# Carbon footprint of clinical trials: A high-level literature review

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#### Abstract

Thousands of clinical trials are conducted globally each year. Yet, little is known about their environmental impact. This paper presents the results of a high-level literature review of the carbon footprint of clinical trials. Five papers were identified and their contents summarised qualitatively. All papers were authored by UK researchers. Carbon footprint metrics from 14 trials were presented in carbon dioxide equivalents (CO<sub>2</sub>e). Emissions were broken down by three broadly defined clinical trial activities: operations, travel, and supplies. Recommendations for carbon reduction are discussed. The review showed a dearth of publications on greenhouse gas emissions generated by clinical trials. More work in this area is needed to achieve sustainable, low carbon clinical research.

#### Introduction

he pharmaceutical industry is among the highest producers of greenhouse gas emissions.<sup>1</sup> One of its key carbon intensive activities is clinical research. Thousands of clinical trials are conducted globally each year. As of January 13, 2022, a total of 400,873 studies are listed in ClinicalTrials.gov. Yet, the current regulatory landscape of healthcare products does not take into account the environmental impact of clinical trials.

#### Search protocol and selection

To learn more about the carbon footprint of clinical trials, a high-level review of literature was conducted. A PubMed search conducted on December 30, 2021 using the terms "clinical trials AND carbon footprint" with no filters yielded a disappointing 12 publications. The retrieved publications were screened for eligibility based on relevance to the topic. Of the 12 publications identified, only four were deemed eligible and further scrutinised. A manual search of the identified publications revealed one relevant paper which was also included. The 5 papers included are summarised below (see Table 1).

#### Methodology to estimate emissions

Three papers reported relevant data on greenhouse gas emissions of select clinical trials and followed similar methodology. Data from 14 trials were collected retrospectively on all trial elements that would generate carbon emissions according to the greenhouse gas (GHG) reporting protocol<sup>2</sup> developed by the World Business Council for Sustainable Development. Using the GHG calculation tools, emissions of the clinical trials were expressed in carbon dioxide equivalents (CO2e) using generally accepted conversion factors. Sources of emissions were broken down by different trial activities, roughly categorised as operation of coordination centre or study site (i.e., fuel for electricity, waste disposal, water), travel (i.e., trial staff commute, trial-related travels), and trial supplies (i.e., manufacture and distribution of drugs, documents, and other equipment).

#### **Publications retrieved**

1. Sustainable Trials Study Group (2007). Towards sustainable clinical trials.

The oldest publication identified by PubMed, this paper<sup>3</sup> is probably the first published report quantifying greenhouse gas emissions of a clinical trial. The CRASH trial was a multicentre, international study conducted between April 1999 and May 2004 to evaluate the effect of corticosteroids on death and disability in adults with head injury. The analysis was performed by the Sustainable Trials Study Group, a group convened by the London School of Hygiene and Tropical Medicine. The group's mandate was to find ways of reducing greenhouse gas emissions from clinical trials.

There is a dearth of publications on greenhouse gas emissions generated by clinical trials. It is clear that more work needs to be done in this field of research.

Based on a one-year carbon audit, the estimated emission of the whole trial was 630 tonnes CO<sub>2</sub>e. There were 10,008 participants and 1945 primary endpoint events, amounting to greenhouse gas emissions of 63 kgCO<sub>2</sub>e per participant or 324 kgCO<sub>2</sub>e per primary endpoint event. Operation of the coordination centre accounted for the majority of the emissions (39%). Key carbon reduction recommendations include simplifying study design and processes, and minimising travel. This paper mentions the contribution of clinical trial documentation to a study's carbon footprint, thus directly linking medical writing to carbon emissions.

#### Lyle et al. (2009). Carbon cost of pragmatic randomised controlled trials: retrospective analysis of sample of trials.

To the best of current knowledge, this is the first and only meta-analysis<sup>4</sup> published to date on the CO<sub>2</sub> emissions of clinical trials. Though not identified during the PubMed search, this paper was cited by three papers retrieved by the initial search. This retrospective study analysed 12 pragmatic (see Merali & Wilson<sup>5</sup> on the definition of pragmatic vs. explanatory trials), randomised, controlled trials (RCTs) funded by the Health Technology Assessment programme of UK's National Institute for Health Research (NIHR) from 2002 to 2003. The CRASH trial previously presented was not eligible for inclusion in the analysis. The 12 trials involved more than 4800 participants and a wide range of

> healthcare interventions, including pharmaceuticals, devices, and psychological therapies.

> In addition to metrics related to site operation, travel, and supplies, this paper also calculated emissions related to information technology equipment used in the trials. Interestingly, freight distribution of trial documentation was not considered in the metrics, probably due to use of electronic rather than paper-based documents.

> The mean emission estimates were 306 kg  $CO_2e$  per participant and 78 tonnes  $CO_2e$  per trial. The largest proportion of emissions



came from staff commute (26%) and operations (23%) whereas information technology footprint was lowest (2%; see Table 1).

Data from this analysis were used in developing the NIHR Carbon Reduction Guidelines  $(p.19).^6$ 

#### Subaiya et al (2011). Reducing the environmental impact of trials: a comparison of the carbon footprint of the CRASH-1 and CRASH-2 clinical trials.

This paper<sup>7</sup> follows up on the 2007 paper<sup>3</sup> and compared the original CRASH trial with a similar study (designated as CRASH-1 and CRASH-2, respectively). CRASH-2 was conducted between May 2005 and February 2010, starting one year after CRASH-1 ended. The two trials were of similar design but CRASH-2 made a greater effort to reduce the carbon footprint using several of the strategies outlined in the NIHR carbon reduction recommendations. CRASH-2 recruited approximately twice the number of participants (N=20,211) but emitted 73% less carbon per randomised patient than CRASH-1 (25 kg vs 92 kg CO<sub>2</sub>e per participant; Table 1). The main drivers for lower CO2 emissions in CRASH-2 were increased efficiency in study design, recruitment and conduct, and more compact trial supplies.

The emission data presented for CRASH-1 in this paper slightly differed from CO<sub>2</sub>e reported in the 2007 CRASH paper.<sup>1</sup> As carbon calculation tools are regularly updated, the different values were most likely due to different metrics (e.g., updated tools and conversion factors).

#### 4. Pencheon (2011). Managing the environmental impact of research.

This was a commentary<sup>8</sup> on the environmental impact of healthrelated research, particularly clinical trials. It heavily cited and reported data from the 2011 CRASH-2 vs CRASH-1 paper by Subaiya et al.<sup>7</sup> Recommendations were broader and went beyond just clinical trials and covered the whole life cycle analysis of health interventions. Examples are finding ways to "incorporate the

environmental cost as well as the financial cost into the process of commissioning research" and the proposal to calculate "potential health gain per tonne of carbon expended".

### 5. Adshead et al (2021). A strategy to reduce the carbon footprint of clinical trials.

Approximately 10 years passed before another paper  $^9\,$  on this topic was published. This

commentary builds on the four previous publications and extrapolated the CO<sub>2</sub>e estimates in these papers to the roughly 350,000 clinical trials registered in ClinicalTrials.gov to arrive at an estimated 27.5 million tonnes of emission gases attributable to clinical trials globally.

The paper also cites new developments in this field over the last decade. Results from the previous carbon footprint studies<sup>3,4,7</sup> were used to

The need for reliable clinical trial data has to be weighed against the urgency of the climate crisis. develop the UK NIHR Carbon Reduction Guidelines.<sup>6</sup> A carbon footprint measuring tool is being tested by the Sustainable Healthcare Coalition. These tools will assist in building CO<sub>2</sub> reduction strategies into study planning and design.

The paper calls for more transparency of the environmental impact of trials and proposes a

thorough environmental cost-benefit assessment to justify the need for conducting a trial based on systematic review of literature and clinical trial registries.

An interesting proposal by this paper is the potential policing of clinical trial  $CO_2$  emissions by regulatory agencies, ethics committees, and biomedical journals. While this suggestion has some merits, the authors concede it comes with

#### Table 1. Publications on the carbon footprint of clinical trials

Publication / Type	Source of trial data / Trial information	<b>Greenhouse gas</b> kg per participant	<b>emission estimates (</b> i tonnes per trial per year	i <b>n CO<sub>2</sub>e)</b> <sup>b</sup> tonnes for whole trial	other metrics reported
Sustainable Trials Study Group, 2007 / original research	CRASH Trial <sup>a</sup> / Multicentre international trial of 10,008 participants over 5.1 years	63	126	630	324 kg per primary endpoint event
Lyle et al., 2009 / meta-analysis	12 pragmatic RCTs funded by the HTA programme of >4800 participants during 2002 and 2003 Mean number of centres: 16, in the UK only Mean number of participants: 402	Mean: 306.2 Range: 80.0 to 883.7	Total: 222.3 Mean: 18.1 Range: 8.9 to 30.1	Total: 941.2 Mean: 78.4 Range: 42.1 to 112.7	Mean: 0.1 kg per £ spent Mean: 5.6 tonnes per 1 full time staff
Subaiya et al., 2011 / original research	CRASH-1 Trial <sup>a</sup> Multicentre international trial of 10,008 participants over 5.1 years	92	181.3	924.6	NI
	CRASH-2 Trial Multicentre international trial of 20,211 participants over 4.7 years	25	108.2	508.5	NI
Pencheon, 2011 / commentary	Refers to data provided by Subaiya et al.				
Adshead et al., 2021 / commentary	350,000 trials registered in ClinicalTrials.gov as of June 16, 2021	NI	NI	NI	27.5 million tonnes (cumulative)
<sup>a</sup> CRASH trial and CRASH-1	trial are the same but the values reported in the 2 papers differ, possi	ibly due to different met	rics.		

<sup>a</sup> CRASH trial and CRASH-1 trial are the same but the values reported in the 2 papers differ, possibly due to different metrics.

<sup>b</sup> Calculations were according to the greenhouse gas reporting protocol<sup>2</sup> http://www.ghgprotocol.org/ but scoping and conversion factors could potentially differ.

Abbreviations: CO2e = carbon dioxide equivalents; NI = no information provided; NIHR = National Institute for Health Research; RCT = randomised controlled trials

additional bureaucratic burden. Clearly, the need for reliable clinical data has to be weighed against the urgency of the climate crisis.

#### Discussion and synthesis

This review identified important information on

the carbon footprint of clinical trials and opportunities for carbon reduction. This information is a good starting point towards sustainable and low carbon clinical research.

A total of five papers on the carbon footprint of clinical trials were reviewed and summarised

(Table 1). Two papers were commentaries, two were original research that provided data on the CRASH trials whereas one reported a metaanalysis of 12 pragmatic RCTs. Data from a total of 14 trials were summarised.

The main clinical trial activities that drive

Clinical trial activities as CO <sub>2e</sub> contributor (% of total trial emission)	Recommendations to reduce emissions
<ul> <li>Coordination centre operations (39%)</li> <li>Distribution of drugs and documents to sites (28%)</li> <li>Trial-related travel (23%)</li> <li>Trial team commuting (5%)</li> <li>Deliveries related to production of trial drugs (5%)</li> </ul>	<ul> <li>Reduce bureaucracy (regulatory agencies and ethics committees)</li> <li>Simplify study designs</li> <li>Choose better research questions</li> <li>Reduce travel</li> <li>Avoid unnecessary data collection</li> <li>Save electricity by using renewable-energy resources</li> <li>Use systematic reviews to answer research questions first before proposing new trials</li> </ul>
<ul> <li>Trial team work commute (26%)</li> <li>Study centres operations (23%)</li> <li>Staff trial-related travel (19%)</li> <li>Trial participants' travel (16%)</li> <li>Manufacture and distribution of trial supplies (14%)</li> <li>Information technology equipment (2%)</li> </ul>	<ul> <li>Minimise trial-related travel</li> <li>Reduce number of face-to face study visits</li> <li>Develop tools and methods to allow the carbon cost of a trial to be considered at the planning stage (e.g., use NIHR carbon reduction guidelines)</li> </ul>
<ul> <li>Distribution of trial drugs (48%)</li> <li>Coordination centre operation (30%)</li> <li>Trial-related travel (21%)</li> <li>Trial team commuting (1%)</li> <li>Coordination centre operation (37%)</li> <li>Distribution of trial drugs (32%)</li> <li>Trial-related travel (29%)</li> </ul>	<ul> <li>Improve trial efficiency (e.g., recruitment, data entry, validation, monitoring)</li> <li>Reduce travel (e.g., web-based training, teleconferences)</li> <li>Improve logistics (e.g., more compact materials, lighter packaging)</li> </ul>
	<ul> <li>Embed sustainability as a core part of research governance</li> <li>Have a more holistic and enlightened view to the process of conducting research</li> <li>Incorporate the environmental cost well as the financial cost into the process of commissioning research</li> <li>Make valid comparisons and use consistent metrics</li> </ul>
NI	<ul> <li>Confirm through systematic reviews the necessity of a trial (i.e., cost-benefit analysis)</li> <li>Make carbon footprint measures a part of study design</li> <li>Provide funding incentives for carbon reduction</li> <li>Use NIHR carbon reduction guidelines</li> <li>Involve regulatory bodies, ethics committees, and biomedical journals in policing carbon footprint</li> <li>Develop a tool to measure reliably the carbon footprint of trials and identify which elements are carbon-heavy</li> </ul>

emissions are the study site operation, trialrelated travel, and trial supplies. Key recommendations to reduce carbon footprint include more efficient study designs and conduct, and minimising trial-related travel. Most of the recommendations (Table 1) by these papers have been incorporated in the UK NIHR Carbon Reduction Guidelines.<sup>6</sup>

There are a number of caveats that may limit the generalisability of the review results. Only one database (PubMed) was used for the literature search. All five papers identified were from the UK. The meta-analysis included only UK pragmatic RCTs funded by the NIHR Health Technology Assessment programme. No data from explanatory clinical trials sponsored by the industry are available. Also, all these studies were performed before 2020. Clinical trial conduct has

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changed drastically during the pandemic, restricting travel, and relying on remote monitoring and virtual meetings.

Literature on the greenhouse gas emissions of clinical trials was surprisingly sparse. This dearth of publications on the carbon cost of clinical research indicates a domain that is underserved. Some of the gaps identified that warrant more research are:

- Development of harmonised and validated carbon footprint quantification metrics.
- Incorporation of carbon metrics and reduction strategies in trial planning and design.
- Involvement of funders, regulatory agencies, ethics committees, biomedical journals, and other governance bodies in the disclosure and management of the carbon profile of clinical trials.
- Data from other countries, especially the US, China, and the European Union.
- Data on carbon emissions generated by other research types and study designs.

Though not explicitly mentioned in these papers, in one way or another, medical writers and communicators are involved in clinical trials, and thus, contribute to the emissions. We can also play an active role in the decarbonisation process of clinical research (see also p. 22, Table 1, Uegaki paper).

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The opinions expressed in this article are the author's own and not necessarily shared by her employer or EMWA.

#### **Disclosures and conflicts of interest**

The author is employed in the pharmaceutical industry.

#### Data availability statement

Search results in PubMed are available for sharing. All five papers summarised are open access. Please contact the author for more information.

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# On the Carbon Reduction Guidelines of UK's National Institute for Health Research (NIHR)

#### What are the NIHR Carbon Reduction Guidelines?

nder the Climate Change Act of 2008, the UK government has committed to significantly reduce UK greenhouse gas emissions by 2050. Healthcare is one of the key drivers of these emissions.

The National Institute for Health Research (NIHR) guidelines are part of the National Health Services (NHS)'s commitment to meet the targets set by the Climate Change Act.

"The NHS has a carbon footprint of about 21 million tonnes of CO2 per year, representing around 25% of public sector greenhouse gas emissions... As the leading funder of health research in the NHS, the NIHR must play a role in reducing carbon emissions from health research."

The guidelines were published on July 30, 2019. There are plans to update these guidelines soon.

## Who should use the guidelines and how should they be used?

The guidelines are "aimed at researchers conducting research funded by the NIHR and

outlines some approaches for reducing the greenhouse gas emissions from health research." However, the principles of the guidelines are applicable to all research, regardless of the type of research, source of funding, or geography.

The guidelines are not mandatory; they provide a framework to reduce the carbon footprint of clinical research without adversely impacting the quality, validity, and reliability of research.

#### Who developed the guidelines?

The guidelines were developed by UK researchers based on data published in two research papers:

- Sustainable Trials Study Group. Towards sustainable clinical trials. BMJ. 2007 Mar 31; 334(7595):671–3. doi:10.2471/BLT.19.249508.
- Lyle K, Dent L, Bailey S, et al. Carbon cost of pragmatic randomised controlled trials: retrospective analysis of sample of trials. BMJ. 2009 Oct 30;339:b4187. doi: 10.1136/bmj.b4187.

# What are some of the key recommendations of the guidelines?

The recommendations of the guidelines fall under two main categories: sensible study design and reducing the environmental impact of the NHS through research.

#### The high-level headings are as follows:

- Setting the research question and making full use of existing evidence
- Efficient study design
- Study set up and conduct
- Avoiding unnecessary data collection
- Sensible clinical trial monitoring
- Good practice in reporting research
- Reducing the environmental impact of the NHS through research

The NIHR Carbon Reduction Guidelines are available at

https://www.nihr.ac.uk/documents/the-nihrcarbon-reduction-guidelines/21685

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