stage. Second, variables such as KRT rates are directly reported to the ISN–GKHA and not represented within the GBD; they are not modelled, resulting in higher missingness. We did not impute these values because missingness was not random. Given that missingness was inversely correlated with income level, and assuming that countries with missing kidney transplantation incidence perform fewer kidney transplantations than their peers, our results are biased toward the null. Our research group is actively working to address these gaps in global data. Third, our data sources do not include subnational-level data, such as KRT quality metrics (frequency of dialysis sessions), centre-level kidney transplantation rates, or median patient age at transplantation, all of which could affect the KRT rate–mortality relationship and increase susceptibility to ecological fallacy. We suspect that these variations are likely collinear with GDP-PC, which was included in our models, and that their potential effect on our results is small. Finally, our model did not include morbidity or mortality from diseases precipitated by chronic kidney disease, or from kidney donation by living donors. Given that the former almost certainly outweighs the latter (chronic kidney disease contributed to 1·4 million cardiovascular disease-related deaths in 2017[3]), on balance, we expect that our results are biased towards the null.

We present, to our knowledge, the first compilation of evidence of global estimates of the potential mortality benefit of increasing kidney transplantation rates in countries across the GDP spectrum. The current global trend of dialysis programme expansion without concomitant increases in kidney transplantation access is an inappropriate use of resources. Income-based disparities in data availability, KRT rates, and chronic kidney disease mortality are concerning given anticipated increases in the need for KRT, particularly among LICs and LMICs. We used robust, consistent metrics to facilitate international comparisons and provide easily interpretable data that could be useful to policy makers. Future work should focus on increasing the availability and quality of primary data, defining barriers and facilitators to transplantation programme development, and longitudinal studies to estimate the mortality benefits and cost–utility of transplantation and dialysis in low-income settings. Together, these data can provide policy makers with the necessary evidence to appropriately direct resources towards the growing disease burden of chronic kidney disease.

Contributors

AZ-L was involved in study conceptualisation, data curation, formal data analysis, investigation (data collection), design of methodology, project administration, provision of statistical analysis resources and software, validation of reproducibility of the results, visualisation in tables and figures, and writing of the initial draft and revised manuscript. ST and AG were involved in design of methodology, validation of reproducibility of the results, and writing of the initial draft and revised manuscript. IGO and AKB were involved in validation of reproducibility of the results, supervision, and writing. MTS, FAM, FA, PB, VO, DT, EM, SS, PS, NA, and JWS were involved in validation of reproducibility of the results, supervision, and writing of the initial draft and revised manuscript. SMB was involved in study conceptualisation, design of methodology, supervision, and writing of the initial draft and revised manuscript. TJH was involved in formal data analysis, validation of reproducibility of the results, and writing of the initial draft and revised manuscript. JR was involved in study conceptualisation, formal data analysis, design of methodology, supervision, validation of reproducibility of the results, visualisation in tables and figures, and writing of the initial draft and revised manuscript. AZ-L, TJH, and JR accessed and verified the underlying data. All authors had access to the data, approved the final version of the manuscript, and accept responsibility for the decision to submit for publication.

Declaration of interests

AKB reports grants from the Canadian Institute of Health Research and the Heart and Stroke Foundation of Canada; honoraria and/or consultancy fees from Amgen, Bayer, GlaxoSmithKline, and Otsuka; and is Co-chair of the International Society of Nephrology–Global Kidney Health Atlas and an Associate Editor of the *Canadian Journal of Kidney Health and Disease*. EM is a Principal Investigator on a US National Institutes of Health grant (U01AI152153); reports honoraria and travel funding from Astellas for educational work in India; and serves on the board of directors for US Enterprises of University of Stellenbosch. JWS is Principal Investigator on a US Health Resources and Services Administration grant (K08-HS028672) and a Co-principal Investigator on a US National Institutes of Health grant (R01-DK137466). PS participates on the advisory board of Minutia (a company developing strategies for monitoring viability of cell-based therapies for diabetes). All other authors declare no competing interests.

Data sharing

The data used in this study (country-level population, gross domestic product per capita, World Bank income level, chronic kidney disease prevalence, kidney replacement therapy rates, chronic kidney disease disability-adjusted life-years, and chronic kidney disease mortality) are publicly available on the websites of the institutions that manage them: the World Bank, the Institute for Health Metrics and Evaluation, the International Society of Nephrology, and the Global Observatory on Donation and Transplantation. The code used for statistical analysis is publicly available at https://github.com/azambeli/CKD_Global_Burden/. No individual-level data were used in this study.

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