Clinical Kidney Journal

Sustainable Nephrology TASK FORCE

Clinical Kidney Journal, 2024, vol. 17, no. 8, sfae181

https://doi.org/10.1093/ckj/sfae181
Advance Access Publication Date: 17 June 2024
Editorial Comment

EDITORIAL COMMENT

An urgent call for environmental accountability in nephrology clinical trials

Anna Julie Peired [1], Ivo Laranjinha[2], Gulay Demirtas[3], Ana Carina Ferreira [4,5], Sonja Gracin[6], Susi Knoeller[7] and Maryvonne Hourmant[8]; on behalf of the Sustainable Nephrology Task Force of the ERA

[1]Department of Clinical and Experimental Biomedical Sciences "Mario Serio", University of Florence, Florence, Italy, [2]Nephrology Department, Unidade Local de Saúde de Lisboa Ocidental, Lisbon, Portugal, [3]Department of Nephrology, University of Health Sciences, Antalya Training and Research Hospital, Antalya, Turkiye, [4]Department of Nephrology – Hospital Curry Cabral – ULS São José, Lisbon, Portugal, [5]Nova Medical School, Lisbon, Portugal, [6]Transplantation Centre, University Hospital Sahlgrenska, Gothenburg, Sweden, [7]Department of Nephrology and Transplantation, GesundheitNord, Klinikum Bremen Mitte, Bremen Germany and [8]Service de Néphrologie et Immunologie Clinique, University Hospital of Nantes, Nantes, France

Correspondence to: Anna Julie Peired; E-mail: annajulie.peired@unifi.it

The carbon footprint (CF) of the healthcare sector is estimated to account for 4.4% of the total world emissions of carbon dioxide equivalent (CO_2e) [1]. Clinical trials (CTs) play a substantial role in knowledge and innovation, but require important human and material resources. Despite increasing global concern for environmental sustainability, few studies have assessed the environmental impact of CTs and the strategies to mitigate their effects [2]. All available reports emphasize the substantial CO_2e emissions associated with CTs, yet just one specifically addresses nephrology trials. Recognizing this knowledge gap, the ERA Sustainable Nephrology Task Force (SNTF) calls for urgent attention and action to introduce sustainability in nephrology CTs.

In 2021, there were 350 000 CTs registered on ClinicalTrials.gov, resulting in 27.5 million tonnes CO_2e emissions (over 78 tonnes CO_2e per CT) [2]. Estimates from the Sustainable Healthcare Coalition suggest that CT emissions could reach 100 million tonnes CO_2e per year.

Pharmaceutical companies increasingly commit to measuring and curbing the CO_2e emissions of their CTs. Two industry-sponsored studies have been published—the first estimated the CO_2e emissions from all in-scope activities involved in a phase 1 CT to be over 17 tonnes CO_2e [3]. Travel and study site activities were the main contributors. The authors describe opportunities for CO_2e reductions, such as decentralized CT sites and a shift of sponsor employees and study participants to electric vehicles. The second study reported the life cycle assessment (LCA) of three multicenter randomized CTs (mrCTs) [4]. They evaluated the CF of each CT (ranging from 1437 to 2500 tonnes CO_2e), and determined the main factors driving emissions, notably travel and trial site management, transport of study drugs to trial sites and sample life cycle (sample collection, shipment, analysis and storage, manufacturing and distribution of laboratory kits). Furthermore, the study delineated strategies for reducing CF, such as minimizing unused stored samples and study drug or material, while also establishing a replicable framework.

Despite the complexity of CT management, several studies have demonstrated the possibility of reducing CO_2e emissions.

Received: 17.5.2024; Editorial decision: 16.6.2024

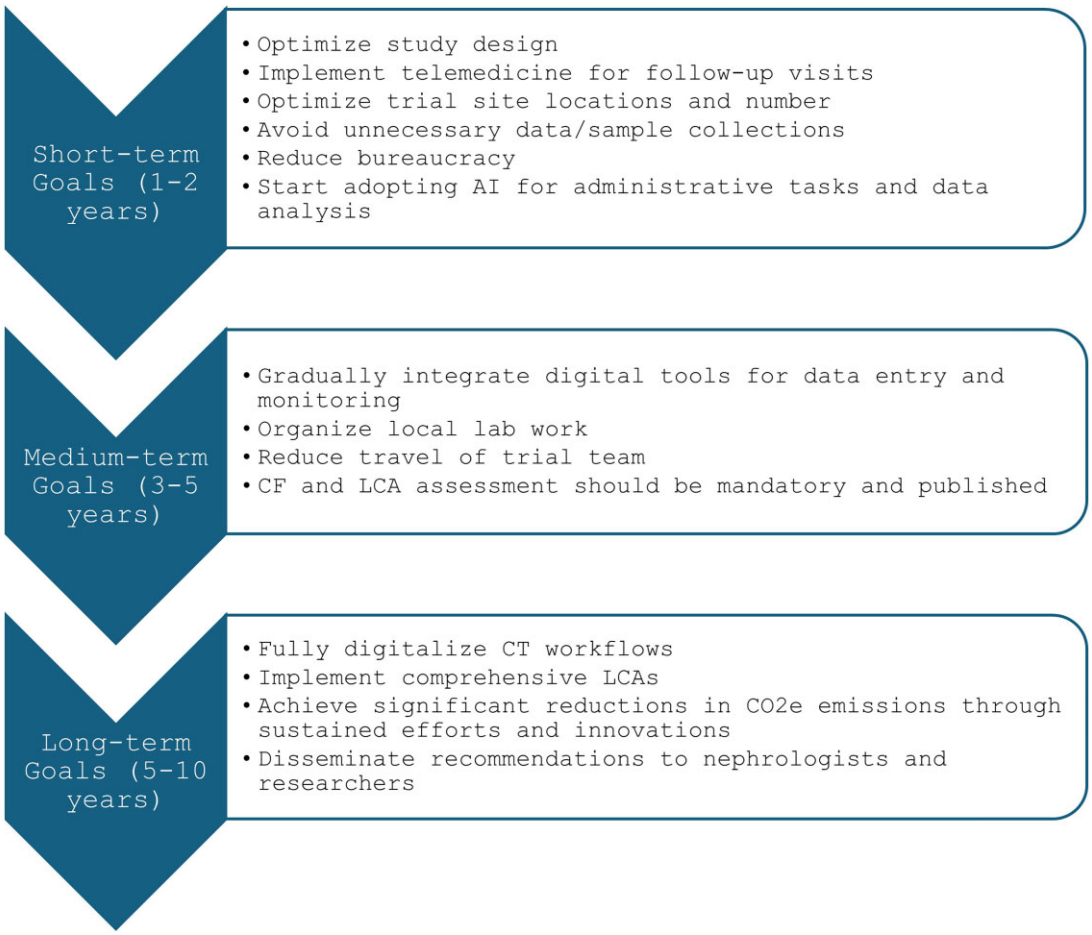

Figure 1: Roadmap for improving the CF of nephrology CTs.

Clinical Randomisation of an Antifibrinolytic in Significant Haemorrhage (CRASH)-1 and CRASH-2 are two international mrCTs with similar design [5]. In CRASH-2, efforts to reduce CO_2e emissions resulted in a 45% overall decrease and a 73% decrease per patient. These efforts, based on the strategies outlined in the National Institute for Health and Care Research (NIHR) carbon reduction guidelines, include faster patient recruitment, lighter trial materials (resulting in lower CO_2e emission arising from shipment) and direct data entry.

The only nephrology CT evaluating CF was the NightLife study, an mrCT assessing the impact of in-center nocturnal hemodialysis on quality of life [6]. Interestingly, the CF decreased when the study had to be reorganized because of the COVID-19 pandemic. A saving of 136 tonnes of CO_2e was obtained by installing remote conferencing, eliminating every travel and promoting teleworking. Innovative data collection methods were implemented, such as virtual interviews using common conference software programs and "photovoice."

Nephrology CTs face unique challenges stemming from the specific nature of kidney diseases. Indeed, successful trials would require recruitment of a large number of patients across multiple sites, leading to longer study durations and increased logistical complexity. As many kidney diseases have a progressive course, long-term follow-up is required to assess disease progression, treatment efficacy and safety. Moreover, most nephrology trials include drug interventions [7], and drugs are major contributors to CO_2e emissions. Due to the risk of medication overdose resulting from impaired renal function, patients require more frequent monitoring. This complexity, together with the multipathological state of patients, makes it challenging for nephrology trials to be environmentally friendly, and necessitates a tailored framework for assessing their CF [8].

Based on published studies, practical steps could be implemented, such as optimization of trial site locations and numbers, avoiding unnecessary data/biological sample collection, favoring local lab work to avoid shipping biological samples, and reducing travel for both patient and the trial team (Fig. 1). A systematic assessment of existing evidence concerning the objective of the study, as recommended by the NIHR guidelines in 2019, would allow excluding studies lacking significance and novelty [2]. Novel trial designs, such as those employed in basket and umbrella trials, evaluate targeted therapies across multiple diseases or assess multiple therapies for a single disease. These approaches shift the focus from specific interventions for a single disease, to evaluating multiple interventions concurrently [9]. This methodology has the potential to enhance the current framework of CTs by reducing time, complexity and costs, consequently lowering the CF of the CTs. Another strategy involves the full digitiziation of the workflow. Supported by The Sustainable Markets Initiative Health Systems Task Force, a collaboration of public and private entities including major pharmaceutical companies, this

approach advocates for digital integration from study design to site selection, participant enrollment, monitoring and management and data analysis. As proposed by CT organizers themselves, we are convinced that full digitalization will be mandatory in the coming years. The cloud-based electronic health record system Epic is already widely used in the USA and Canada, offering features like patient engagement, telehealth, interoperability and extensive medical record management. Digital tools offer efficiency gains and resource savings, but challenges such as managing exchanges of large data volume, logistical complexities, lack of interoperability, ingrained cultures and behaviors, cost of digital solutions and regulatory hurdles must be addressed. As on-site patient visits will be replaced with telemedicine, there will be an increased need for the shipment of biological samples and medications to and from participants' home. Despite these obstacles, the potential benefits of digitalization in reducing environmental impact are substantial.

The integration of artificial intelligence (AI) in clinical nephrology could improve diagnostic accuracy and treatment outcomes, contribute to CT efficiency, costs reduction and improve patients' experience [10]. AI could improve the sustainability of nephrology CT through: the automatization of administrative tasks, saving time for healthcare workers; analysis of complex data in a shorter amount of time with greater precision; use of digital twins (virtual patient modeling to predict outcomes and enroll suitable candidates); and remote monitoring of vital signs and anthropometric data connected to decision algorithms; and speeding up the CT workflow. AI and machine learning techniques have been developed to predict the progression of chronic kidney disease (CKD), offering opportunities for timely intervention and personalized management strategies. Although AI utilizations in healthcare hold promise, they remain relatively nascent and underused. Thus, it is crucial to carefully evaluate the balance between AI positive advancements and its negative environmental impact. Indeed, CO_2e emissions are present throughout its life cycle—from programming and development to use—due to high energy and resource demands alongside the risk of exacerbating climate and environmental injustices by perpetuating existing inequalities in resource access and opportunities.

The world of clinical research is changing and pharmaceutical companies, international organizations and regulatory bodies are stepping in to make CTs more sustainable (https://www.clinicalleader.com/doc/the-current-state-of-sustainability-in-clinical-trials-0001). Of note, the Innovative Health Initiative, a partnership between the EU and various European industry associations, aims to drive health research innovation and fund projects addressing environmental concerns. Similarly, the Accelerating Clinical Trials in the EU (ACT EU) initiative, by the European Medicines Agency, the European Commission and the Heads of Medicines Agencies, focuses on transforming CT processes and prioritizing actions to make trials more sustainable.

Since 2020, the Coalition for Reducing Bureaucracy in Clinical Trials, a broad cross-disciplinary coalition of medical societies and patient advocates, has issued recommendations to make CTs less bureaucratic and more patient-centered, efficient and cheaper. The proposed measures, including digitalization and streamlining processes, and harmonization of requirements, aim to reduce administrative burdens and improve protocol design, contributing to lower environmental impact. EASi-KIDNEY is an mrCT testing a new drug to treat patients with CKD, starting in 2024. This is the first nephrology CT to apply some of the recommendations of the Coalition.

In addition, policymakers should implement measures that require a mandatory LCA when investigating a new drug, as well as CF assessment to be included in grant and CT applications. Journals could also mandate reporting of the CF of published trials, with the quantification of the CF of interventions and comparators, alongside a discussion of whether the knowledge gained justifies the carbon consumed [2]. Additionally, CF and LCA should become mandatory in trials comparing therapeutic strategies, either as secondary objectives or as ancillary studies, like medico-economic studies (months of dialysis avoided, CO_2e, waste and water saved, etc.). Further efforts should focus on the dissemination of recommendations to nephrologists and researchers, who should advocate for sustainability in CTs, requiring a sustainable approach from the industry in the management of CTs.

Implementing sustainability measures may entail initial costs, which can be mitigated through long-term savings from reduced travel and shipping expenses, support from funding bodies for sustainability initiatives, and efficiency gains achieved via digital tools and AI.

With the present call, the SNTF urges the nephrology community to pledge sustainable CTs, recognizing the pressing need to understand and mitigate their environmental impact. A collective effort from nephrologists, researchers, pharmaceutical companies, industry partners, research and medical institutions, and funding bodies is essential to raise awareness and prioritize sustainability in CTs. Encouraging the sharing of best practices and the establishment of a collaborative platform for ongoing research and knowledge exchange is crucial. Finally, addressing the CF of CTs is not only an environmental imperative, it also aligns with ethical considerations in patient care, as environmental degradation is deeply intertwined with patient health.

ACKNOWLEDGEMENTS

The Sustainable Nephrology Task Force is an official body of the ERA.

AUTHORS' CONTRIBUTIONS

A.J.P. and M.H. wrote the manuscript. I.L., G.D., A.C.F., S.G. and S.K. were responsible for the critical revision of the manuscript. The final version of the manuscript was seen and approved by all authors.

CONFLICT OF INTEREST STATEMENT

A.C.F. is member of the *CKJ* Editorial Board.

REFERENCES

1. Pichler PP, Jaccard IS, Weisz U *et al*. International comparison of health care carbon footprints. *Environ Res Lett* 2019;**14**:064004.
2. Adshead F, Al-Shahi Salman R, Aumonier S *et al*. A strategy to reduce the carbon footprint of clinical trials. *Lancet* 2021; **398**:281–2. https://doi.org/10.1016/S0140-6736(21)01384-2
3. LaRoche JK, Alvarenga R, Collins M *et al*. Climate footprint of industry-sponsored clinical research: an analysis of a phase-1 randomised clinical study and discussion of opportunities to reduce its impact. *BMJ Open* 2024;**14**:e077129. https://doi.org/10.1136/bmjopen-2023-077129

4. Mackillop N, Shah J, Collins M *et al.* Carbon footprint of industry-sponsored late-stage clinical trials. *BMJ Open* 2023;**13**:e072491. https://doi.org/10.1136/bmjopen-2023-072491
5. Subaiya S, Hogg E, Roberts I. Reducing the environmental impact of trials: a comparison of the carbon footprint of the CRASH-1 and CRASH-2 clinical trials. *Trials* 2011;**12**:31. https://doi.org/10.1186/1745-6215-12-31
6. Quann N, Burns S, Hull KL *et al.* Reducing the carbon footprint of research: experience from the NightLife study. *BMJ Open* 2023;**13**:e070200. https://doi.org/10.1136/bmjopen-2022-070200
7. Inrig JK, Califf RM, Tasneem A *et al.* The landscape of clinical trials in nephrology: a systematic review of Clinicaltrials.gov. *Am J Kidney Dis* 2014;**63**:771–80. https://doi.org/10.1053/j.ajkd.2013.10.043
8. Griffiths J, Fox L, Williamson PR. Quantifying the carbon footprint of clinical trials: guidance development and case studies. *BMJ Open* 2024;**14**:e075755. https://doi.org/10.1136/bmjopen-2023-075755
9. Kotwal S, Perkovic V, Heerspink HJL. Platform clinical trials within nephrology-interpreting the evidence. *Am J Kidney Dis* 2022;**80**:143–6. https://doi.org/10.1053/j.ajkd.2022.01.430
10. Askin S, Burkhalter D, Calado G *et al.* Artificial Intelligence applied to clinical trials: opportunities and challenges. *Health Technol* 2023;**13**:203–13. https://doi.org/10.1007/s12553-023-00738-2

Received: 17.5.2024; Editorial decision: 16.6.2024