

it does not encompass broader ecological aspects. Therefore, emissions estimates are likely underrepresented and the total ecological impact will be even higher (17, 20). Further progress can then be made in accordance with the strategies set out in various guidance documents.

In the context of the above-mentioned information, digital and decentralized clinical trial (DCT) models should offer one of the most effective approaches for reducing carbon emissions. Kohl et al. estimate that typical paper-based study can lead to approximately 4,885 kg of CO₂; transitioning to a fully digitized clinical trial can reduce emissions by approximately 90%. Digitization alone (by migrating informed consent forms, forms and questionnaires, case report forms, and essential documents such as master files and site files to electronic platforms) can eliminate the need for vast amounts of paper – up to 164,800 sheets of paper in an average clinical trial (equivalent roughly to a stack of paper higher than 16 metres and 799 kg CO₂) (21). Decentralization facilitates remote data collection by allowing participants to complete some study procedures without travelling to clinical trial sites, with telemedicine consultations replacing in-person visits. This model not only reduces emissions – an estimated 237 kg of CO₂ emissions per an average clinical trial with 9 visits – but also decreases the time and financial burden placed on participants. Remote physiological monitoring (e.g., blood pressure or heart rate) can be performed using digital health technologies and wearables, offering additional benefits such as longitudinal monitoring, monitoring in real-world environments, and immediate transmission to investigators. Biological samples, such as saliva, stool or urine, can be collected via courier services and delivered directly to laboratories, while the sample-collection materials can be sent directly to participants. Clinical research associates can likewise conduct site oversight remotely through virtual meetings. It can save an additional 3,808 kg of CO₂ per average clinical trial with five monitoring visits of each of ten centres by car depending on travelling distance (16, 21, 22). Beyond these approaches, other emerging trends (e.g., integration of artificial intelligence for trial optimization, increa-

sed use of real-world data, virtual clinical trials) can be expected to further enhance both the efficiency and environmental performance of clinical trials.

However, DCT models introduce new forms of energy demand – computer and server operation, digital communication, etc. Kohl et al. provided approximate estimates of these alternative sources of emissions: energy needed for filling out questionnaires on computers or smartphones (counted as 1 minute per page), video consultations (approximately 1 hour with each centre), email communication (estimated at 12 per participant), and server operation (assuming 0.04 kW/h) for maintaining the trial platform over a 2-year period. In total, these activities generate an estimated 486 kg of CO₂, which is still substantially less compared to the traditional clinical trial (21). DCTs also support inclusivity, even though disparities in digital literacy, variability in internet access, device validation requirements to bring accurate results, and the need for robust data protection frameworks pose additional challenges (23, 24). Higher initial costs for digital health technologies, alongside other challenges (e.g., resistance from clinical sites, regulatory uncertainties, the need for staff training and infrastructure adaptation) can be another issue. However, ultimately, DCTs have the potential to yield long-term cost savings (16).

An illustration is provided by the PROMOTE study, a DCT conducted during the Covid-19 pandemic among pregnant women. The decentralized design reduced the environmental burden from approximately 123.9 kg of CO₂ to 3 kg of CO₂ (a 41-fold reduction). In addition, the decentralized design improved participant recruitment (22).

Regulatory framework, initiatives, and education in the field of “green” clinical trials

Although many countries have committed to achieving net zero by 2050, sustainability considerations for clinical trials are not incorporated in their regulatory frameworks or requirements. Major bodies acknowledge the importance of clinical trial sustainability and have begun to work on guidelines to promote more efficient and lower-carbon trial

design (25). However, the absence of binding legal framework means that “greener” trial practices still remain voluntary. Unfortunately, even the ethics committees have not yet received guidelines on how to properly formulate recommendations and assess environmental aspects in clinical trials (25, 26).

Multiple groups and activities are emerging to advance environmental sustainability within clinical research. The *Sustainable Healthcare Coalition* plays a central role in accelerating and amplifying decarbonizing action (27). The strength of their voice in this area is demonstrated by the fact that they were invited to collaborate with the global platform of *Sustainable Markets Initiative* (SMI) (16, 18, 28, 29). Similarly, the *Institute of Cancer Research* (ICR), in collaboration with the NIHR and the UK Clinical Research Collaboration (UKCRC), is actively integrating sustainability principles into healthcare and clinical trial designs (30). SMI and ICR are both part of the *iLCCT consortium* that developed the clinical trials carbon calculator (18, 19). The Medical Research Council and National Institute of Health and Care Research (MRC-NIHR) Trial Methodology Research Partnership has established the *Greener Trials Group* which shares methodologies for reducing emissions, waste, and water use in clinical trials or provides guidance for carbon footprint estimation. Their online resources represent one of the most comprehensive repositories currently available (20, 30, 31). The *Breast International Group* (BIG) is another group active in this field, organizing events to discuss challenges ranging from CO₂ emissions in cancer research to climate-related disruptions of clinical trial operations (32). The Health Research Board of the Trials Methodology Research Network (HRB-TMRN) discussed sustainable clinical trials in their online conference, too (33).

These examples illustrate only a subset of the efforts currently devoted to sustainability in clinical trials. It is encouraging that sustainable clinical research has been gaining increasing recognition. Although many of the above-mentioned groups are primarily based in the UK, they maintain international collaborations and outreach.

Unfortunately, there remains a notable lack of comprehensive, structured training