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Dialysis Outcomes Across Countries and Regions: A Global Perspective From the International Society of Nephrology Global Kidney Health Atlas Study

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Introduction: Kidney failure treated with hemodialysis (HD), or peritoneal dialysis (PD) is a major global health problem that is associated with increased risks of death and hospitalization. This study aimed to compare the incidence and causes of death and hospitalization during the first year of HD or PD among countries.

Methods: The third iteration of the International Society of Nephrology Global Kidney Health Atlas (ISN-GKHA) was conducted between June and September 2022. For this analysis, data were obtained from the cross-sectional survey of key stakeholders from ISN-affiliated countries.

Results: A total of 167 countries participated in the survey (response rate 87.4%). In 48% and 58% of countries, 1% to 10% of people treated with HD and PD died within the first year, respectively, with cardiovascular disease being the main cause. Access-related infections or treatment withdrawal owing to cost were important causes of death in low-income countries (LICs). In most countries, <30% and <20% of patients with HD and PD, respectively, required hospitalization during the first year. A greater proportion of patients with HD and PD in LICs were hospitalized in the first year than those in high-income countries (HICs). Access-related infection and cardiovascular disease were the commonest causes of hospitalization among patients with HD, whereas PD-related infection was the commonest cause in patients with PD.

Conclusion: There is significant heterogeneity in the incidence and causes of death and hospitalization in patients with kidney failure treated with dialysis. These findings highlight opportunities to improve care, especially in LICs where infectious and social factors are strong contributors to adverse outcomes.

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/ idney failure is a major global health problem and significant contributor to morbidity, mortality, and health care cost.¹ The global median prevalence of kidney failure treated with maintenance HD or PD continues to rise, and most recent estimates put it at 823 per million population.² This figure reflects both the increasing incidence of kidney failure worldwide as well as gradual improvements in patient survival on HD and PD.^{3,4} The rising prevalence of kidney failure treated with dialysis places significant strain on health services and health systems. On average, costs of treatment for kidney failure with maintenance HD and PD were US \$19,380 and US \$18,959 per person per year, respectively.² In addition, patients treated with dialysis have high rates of hospital admission and readmission, which further increases cost and resource burden and is associated with an increased risk of death.5,6

Death and hospitalization among patients with kidney failure treated with dialysis represent important metrics of the quality and effectiveness of care. Quantifying the incidence and causes of such events allows benchmarking within and between countries and enables the identification of any unexpected or unwarranted variations in care.^{7,8} Moreover, such data could be used to facilitate the optimal and equitable allocation of resources to address specific deficiencies. Although many published studies have reported the incidence of death in patients with kidney failure treated with dialysis, almost all cohorts originate from HIC, especially those in North America, and few report the incidence and causes of hospitalization.^{3-5,9} In particular, the dialysis outcomes practice patterns study has made significant progress in this area, although its findings are limited by a paucity of data from LICs and small overall scope (only 14 countries for HD and 7 countries for PD).^{10,11} Extrapolation of existing data to other regions of the world and income groups is prohibited by obvious differences in healthcare systems and policies. Therefore, we used data from the 2023 iteration of the ISN-GKHA to evaluate the burden and causes of first-year deaths and hospitalizations in patients with kidney failure treated with dialysis.

METHODS

The third iteration of the ISN-GKHA was a multinational cross-sectional survey conducted and administered electronically to representatives of 191 countries with ISN affiliate societies between 1 July and 30 September 2022. Countries were categorized by World Bank income group classification and the 10 ISN regions (Africa, Eastern and Central Europe, Latin America, the Middle East, North America and the Caribbean, North and East Asia, Oceania and Southeast Asia, Newly Independent States and Russia, South Asia, and Western Europe).

A comprehensive description of the sampling approach, survey development, data handling, and statistical analysis for the ISN-GKHA has been described elsewhere.¹² Although the overall methodology of the ISN-GKHA involved a literature review and survey components, only survey data were used in this study. In short, a multinational cross-sectional survey of key opinion leaders from each country was carried out to collect details on national kidney care practices. Key opinion leaders included nephrologists, leaders of consumer representative organizations, and policymakers. Further assistance from international collaborators, ISN leaders, regional board members, and key project leaders was also sought to review the consistency of regional data. The survey was available in English, French, and Spanish and was distributed to key stakeholders in countries via an online platform, REDCap (www.project-redcap.org). The survey is presented in Supplementary Appendix S1. The project was approved by the University of Alberta research ethics committee (protocol number: PRO00063121).

The survey was designed in modules that corresponded to each of the 6 building blocks of health systems toward universal health coverage. One module included data on the outcomes of people receiving dialysis, including hospitalization and death. These data were collected for the first time in this iteration of the GKHA. Questions covered an estimate of the proportion of patients who died in the first year of dialysis and the causes of death, categorized as cardiovascular disease (ischemic heart disease, arrhythmia, cerebrovascular disease), access-related infection (infected arteriovenous fistula/graft, catheter-related bacteremia, PD-related peritonitis, exit site or tunnel tract infection), other infection, malignancy, dialysis withdrawal for social reasons, dialysis withdrawal for financial reasons, other and unknown. Estimates of the proportion of people who died within the first year of PD or were hospitalized within the first year of HD or PD were categorized as "0%," "1 to 10%," "11 to 25%,"

CLINICAL RESEARCH -

"26 to 50%," and ">50%." Estimates of the proportion of people who died within the first year of HD were categorized as "0%," "1 to 10%," "11 to 50%," "51 to 75%," and ">75%." Questions also covered the proportion of patients who were hospitalized in the first year of dialysis and the cause of hospitalization. Cause of hospitalization was categorized as cardiovascular disease (ischemic heart disease, arrhythmia, cerebrovascular disease), access malfunction (arteriovenous fistula/graft malfunction, blocked central venous catheter, blocked PD catheter, PD catheter tip migration), access-related infection, other infection, or other cause.

Data quality was ensured through extensive consultation with ISN regional leaders. Any ambiguities were clarified with the regional board, and any remaining inconsistencies were systematically addressed with key stakeholders. Additional data validation was performed at the national and regional levels by triangulating the findings with published literature and grey literature. The data collected were presented as frequency (percentage) or median (interquartile range), as appropriate.

RESULTS

A total of 167 of 191 countries (87.4%) participated in the survey, comprising 97.4% of the world's population. Responses to the dialysis outcomes domain of the survey were received from 159 of the 162 countries in which HD was available (98.1%) and from 128 of the 130 countries (98.5%) in which PD was available. Complete details on the population coverage and response rate of the survey have been previously published.² The affiliations of survey respondents were nephrologists (81%), non-nephrologist physicians (5%), non-physician health care professionals (2%), administrators/policymakers (4%), and others affiliated with advocacy groups for people living with kidney disease (5%).

Death in the First Year of HD

Overall, 77 countries (48%) reported that 1% to 10% of people treated with HD died in the first year of dialysis, whereas 50 countries (31%) reported that 11% to 50% died within the first year of initiating HD (Figure 1a; Supplementary Figures S1 and S2). Only 3 countries (Gabon, Morocco, and Luxembourg) reported that 0% of patients died in the first year of HD. First-year mortality rates exceeding 50% were reported by 6 African countries: 4 countries (Cameroon, Republic of Congo, Madagascar, and Mali) and 2 countries (Burkina Faso and Nigeria) reported that 51% and 75% and >75% of people on HD died within the first year of initiation, respectively. Of note, the proportion of first-year mortality was unknown in 23 countries (14%).

There was a first-year mortality gradient across LICs, lower-middle income countries (LMICs), upper-middle countries and HICs (Figure 1a).

Cause of Death in the First Year of HD

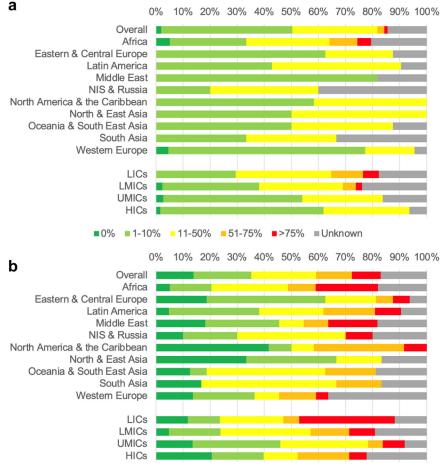
The commonest cause of death among people treated with HD was reported as cardiovascular disease by 123 countries (77%) overall, ranging from 33% of African countries to 100% of Eastern & Central Europe, North & East Asian, and South Asian countries (Figure 2a). Overall, access-related infections were the second most frequently reported causes of death (17 countries; 11%), especially in Africa (11 countries, 28%). Infection from other sources was the most common cause of death in only 1 country (Mauritania), whereas dialysis withdrawal due to cost of care was the commonest cause of death in 5 African countries (Republic of Congo, Madagascar, Nigeria, Togo, Uganda) and 1 Latin American country (Haiti), all of which are LICs or LMICs. The most common cause of death was unknown in 11 countries (7%), of which 8 countries were in Africa. A descending gradient across ascending income levels was seen in terms of access-related infections.

Hospitalization in the First Year of HD

The median proportion of people treated with HD requiring at least 1 hospitalization in the first year of dialysis was 21% and 30% overall. Only 17 countries (11%) reported >50% of first-year hospitalization, of which 9 were in Africa (Figure 1b; Supplementary Figures S3 and S4). Higher first-year hospitalization proportions were seen with lower income levels (Figure 1b). Access-related infections (infected arteriovenous fistula/graft, central venous catheter-related bacteremia) and cardiovascular disease represented the 2 commonest causes of first-year hospitalization in patients with HD as reported by 51 (32%) and 48 countries (30%), respectively (Figure 2b). Access malfunction (malfunction of arteriovenous fistula /graft, blocked central venous catheter) was reported as the most common cause of hospitalization by an additional 28 countries (18%). Infections were the commonest cause of hospitalization in 76% of LICs (access-related infections: 10 countries; infections from other sources: 3 countries), whereas cardiovascular diseases represented the most common cause of hospitalization in 43% of HICs (Figure 2b).

Death in the First Year of PD

In people treated with PD, the proportion who died within the first year on dialysis was between 1% and 10% in 74 countries (58%), 11% and 20% in 18 countries (14%), and 21% and 30% in 5 countries (4%). No country reported >30% first-year mortality



■ 1-10% ■ 11-20% = 21-30% = 31-50% ■ >50% ■ Unknown

Figure 1. Proportion (national average) of patients with kidney failure on hemodialysis who (a) died or (b) required at least one hospitalization, in the first year of dialysis. HICs, high income countries; LICs, low-income countries; LMICs, lower-middle income countries; NIS, Newly Independent States; UMICs, upper-middle income countries. Data are presented as proportions (in percentages) of countries per region or income category.

on PD, but the proportion of patients who died was unknown in 31 countries (24%). An ascending gradient rin mortality was noted across descending income levels in patients on PD (Figure 3a; Supplementary Figures S5 and S6).

Cause of Death in the First Year of PD

The commonest cause of death among people treated with PD was cardiovascular disease in 85 countries (66%) and PD-related infections (i.e., PD-related peritonitis, exit-site, or tunnel tract infection) in 19 countries (15%) (Figure 4a). Dialysis withdrawal due to cost of care was the most common cause of death in 3 African countries (Republic of Congo, Democratic Republic of Congo, Nigeria), and withdrawal due to social reasons in 1 country from the Middle East (Syria). PD withdrawal due to cost or social reasons was reported as the most common cause of mortality in LICs only (Figure 4a).

Hospitalization in the First Year of PD

The proportion of people treated with PD requiring at least 1 hospitalization in the first year of dialysis was

Kidney International Reports (2024) 9, 2410-2419

1% and 10% in 30 countries (23%), 11% and 20% in countries (30%), 21% and 30% 39 in 15 countries (12%), and unknown in 34 countries (27%). Again, a strong gradient of hospitalization was seen across income levels (Figure 3b; Supplementary Figures S7 and S8). The commonest causes of first-year hospitalization were PD-related infections, cardiovascular diseases, access malfunction (PD catheter block, catheter tip migration) and unknown in 65 (51%), 27 (21%), 17 (13%), and 14 countries (11%), respectively (Figure 4b). Similar to the findings for people treated with HD, PD-related infections were the most common causes of hospitalization in 75% of LICs; in contrast, cardiovascular diseases and PD-related infections were the commonest causes in 30% and 39% of HICs, respectively (Figure 4b).

DISCUSSION

Fewer than 10% of people treated with HD and PD died within the first year in most countries. Only countries in Africa reported that >50% or >75% of



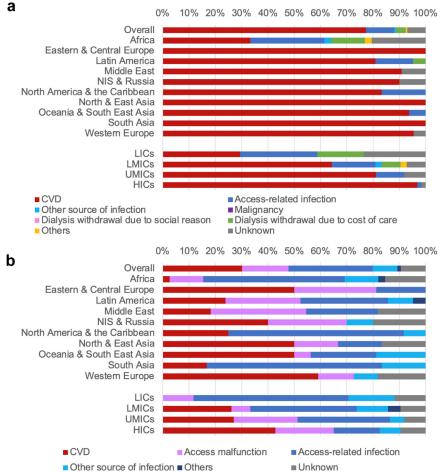


Figure 2. Commonest cause of (a) death or (b) hospitalization among hemodialysis patients. CVD, cardiovascular disease; HICs, high income countries; LICs, low-income countries; LMICs, lower-middle income countries; NIS, Newly Independent States; UMICs, upper-middle income countries. Data are presented as proportions (in percentages) of countries per region or income category. Cardiovascular disease: ischemic heart disease, arrhythmia, cerebrovascular disease. Access malfunction: malfunction of arteriovenous fistula/graft, blocked central venous catheter. Access-related infection: infected arteriovenous fistula/graft, central venous catheter-related bacteremia. Other sources of infection: pneumonia, gangrene of limbs, etc.

people treated with HD died in the first year. No countries reported first-year mortality of >30% in people treated with PD. The commonest cause of death for patients on HD and PD was cardiovascular diseases. Access-related infections and withdrawal owing to the cost of care were also important causes of death in LICs. Fewer than 30% of people receiving HD and 20% of people treated with PD required hospitalization within the first year in most countries. Access-related infections and cardiovascular diseases were the most common causes of hospitalization among patients with HD in LICs and HICs, respectively. PD-related infections were the most common causes in patients with PD across all income groups. The burden of first-year hospitalization was higher in LICs, where the cause of hospitalization was most often access-related infections.

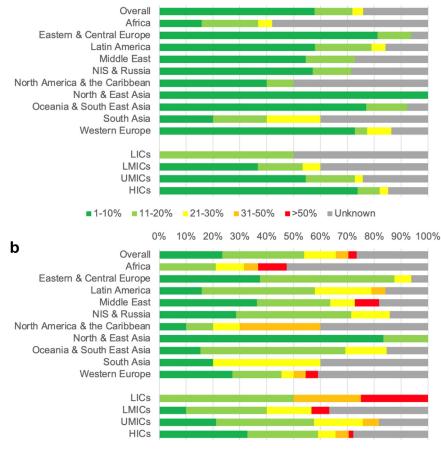
This study provides important global insights into early outcomes for people treated with HD or PD. In keeping with previous studies, mortality among

people on HD was found to be high, with more than one-third of countries in the present study reporting that greater than 10% of patients die in the first year of therapy.^{4,13-15} Of particular concern, 2 countries in Africa reported first-year HD mortality that exceeded 75% of patients, and no data on mortality were available for a high proportion of LICs and LMICs. Monitoring first-year mortality is an important marker of the quality and effectiveness of care and should be treated as a key performance indicator for HD units and hospitals. The most common cause of death among patients with HD overall was cardiovascular diseases, which aligns with findings from previous studies.¹⁶ Access-related infections and dialysis withdrawal due to unaffordability were important and potentially preventable causes of death on HD in LICs and in African countries. The latter finding reflects the notably high out-of-pocket payments for the delivery of HD in these settings.¹⁷





0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%



■ 1-10% ■ 11-20% ■ 21-30% ■ 31-50% ■ >50% ■ Unknown

Figure 3. Proportion (national average) of patients with kidney failure on peritoneal dialysis who (a) died or (b) require at least one hospitalization, in the first year of dialysis. HICs, high income countries; LICs, low-income countries; LMICs, lower-middle income countries; NIS, Newly Independent States; UMICs, upper-middle income countries. Data are presented as proportions (in percentages) of countries per region or income category.

Data on hospitalization during the first year of HD are particularly relevant because this information is not frequently collected or reported by kidney disease registries. Although fewer than half of people treated with HD were hospitalized in the first year overall, as many as one-third of LICs reported first-year hospitalization of >75% of patients. This may be explained by the cause of hospitalization. For example, the most common reason for hospitalization in LICs was accessrelated infections. Limited public funding and high out-of-pocket costs for permanent HD access in LICs result in higher use of central venous catheters, 18,19 which increases the risk of bloodstream infection.^{20,21} Furthermore, in HIC where cost of hospitalization is high, access-related infection may be treated in the outpatient setting rather than as an inpatient. In light of these findings, public funding for HD should also cover the cost of access creation or tunneled catheter insertion, especially in LICs and LMICs because this approach could potentially reduce access-related hospitalizations, mortality, and healthcare costs.

Outcomes for patients on PD were marginally better than for those on HD, with first-year mortality being <10% and first-year hospitalization being <20% in the majority of participating countries. Differences between PD and HD may reflect the availability of PD and HD across income groups (i.e., PD available in 4 LICs vs. HD available in 17 LICs), lack of data on PD outcomes from 50% of LICs and 40% of LMICs, or differences in modality selection at the patient level. Cardiovascular diseases were the leading cause of death in the first year of PD in most countries, except in Africa where infections (PD-related or other) and dialysis withdrawal owing to cost of care were the most common causes of death. This further reinforces inequities in the affordability of KRT and in the availability of effective infection prevention strategies.

The results of this study have important implications for health policy and health system governance. Dialysis withdrawal owing to cost of care was only reported as a cause of death in LICs and LMICs, demonstrating significant disparity and inequity

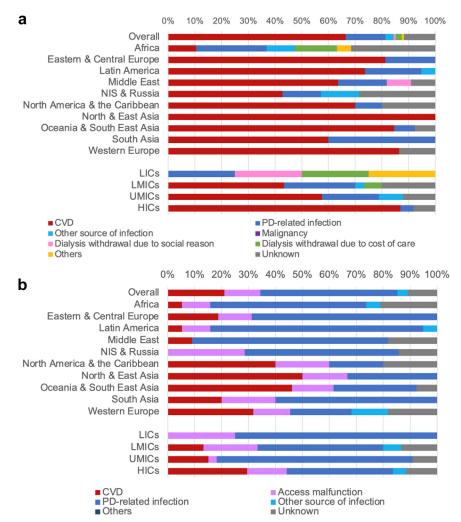


Figure 4. Commonest cause of (a) death or (b) hospitalization among peritoneal dialysis patients. CVD, cardiovascular disease; HICs, high income countries; LICs, low-income countries; LMICs, lower-middle income countries; NIS, Newly Independent States; UMICs, upper-middle income countries. Data are presented as proportions (in percentages) of countries per region or income category. Cardiovascular disease: ischemic heart disease, arrhythmia, cerebrovascular disease. Access malfunction: PD catheter block, catheter tip migration. PD-related infection: peritonitis, exit-site, or tunnel tract infection. Other sources of infection: pneumonia, gangrene of limbs, etc.

between income groups as well as catastrophic health expenditures in these income groups. Dialysis is expensive, the cost of its delivery varies greatly across countries, and out-of-pocket costs to patients are common in many countries. For example, the median annual cost of dialysis is approximately US \$19,000 per person, with disproportionate cost coverage from governments influenced by the country's wealth (51% of HICs require no copayment for PD compared with 0% of LICs). The cost burden of dialysis to patients must be interpreted in the context of expected income for people in the region. As defined by the World Bank, the gross national income per capita is \leq US \$1025 in LICs and \leq US \$3995 in LMICs, which is significantly lower than the median annual cost of dialysis in these countries (median annual HD cost US \$9065 in LICs, US \$10,114 in LMICs).² This makes dialysis unattainable or unsustainable for many, as

observed in this study. For this reason, among LICs and LMICs, especially in Africa, there are opportunities to access acute PD but not chronic PD because of the cumulative cost of the latter, limiting dialysis treatment to those who are likely to recover from acute kidney injury.²

The resource capacity at a country level also plays a key role in the quality and accuracy of data capture. For example, among countries in Africa, >50% indicated an "unknown" proportion of patients with kidney failure on PD who died in the first year of dialysis. Based on available data, patients who start PD in Africa may be quoted to have an 11% and 20% risk of death in the first year (according to 21% of responding countries) but given the many countries that did not report these data, the true proportion could be substantially higher, possibly even exceeding 30% per year. The distribution of "unknown" data were inverse to income group, as demonstrated in previous iterations of the ISN-GKHA and by a review on the global status of kidney failure registries.^{7,8,22} Established kidney registries also have gaps in data collection. For outcomes such as mortality rate or cause of death, there is near 90% data capture, compared with hospitalizations which are currently captured by <20% of established registries.²² Perhaps these differences could explain the absence of a gradient in "unknown" proportion of hospitalization for HD and PD across World Bank groups, which were clearly demonstrated for mortality.

This study has several strengths. Firstly, its findings are based on 1 of the largest global surveys on kidney care and it used data from as many as 167 countries. Next, its analyses are categorized by ISN regions and world bank income groups so that direct comparisons can be made. However, it also has several limitations, largely relating to its survey design and generation of data from best estimates rather than from national health records or kidney registries. As such, it is prone to recall bias, lack of granular data (including on the specific cause of death and hospitalization), and reliance on responder knowledge. Importantly, estimates of the burden of death and hospitalization were provided by key opinion leaders from each country rather than being derived from local or national registries, large observational studies, or other objective sources. Although responses were externally verified for consistency, survey responses may have been prone to bias, including social desirability bias. Moreover, there are inherent challenges in assessing both causes of death and hospitalization and misclassification is common

CONCLUSION

Published data in the form of registry reports and prospective studies such as Dialysis Outcomes Practice Patterns Study have improved our knowledge regarding the risk and burden of adverse outcomes associated with kidney failure including hospitalization and mortality. Our data represents the first global effort to document the burden of these adverse outcomes across all world regions irrespective of country economic ranking. We have demonstrated significant global disparities in HD and PD outcomes across income groups and world regions. Available data highlight several areas for development, especially in LICs where infections and social factors are major contributors to death and hospitalization. Routine collection of outcome data in people receiving HD or PD is imperative as a marker of quality and to allow reporting, comparison, and benchmarking within and between countries. In LICs, such data could also be leveraged by

nephrology leaders to engage health policymakers about the need for increased public funding for dialysis. In both HICs and LICs, outcome data could be used to quantify the effectiveness of quality improvement initiatives aimed at improving preventable contributors to adverse outcomes, including infectious complications and dialysis access issues.

DISCLOSURE

All authors have completed an ICMJE form. YC reports grants and others from Baxter Healthcare, outside the submitted work. IE reports grants from Fonds de Recherche du Québec-Santé, outside the submitted work. HH reports personal fees from AWAK technology and Baxter Healthcare, and nonfinancial support from Mologic company, outside the submitted work. SA reports personal fees from The International Society of Nephrology, outside the submitted work. SD reports personal fees from The International Society of Nephrology, outside the submitted work. JD reports personal fees from The International Society of Nephrology, outside the submitted work. VJ reports personal fees from GSK, Astra Zeneca, Baxter Healthcare, Visterra, Biocryst, Chinook, Vera, and Bayer, paid to his institution, outside the submitted work. CM reports personal fees from The International Society of Nephrology, outside the submitted work. MN reports grants and personal fees from KyowaKirin, Boehringer Ingelheim, Chugai, Daiichi Sankyo, Torii, JT, Mitsubishi Tanabe, grants from Takeda and Bayer, and personal fees from Astellas, Akebia, AstraZeneca, and GSK, outside the submitted work. AKB reports other (consultancy and honoraria) from AMGEN Incorporated and Otsuka, other (consultancy) from Bayer and GSK, and grants from Canadian Institute of Health Research and Heart and Stroke Foundation of Canada, outside the submitted work; He is also Associate Editor of the Canadian Journal of Kidney Health and Disease and Cochair of the ISN-Global Kidney Health Atlas. DWJ reports consultancy fees, research grants, speaker's honoraria and travel sponsorships from Baxter Healthcare and Fresenius Medical Care, consultancy fees from Astra Zeneca, Bayer, and AWAK, speaker's honoraria from ONO and Boehringer Ingelheim & Lilly, and travel sponsorships from Ono and Amgen, outside the submitted work. He is also a current recipient of an Australian National Health and Medical Research Council Leadership Investigator Grant, outside the submitted work. All the authors declared no competing interests.

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DATA AVAILABILITY STATEMENT

De-identified participant data will be available upon request to the corresponding author.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1. Proportion of people with kidney failure on hemodialysis who died in the first year of dialysis (overall). Figure S2. Proportion of people with kidney failure on hemodialysis who died in the first year of dialysis (by income group).

Figure S3. The proportion of people with kidney failure on hemodialysis who were hospitalized in the first year of dialysis (overall).

Figure S4. Proportion of people with kidney failure on hemodialysis who were hospitalized in the first year of dialysis (by income group).

Figure S5. Proportion of people with kidney failure on peritoneal dialysis who died in the first year of dialysis (overall).

Figure S6. Proportion of people with kidney failure on peritoneal dialysis who died in the first year of dialysis (by income group).

Figure S7. Proportion of people with kidney failure on peritoneal dialysis who were hospitalized in the first year of dialysis (overall).

Figure S8. Proportion of people with kidney failure on peritoneal dialysis who were hospitalized in the first year of dialysis (by income group).

Appendix S1. Global Kidney Health Atlas survey.

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