The Future of Technology-Based Kidney Replacement Therapies: An Update on Portable, Wearable, and Implantable Artificial Kidneys

Fokko P. Wieringa, Swathi Suran, Henning Søndergaard, Stephen Ash, Cian Cummins, Ashesh Ray Chaudhuri, Tugrul Irmak, Karin Gerritsen, and Jeroen Vollenbroek

Worldwide, the number of people who need lifesaving kidney replacement therapy (KRT) steadily increases, but approximately two thirds of them lack access to KRT and therefore die. Access to KRT depends on economic, social, infrastructural, ecological, and political factors. Current KRTs include kidney transplant, peritoneal dialysis, and hemodialysis. The field of xenotransplantation has been opening promising new perspectives recently but needs improvement. Unfortunately, not all patients are suitable for transplant. Peritoneal dialysis and hemodialysis will remain important KRTs, but they are expensive and strongly dependent on infrastructure, with few fundamental changes since the 1980s. The KRT field might learn from the "African mobile phone revolution" that beat infrastructural limitations, lowered costs, and increased access. We provide a nonexhaustive overview of promising ways to increase the mobility of technology-based KRTs by dialysate regeneration, chip-based nanoporous filters, bioreactor-enabling technologies, and using the gut as a "third kidney." In 2018, the Kidney Health Initiative published a road map for innovative KRTs composed by leading innovators, but the pace of innovation is slower than was targeted. Ambitious political statements about realizing this road map can only succeed if the granted funding matches the targeted time scale. Patient-centered international "coopetition" (ie, the act of cooperation between competing entities) seems to offer the quickest pathway to success.

Complete author and article information provided before references.

Correspondence to F.P. Wieringa (fokko.wieringa@imec.nl)

Am J Kidney Dis. 85(6):787-796. Published online February 4, 2025.

doi: 10.1053/j.ajkd.2024.10.015

Introduction

In 2018, the Kidney Health Initiative (KHI) published a road map for innovative approaches to renal replacement therapy, and, that same year, *AJKD* published an excellent Perspective titled "Innovations in Wearable and Implantable Artificial Kidneys" by Salani et al.[1,2] Here we provide an updated Perspective on this matter, which we will relate to these two documents.

It is predicted that, by 2030, approximately 14.5 million people with end-stage kidney disease or chronic kidney failure will need lifesaving kidney replacement therapy (KRT), whereas only approximately one third of these people will actually receive KRT. This implies that a two-thirds majority (mainly located in low-income countries) will not receive KRT and will therefore die.[3] This is due to economic, social, infrastructural, and environmental factors, plus an innovation paradox regarding KRTs that has persisted over a period of 5 decades.[4]

Current KRT modalities include kidney transplant (preferred treatment if the patient is eligible for transplant and a matching donor kidney is available) as well as peritoneal dialysis (PD) and hemodialysis (HD).

Regarding transplantation, there is a persistent lack of donor kidneys from living and deceased donors. However, March 2024 saw a big breakthrough in xenotransplantation: a kidney from a genetically modified pig was successfully transplanted into a patient, who could return home a few weeks after surgery.[5] However, this patient died 2 months later.[6] In April 2024, another patient received an electromechanical left ventricular assist device plus a genetically modified pig kidney that was explanted in June 2024 because of complications from low perfusion episodes, and the patient died July 7, 2024.[7,8] The etiology or cause(s) of death for either of these patients had not been published by the time of manuscript preparation. Despite their short durations, these xenotransplants are true breakthroughs, and xenotransplantation is clearly opening promising new perspectives. Laboratory-cultivated, three-dimensional bioprinted, and other fully biology-based replacement kidneys are also being developed, but these seem much further away on the timeline.

Unfortunately, not all patients are suitable for transplant, and other forms of KRT (and innovations thereof) will remain essential in the foreseeable future.[9] This Perspective will focus on technological and/or technological/biological hybrid forms of KRT, while leaving the description of the exciting perspectives regarding transplant of fully biology–based kidneys to experts in that specific field; see, for example, a recently published excellent review.[10]

PD and HD will remain important KRT modalities, but, in their present forms, they are expensive and strongly dependent on infrastructure for water and electricity (especially HD) as well as on transportation and logistics (both HD and PD), which hampers their uptake in low-income countries. It is highly plausible that decreasing those dependencies can go hand in hand with decreasing treatment costs and increasing mobility, which could result in serving a larger proportion of patients in need of

KRT at the places where they live and work.[11] Mobility is highly desired by patients. A recent study of 498 patients with kidney failure found a willingness to trade a 1% infection risk and a 0.5% risk of death within 5 years to gain complete mobility and freedom from in-center HD.[12] Mobile, affordable, and easy-to-use KRT devices additionally might help to alleviate the internationally observed increasing shortage of nurses in general and nephrology nurses in particular.[13,14]

Here, the kidney community might learn from the "African mobile phone revolution," an interesting (and initially unexpected) leap-frog effect observed within the telecommunication business. After its invention in 1876, the telephone rapidly conquered the Western world. Africa, however, severely lagged behind in cable-based telephone connections, which required costly cable infrastructure on a vast continent. The first mobile call in Africa was made in Zaire (now the Democratic Republic of the Congo) in 1987, and mobile telephony was rapidly adopted by millions of Africans. In 2022, sub-Saharan Africa had 489 million unique mobile phone subscribers, and this is expected to grow to 602 million by 2030.[15,16] In Africa, this growth pace would never have been possible for a purely cable-dependent phone network.

A similar leap-frog effect might be achieved by creating very compact mobile dialysis modalities with far less infrastructural restrictions or even implantable artificial kidneys offering functionality beyond the definitions of HD or PD. Interestingly, the enabling role that chip technology plays for the miniaturization of mobile phones may also apply to the miniaturization of KRTs.

Present KRTs and Main Trends to Increase Their Mobility

Figure 1 provides a graphical summary of the main presently available KRTs, as well as various innovative KRT approaches that are in the pipeline.

Targeted Levels of Portability Within This Article

Air travel has strict rules for baggage size and weight. Typically, the most desirable baggage category is carry-on

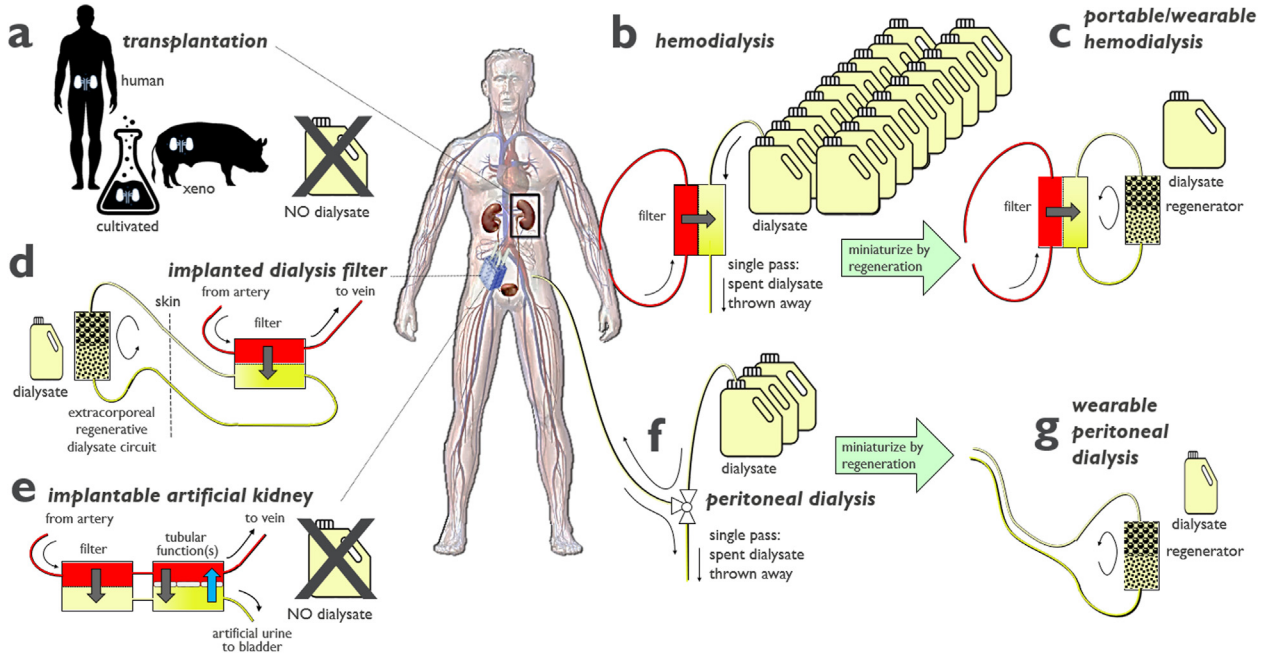

Figure 1. Graphical summary of the main forms of present and future projected kidney replacement therapies. The portable fuel container symbols depict the relative amount of water consumption by the various modalities. (A) Transplant of human kidneys is the present first-choice therapy, but there is a structural shortage of donor kidneys, for which xenotransplantation or laboratory-cultivated kidneys may be solutions. However, not all patients are suited for a transplant, and, to prevent rejection, patients must take immune-suppressive drugs, which increase the risks of cancer and infections. (B) Hemodialysis (HD; in a single-pass method) is the most widely applied form of kidney replacement therapy, but it is costly and not very mobile. (C) Regenerating dialysate in a closed loop can significantly improve HD mobility, but still requires an extracorporeal blood circuit. (D) Implanting the HD filter would eliminate the need for an extracorporeal blood circuit. Only an extracorporeal dialysate circuit would then be needed to perform HD. (E) Adding a bioreactor to an implantable hemofiltration filter could (partly) replace tubular functions. This method goes beyond the definition of HD and forms an autonomous implantable artificial kidney. (F) Peritoneal dialysis (shown here in its simplest form) does not require an extracorporeal blood circuit but requires relatively high dialysate volume. Typically, the dialysate is instilled into the peritoneum, remains there for a few hours, and is then drained. (G) Peritoneal dialysis mobility can be significantly improved by regenerating the dialysate in a closed loop, preferably in a continuous flow mode.

because these bags are much less likely to be damaged or lost during handling, which is crucial for travelers. The International Air Transport Association states that, "as a general guide, carry-on baggage should have maximum length of 22 inches (56 cm), width of 18 inches (45 cm), and depth of 10 inches (25 cm). These dimensions include wheels, handles, side pockets, etc."[17] For this study, we particularly looked for HD devices/prototypes that at least meet this recommendation, but, regarding PD devices (which are typically less bulky), we specifically looked for

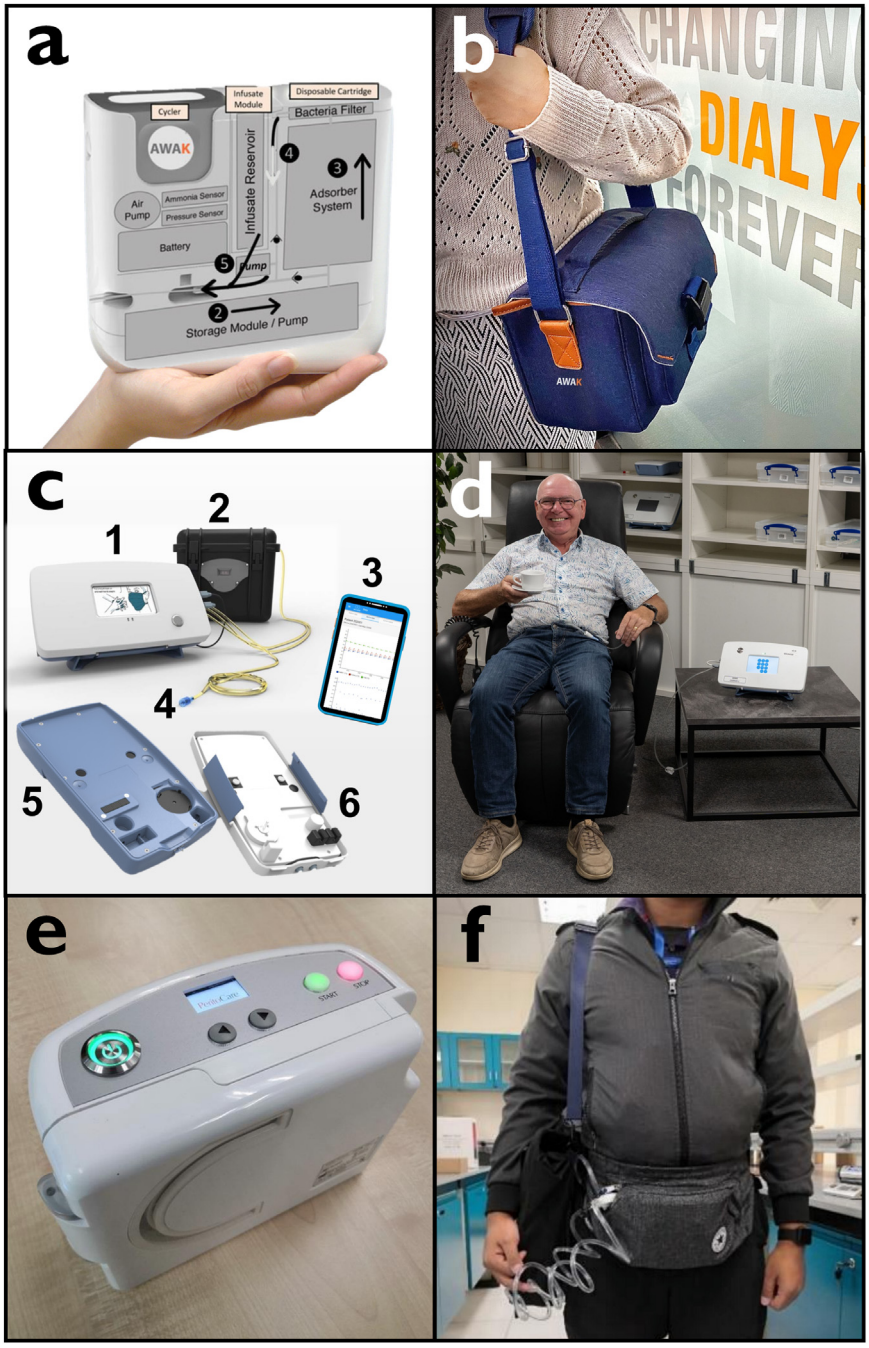

Figure 2. Three types of wearable peritoneal dialysis machines currently in human clinical trials. (A) An AWAK (Automated Wearable Ambulant Kidney) rapidly cycling sorbent-based regenerated dialysate. (B) The AWAK was reengineered and rebranded as a VIVANCE device. (C) The Weakid peritoneal dialysis device (Nanodialysis) uses rapid cycling of regenerated dialysate and includes a mobile unit with sorbents (1), a dialysate reservoir for night treatment (2), a wireless interface to a mobile phone (3), a sterile connection to the catheter (4), a cassette with sorbents (5; shown with device opened up), and a reusable control unit in the front part of the device (6). (D) Weakid mobile unit in use. (E) Peritocare wearable peritoneal dialysis device from IMEN (single-pass, no dialysate regeneration). (F) Peritocare device in mobile use.

wearable systems nearing the market. Implantable (parts of) KRT devices should fit to the approximate dimensions of a regular kidney.

Wearable PD

We describe 3 wearable PD systems that are in human clinical trials but not yet on the market (Fig 2). More exhaustive articles also exist,[3,18] and the not-for-profit organization Home Dialysis Central also maintains a website with home PD devices (https://homedialysis.org/home-dialysis-basics/machines-and-supplies/peritoneal-dialysis-machines).

The Singaporean AWAK (Automated Wearable Artificial Kidney) PD system (Fig 2A) was mentioned in the aforementioned 2018 *AJKD* Perspective.[2] It is a sorbent-based dialysate-regenerating tidal-flow PD device that uses a single-lumen catheter with a tidal flow rate of 2 L/h and a fixed dialysate glucose concentration and can be carried in a shoulder-strap bag. Preliminary human safety trial results with the AWAK PD system have been published.[19,20] Since then, the product has been reengineered (Fig 2B) and, in October 2024, rebranded as VIVANCE (https://vivance.com/).

The Dutch Weakid PD system (Fig 2C and D) is intended for nocturnal use and consists of a mobile console with a clicked-in sorbent cartridge that is supported by an externally connected dialysate reservoir. The mobile console with its clicked-in cartridge can be used optionally as stand-alone KRT during the day for additional clearance. A first-in-human clinical trial in 12 patients is currently ongoing (https://www.nanodialysis.nl/).

In contrast to the aforementioned sorbent-based dialysate-regenerating PD systems, the Malaysian Peritocare PD system is a wearable single-pass PD system. A first-in-human clinical trial in 11 patients was completed in March 2022 (A.A. Hamzah, unpublished data, 2024). The project is still ongoing, led by Azrul Azlan Hamzah, the director of the Institute of Microengineering and Nanoelectronics at Universiti Kebangsaan in Malaysia (personal communication, June 2024; https://www.ukm.my/imen/en/research-fellows/assoc-prof-dr-azrul-azlan-hamzah/).

An interesting additional pathway to increase PD mobility is local dialysate preparation.[21] There is even an initiative ongoing toward achieving this by using solar power.[22]

Portable/Wearable HD and Beyond

The International Electrotechnical Commission (IEC) standard IEC 60601-2-16 contains requirements for the safety and essential performance of HD devices and defines HD as follows: "process whereby concentrations of water-soluble substances in a patient's blood and an excess of fluid of a patient are corrected by bidirectional diffusive transport and ultrafiltration across a semipermeable membrane separating the blood from the dialysis fluid".[23]

Figure 3 shows simplified diagrams and photos of typical stages of miniaturization regarding HD (Fig 3A-E) as well as a technological/biological hybrid implantable artificial kidney (Fig 3F) that goes beyond HD, plus 2 different approaches to make silicon nanoporous membranes (Fig 3G and H) that form key enabling technologies for such implantable devices.[24,25]

It is important to note that the IEC definition does not demand an extracorporeal blood circuit. This is why the principle shown in Fig 3E falls within the IEC definition of HD.

Presently commercially available transportable HD devices use the single-pass principle: when the dialysate has passed through the dialyzer, it is discarded into a drain connected to the sewer system (hence the term "spent dialysate"). Consumption of water and electricity (to heat the water) are therefore large.[26] Figure 3A and B shows a highly simplified typical block diagram and some photos of transportable single-pass HD devices on the market. The pictured examples are not exhaustive. The not-for-profit organization Home Dialysis Central also maintains a website with home HD devices that is periodically updated: https://homedialysis.org/home-dialysis-basics/machines-and-supplies/hemodialysis-machines.

Dialysate-regenerating HD devices circulate a much smaller volume of dialysate through a closed loop in which the dialysate is regenerated. This provides greater freedom for miniaturization into a portable (ie, International Air Transport Association–compatible) or even wearable format. Considerably less water (10- to 20-fold) and electricity are consumed (there is less water to heat). Figure 3C and D shows a simplified block diagram and 2 examples that have reached the stage of in-human clinical trials: the wearable HD device (also referred to as WAK) from Victor Gura (previously described in the 2018 Perspective[2]) and the Neokidney portable HD device from NextKidney, which meets International Air Transport Association carry-on baggage criteria.[27,28] First-in-human trial results of this device were presented during 2024 American Society of Nephrology Kidney Week.[29]

The IEC definition of HD also covers partly implantable HD devices (Fig 3E). Implanting the HD filter renders the extracorporeal blood circuit superfluous. The blood stays in the body and loops through the implanted HD filter, so only an extracorporeal dialysate circuit is needed (eg, by a compact dialysate regeneration device). When the device is not in use, the transcutaneous dialysate catheters (which represent known technology) are simply connected to each other.

Thus, making needles and vascular cannulation obsolete is a giant leap forward. However, ultimately, one would like to get rid of all extracorporeal connections. This may be achieved by a fully implantable artificial kidney with 2 modules: a nanoporous silicon (or other material) wafer-based filter and a bioreactor (containing cultured tubular cells). The bioreactor would reclaim water, maintain

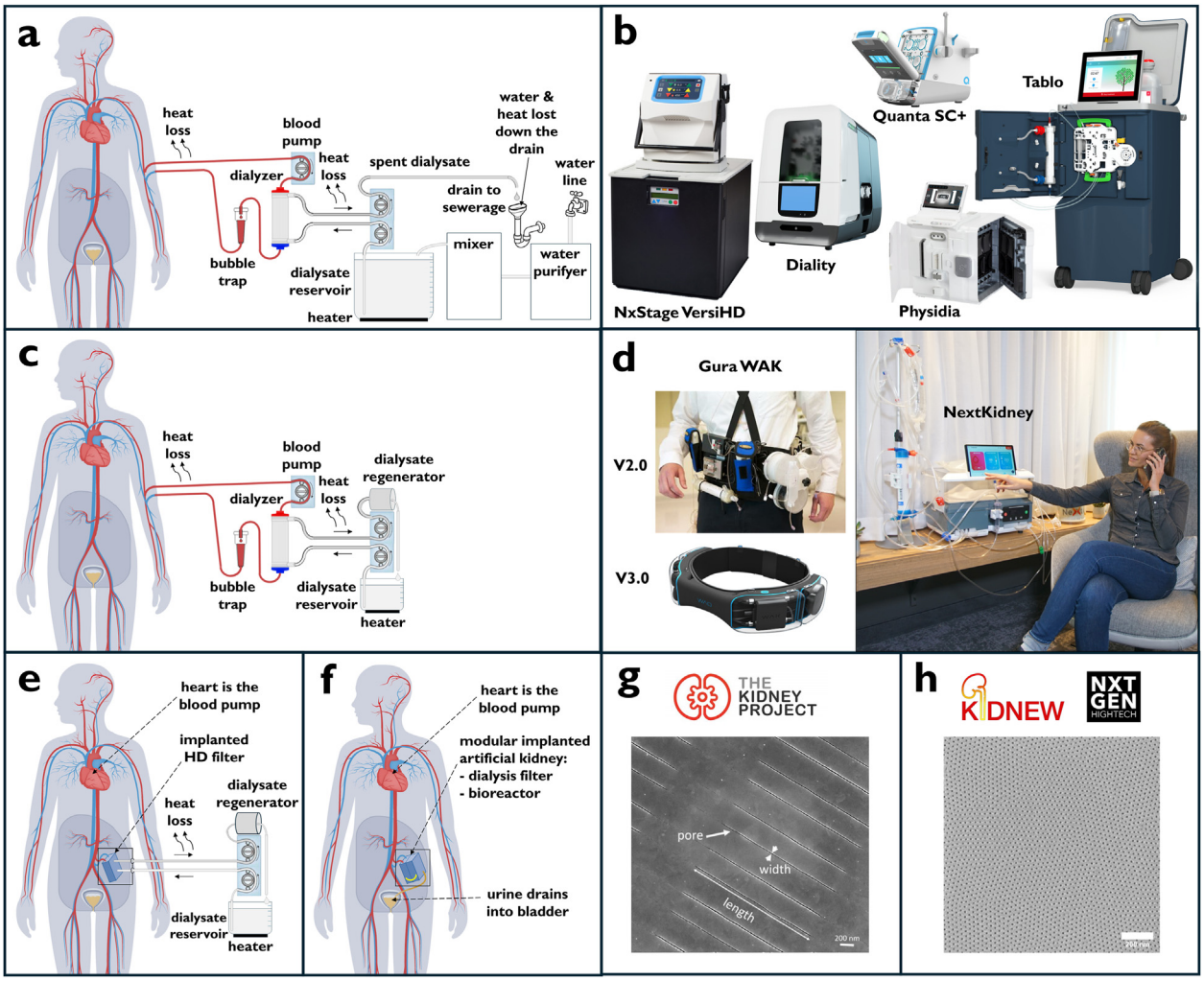

Figure 3. Highly simplified diagrams to illustrate progressive miniaturization of hemodialysis (HD) devices (A-E) and a technological/biological hybrid implantable artificial kidney beyond the definition of HD (F-H). (A) Single-pass HD block diagram. (B) Some examples of existing transportable single-pass HD devices (not exhaustive; photos from manufacturers' websites). No commercial single-pass HD devices were found that meet International Air Transport Association carry-on baggage guidelines. (C) Dialysate-regenerating HD block diagram. (D) Some examples of dialysate-regenerating HD devices that reached human clinical trials and meet International Air Transport Association carry-on requirements for air travel. (E) Partly implantable HD principle. The natural heart forms the blood pump, and an extracorporeal dialysate-regenerating device can be connected to perform dialysis. (F) Fully implantable technological/biological hybrid artificial kidney principle with a nanoporous (eg, silicon wafer–based) filter and a bioreactor. The natural heart also forms the blood pump in this case. (G) Silicon nanoporous membrane of The Kidney Project with patterned slit pores.[24] (H) Silicon nanoporous membrane pore patterning technology as applied by imec in the KIDNEW and NXTGEN HighTech projects.[25] (Original magnification, G and H: approximately ×2; scale bars, G and H: 200 nm.)

homeostasis, and help to actively expel uremic toxins via a urine outlet to the bladder (Fig 3F).[30]

It must be highlighted that the concepts depicted in Fig 3E and F were first defined by David Humes and persistently matured by the research group of William Fissel (Vanderbilt Medical School) and Shuvo Roy (University of California, San Francisco), also known as The Kidney Project.[2,3,31] The Kidney Project has already demonstrated the feasibility of the bioreactor concept and also created a well-defined animal model to test and compare silicon wafer–based nanoporous filters.[32,33] This stepwise modular approach resembles the Apollo project, a classic example of how to decrease risks while making meaningful steps toward an ambitious and complex target. In addition to this US-located project, two European Union–located synergetic consortia, called KIDNEW and NXTGEN HighTech, recently also started working toward these goals, combining their chip-based nanofilters with add-on modular on-chip integrated electronics for sensing, control, actuation, and data storage as well as wireless powering and bidirectional data communication.[11]

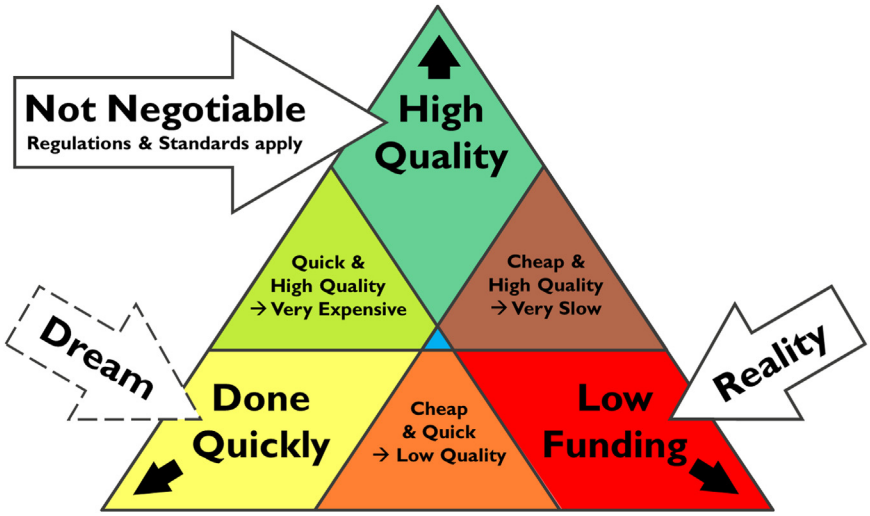

Figure 4. The "Triangle of Project Management." You may choose only 2 of the 3 triangle points, with the third automatically excluded. The NASA moon mission followed the "High Quality" and "Done Quickly" route. This is also the dream of patients needing better kidney replacement therapies, but "Low Funding" is the present reality. Note that the development of complex medical devices in any case requires considerable persistence. For a complex active medical device (eg, a kidney replacement device), it easily takes approximately 10 years from idea to market approval even if all parameters are optimized (depicted by the blue spot in the middle). Released under a CC-BY license from Wieringa et al.[11]

Researchers on both sides of the Atlantic thus work separately on creating a partly implantable HD system (Fig 3E), eventually followed by a technological/biological hybrid implantable artificial kidney (Fig 3F). The underlying silicon wafer–based filter manufacturing technologies of the US- and EU-located consortia are fundamentally different. The Kidney Project uses slit-shaped pores (Fig 3G) with widths tuned by process parameters, but the minimum distance between the individual slit-pores is dictated by the technical limitations of the applied lithographic wafer-stepper generation. Within the KIDNEW and NXTGEN HighTech projects, imec achieves a high pore density by applying molecular self-assembly (Fig 3H), which is fully independent of lithographic wafer-stepper generation and simplifies large-scale manufacturing.[25]

Using the Gut as a "Third Kidney" to Create More Room for KRT Engineering Trade-Offs

The small intestine is mostly impermeable to high-weight molecules but freely permeable to small and charged ions like Na^+, K^+, $Phos^{2-}$, H^+, and (from urea hydrolysis) NH_4^+.[34] In patients with end-stage kidney disease, ≥50% of the urea generated daily passes into the small bowel, where bacteria decompose it into bicarbonate and NH_4^+, which are then resynthesized to urea in the liver. Removing these 5 components via the gut could simplify KRT miniaturization engineering trade-offs. A daily 30-g oral dose of the monovalent-selective cation exchanger zirconium cyclosilicate (efficiently binding K^+ and NH_4^+) can normalize K^+ in patients with end-stage kidney disease and decrease the serum urea nitrogen level by 20%-25% (through removal of NH_4^+).[35-38] A daily 10-g dose can prevent significant hyperkalemia during interdialytic periods.[37] Combination with inorganic H^+–loaded cation exchangers and OH^-–loaded anion exchangers increases binding for Na^+, K^+, $Phos^{2-}$, H^+, and NH_4^+.[39,40] Animal studies of this oral sorbent are ongoing. Adding a hydrophobic gas-permeable coating to the cation-exchanging sorbent particles further increases NH_3 removal.[41,42]

Using the gut as a third kidney opens new perspectives. In the very long run, this approach might help simplify dialysate regeneration to apply a low-cost activated carbon block for removal of remaining organic toxins (many protein-bound), which, to a great extent, cause the actual uremia symptoms.[43-46] Easily suspended, fine-powdered, and tasteless oral sorbent might also become a "kidney support" modality during earlier chronic kidney failure stages before uremia requires KRT.

What Are the Biggest Bottlenecks?

On May 25, 1961, President Kennedy announced "the intention to land a man on the moon and safely return him to Earth before the end of the decade."[47] And the United States indeed did make that miracle happen within the same decade.

On July 10, 2019, President Trump signed the Advancing American Kidney Health executive order.[48] This executive order listed several highly needed improvements for kidney health, including the development of breakthrough technologies like wearable or implantable artificial kidneys, for which the KidneyX prize competition was

established, which leaned on the KHI innovation road map. Yet, despite this order, today, innovation is severely lagging behind the KHI road map schedule. Why?

In both cases, highly ambitious targets were set by US presidents. The essential difference is in the associated budget assignments: in 1962, the US Congress swiftly assigned $531 million to NASA, with a plan to cumulatively invest another estimated $7-$9 billion over the next 5 years.[47] Note that those were US dollars from 1962 (ie, not adjusted for inflation) all focused on a single target.

In contrast, regarding the funding of artificial kidney–related innovations, the public–private KidneyX competition, since 2019, has granted a total of $17.6 million on 76 different KidneyX prize–winning projects.[49] Of course, it is obvious that developing a moon mission is by far more costly than developing an implantable artificial kidney. However, also in 2019, a scientific analysis jointly performed by the Eastern Research Group and the US Department of Health and Human Services estimated "the overall cost of development for a complex medical device at $526.4 million after accounting for the cost of failures and the opportunity cost of capital".[50] A 2022 update of this report confirmed this order of magnitude.[51] It is thus not surprising that the implementation of the KHI innovation road map is lagging behind. The KidneyX concept is superb, but, without an appropriate budget to fuel it, progress will be limited accordingly (Fig 4).

The present situation in Europe is slightly better, but also needs drastic improvement: KIDNEW and the NXTGEN HighTech Biomed04 project, synergistically targeting an artificial kidney, have a total budget of €41 million with a run time to 2030. The European Innovative Health Initiative and Horizon Europe Health cluster should play an essential role in boosting this by including innovation in kidney therapies among Innovative Health Initiative call topics.[11]

In this context, the Malaysian government already made a wise investment with their Peritocare PD project (Fig 2E and F) that focuses on engineering issues to integrate already well-known scientific principles into a relatively simple, but nevertheless innovative, product. Instead of remaining stuck on buying PD devices, fluids, and disposables from abroad (thereby draining significant money from their national economy), they chose to finance an ecosystem that created a PD system in their own country, which was largely unnoticed until the first-in-human results were obtained. This approach (which is viable for miniaturizing single-pass PD) offers the potential to keep the money circulating in their own economy while creating high-tech jobs with future export potential.

For a far more complex product like an implantable artificial kidney, the associated challenges are exponentially bigger. Here, an even bigger bottleneck than funding arises. In 2019, Wieringa and Sheldon stated that "to succeed, the best brains in the world need to work together, and no country in the world holds all the best brains within its own borders. That is why international cooperation should be facilitated to maximize the chance of success. And here the existence of an international road map might help to get things rolling via coopetition".[4]

The good news is that many expert groups around the world know and respect each other, and most would welcome ways to somehow join forces. A research-and-development funding model that encourages international, multidisciplinary approaches to solutions and facilitates international coopetition (whereby all parties see their background intellectual property secured and shared intellectual property is jointly protected) might largely speed up the implementation of the KHI innovation road map.[52,53]

Patients across the world need access to higher-quality, more sustainable, and less costly therapies. To achieve this, patient associations should be closely involved with the international solver community, provide input in regard to standards and regulations, and actively request their governments to facilitate international coopetition.[4,52,54] Persistent patient advocacy helped to strengthen the fight against AIDS[55] and stimulated the development of wearable devices to manage diabetes.[56,57] A type 1 diabetes patient/inventor/engineer even developed his own artificial pancreas and got it CE-marked for sale in the European Union.[58] Kidney patient advocacy might follow these examples to stimulate private–public partnerships and accelerate the adoption of new KRT systems.[59]

Nephrology nurses should also be more strongly involved in the design of new KRTs, and the American Nephrology Nurses Association published an excellent methodology to achieve this.[60] The American Nephrology Nurses Association also has a dedicated Home Dialysis Therapies Task Force[61] and published a plan to combat nephrology nurse shortage.[14]

All these issues match with the Decade of the Kidney initiative, which was started by the American Association of Kidney Patients and joined by the European Federation of Kidney Patients and European Kidney Health Alliance.[62]

Article Information

Authors' Full Names and Academic Degrees: Fokko P. Wieringa, PhD, Swathi Suran, PhD, Henning Søndergaard, MSc, Stephen Ash, MD, Cian Cummins, PHD, Ashesh Ray Chaudhuri, MSc, Tugrul Irmak, PhD, Karin Gerritsen, MD, PhD, and Jeroen Vollenbroek, PhD.

Authors' Affiliations: imec, Holst Centre, Eindhoven (FPW, SS, JV), Department of Nephrology, University Medical Center Utrecht, Utrecht (FPW, TI, KG, JV), and BIOS Lab-on-a-Chip Group, University of Twente, Enschede (JV), The Netherlands; European Kidney Health Alliance Work Group 3 "Breakthrough Innovation," Brussels (FPW, HS, TI) and imec, Leuven (CC, ARC), Belgium; International Electrotechnical Commission TC62D/MT20, Geneva, Switzerland (FPW); Danish Kidney Association, Copenhagen, Denmark (HS); and Department of Medicine, Purdue University, West Lafayette, IN (SA).

Address for Correspondence: Fokko P. Wieringa, PhD, imec, High Tech Campus 31, 5656 AE Eindhoven, The Netherlands. Email: fokko.wieringa@imec.nl

Support: Drs Wieringa, Suran, Cummins, Irmak, Gerritsen and Vollenbroek acknowledge financial support from the European

Innovation Council (KIDNEW, HORIZON-EIC-2022 Pathfinder program, grant agreement no. 101099092), as well as from the Dutch national growth fund (NXTGEN HighTech Biomed04 "Artificial Organs" project). Dr Gerritsen acknowledges additional financial support from COPEDIS (DKF HealthHolland Public–Private Project, code PPS08), CORDIAL (EU HORIZON 2020, grant agreement ID 945207), and KitNewCare (Horizon-HLTH-2023-CARE-04, project 101137054). Dr Vollenbroek acknowledges that this project is part of the project MICROMERULUS with project number OCENW.XS24.1.159, which is financed by the Dutch Research Council. None of the above funders had a role in defining the content of this manuscript.

Financial Disclosure: Dr Wieringa is a technology consultant to NextKidney and in 2019 provided free-of-charge advice on regulatory and standardization aspects for the Peritocare project at the Institute of Microengineering and Nanoelectronics in Malaysia (he has no financial interest in this project). Dr Ash is coinventor of several oral sorbents described in the article and owns shares in these products. Drs Wieringa, Suran, Cummins, Gerritsen, and Vollenbroek are coinventors (but not owners) of various patents regarding innovative KRTs. The remaining authors declare that they have no relevant financial interests.

Acknowledgements: Dr Wieringa thanks the European Dialysis and Transplant Nurses Association/European Renal Care Association for their invitation to present parts of this article during their 52nd Annual Congress (Athens, Greece; September 21, 2024).

Peer Review: Received June 9, 2024, in response to an invitation from the journal. Evaluated by 4 external peer reviewers, with direct editorial input from an Associate Editor and a Deputy Editor. Accepted in revised form November 30, 2024.

References

1. Kidney Health Initiative. Technology roadmap for innovative approaches to renal replacement therapy. October 2018. Accessed October 11, 2024. https://www.asn-online.org/g/blast/files/KHI_RRT_Roadmap1.0_FINAL_102318_web.pdf
2. Salani M, Roy S, Fissell WH. Innovations in wearable and implantable artificial kidneys. *Am J Kidney Dis*. 2018;72(5):745-751. doi:10.1053/j.ajkd.2018.06.005
3. Groth T, Stegmayr BG, Ash SR, et al. Wearable and implantable artificial kidney devices for end-stage kidney disease treatment: current status and review. *Artif Organs*. 2023;47(4):649-666. doi:10.1111/aor.14396
4. Wieringa FP, Sheldon M. The Kidney Health Initiative innovation roadmap for renal replacement therapies: building the yellow brick road, while updating the map. *Artif Organs*. 2020;44(2):111-122. doi:10.1111/aor.13621
5. Mallapaty S, Kozlov M. First pig kidney transplant in a person: what it means for the future. *Nature*. 2024;628(8006):13-14. doi:10.1038/d41586-024-00879-y
6. Bowman E. The first person to receive a genetically modified pig kidney transplant has died. *National Public Radio: SCIENCE*. May 12, 2024. Accessed June 5, 2024. https://www.npr.org/2024/05/12/1250835113/pig-kidney-transplant-richard-slayman
7. Sealy A. Transplant patient stable and on dialysis after pig organ removed due to 'unique challenges' with heart, kidney health. *CNN*. May 31, 2024. Accessed June 5, 2024. https://edition.cnn.com/2024/05/31/health/pig-kidney-transplant-removal/index.html
8. Lewis T. Woman becomes first person to receive both pig kidney transplant and heart pump. *Sci Am*. April 24, 2024. Accessed June 5, 2024. https://www.scientificamerican.com/article/woman-receives-genetically-modified-pig-kidney-transplant-after-heart-pump/
9. Pereira Cabral B, Bonventre JV, Wieringa F, Mota FB. Probing expert opinions on the future of kidney replacement therapies. *Artif Organs*. 2021;45(1):79-87. doi:10.1111/aor.13784
10. Vadori M, Cozzi E. Current challenges in xenotransplantation. *Curr Opin Organ Transplant*. 2024;29(3):205-211. doi:10.1097/MOT.0000000000001146
11. Wieringa FP, Bolhuis D, Søndergaard H, et al. Transportable, portable, wearable and (partially) implantable haemodialysis systems: comparison of technologies and readiness levels. *Clin Kidney J*. 2024;17(9):sfae259. doi:10.1093/ckj/sfae259
12. Wilson L, Gress AF, Frassetto L, et al. Patient preference trade-offs for next-generation kidney replacement therapies. *Clin J Am Soc Nephrol*. 2024;19(1):76-84. doi:10.2215/CJN.0000000000000313
13. Boniol M, Kunjumen T, Nair TS, Siyam A, Campbell J, Diallo K. The global health workforce stock and distribution in 2020 and 2030: a threat to equity and "universal" health coverage? *BMJ Glob Health*. 2022;7(6):e009316. doi:10.1136/bmjgh-2022-009316
14. Brown JS, Gomez N, Harper M, Olivares R. Combating the nursing shortage: recruitment and retention of nephrology nurses. *Nephrol Nurs J*. 2023;50(1):49-53.
15. Etzo S, Collender G. The mobile phone "revolution" in Africa: rhetoric or reality? *Afr Aff (Lond)*. 2010;109(437):659-668. doi:10.1093/afraf/adq045
16. GSM Association. *The mobile economy Sub-Saharan Africa 2023*. Accessed June 5, 2024. https://www.gsma.com/solutions-and-impact/connectivity-for-good/mobile-economy/wp-content/uploads/2023/10/20231017-GSMA-Mobile-Economy-Sub-Saharan-Africa-report.pdf
17. International Air Transport Association. Passenger baggage rules. Accessed February 9, 2024. https://www.iata.org/en/programs/ops-infra/baggage/check-bag/
18. Foo MWY, Htay H. Innovations in peritoneal dialysis. *Nat Rev Nephrol*. 2020;16(10):548-549. doi:10.1038/s41581-020-0283-8
19. Htay H, Gow SK, Jayaballa M, et al. Preliminary safety study of the automated wearable artificial kidney (AWAK) in peritoneal dialysis patients. *Perit Dial Int*. 2022;42(4):394-402. doi:10.1177/08968608211019232
20. Foo MWY, Brown EA, Jain A, et al. Prepivotal study exploring safety, efficacy, and usability of the automated wearable artificial kidney (AWAK) PD device. *J Am Soc Nephrol*. 2024;35(10)(suppl). doi:10.1681/ASN.20246r4yry1n
21. Sharma S, Shamy OE, Wilmington A, et al. Performance evaluation of an automated peritoneal dialysis solution generation system in patients using automated peritoneal dialysis. *Kidney Int Rep*. 2024;9(6):1752-1757. doi:10.1016/j.ekir.2024.03.010
22. Talbot B, Davies S, Burman J, et al. The point-of-care peritoneal dialysis system early evaluation study (POC-PDEE): a pilot proof-of-principal study of the Ellen Medical devices point-of-care affordable peritoneal dialysis system. *Perit Dial Int*. 2025;45(1):52-56. doi:10.1177/08968608231209850
23. International Electrotechnical Commission. IEC 60601-2-16: 2018. Particular requirements for basic safety and essential performance of haemodialysis, haemodiafiltration and haemofiltration equipment. April 20, 2018. Accessed December 20, 2024. https://www.iecee.org/certification/iec-standards/iec-60601-2-162018
24. Iqbal Z, Moses W, Kim S, Kim EJ, Fissell WH, Roy S. Sterilization effects on ultrathin film polymer coatings for silicon-

based implantable medical devices. *J Biomed Mater Res B Appl Biomater*. 2018;106(6):2327-2336. doi:10.1002/jbm.b.34039
25. Suran S, Lindeboom L, Wieringa FP, et al. Silicon nanoporous filter technology: towards artificial kidneys. In: *Euromembrane Prague 2024:* Book of Abstracts. 2024. ; pp. 875-875. Accessed October 8, 2024. https://euromembrane2024.cz/wp-content/uploads/2024/09/Book-of-Abstracts-EuroMembrane2024-small.pdf
26. Bendine G, Autin F, Fabre B, et al. Haemodialysis therapy and sustainable growth: a corporate experience in France. *Nephrol Dial Transplant*. 2020;35(12):2154-2160. doi:10.1093/ndt/gfz284
27. Gura V, Rivara MB, Bieber S, et al. A wearable artificial kidney for patients with end-stage renal disease. *JCI Insight*. 2016;1(8):e86397. doi:10.1172/jci.insight.86397
28. Wieringa F. Die zukunft der nierenersatztherapie. *Nephrol Akt*. 2023;27(1):26-30. doi:10.1055/a-1989-4035
29. Lau TW, Bluechel C, Khaopaibul P, Tan HJ, Toh YE, Haroon S. First-in-human trial of the NeoKidney portable hemodialysis device sorbent system [abstract]. *J Am Soc Nephrol*. 2024;35(10)(suppl):41. doi:10.1681/ASN.2024r0ax6776
30. Ramada DL, de Vries J, Vollenbroek J, et al. Portable, wearable and implantable artificial kidney systems: needs, opportunities and challenges. *Nat Rev Nephrol*. 2023;19(8):481-490. doi:10.1038/s41581-023-00726-9
31. Humes HD, Buffington D, Westover AJ, Roy S, Fissell WH. The bioartificial kidney: current status and future promise. *Pediatr Nephrol*. 2014;29(3):343-351. doi:10.1007/s00467-013-2467-y
32. Kim EJ, Chen C, Gologorsky R, et al. Feasibility of an implantable bioreactor for renal cell therapy using silicon nanopore membranes. *Nat Commun*. 2023;14(1):4890. doi:10.1038/s41467-023-39888-2
33. Moyer J, Wilson MW, Sorrentino TA, et al. Renal embolization-induced uremic swine model for assessment of next-generation implantable hemodialyzers. *Toxins (Basel)*. 2023;15(9):547. doi:10.3390/toxins15090547
34. Ash SR. Sorbents in treatment of uremia: a short history and a great future. *Semin Dial*. 2009;22(6):615-622. doi:10.1111/j.1525-139X.2009.00657.x
35. Roger SD, Lavin PT, Lerma EV, et al. Long-term safety and efficacy of sodium zirconium cyclosilicate for hyperkalaemia in patients with mild/moderate versus severe/end-stage chronic kidney disease: comparative results from an open-label, Phase 3 study. *Nephrol Dial Transplant*. 2021;36(1):137-150. doi:10.1093/ndt/gfz285
36. Wadhwa NK, Kline JA, Adapa SR. The role of patiromer in delaying the onset of renal replacement therapy in patients with advanced renal failure. *Case Rep Nephrol*. 2021;2021:6987456. doi:10.1155/2021/6987456
37. Fishbane S, Ford M, Fukagawa M, et al. A phase 3b, randomized, double-blind, placebo-controlled study of sodium zirconium cyclosilicate for reducing the incidence of predialysis hyperkalemia. *J Am Soc Nephrol*. 2019;30(9):1723-1733. doi:10.1681/ASN.2019050450
38. Roger SD, Spinowitz BS, Lerma EV, et al. Sodium zirconium cyclosilicate increases serum bicarbonate concentrations among patients with hyperkalaemia: exploratory analyses from three randomized, multi-dose, placebo-controlled trials. *Nephrol Dial Transplant*. 2021;36(5):871-883. doi:10.1093/ndt/gfaa158
39. Ash SR. Oral sorbents for small, charged uremic toxins, and carbon block for regeneration of dialysate: fourth down and long. *Artif Organs*. 2023;47(1):217-221. doi:10.1111/aor.14459
40. Ash SR, Carr DJ. Oral sorbent for removing toxins of kidney failure combining anion and cation exchangers. US patent 10,668,098 B2. June 2, 2020. https://patentimages.storage.googleapis.com/ec/8a/5e/a88cf45bc9fce9/US10668098.pdf
41. Richards E, Ye SH, Ash SR, Li L. A perfluorocarbon-coated ZrP cation exchanger with excellent ammonium selectivity and chemical stability: an oral sorbent for end-stage kidney disease (ESKD). *Langmuir*. 2023;39(22):7912-7921. doi:10.1021/acs.langmuir.3c00753
42. Richards E, Ye SH, Ash SR, Li L. Developing a selective zirconium phosphate cation exchanger to adsorb ammonium: effect of a gas-permeable and hydrophobic coating. *Langmuir*. 2022;38(28):8677-8685. doi:10.1021/acs.langmuir.2c01194
43. Cornelis T, Eloot S, Vanholder R, et al. Protein-bound uraemic toxins, dicarbonyl stress and advanced glycation end products in conventional and extended haemodialysis and haemodiafiltration. *Nephrol Dial Transplant*. 2015;30(8):1395-1402. doi:10.1093/ndt/gfv038
44. Chinnappa S, Tu YK, Yeh YC, Glorieux G, Vanholder R, Mooney A. Association between protein-bound uremic toxins and asymptomatic cardiac dysfunction in patients with chronic kidney disease. *Toxins (Basel)*. 2018;10(12):520. doi:10.3390/toxins10120520
45. Sirich TL, Aronov PA, Plummer NS, Hostetter TH, Meyer TW. Numerous protein-bound solutes are cleared by the kidney with high efficiency. *Kidney Int*. 2013;84(3):585-590. doi:10.1038/ki.2013.154
46. Meyer TW, Lee S, Whitmer LC, Blanco IJ, Suba JK, Sirich TL. Increasing the clearance of protein-bound solutes by recirculating dialysate through activated carbon. *Kidney360*. 2023;4(6):e744-e750. doi:10.34067/KID.0000000000000155
47. Ostovar M. The decision to go to the moon: President John F. Kennedy's May 25, 1961 speech before a joint session of congress. *NASA History Communications*. September 22, 1998. Accessed June 5, 2024. https://www.nasa.gov/history/the-decision-to-go-to-the-moon/
48. Executive Order 13879. Advancing American Kidney Health. *Fed Regist*. 2019;84(125):33817-33819. Accessed March 27, 2024. https://www.federalregister.gov/documents/2019/07/15/2019-15159/advancing-american-kidney-health
49. KidneyX Innovation Accelerator. All KidneyX Prize Winners. Accessed June 5, 2024. https://www.kidneyx.org/prize-winners/
50. Sertkaya A, Jessup A, Devries R. Cost of developing a therapeutic complex medical device for the U.S. market. Paper presented at Harvard Center for Risk Analysis "Risk Assessment, Economic Evaluation, and Decisions" workshop; September 26-27, 2019. Accessed June 7, 2024. https://www.hsph.harvard.edu/wp-content/uploads/sites/1273/2019/09/Sertkaya-Jessup-DeVries-2019.pdf
51. Sertkaya A, DeVries R, Jessup A, Beleche T. Estimated cost of developing a therapeutic complex medical device in the US. *JAMA Netw Open*. 2022;5(9):e2231609. doi:10.1001/jamanetworkopen.2022.31609
52. Wieringa F, Søndergaard H, Ortiz A. Coordinating efforts to optimize next-generation kidney replacement therapies: the European Kidney Health Alliance work group 'breakthrough innovation.' *Clin Kidney J*. 2023;16(6):885-890. doi:10.1093/ckj/sfad016
53. Bonventre JV, Hurst FP, West M, Wu I, Roy-Chaudhury P, Sheldon M. A technology roadmap for innovative approaches to kidney replacement therapies. *Clin J Am Soc Nephrol*. 2019;14(10):1539-1547. doi:10.2215/CJN.02570319
54. Wieringa FP, Sheldon MI, Hidalgo-Simon A. Regulatory approaches to stimulate innovative renal replacement therapies. *Nat Rev Nephrol*. 2020;16(10):546-547. doi:10.1038/s41581-020-0275-8

55. Dubé K, Peterson B, Jones NL, et al. Community engagement group model in basic and biomedical research: lessons learned from the BEAT-HIV Delaney Collaboratory towards an HIV-1 cure. *Res Involv Engagem*. 2023;9(1):39. doi:10.1186/s40900-023-00449-y
56. van Bon AC, Blauw H, Jansen TJP, et al. Bihormonal fully closed-loop system for the treatment of type 1 diabetes: a real-world multicentre, prospective, single-arm trial in The Netherlands. *Lancet Digit Health*. 2024;6(4):e272-e280. doi:10.1016/S2589-7500(24)00002-5
57. Edelman S, Cheatham WW, Norton A, Close KL. Patient perspectives on the benefits and challenges of diabetes and digital technology. *Clin Diab*. 2024;42(2):243-256. doi:10.2337/cd23-0003
58. Koops R. A journey from becoming a diabetes type 1 patient to realizing a CE-marked artificial pancreas. Proc ESAO 2024. *Int J Artificial Organs*. 2024;47(7):2024:421-565. doi:10.1177/03913988241279540
59. Dember LM. What patients teach us about patient engagement in research. *Clin J Am Soc Nephrol*. 2022;17(2):176-178. doi:10.2215/CJN.16561221
60. Jónsdóttir AA, Lazo GR, Kessler LG, Smith NC, Kim JE. Nephrology nurses' perspectives for the designs of mobile hemodialysis devices: a human factors engineering approach. *Nephrol Nurs J*. 2022;46(6):481-530.
61. Bednarski D, Painter D, Pryor L, Villaran T, Walz D, Kurosaka AT. Registered nurse in home dialysis therapies and future implications. *Nephrol Nurs J*. 2023;50(1):13-21.
62. Vanholder R, Conway PT, Gallego D, Scheres E, Wieringa F. The European Kidney Health Alliance (EKHA) and the Decade of the Kidney™. *Nephrol Dial Transplant*. 2023;38(5):1113-1122. doi:10.1093/ndt/gfac211