Journal of Clinical Epidemiology 181 (2025) 111733

Journal of Clinical Epidemiology

ORIGINAL RESEARCH

Carbon emissions associated with clinical trials: a scoping review

Frank You[a,*], Taylor Coffey[a], Daniel Powell[b], Paula R. Williamson[c], Katie Gillies[a]

[a]*Aberdeen Centre for Evaluation, University of Aberdeen, Aberdeen, UK*
[b]*Health Psychology, Institute of Applied Health Sciences, University of Aberdeen, Aberdeen, UK*
[c]*Department of Health Data Science, University of Liverpool, Liverpool, UK*

Accepted 18 February 2025; Published online 22 February 2025

Abstract

Objectives: To review and synthesize available evidence on carbon emissions associated with clinical trials to inform future research on design and delivery of greener trials.

Study Design and Setting: We performed a scoping review by following the Joanna Briggs Institute guidance and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews. A systematic search was conducted on MEDLINE (Ovid) from January 1, 2007, to April 15, 2024, with no geographic and language restrictions complemented by forward and backward citation analysis (snowballing). We included all types of research literature within the context of clinical trials reporting any aspect related to trial specific carbon emissions.

Results: Twenty-two articles were identified as eligible and included in the review. Most included studies (n = 17, 77%) were published between 2020 and 2024. Over half of the included studies (n = 13, 59%) were primary research articles with the majority reporting carbon audits of trials and their associated processes. The remaining literature comprised secondary studies (n = 3, 14%) and opinion pieces (n = 6, 27%). Diverse and evolving approaches to studying trial-related carbon emissions were identified alongside several carbon hotspots including those associated with trial-related travel, trial facilities, and sample lifecycle.

Conclusion: The literature on carbon emissions associated with clinical trials has focused on studies reporting carbon audits of trials and their associated processes. Efforts have been made to quantify the trial carbon output with variability in methods and carbon output. Despite the development and evolution of carbon measurement tools, strategies to mitigate trial specific carbon emissions are still much in need.

Keywords: Carbon footprint; Clinical trials; Trials methodology; Greener trials; Scoping review; Environmental sustainability

1. Introduction

Clinical trials are a cornerstone of evidence-based medicine and health care. By evaluating the safety, efficacy, and potential benefits of medical interventions with scientific rigor, clinical trials provide evidence to advance medical knowledge [1,2]. The evidence generated from clinical trials enables health-care professionals and policymakers to make informed decisions about patient care, improving personal and public health outcomes [3].

However, clinical trials have unintended environmental impacts, particularly in terms of their carbon footprint, commonly measured in carbon dioxide equivalent (CO_2e) [4–6]. In 2007, the Sustainable Trials Study Group (‘‘the Group’’ comprised clinical researchers and trialists) concluded that clinical trials had substantial carbon emissions [4]. By measuring the carbon footprint of the Corticosteroid Randomisation After Significant Head Injury (CRASH-1) trial (an international multicenter trial evaluating the effect of corticosteroids on patients with brain

Funding: This project is supported by funding from MRC TMRP DTP (MR/W006049/1). Paula R Williamson is supported by funding from NIHR (NIHR163807).

* Corresponding author. Aberdeen Centre for Evaluation, University of Aberdeen, 3rd Floor, Health Sciences Building, Foresterhill Campus, Aberdeen, AB25 2ZD, UK.

E-mail address: s.you.23@abdn.ac.uk (F. You).

https://doi.org/10.1016/j.jclinepi.2025.111733

Plain Language Summary

Clinical trials are important to the development of medicine and health care but they have great unintended environmental impacts, especially in the form of carbon emissions. We looked at the literature to understand how carbon emissions generated by clinical trials were measured, which components across trials were carbon heavy, and what could be done to reduce the carbon output of clinical trials. We found 22 relevant articles of which 13 were primary research studies. Twelve of these primary studies measured carbon output of a range of trials. Their results varied considerably because of the variability of a host of factors, such as the number of trials analyzed, trial duration, geographical scope, trial processes measured and methods for quantifying carbon emissions. Despite varied definitions of carbon hotspots, several trial activities, including trial-related travels and meetings, trial facilities, and sample and laboratory activities, were found to be carbon heavy across studies. The remaining primary research surveyed the awareness of trial carbon impact. The rest of the 22 articles consist of three secondary research studies and six opinion papers. All of them called for attention to the carbon emissions of clinical trials and offered recommendations for reducing the carbon footprint of trials. This review identified evidence that was dedicated to measuring carbon footprint of clinical trials. Despite the challenge to compare their results because of their different approaches to carbon measurement, several carbon intensive trial processes were found to be common across studies. We still require research on how to minimize the carbon output of clinical trials.

injuries), the Group identified the energy consumption of research premises and distribution of interventions (ie, drugs) and delivery of trial documents to hospitals as carbon intensive. Other processes across the trial lifecycle, such as trial-related travel and trial team commuting, also left a large carbon footprint [4]. The Group calculated that the 5-year CRASH-1 trial had accounted for 630 tonnes of CO_2e. To put this figure in perspective, it is equivalent to the annual carbon footprint of 105 UK citizens [5] or the greenhouse gas emissions of 383 return flights from London to New York [6,7].

By measuring the carbon emissions of a single trial, the Group began to highlight the issue but not the scale of problem. A subsequent carbon audit of 12 randomized controlled trials (RCTs) estimated an average carbon output of 78.4 tonnes of CO_2e per trial [8]. By the end of 2023, a total of 477,237 trials had been registered on ClinicalTrials.gov [9]. Assuming each of these trials generated a similar carbon output, they have potentially accounted for over 37 million tonnes of CO_2e which was close to the carbon footprint of Norway's annual energy consumption [10]. As the number of clinical trials continues to rise, their associated unregulated carbon emissions are likely to escalate and worsen human-induced climate change [11−13]. It is, therefore, imperative to ensure patient-acceptable and efficient conduct of clinical trials without unnecessary carbon output.

Since the publication of the carbon audit of CRASH-1, a small number of key research studies have been conducted on the carbon output of trials [14,15]. The previously mentioned carbon audit of 12 trials identified carbon intensive areas within trials where carbon reduction measures could be taken (eg, study centers' fuel use and trial team related travel) [8]. These results directly informed the UK's National Institute for Health and Care Research (NIHR) Carbon Reduction Guidelines, first published in 2010, which provided guidance on carbon reduction in all research types, not just trials [16]. More recently, there has been interest in developing standardized carbon tools for quantifying the carbon footprint of clinical trials [17,18]. With the growing interest and need to design and deliver greener trials, methodological research in the area is considered a priority [14].

Despite the growing interest and concern about the carbon emissions associated with clinical trials, publications of research evidence in this area have been slow to emerge. Relevant studies and evidence remain fragmented. A systematic synthesis of the evidence is, therefore, required to establish a knowledge base that will inform the direction of future research on the design and conduct of greener trials. A scoping review is considered most appropriate to serve this purpose. Conventional approaches to evidence synthesis, such as systematic reviews, usually evaluate the quality of evidence to confirm or refute a current practice of a rather well defined and established area [19]. A scoping review, in contrast, maps and summarizes the breadth and extent of available evidence across a heterogeneous research body in a research field, especially an emerging one, like greener trials [19−21]. A scoping review is particularly useful for examining how research is conducted on a certain field [19]. It also illuminates where research gaps are and whether a systematic review with a meta-analysis is required as a next step [19,20].

The aim of this scoping review was to establish an evidence base to inform the methodological development for the design and delivery of greener trials.

What is new?

Key findings

- Most primary studies identified focused on quantifying the carbon footprint of clinical trials.
- There is variability of methods in quantifying trial-related carbon emissions across included studies.
- Common carbon hotspots associated with clinical trials include trial-related travel, trial facilities, and sample lifecycle.

What this adds to what is known?

- There is heterogeneity in tool development and application for measuring carbon in clinical trials.

What is the implication and what should change now?

- Interventions for reducing trial-related emissions are lacking.
- Behavioral science may offer insight in developing trial specific carbon mitigation strategies.

The objectives of this review were to

i. Identify and describe the extent of evidence that explored any aspect of carbon emissions associated with clinical trials including both the delivery of trial processes (eg, trial centers'/units' energy consumption, patients' trial-related travels) and the development/production of interventions (eg, manufacturing of placebos) beyond standard care;
ii. Identify research gaps across relevant studies and propose recommendations to inform future methodological research on greener trials.

2. Methods

This review followed the framework of the Joanna Briggs Institute guidance for scoping reviews [22] and is reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension for Scoping Reviews [23]. A protocol specifying the review's objectives and methods was developed and registered on the Open Science Framework Registry on 4 April 2024 (https://osf.io/hgu34) [24].

2.1. Eligibility (inclusion/exclusion) criteria

This review adopted the Participant, Concept, Context (PCC) approach for developing eligibility criteria. We included research literature that met the following PCC criteria in this scoping review.

2.1.1. Participants

Participants, in this review, refer to studies that align with our review objectives. All types of literature that explored environmental impacts of carbon emissions associated with clinical trials, regardless of the trial type (eg, explanatory and pragmatic), phase, duration, scale, and source of funding, were included.

2.1.2. Concept

Exploration of trial-related carbon emissions included, but was not limited to, quantifying and measuring output of carbon dioxide generated from trial-related activities, trial teams' experiences of reducing carbon output of trials, or recommendations to address the carbon emissions associated with clinical trials.

2.1.3. Context

All settings (eg, countries, publicly or industry-funded projects) related to the design, conduct, analysis, and reporting of clinical trials were considered.

We considered all study types (eg, primary and secondary research) and designs (eg, qualitative, quantitative, and mixed methods) that met the inclusion criteria. We also considered commentaries, editorials, letters, and opinion papers published in peer-reviewed journals and unpublished studies from preprint servers.

We excluded studies or articles that were published before the publication of the Group's carbon audit on the CRASH-1 trial in January 2007 [4].

2.2. Search strategy

A search strategy was developed by the lead author (F.Y.) in consultation with an information scientist and encompassed two main concepts. The first was ''environmental impact'' comprising terms such as ''carbon footprint'' and ''environmental sustainability'' as inspired by previous studies on assessing environmental impacts of health technology [25,26]. The second concept was ''clinical trial'' and its associated terms. These two concepts guided our literature search in MEDLINE (Ovid). The search strategy also employed controlled terms, such as Medical Subject Headings wherever applicable in the database, and keywords. A list of the search terms and complete search strategy is presented in Appendix I. Our search strategy aimed to locate relevant literature from the publication of the carbon audit of CRASH-1 from January 1, 2007, to April 15, 2024. There were no restrictions on language and place of publication.

In addition, a snowballing approach developed by Claes Wohlin was adopted to complement the literature search [27]. Snowballing referred to systematically identifying additional papers of interest by examining where included

studies had been cited. Snowballing enabled identification of relevant papers using different terminology on the same subject which might likely be missed by the search on databases [27]. Once the included studies from the database search were determined, an alternate process of backward (ie, examining reference lists of the included studies for additional papers) and forward snowballing (ie, identifying additional papers citing the included studies) was iterated for three rounds using Google Scholar (https://scholar.google.co.uk) between May 13, 2024, and May 27, 2024. Duplicated papers discovered during the iteration were removed.

Two preprint servers for health sciences, medRxiv, and bioRxiv, were searched for unpublished papers relevant to our review objectives. Studies shared by members of the Medical Research Council National Institute for Health and Care Research Trials Methodology Research Partnership (MRC NIHR TMRP) ''Greener Trials'' subgroup were also sourced in the literature search. Given the coverage of the literature search, complemented by the snowballing approach and the aforementioned reference sources, we considered the gray literature search on Google Scholar as initially presented in the review protocol unnecessary [24].

2.3. Record screening and selection

Titles and abstracts of the identified articles from the database search were collated and imported into EndNote (web version) and transported into Rayyan, a web-based app for systematic reviews, for screening [28,29]. Duplicates were removed manually before one reviewer (F.Y.) started screening the abstracts according to the inclusion/exclusion criteria. A select 10% of the abstracts were reviewed by another team member (K.G.) for eligibility. Discrepancies were discussed and settled between the two reviewers. Full-text screening of potentially eligible papers was undertaken by F.Y. with two other members (K.G. and T.C.) clarifying uncertainties until a consensus was reached by discussion.

Once the eligible articles had been identified for inclusion, F.Y. performed the snowballing search on the included articles. Titles and abstracts of the papers collected from the backward and forward snowballing were screened against the eligibility (inclusion/exclusion) criteria. Those fitting the inclusion criteria were examined in full text before they were determined to be included for this scoping review. The result of three iterations of the snowballing was reviewed by K.G. and T.C. Any disagreement over the screening result was resolved through discussion among the three reviewers. F.Y. performed abstract and title screening on articles sourced from medRxiv and bioRxiv.

2.4. Data extraction

F.Y. extracted relevant data using a data extraction form developed from the template of the ''Data collection form for intervention review – RCTs and non-RCTs'' [30]. A pilot data extraction on three included studies of different designs was performed by F.Y. and reviewed by K.G. and T.C. The data extracted from each article included author(s), year

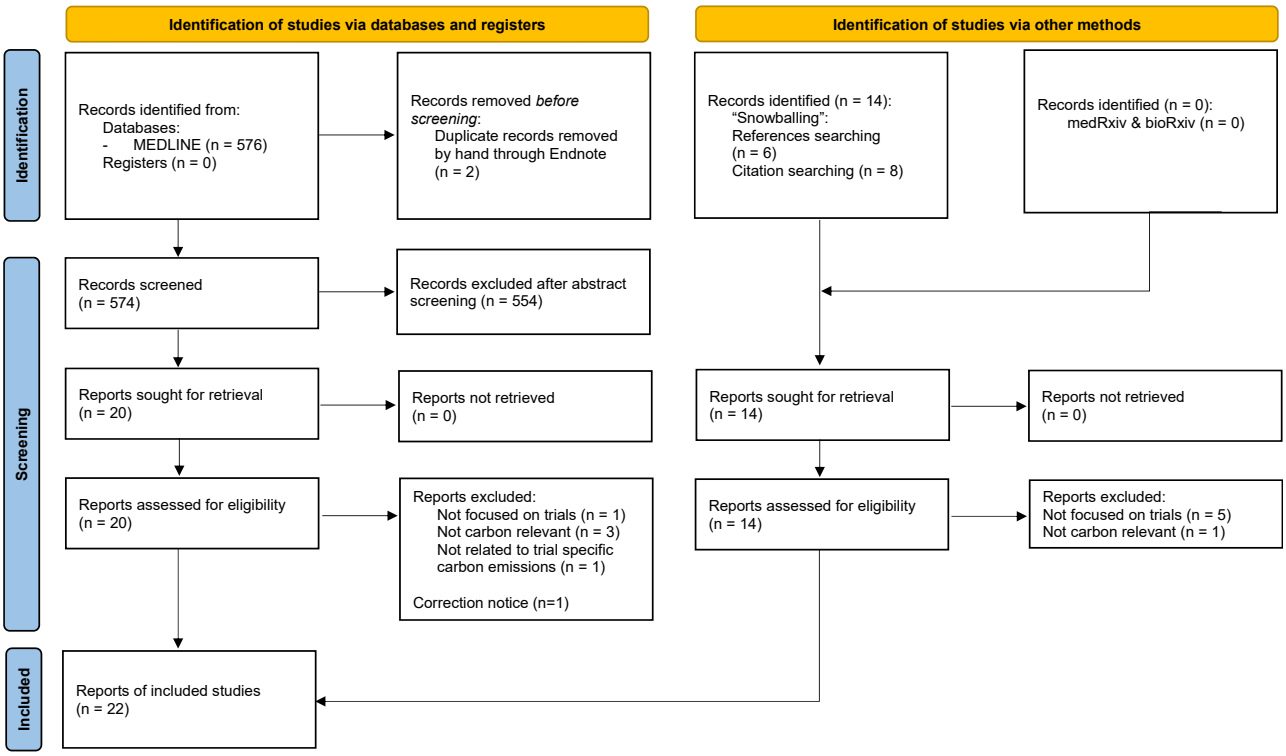

Figure 1. PRISMA diagram. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

and journal of publication, type of evidence source, country of origin, language of publication, study aim, and sample size, where appropriate. Key findings related to the scoping review objectives, such as trial-specific carbon emissions reported in the study outcomes, sources of carbon output within trials, limitations of the study, and recommendations to address the carbon impacts of clinical trials as proposed in the study, were also extracted and summarized.

2.5. Data analysis and presentation

Data relating to the study characteristics of the included articles were summarized with descriptive statistical analysis and presented in a chart. Narrative synthesis was conducted to summarize findings related to the review objectives. No quality assessment of the included articles was conducted since this scoping review was to understand the breadth of the emerging evidence regarding the carbon emissions linked to clinical trials, not to critique the quality of included articles.

3. Results

The PRISMA diagram (Fig 1) represents the results of the screening process to identify eligible articles. The database search yielded 576 articles. After removing two duplicates, 574 remaining titles and abstracts were screened with 20 articles retrieved for full-text screening. The full-text screening resulted in 14 articles meeting the eligibility criteria. An additional 14 articles were identified during snowballing, of which eight fulfilled the eligibility criteria. In total, 22 articles met the eligibility criteria for inclusion of this review and for further data extraction.

3.1. Summary of study characteristics

Most of the included studies (n = 17, 77%) were published within the last 5 years (Fig 2). Nearly half of the included studies were authored by researchers based in the UK (n = 9, 41%) followed by international teams led mostly by countries in the global north (e.g., Canada) (n = 6, 27%). The authors of the remaining studies were based in Australia (n = 2, 9%), Switzerland (n = 2, 9%), India (n = 1, 4%), and the US (n = 1, 4%). One included article did not report where the author was based or affiliated to. All included studies were published in English.

3.2. Types of research

More than half of the included studies reported on original research generating primary data (n = 13, 59%). The remaining studies encompassed secondary research papers (n = 3, 14%) and other literature types that comprised mainly commentaries and opinion papers (n = 6, 27%).

Almost all included primary research articles (n = 12, 92%) quantified the carbon emissions of clinical trials in terms of CO_2e from at least one trial process [4,8,15,17,18,31–38]. The remaining primary research study reported an international survey investigating whether academic and government research bodies were aware of and were taking action to reduce the carbon footprint of their clinical trials [39].

The secondary research articles comprised one literature review on the carbon footprint of clinical trials [40], one gap analysis that argued the need to take environmental impacts in the design and execution of decentralized clinical trials into account [41], and one secondary data analysis that sought to link qualitative data on patients' decision-making factors in recruitment and retention to carbon sources in clinical trials [42].

Nearly all remaining included articles, mainly comprising commentaries and opinion papers, argued for the urgency to address trial-related carbon emissions in relation to climate change (n = 5, 83%) [14,43–46]. Most of them proposed carbon reduction recommendations for designing and conducting trials. One additional study reflected on how

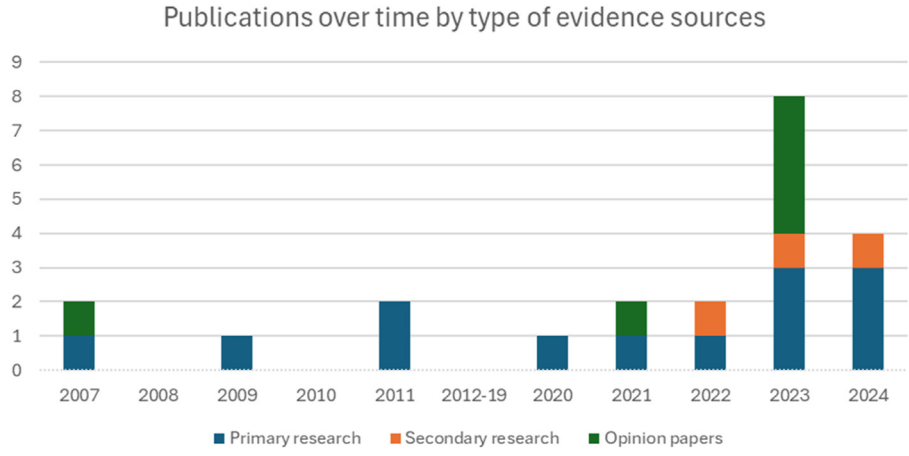

Figure 2. Type of evidence sources mapped over time.

adaptation of a new practice in international clinical trials had led to carbon efficient conduct of trials [47].

There were several areas of interest in common across the included studies. They encompassed how carbon footprint of clinical trials was quantified, which trial process(es) were carbon intensive, and what should be done to reduce trial-related carbon emissions. For the purpose of this review, we will focus on reporting the findings of the 12 included primary research studies that covered these common areas of interest [4,8,15,17,18,31−38].

3.3. Quantifying carbon footprint of clinical trials

Table 1 summarizes the 12 primary studies that performed some form of carbon audit to measure the carbon footprint of sample trials. The scope of trial activities being assessed for their carbon footprint varied considerably across the 12 studies, making it challenging to compare their findings directly. The reported carbon emissions ranged from one tonne of CO_2e associated with patients' travel to clinics in a single trial lasting for 6 months to 5573 tonnes of CO_2e generated from multiple processes in three international Phase-III trials involving both investigative medicinal product (IMP) and non-IMP with varied durations [34−36]. The variation in the reported CO_2e can be attributed to a host of variables including the number of trials analyzed, intervention type, trial population, geographical scope, trial duration, funding source, trial processes measured, and carbon quantification approaches.

Five of the 12 studies drew data from a single trial (42%) [4,32,34,37,38], while the remaining seven studies (58%) reported results of multiple trials ranging from 2 to 68 [8,15,17,18,31,33,36]. The sample trials encompassed diverse interventions including IMPs and non-IMPs (eg, on-site medical treatment, patient-administered therapy, and behavioral interventions). Participant numbers varied greatly from 39 to 20,211 [15,38]. The trials themselves ranged from single-site to multicenter designs and were conducted either within a single country or internationally, lasting from 6 months to 8 years [17,34,35]. Ten of the 12 studies (83%) were publicly funded [4,8,15,17,18,31−35,37], while two were sponsored by the pharmaceutical industry [36,38].

Seven of the 12 carbon audit studies assessed the carbon footprint across a broad range of trial processes within their sample trials [4,8,15,17,18,36,38]. Early studies focused primarily on the carbon impact of the trial conduct phase and strategies for emissions reduction [4,8,15]. Most of them reported the challenge of distinguishing carbon emissions associated with the trial processes from overall settings where the sample trials were embedded [4,8]. In contrast, more recent studies broadened their scope to encompass the entire trial lifecycle. For example, Griffiths et al developed a comprehensive process map covering trial design, conduct, analysis, and reporting stages and grouped core trial activities above routine care into 10 modules to guide carbon footprinting exercises [17,18]. In addition, two industry-sponsored audits included the carbon footprint of manufacturing investigational products (IPs) such as drugs and placebos which were not included in the carbon audits of publicly funded trials [36,38]. They demarcated trial-related carbon emissions with clear inclusion and exclusion criteria [36,38]. None of the 12 studies, however, accounted for emissions from infrastructure construction or equipment manufacturing used in trials.

Five other included studies among the 12 carbon audit papers quantified the carbon footprint of discrete aspects or components of their sample trials [31−35,37]. Chakladar et al reported the carbon emissions associated with paper consumption in applications to a single UK research ethics committee across 68 trials [31]. Coleman et al assessed the emissions linked to Christmas cards used as an intervention to improve participants retention within a study within a trial design [33]. Williams et al examined the carbon footprint of patients' travel to clinics for the trial purposes when evaluating the feasibility of incorporating environmental impact to analyze the cost of clinical trials [34,35]. Similarly, Vergunst et al focused solely on the carbon footprint associated with patients' interactions with health professionals in their sample trial [32].

The methods used for quantifying carbon emissions in clinical trials varied substantially across the reviewed studies. Two primary approaches to carbon auditing were identified. Nearly all of the 12 included carbon audit studies employed a bottom-up approach [4,8,15,17,18,31,33−38], which involved gathering data on specific trial activities at an operational level (eg, volume, frequency, duration or costs) and applying carbon conversion factors to estimate emissions. Early audits using this method focused on particular processes or trial periods, while later studies broadened the scope. For example, the Group and Subaiya et al calculated emissions by multiplying 1-year figure of the trial carbon output to total duration of their sample trials [4,15], and Chakladar et al converted paper consumption for ethics applications into CO_2e value [31]. The two industry-sponsored carbon audits reported using life cycle assessment (LCA) which was a prominent bottom-up method for assessing the potential environmental impacts associated with every process in a life cycle of a product or service [36,38]. Of the bottom-up studies, 10 out of 11 were retrospective [4,8,15,17,18,31,33−36,38], with two including both completed and ongoing trials [17,36] and one assessing emission savings within an active trial [37].

An alternative approach, the top-down method, relies on proxy data to represent collections of trial-related activities when estimating carbon footprints. For instance, Vergunst et al applied an input-output analysis by converting trial process expenditures into CO_2e to evaluate the Triple Bottom Line (TBL) framework, which assesses environmental, economic, and social impacts in trials [32]. This method involved scaling organizational financial data and applying established conversion factors to estimate emissions for specific activities [32].

Table 1. Quantifying carbon footprint of clinical trials (12 included carbon audit studies).

Study (first author, publication year)	Carbon audit design	Sample trials					Methods
		Number of sample trials	Context	Phase	Population of trial participants	Funding	Approach
Sustainable Trials Study Group, 2007	Retrospective	1	International multicenter IMP 5 years	Not reported	10,008	Public	Bottom up (1-year)
Lyle, 2009	Retrospective	12	National multicenter Including IMP and non-IMP duration varied	Not reported	Over 4800	Public	Bottom up
Subaiya, 2011	Retrospective	2	International multicenter IMP 5 years	Not reported	10,008-20,211	Public	Bottom up (1-year)
Chakladar, 2011	Retrospective	68	Varied	Varied	Not reported	Public	Bottom up
Vergunst, 2020	Retrospective	1	National multicenter non-IMP 1 year	Not reported	333	Public	Top down (input-output analysis)
Coleman, 2021	Retrospective	8	Varied	Varied	380-1147	Public	Bottom up
Williams, 2022 (2024)[b]	Retrospective	1	National single site non-IMP 6 months	Not reported	100	Public	Bottom up
Mackillop, 2023	Retrospective, current, prospective	3	International multicenter IMP and non-IMP varied duration	III	668-4744	Industry	Bottom up (LCA)
Quann, 2023	Current	1	National multicenter non-IMP	Not reported	Not reported	Public	Bottom up
LaRoche, 2024	Retrospective	1	National single site IMP	I	39	Industry	Bottom up (LCA)
Griffiths, 2024a	Retrospective	2	International and national multicenter IMP and non-IMP	Varied	47-1962	Public	Bottom up
Griffiths, 2024b[c]	Retrospective, current	10	International and national Single and multicenter IMP and non-IMP 2.5 – 8 years	Varied	80-12,580	Public	Bottom up

[a] The bold indicates the trial process(es) being measured for carbon output in the corresponding carbon audit. ''Multiple'' refers to more than one trial process having carbon footprint. ''Single'' indicates that only one type of trial activity or process was assessed.

[b] Correction notice of the original study published in 2024 [35].

[c] This preprint article was peer reviewed and published as ''What is the carbon footprint of academic clinical trials? A study of hotspots in 10 trials'' on October 16, 2024 [48].

Table 1. (cont.)

Methods			Trial process(es) measured[a]			
Conversion factor(s) reported	Scope of trial activities defined	Distinction between trial-specific activities and routine care	Design	Conduct	Analysis and reporting	Total carbon footprint in tonnes of CO2e (range)
Yes	Yes	Unable to make distinction		**Multiple**		630
Yes	Yes	Unable to make distinction		**Multiple**		941.2 (42.1-112.7)
Yes	Yes	Not reported		**Multiple**		1433.1 (508.5-924.6)
No	No	Not reported	**Single**			3.4
Yes	No	Not reported		**Single**		804
No	No	Not reported		**Single**		0.226
Yes	No	Not reported		**Single**		1
Yes	Yes	High level map to demarcate common trial activities		**Multiple**	**Multiple**	5573 (1437-2498)
Yes	No	Not reported		**Single**		32.32 (carbon saved)
Yes	Yes	LCA boundary reported		**Multiple**	**Multiple**	17.7
Yes	Yes	10 modules of trial activities beyond routine care	**Multiple**	**Multiple**	**Multiple**	161.3 (72-89)
Yes	Yes	10 modules of trial activities beyond routine care	**Multiple**	**Multiple**	**Multiple**	1322.8 (15-765)

Ten of the 12 carbon audit studies (83%) reported the sources of emission conversion factors [4,8,15,17,18,32,34,36−38]. Several studies used established protocols like the World Business Council's greenhouse gas guidelines or NHS Footprinting Reports [4,8], while others relied on varied data sources such as Ecoinvent and the IPCC's global warming potential calculations [15,17]. Publicly funded research predominantly utilized accessible, country-specific tools, such as Ecoinvent (V.2.2 GOV UK) conversion factors and the Australian Department of Industry's emission factors for gasoline [17,34]. In contrast, the two industry-sponsored audits employed tools specifically developed for pharmaceutical applications, such as the Association of the British Pharmaceutical Industry's (ABPI) sustainability tool, which enabled the quantification of carbon emissions from the manufacturing of IPs [36,38]. These variations in assessment techniques compounded with the diverse trial profiles contributed not only to the great variability in reported carbon outputs but also in the identification and categorization of carbon hotspots which we will cover in the next section.

3.4. Identifying "carbon hotspots" across trials

Seven of the 12 included carbon audits reported major carbon sources or ''carbon hotspots'' when assessing the carbon footprint of their sample trials as summarized in Table 2 [4,8,15,17,18,36,38]. These studies exhibited notable variability in defining and presenting ''carbon hotspots'' within clinical trials and reflected evolving understanding and methodology. Early studies [4,8,15], while highlighting areas which were particularly carbon heavy in their sample trials, did not explicitly define carbon hotspots or provide specific criteria or thresholds. They presented major carbon contributors in varied forms, such as proportion to overall carbon output and emissions per patient [4,15]. Clearer definitions started to emerge in later studies where carbon hotspots referred to key trial activities or processes with significant contribution to overall carbon footprint within trials [36]. Griffiths et al even adopted a quantifiable threshold by considering trial processes, which they grouped into 10 modules, contributing over 10% of total carbon output as carbon hotspots [17]. In addition to presenting the percentage of emissions by each module, Griffiths et al reported the top three carbon hotspots of each trial in their study and identified the common hotspots across them [17]. Given the variability in definition and presentation, it is challenging to make a conclusive comparison of the reported carbon hotspots between studies.

However, some areas consistently stood out as major carbon contributors or hotspots common across the seven audits despite different groupings. All of the seven audits reported trial related travel and meetings by both trial staff and participants as one of the hotspots in their sample trials [4,8,15,17,18,36,38]. Carbon emissions associated with trial facilities including clinical trial units (CTUs) or coordination centers (eg, electricity, energy consumption, waste disposal and staff commuting to work) [4,8,15,17,18], trial site [38], and sponsor facilities were also reported as major carbon sources in six of the seven audits [38]. Sample lifecycle as well as the transport and processing of laboratory samples were reported to be particularly carbon heavy in trials that required international shipment and long-term storage with energy intensive freezers [17,36,38]. Carbon generated from distribution and deliveries of trial treatment and documents were featured highly in two studies [4,15].

3.5. Recommendations for reducing trial carbon footprint

Almost all included studies in this review ($n = 22$) proposed recommendations for reducing trial-related carbon emissions. These recommendations encompass actions to be implemented by a host of relevant parties (eg, trial governing bodies, funders, publishers, and trialists) across different trial stages including design, conduct, analysis, and reporting.

Key recommendations for simplifying and streamlining the design of trials to reduce the associated carbon output are mainly twofold. First, recommendations to consider environmental impacts, cost, and decarbonization strategies as core components, especially in governance and funding applications, as well as outcome measures [14,17,32,34,39−41,43,44]. For example, available online carbon calculators were recommended to be used prospectively to estimate the carbon footprint of planned trials [39]. Environmental accreditation schemes such as LEAF and My Green Lab can be leveraged to encourage the planning of green trials [17]. Funding incentives can be offered to trial designs that take carbon impacts into account along with having carbon mitigation strategies in place [14,38,46]. Second, avoiding research waste by conducting systematic reviews and cost-benefit analyses to evaluate the necessity of new trials is recommended [4,14,17,39,44−46].

Recommendations for reducing carbon emissions associated with the conduct phase of trials were targeted mostly at identified carbon hotspots in the carbon audit studies. For example, four studies suggested trial units adopt renewable energy to address CTU emissions [4,17,38,39], nine studies proposed minimizing trial-related travel for both trial staff and patients by, for example, decentralizing trial conduct and using web-based communication as much as possible [4,8,15,17,37−39,41,45]. Other recommendations included using existing resources such as NIHR Carbon Reduction Guidelines to implement carbon reduction strategies in trials [14,46], involving environmental scientists or specialists to perform the LCA over trial processes [34,35], and redesigning recipes with less carbon heavy ingredients for inparticipant care [38]. With regard to reporting, adding a requirement to publish the carbon output or carbon relevant data of trials has been recommended [18,39,41].

Table 2. Identifying "carbon hotspots" across trials (7 included carbon audit studies assessing carbon footprint of multiple trial activities/processes)

Study (first author, publication year)	Definition of "carbon hotspots"	Criteria/Threshold	Presentation of carbon hotspots	Carbon hotspots identified				
				Trial facilitates[a]	Trial-related travel and meetings[b]	Sample and laboratory activities	Treatment distribution and delivery	Trial supplies and equipment
Sustainable Trials Study Group, 2007	Not explicitly defined (Areas with high proportion of CO_2e emissions reported)	None specified	Proportion (%) of contribution to total emissions	✓	✓		✓	
Lyle, 2009	Not explicitly defined (Areas with significant CO_2e emissions reported)	None specified	Quantitative breakdown using average CO_2e per trial value	✓	✓			
Subaiya, 2011	Not explicitly defined (Significant sources of greenhouse gas (GHG) emissions reported)	None specified	Comparative analysis of emission using per patient metrics	✓	✓		✓	
Mackillop, 2023	Key activities or processes with significant carbon footprint	High-contributing activities; no specified threshold	Quantified emissions with percentage contribution to total emissions		✓	✓		
LaRoche, 2024	Significant contributors to GHG emissions within the trial lifecycle	High-contributing activities, no specified threshold	Quantified emissions with percentage contribution to total emissions	✓	✓	✓		
Griffiths, 2024a	Trial activities or processes with substantial GHG emissions	>10% of total emissions	Quantified emission with percentage by predefined module	✓	✓			
Griffiths, 2024b	Activities contributing to >10% of total GHG emissions	>10% of total emissions	Quantified emission with percentage by predefined module Top 3 carbon hotspots	✓	✓	✓		✓

[a] Trial facilities encompass carbon emissions associated with the operation of clinical trial units (CTUs)/coordination centers/trial sites including electricity and energy use.

[b] Trial-related travel includes travel by trial staff (eg, monitoring visits, meetings and conferences) and patients/participants (eg, trial-specific assessment beyond standard care).

4. Discussion

This scoping review synthesized the evidence on carbon emissions associated with clinical trials reported to date. We identified various types of evidence that explored the carbon impact of clinical trials, most of which were published over the last 5 years. The emerging body of evidence comprised mostly primary studies performing carbon audits to quantify the carbon footprint of clinical trials. The diverse profiles of the sample trials across the carbon audits made it hard to compare the studies conclusively. However, it was evident that efforts are being made to develop reliable and standardized methods for measuring trial carbon footprints. A preprint of a systematic review on assessing trials' carbon footprint has recently been published [49]. Despite the similarity in the scope of investigation, there are marked differences in search strategy, analyzed evidence, and presentation of results between the two reviews. However, some of the key findings are comparable across the two reviews and reinforce their importance.

In contrast with earlier carbon audit studies, recent publications reported more comprehensive mapping of trial processes. For example, Mackillop et al and Griffiths et al mapped overall trial processes in their carbon assessment of industry-sponsored and publicly funded trials respectively, despite in different groupings [17,18,36]. The authors detailed key steps in developing their research strategies, clearly provided sources of carbon conversion factors, and defined each mapped process in detail. The importance of distinguishing carbon emissions specifically associated with clinical trials from nontrial activities, for example, routine care, were highlighted [17,18,41]. In their most recent studies, Griffiths et al dedicated to sifting trial-related carbon emissions from those generated from standard of care to improve the precision in capturing trial specific carbon footprint [17,18]. The comprehensive process maps did not only enable identification of common carbon sources across different trial settings but also their nuanced differences. For example, CTU emissions including the

number of staff commuting would be significantly higher in countries with more energy intensive grids, such as China and US [36]. Country specific carbon conversion factors would, therefore, be desirable to account for those differences. However, carbon calculation relies much on assumptions of estimated variables, such as distance traveled by staff, especially in retrospective research design. Those assumptions may not be necessarily correct or valid and were often context dependent. These might render inaccurate estimation at best and compromise the reliability of the carbon audit at worst.

While the tools for quantifying trial-related carbon emissions are being trained for reliability, accuracy and specificity, they have helped identify the carbon hotspots which were common in trials across the carbon audit studies such as CTU emissions and trial-related travel. By targeting the identified hotspots for change, it has the potential to reduce trial-related carbon emissions. Development of carbon mitigation strategies to target the identified carbon hotspots will also benefit from contributions across disciplines such as climate science, ecology, and health sciences. Many activities within a trial involve human behavior which requires people to perform particular actions in particular settings, so effective reduction of trial-related carbon output might hinge on changing how people perform those actions. Behavioral sciences may offer invaluable insights as previous studies have reported how behavioral approaches could inform trials methodology research [50,51].

Most of the included studies proposed recommendations for minimizing the carbon footprint of clinical trials. They ranged from funding requirements to efficient trial design which all required efforts from a range of relevant parties. Most of the studies' authors agreed that promoting awareness of trial-related carbon impact and incorporating carbon cost in during trial design would be an upstream measure to prevent unnecessary carbon emissions from trials. Some recommended measures proposed in the included studies have already been adopted such as reducing trial-related travel by conducting meetings, visits, conferences, and assessments for trial purposes virtually or remotely. The COVID-19 pandemic was a catalyst for some of these changes but many have remained postpandemic and extended to other aspects of trial conduct. For example, Thiemer et al reported how the delivery of training and the conduct of international clinical trials have been transformed into a more environmentally sustainable format [47]. The merit of this change in practice must be assessed in balance against the impacts on the trial. For example, while virtual appointments may reduce the carbon footprint of patients' travel to trial sites, patients' preference for face-to-face assessments may discourage participant recruitment and retention, which may in turn cause the waste of research resources [38]. Piltonen et al's study was an attempt to address this research gap by exploring how known influences on participant recruitment and retention may also be relevant for design and conduct of greener trials [42].

4.1. Strengths and limitations

This scoping review addresses specifically trial-related carbon emissions which is among the first of its kind. We examined the implications of the carbon footprint unique to trial processes which will be invaluable to inform trials methodology research on greener trials. Given our focus on clinical trials, publications that explored environmental impacts of health-care research in general that included trials were excluded [16,52,53]. This scoping review was conducted by following a predefined protocol for promoting accessibility and transparency [24]. The data generated in this review was made publicly available so that others may examine these for additional purposes.

Given the nature of this scoping review, we did not perform formal quality assessment or assessment of applicability on the data drawn from the included studies. This is due to the heterogeneity of the literature examined, especially in an emerging field of study. Our literature search through snowballing yielded eight eligible articles which amounted to 36% of all included studies. Among the articles emerging from the snowballing exercises, one was published after completion of our database search [42], two were preprint articles which were recently made available [17,44]. The remaining five articles that had been missed from our database search implied our database search strategy may have been insufficiently sensitive [8,31,32,40,46]. The scope of investigation of this review was also limited to trial specific carbon emissions without examining other forms of environment impact, such as material waste and other greenhouse gases [54], which will require further studies.

5. Conclusion

This scoping review synthesized evidence of carbon emissions linked to clinical trials to date. Efforts have been made to quantify carbon footprint of trials by measuring a variety of activities using a range of tools and approaches, making direct comparisons difficult. Certain carbon hotspots have been identified across studies while carbon quantification tools for trial specific emissions continue in development. Recommendations to address the carbon impacts of trials have been suggested but now require implementation.

CRediT authorship contribution statement

Frank You: Writing − review & editing, Writing − original draft, Visualization, Methodology, Formal analysis, Data curation, Conceptualization. **Taylor Coffey:** Writing − review & editing, Supervision, Methodology. **Daniel Powell:** Writing − review & editing,

Visualization, Supervision. **Paula R. Williamson:** Writing − review & editing, Supervision, Methodology. **Katie Gillies:** Writing − review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

There are no competing interests for any author.

Acknowledgments

We thank MRC NIHR TMRP ''Greener Trials'' subgroup for discussion and contributing to idea development of this review. We also thank Paul Manson, Information Officer of the ACE at the University of Aberdeen, for advice on developing the search strategy.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jclinepi.2025.111733.

Data availability

Data will be made available on request.

References

[1] Cook JA. An introduction to clinical trials. Oxford, UK: Oxford University Press; 2023.
[2] Jager W. The importance of clinical trials in advancing medical research. Ann Clin Trials Vaccines Res 2023;13(3):93−8.
[3] Friedman LM, Furberg CD, DeMets DL, Reboussin DM, Granger CB. Introduction to clinical trials. In: Friedman LM, Furberg CD, DeMets DL, Reboussin DM, Granger CB, editors. Fundamentals of Clinical Trials. Cham: Springer International Publishing; 2015:1−23.
[4] Sustainable Trials Study Group. Towards sustainable clinical trials. BMJ 2007;334(7595):671−3.
[5] Lebreton T. What's the average carbon footprint in the UK? 2023. Available at: https://www.theecoexperts.co.uk/blog/average-carbon-footprint-uk. Accessed July 23, 2024.
[6] Ritchie H. Which form of transport has the smallest carbon footprint? 2023. Available at: https://ourworldindata.org/travel-carbon-footprint. Accessed July 23, 2024.
[7] How far is New York, NY, from London? Available at: https://www.airmilescalculator.com/distance/lhr-to-jfk/. Accessed July 23, 2024.
[8] Lyle K, Dent L, Bailey S, Kerridge L, Roberts I, Milne R. Carbon cost of pragmatic randomised controlled trials: retrospective analysis of sample of trials. BMJ 2009;339:b4187.
[9] Trends, charts, and maps. Available at: https://classic.clinicaltrials.gov/ct2/resources/trends. Accessed January 13, 2024.
[10] World emissions clock. Available at: https://worldemissions.io/. Accessed February 29, 2024.
[11] Richardson K, Steffen W, Schellenhuber HJ, Munasinghe M, Al WE. Climate change: global risk, challenges and decisions - synthesis. Copenhagen, Denmark: University of Copenhagen; 2009.
[12] Costello A, Abbas M, Allen A, Ball S, Bell S, Bellamy R, et al. Managing the health effects of climate change: *lancet* and university college London Institute for global health commission. Lancet 2009;373(9676):1693−733.
[13] Papies EK, Nielsen KS, Soares VA. Health psychology and climate change: time to address humanity's most existential crisis. Health Psychol Rev 2024;6:1−31.
[14] Adshead F, Al-Shahi SR, Aumonier S, Collins M, Hood K, McNamara C, et al. A strategy to reduce the carbon footprint of clinical trials. Lancet 2021;398(10297):281−2.
[15] 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.
[16] NIHR carbon reduction guidelines. Available at: https://www.nihr.ac.uk/documents/nihr-carbon-reduction-guidelines/21685#nihr-carbon-guidelines-key-recommendations-for-researchers. Accessed January 13, 2024.
[17] Griffiths J, Adshead F, Salman RA, Anderson C, Bedson E, Bliss J, et al. Quantifying the carbon footprint of academic clinical trials: building the evidence base and hotspot identification [Preprint] (Version 1). Durham, NC: Research Square Company; 2024.
[18] Griffiths J, Fox L, Williamson PR, Low Carbon Clinical Trials Group. Quantifying the carbon footprint of clinical trials: guidance development and case studies. BMJ Open 2024;14(1):e075755.
[19] Munn Z, Peters MDJ, Stern C, Tufanaru C, McArthur A, Aromataris E. Systematic review or scoping review? Guidance for authors when choosing between a systematic or scoping review approach. BMC Med Res Methodol 2018;18(1):143.
[20] Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol Theor Pract 2005;8(1):19−32.
[21] Peters MDJ, Godfrey C, McInerney P, Khalil H, Larsen P, Marnie C, et al. Best practice guidance and reporting items for the development of scoping review protocols. JBI Evid Synth 2022;20(4):953−68.
[22] Peters MDJ, Marnie C, Tricco AC, Pollock D, Munn Z, Alexander L, et al. Updated methodological guidance for the conduct of scoping reviews. JBI Evid Implement 2021;19(1):3−10.
[23] Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA extension for scoping reviews (PRISMA-ScR): checklist and explanation. Ann Intern Med 2018;169(7):467−73.
[24] You FS, Coffey T, Powell D, Williamson P, Gillies K. Environmental impacts of carbon emissions associated with clinical trials: a scoping review protocol. Frankfurt, Germany: Open Science Framework (OSF) Registries; 2024.
[25] Polisena J, De Angelis G, Kaunelis D, Gutierrez-Ibarluzea I. Environmental impact assessment of a health technology: a scoping review. Int J Technol Assess Health Care 2018;34(3):317−26.
[26] Guirado-Fuentes C, Abt-Sacks A, Trujillo-Martín MDM, García-Pérez L, Rodríguez-Rodríguez L, Carrion I, et al. Main challenges of incorporating environmental impacts in the economic evaluation of health technology assessment: a scoping review. Int J Environ Res Public Health 2023;20(6):4949. https://doi.org/10.3390/ijerph20064949.
[27] Wohlin C. Guidelines for snowballing in systematic literature studies and a replication in software engineering. Proceedings of the 18th International Conference on Evaluation and Assessment in Software Engineering. Frankfurt, Germany: Open Science Framework (OSF) Registries; 2014.
[28] Rayyan—a web and mobile app for systematic reviews. Syst Rev 2016;5(1):210.
[29] Khabsa M, Ahmed E, Ihab I, Hossam H, Mourad O. Learning to identify relevant studies for systematic reviews using random forest and external information. Mach Learning 2016;102(3):465−82.
[30] Cochrane handbook for systematic reviews of interventions. Chichester, UK: Cochrane; 2023: version 6.4.
[31] Chakladar A, Eckstein S, White SM. Paper use in research ethics applications and study conduct. Clinical medicine 2011;11(1):44.
[32] Vergunst F, Berry HL, Rugkåsa J, Burns T, Molodynski A, Maughan DL. Applying the triple bottom line of sustainability to healthcare research—a feasibility study. Int J Qual Health Care 2020;32(1):48−53.
[33] Coleman E, Arundel C, Clark L, Doherty L, Gillies K, Hewitt C, et al. Bah humbug! Association between sending Christmas cards to trial participants and trial retention: randomised study within a trial conducted simultaneously across eight host trials. BMJ 2021;375:e067742.

[34] Williams JTW, Bell KJL, Morton RL, Dieng M. Exploring the integration of environmental impacts in the cost analysis of the pilot MEL-SELF trial of patient-led melanoma surveillance. Appl Health Econ Health Pol 2023;21(1):23−30.
[35] Williams JTW, Bell KJL, Morton RL, Dieng M. Correction: exploring the integration of environmental impacts in the cost analysis of the pilot MEL-SELF trial of patient-led melanoma surveillance. Appl Health Econ Health Pol 2024;22(2):271−2.
[36] Mackillop N, Shah J, Collins M, Costelloe T, Öhman D. Carbon footprint of industry-sponsored late-stage clinical trials. BMJ Open 2023;13(8):e072491.
[37] Quann N, Burns S, Hull KL, Cluley V, Richardson C, MacConaill K, et al. Reducing the carbon footprint of research: experience from the NightLife study. BMJ Open 2023;13(4):e070200.
[38] Keith LaRoche J, Alvarenga R, Collins M, Costelloe T, De Soete W, Faludi J, 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(1):e077129.
[39] Hoffmann J, Bauer A, Grossmann R. The carbon footprint of clinical trials: a global survey on the status quo and current regulatory guidance. BMJ Glob Health 2023;8(9):e012754. https://doi.org/10.1136/bmjgh−012754.
[40] Billiones R. Carbon footprint of clinical trials: a high-level literature review. Med Writ 2022;31:14−8.
[41] Singh P, Burden AM, Natanegara F, Beckman RA. Design and execution of sustainable decentralized clinical trials. Clin Pharmacol Ther 2023;114(4):802−9.
[42] Piltonen E, Goulao B, Gillies K. Designing greener participant-centred trials: an analysis of 'carbon relevant'factors within items that influence participants' decisions about trial recruitment and retention. Trials 2024;25(1):260.
[43] McMichael AJ, Bambrick HJ. Greenhouse-gas costs of clinical trials. Lancet 2007;369(9573):1584−5.
[44] Athalye S, Baraskar S, Mittra S, Wolff-Holz E. Aligning environmental, social, and governance to clinical development: moving towards more sustainable clinical trials [preprint]. SSRN. Available at: https://ssrn.com/abstract=4590749. Accessed July 23, 2024.
[45] Rahman S, Ryan S, Kim J, Kenney P, Ghali F. Clinical trials and climate change: doing our Part While pursuing progress. Eur Urol Focus 2023;9(6):861−2.
[46] Cuffari B. The carbon footprint of clinical trials. News-Medical; 2023. Available at: https://www.news-medical.net/health/The-Carbon-Footprint-of-Clinical-Trials.aspx. Accessed June 20, 2024.
[47] Thriemer K, Degaga TS, Alam MS, Adhikari B, Tripura R, Hossain MS, et al. Adapting international clinical trials during COVID-19 and beyond. Clin Trials 2023;20(3):237−41.
[48] Griffiths J, Adshead F, Al-Shahi SR, Anderson C, Bedson E, Bliss J, et al. What is the carbon footprint of academic clinical trials? A study of hotspots in 10 trials. BMJ Open 2024;14(10):e088600.
[49] Jean C, Layese R, Canouï-Poitrine F, Grimaldi D, Audureau E, Leemans M, et al. Assessing the carbon footprint of clinical trials: a systematic review. medRxiv 2024. https://doi.org/10.1101/2024.11.12.24317142.
[50] Coffey T, Williamson PR, Gillies K. On behalf of the Trials Methodology Research Partnership, Working Groups. Understanding implementation of findings from trial method research: a mixed methods study applying implementation frameworks and behaviour change models. Trials 2024;25(1):139.
[51] Gillies K, Brehaut J, Coffey T, Duncan EM, Francis JJ, Hey SP, et al. How can behavioural science help us design better trials? Trials 2021;22(1):882.
[52] D'Souza J, Samuel G. Clinical research risks, climate change, and human health. JAMA 2023;330(23):2247−8.
[53] Accelerating the delivery of net zero health systems- an overview of practical recommendations and actions in support of healthy people, planet, and society. Manchester, UK: The Sustainable Markets Initiative Health Systems Task Force, in collaboration with BCG; 2022.
[54] Darlington E, Frost H, Patel A, Descamps T, Loong H, Alt M, et al. Assessment of the environmental impact of clinical trials. London, UK: National Cancer Research Institute (NCRI); 2021.