# Framework for establishing integrated kidney care programs in low- and middle-income countries

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Secular increases in the burden of kidney failure is a major challenge for health systems worldwide, especially in lowand middle-income countries (LMICs) due to growing demand for expensive kidney replacement therapies. In LMICs with limited resources, the priority of providing kidney replacement therapies must be weighed against the prevention and treatment of chronic kidney disease, other kidney disorders such as acute kidney injury, and other noncommunicable diseases, as well as other urgent public health needs. Kidney failure is potentially preventable—not just through primary prevention of risk factors for kidney disease such as hypertension and diabetes, but also by timely management of established chronic kidney disease. Among people with established or incipient kidney failure, there are 3 key treatment strategies—conservative care, kidney transplantation, and dialysis—each of which has its own benefits. Joining up preventive care for people with or at risk for milder forms of chronic kidney disease with all 3 therapies for kidney failure (and developing synergistic links between the different treatment options) is termed "integrated kidney care" and has potential benefits for

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patients, families, and providers. In addition, because integrated kidney care implicitly considers resource use, it should facilitate a more sustainable approach to managing kidney failure than providing one or more of its components separately. There is currently no agreed framework that LMIC governments can use to establish and/or scale up programs to prevent and treat kidney failure or join up these programs to provide integrated kidney care. This review presents a suggested framework for establishing integrated kidney care programs, focusing on the anticipated needs of policy makers in LMICs.

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he prevalence of kidney failure and its major risk factors (including chronic kidney disease [CKD]) are increasing worldwide, and the most rapid growth is observed in low- and middle-income countries (LMICs).<sup>1</sup> The corresponding increase in the burden of kidney failure is a major challenge for health systems, especially in LMICs, due to growing demand for expensive kidney replacement therapies such as dialysis.<sup>2</sup> In LMICs with limited resources, the priority of providing costly kidney replacement therapies must be weighed against the prevention and treatment of

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CKD, other kidney disorders such as acute kidney injury, and other non-communicable diseases, as well as other urgent (public) health needs such as sanitation, clean water, infectious diseases, and reproductive health.

In a systematic review in sub-Saharan Africa, presumed and known mortality among adults and children was high, and was >95% when patients were unable to access dialysis. Among patients who did start dialysis, mortality remained high, largely because of late presentation, frequent dialysis discontinuation, and suboptimum dialysis quality. Overall, only about 10% of adults with incident end-stage kidney disease and 35% of children remained on dialysis for at least 3 months.<sup>3</sup>

Kidney failure is potentially preventable-not just through primary prevention of risk factors for kidney disease such as hypertension and diabetes, but also by timely management of established CKD. Among people with established or incipient kidney failure, there are 3 key treatment strategies: conservative care, kidney transplantation, and dialysis, each of which has its own benefits. Joining up effective preventive care for people with or at risk for milder forms of CKD with all 3 therapies for kidney failure (and developing synergistic links between the different treatment options) is termed "integrated kidney care" and has potential benefits for patients, families, and providers. In addition, because integrated kidney care implicitly considers resource use, it should facilitate a more sustainable approach to improving the health of people with kidney failure than providing one or more of its components separately.

LMICs are responding to the challenges of kidney failure in different ways,<sup>4</sup> with variable provision of the 4 components of integrated kidney care, and few adopting a coordinated strategy. The variability in approaches may be due to differences between countries in the actual or perceived burden of disease, available human or financial resources, and cost structures (e.g., relative cost of labor vs. supplies), but also cultural considerations, political context, and competing interests from other stakeholders (including governments, other payers, patients and families, drug and device companies, dialysis providers, nephrologists, and other health care workers).<sup>5</sup> Decisions to establish dialysis services without sufficient consideration of the other components of a kidney care strategy are of particular concern-and are often made without effective representation and guidance from the kidney community.

There is currently no agreed framework that LMIC governments can use to establish and/or scale up programs to prevent and treat kidney failure. Individual countries have placed variable priority on establishing and maintaining the different aspects of kidney care programs, and accordingly there has been considerable heterogeneity between and within countries in terms of the relative investment devoted to prevention, conservative care, kidney transplantation, and dialysis care. The current approach to kidney failure in many countries is neither sufficient (in terms of providing equitable access to high-quality care) nor sustainable (for the patient, health system, economy, and society) and demands the urgent attention of governments and policy makers. Whereas countries are free to set their own health priorities (and allocate resources accordingly), it is important that these decisions be made in the context of high-quality and accurate information about the expected benefits and costs of the different components of a coordinated kidney care program—and the potential synergies associated with a coordinated approach.

In this review, we present a suggested framework for establishing integrated kidney care programs in LMIC (Figure 1).

# Framework that LMIC governments can use to establish and/or scale up programs for preventing and treating kidney failure

Because no country has infinite resources, choices must be made about which health services to fund-ideally supported by high-quality evidence on the costs and consequences of the various options. Most relevant to kidney care specifically: the high cost of dialysis treatment and the morbidity and mortality associated with kidney failure emphasize the potential value of primary and secondary prevention. The expertise, generic medications, and diagnostic tests required to slow or prevent progressive kidney function loss are relatively inexpensive and could be scaled and spread in conjunction with other programs for non-communicable diseases prevention and control.<sup>6</sup> Given that the cost per quality-adjusted life-year associated with providing such preventive care is markedly more favorable than dialysis care,<sup>6</sup> it does not seem rational to provide publicly funded kidney replacement until the majority of citizens have access to publicly funded preventive care. Similarly, because not all patients with kidney failure will benefit from and/or have access to kidney replacement, expanded access to conservative care will improve patient outcomes and the experience of patients and families-and providing access to publicly funded conservative care should take priority over implementing kidney replacement programs in LMICs.

When kidney replacement treatment is contemplated, kidney transplantation, compared with dialysis, offers the best outcomes at the lowest costs.<sup>7</sup> Although dialysis is required to support kidney transplant services, in many LMICs, dialysis should be considered as a bridge to transplantation rather than a definitive chronic treatment. Although hemodialysis (HD) is often considered first by countries seeking to develop a dialysis program, peritoneal dialysis (PD) usually offers similar outcomes at lower costs.<sup>8,9</sup> Therefore, in most LMICs, PD should be prioritized over HD when resources are limited.

Although these general principles (summarized in Table 1) are widely accepted, there are some practical barriers to their application. First, kidney transplantation requires multiple ancillary components (e.g., living and deceased donor services, surgical expertise and facilities, tissue-typing laboratories, ability to perform and interpret kidney biopsies) that may be difficult for LMICs to develop and sustain.<sup>10</sup> Because these services all involve certain fixed costs that are amortized



**Figure 1 Potential infographic that could be used to support decision-makers in implementing integrated kidney care.** The size of each section of the triangle has been drawn in proportion to the associated health gains and, thus, the priority for investment. The figure illustrates that of the components of integrated kidney care, treatments that delay or prevent progression from kidney disease to kidney failure should be the highest priority, and hemodialysis (HD) should be the lowest priority. Within the various modalities available for kidney replacement among people with kidney failure, kidney transplantation should be the highest priority and HD should be the lowest priority. However, within countries that choose to offer kidney replacement, a mix of all 3 modalities will often be most appropriate. Treatments that delay or prevent progression from kidney disease to kidney failure include those aimed at treatment of the primary kidney disease, such as immunosuppressive medications for people with lupus nephritis.

across the total number of transplants done, the cost per transplant can be unreasonably high in settings where programs are new and/or low numbers of transplants are performed. One option for countries in this position could be to send patients who have a living donor abroad for the transplant procedure, with postoperative and chronic follow-up done locally. This option will require development of linkages to neighboring countries with established transplant infrastructure-but which also can provide culturally appropriate care to the potential living donors and recipients, and which have the requisite safeguards to prevent organ trafficking and exploitation of donors. Alternatively, partnerships between countries or between medical institutions in said countries can be established, where surgical expertise and resources can be sent periodically to perform kidney transplantation in countries that lack these resources. These partnerships can evolve into long-term relationships where the country with an established kidney transplant infrastructure can help to establish a similar system in their partner country. This would significantly reduce the risk of organ trafficking and donor exploitation and may significantly reduce the cost for patients. This model is currently being implemented in a partnership among Iran, Tajikistan, and Azerbaijan. For these 2 options to be successful, the list of work-up procedures for potential donors should be developed and implemented, and the possibility of using relative-only or relative and emotional donors should be adjusted in accordance with the local regulations. In addition, after appropriate translation into local languages and adaptation to the local

## Table 1 | Principles of integrated kidney care

- Treatments to slow or prevent progression of kidney disease to kidney failure are effective, highly cost-efficient, have synergies for the prevention and management of diabetes and vascular disease, and are easily integrated with other programs aimed at NCD prevention and control. Such preventive care should be the highest priority for kidney care programs in LMICs.
- Treatments aimed at managing symptoms among those with kidney failure who do not have access to or who prefer not to receive kidney replacement are known as "conservative care" and should be established in parallel with preventive care programs.
- Among forms of kidney replacement, kidney transplantation is associated with the best clinical outcomes at the lowest cost. Kidney transplantation is the optimal form of kidney replacement for the large majority of patients with kidney failure.
- PD is associated with outcomes that are similar to those for hemodialysis, but usually at lower cost. For LMICs that are contemplating chronic dialysis programs, PD should be prioritized over hemodialysis, for its cost-savings benefits. Establishing facilities for the local manufacture of PD solutions in these countries, and paying medical staff to train patients in using PD, may help to ensure that the potential economic benefits of PD are realized in all settings.

LMICs, low- and middle-income countries; NCD, noncommunicable disease; PD, peritoneal dialysis.

context, implementation of international guidelines on the Evaluation and Care of Living Kidney Donors and Transplant Recipients<sup>11</sup> should be considered as part of postoperative care for both the recipient and the donor. Again, partnerships with higher-income countries may help to provide the necessary training and education to adapt and implement such guidance. If the option of going abroad for transplantation appears to be more feasible, the travel expenses for the recipient and donor, and the cost of surgery should be estimated and weighted over the local resources, to minimize undue financial burden on the patient and their family.

However, these options should only be seen as a bridge to developing the infrastructure, skills, and workforce to develop a national program within the home country. Development of these programs should be national in scope so that development of the service is in line with national priorities. Second, patients whose transplant fails will die of kidney failure without dialysis support. Therefore, even in settings where kidney transplantation is successfully implemented as the preferred mode of kidney replacement, some dialysis capacity will be required. Third, although PD is generally cheaper than HD, there are settings where this is not the case—especially those where PD fluids and supplies are expensive (e.g., due to tariffs or lack of competition), or where skilled labor is relatively cheap (favoring HD because nursing care is a key driver of costs for this therapy but is not much needed to provide PD<sup>12</sup>). Therefore, there may need to be some flexibility in applying these principles in different settings. With support and training by the International Society of Nephrology and some nongovernmental organizations (such as with Saving Young Lives), a PD program for acute kidney injury must be implemented in most LMICs where kidney replacement therapy is not available. Nearly 200 patients in sub-Saharan Africa have been treated by these programs, despite limited financial and administrative support and a lack of awareness in the communities of the importance of early diagnosis and treatment of acute kidney injury.<sup>13</sup>

The 4 principles in Table 1 are supported by evidence, yet such evidence is not always summarized in a format that is useful to decision-makers, may not apply to all LMIC settings, and may not have been recently updated. To be maximally useful to decision-makers in LMICs, new evidence summaries (rapid reviews, systematic reviews, economic analyses) are required that will provide updated and accessible information to support decision-making on kidney care programs. In addition, specific analyses that translate the general principles into more quantitative decision rules would be beneficial. For example, identifying the threshold cost for PD fluids at which PD becomes more expensive than HD would help to identify settings in which principle 4 may not apply. Therefore, there is an urgent need to produce and disseminate these summaries in partnership with end users.

There are several models that could be considered for organizing and funding kidney care programs, each with their own advantages and disadvantages. A summary of these models would be a useful adjunct to the summary of evidence related to the clinical services that should be provided, and should be developed and disseminated in parallel with the former. Table 2 indicates some strategies that LMIC might use to develop a model of integrated kidney care, based on the experience of successful initiatives in countries such as Taiwan and Japan, recognizing that not all such initiatives will be feasible, especially in low-income countries. Attempts to establish integrated kidney care should ideally be linked to other initiatives aimed at non-communicable diseases prevention and control, such as efforts to establish universal health coverage.<sup>14</sup>

Finally, decision-makers in LMICs would benefit from a tool that describes and justifies the principles behind establishing a national kidney care program, including the 2 forms of evidence summary discussed herein. This tool should present the principles in Table 1, but also identify the preparatory work that countries must do before applying the principles (e.g., assess burden of kidney disease and kidney

Strategies	Partners	Actions
Understand the burden of kidney disease and	National health administration	CKD/ESKD registry
kidney failure at national and local levels	National nephrology society	Epidemiology study
		Risk factor identification
		Target population
Integrated kidney care committee at national	National health administration	CKD prevention program
or nephrology society level	National nephrology society	Multidisciplinary care program
	Nephrologist as core leadership	Replacement therapy quality control
		Kidney transplantation promotion
Standardization for integrated kidney care	National health administration	Dialysis guideline
	National nephrology society	CKD guideline (translation and implementation of KDIGO
	International society (e.g., ISN)	CKD evaluation and management guidelines should be considered)
Implementation of integrated kidney care	Primary and secondary care physicians	Multidisciplinary and multiprofessional care approaches
	Multidiscipline health care professions	<b>F</b> 11 11 11
Sustainability and quality improvement	National health administration	Funding assurance and health care coverage
Outcome measures	National health administration National nephrology society	Annual report and outcome assessment

Table 2 | Suggested strategies for developing an integrated kidney care program

CKD, chronic kidney disease; ESKD, end-stage kidney disease; ISN, International Society of Nephrology; KDIGO, Kidney Disease: Improving Global Outcomes.

failure, identify existing human capacity and relevant infrastructure, consider and agree on health policy priorities). The tool should also make explicit the above-mentioned factors that may prevent a country from developing kidney care services in the order implied by the 4 principles, as well as suggesting some metrics that help to inform countries when offering a more sophisticated kidney care program (e.g., what proportion of the population should have reasonable access to preventive services and conservative care before a kidney transplantation program is implemented). Which specific metrics to use presents an ethical challenge that LMICs will have to acknowledge in order to define metrics that are culturally sensitive, while keeping in mind the limited resources available in these countries.

## Conclusions

LMICs are responding to the challenge of kidney failure in different ways, and few if any have determined how to effectively provide all 4 components of an integrated kidney care strategy. This review presents a suggested framework for establishing integrated kidney care programs that will help to improve the health of all those with kidney disease or kidney failure, especially those in LMICs.

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#### REFERENCES

- 1. Webster AC, Nagler EV, Morton RL, et al. Chronic kidney disease. *Lancet*. 2017;389:1238–1252.
- Mushi L, Marschall P, Flessa S. The cost of dialysis in low and middleincome countries: a systematic review. BMC Health Serv Res. 2015;15:506.
- 3. Ashuntantang G, Osafo C, Olowu WA, et al. Outcomes in adults and children with end-stage kidney disease requiring dialysis in sub-Saharan Africa: a systematic review. *Lancet Global Health*. 2017;5:E408–E417.
- Stanifer JW, Muiru A, Jafar TH, et al. Chronic kidney disease in low- and middle-income countries. *Nephrol Dial Transplant*. 2016;31:868–874.
- Jha V, Arici M, Collins AJ, et al. Understanding kidney care needs and implementation strategies in low- and middle-income countries: conclusions from a "Kidney Disease: Improving Global Outcomes" (KDIGO) Controversies Conference. *Kidney Int.* 2016;90:1164–1174.
- Couser WG, Remuzzi G, Mendis S, et al. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. *Kidney Int*. 2011;80:1258–1270.
- Tonelli M, Wiebe N, Knoll G, et al. Systematic review: kidney transplantation compared with dialysis in clinically relevant outcomes. *Am J Transplant*. 2011;11:2093–2109.
- Pike E, Hamidi V, Ringerike T, et al. More use of peritoneal dialysis gives significant savings: a systematic review and health economic decision model. J Clin Med Res. 2017;9:104–116.
- Liu F, Quock T, Burkart J, et al. Economic evaluations of peritoneal dialysis and hemodialysis: 2004–2012 [version 1; referees: 1 approved, 1 approved with reservations]. *F1000Research*. 2013;2:273. https://doi.org/ 10.12688/f1000research.2-273.v1.
- Ready AR, Nath J, Milford DV, et al. Establishing sustainable kidney transplantation programs in developing world countries: a 10-year experience. *Kidney Int.* 2016;90:916–920.
- Lentine KL, Kasiske BL, Levey AS, et al. KDIGO clinical practice guideline on the evaluation and care of living kidney donors. *Transplantation*. 2017;101:S1–S109.
- 12. Karopadi AN, Mason G, Rettore E, et al. Cost of peritoneal dialysis and haemodialysis across the world. *Nephrol Dial Transplant*. 2013;28:2553–2569.
- **13.** Abdou N, Antwi S, Koffi LA, et al. Peritoneal dialysis to treat patients with acute kidney injury—the Saving Young Lives experience in West Africa: proceedings of the Saving Young Lives session at the First International Conference of Dialysis in West Africa, Dakar, Senegal, December 2015. *Perit Dial Int.* 2017;37:155–158.
- World Health Organization. Universal Health Coverage (UHC) and World Health Day. Available at: https://www.un.org/en/observances/universalhealth-coverage-day/resources. Accessed January 11, 2020.
- Harris DCH, Davies SJ, Finkelstein FO, et al. Increasing access to integrated ESKD care as part of universal health coverage. *Kidney Int.* 2019;95:S1–S33.