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Climate footprint of industry-sponsored in-human clinical trials: life cycle assessments of clinical trials spanning multiple phases and disease areas

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ABSTRACT

Objective This study aims to calculate the global warming potential, in carbon dioxide (CO_2) equivalent emissions, from all in-scope activities involved in phase 1, 2, 3 and 4 clinical trials spanning multiple disease areas.

Design The study design involved a retrospective analysis of completed clinical trials.

Setting Select set of seven clinical trials conducted between 2018 and 2023 and sponsored by Johnson & Johnson Innovative Medicine: TMC114FD1HTX1002, 77242113PSO2001, 42756493BLC2002, 54767414MMY3012, VAC18193RSV3006, R092670PSY3016 and 28431754DIA4032

Participants While participants and the public were involved in all seven trials, the life cycle assessments (LCAs) were performed as an independent retrospective analysis after the clinical trials were completed. As a retrospective analysis, we leveraged clinical trial documentation and interviews with the sponsor trial staff and trial site staff. None of the participating trial subjects were involved specifically in the LCA analysis, nor was any personal identifying information from the trial subjects collected or shared.

The underlying clinical trials were performed in accordance with the Declaration of Helsinki and Guidelines for Good Pharmacoepidemiology Practice. All participating investigators were required to obtain full governing board approval for conducting research involving humans. Sponsor approval and continuing review were obtained through the appropriate Institutional Review Board/Ethics Committee (IRB) and Health Authority channels. For academic investigative sites that did not receive authorisation to use the central IRB, full board approval was obtained from their respective governing IRBs, and documentation of approval was submitted to Johnson & Johnson Innovative Medicine, LLC, before the site's participation and initiation of any trial procedures. All registry participants provided written informed consent and authorisation before participating.

Primary outcome measure Primary outcome measure CO_2 equivalents (CO_2e) for in-scope clinical trial activities calculated according to Intergovernmental Panel on Climate Change 2021 impact assessment methodology.

Results The TMC114FD1HTX1002 phase 1 trial was the smallest trial both in terms of number of patients (39) and sites (1) and had the smallest emissions at 17 648 kgCO_2e. The 54767414MMY3012 phase 3 trial was not the largest trial in terms of number of participating patients (517) but had the largest number of participating sites (129) and had the largest emissions at 3 107 436 kg CO_2e. Across all seven trials analysed, the mean emissions per patient were 3260 kg CO_2e. When the overall trial footprints are broken down by phase, the phase 2 mean per patient was 5722 kg CO_2e and the phase 3 mean per patient emissions were 2499 kg CO_2e. The five largest contributors of greenhouse gas (GHG) emissions were drug product (50% mean), patient travel (10% mean), travel for on-site monitoring visits (10% mean), collection and processing of laboratory samples (9% mean) and sponsor staff commuting (6% mean). Patient travel was the only consistent GHG hotspot across all seven trials, as other hotspots appeared intermittently in some trials but not others based on variations in trial design. Across the multisite phase 2, 3 and 4 trials we analysed, a combination of the observed five largest contributors to GHG emissions were responsible for no less than 79% of GHG emissions for any one trial.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first study comparing greenhouse gas (GHG) emissions from industry-sponsored clinical trials spanning all four phases of clinical development and across different disease areas.
⇒ Study limitations are associated largely with the available data, and the data gaps, such as lack of visibility to the associated GHG emissions of some drug products, were filled by proxy values or assumptions.
⇒ The involved trials were selected to show diversity and may not be representative of all trials of their type.
⇒ Due to resource limitations, the sample size remains limited.
⇒ Despite the limitations, overall, the assessment is a reasonable estimate of the GHG emissions and key drivers of GHG emissions for this subset of clinical trials.

Conclusions Based on our LCAs of seven clinical trials spanning all four phases of development and multiple disease areas, there are five activities that drive no less than 79% of the average clinical trial's GHG footprint. These are drug product manufacture, packaging, and distribution; patient travel; on-site monitoring visit travel; the collection, transport and processing of laboratory samples; and sponsor staff commuting between their homes and the office. Understanding the activities that drive GHG emissions in clinical trials can both guide trial designers in avoiding or minimising reliance on these activities when designing new trials and guide trial sponsors in taking targeted actions to reduce GHG emissions from these activities where their use cannot be avoided.

Trial registration number TMC114FD1HTX1002 (ClinicalTrials.gov: NCT04208061), 77242113PSO2001 (ClinicalTrials.gov: NCT05364554), 42756493BLC2002 (ClinicalTrials.gov: NCT03473743), 54767414MMY3012 (ClinicalTrials.gov: NCT03277105), VAC18193RSV3006 (ClinicalTrials.gov: NCT05070546), R092670PSY3016 (ClinicalTrials.gov: NCT04072575) and 28431754DIA4032 (ClinicalTrials.gov: NCT04288778).

INTRODUCTION

Historically, life cycle assessments (LCAs) of pharmaceuticals have been process or product driven, either focusing on part of the pharmaceutical supply chain[1–3] or assessing the footprint of a product.[4] However, LCA boundaries have gradually expanded, and a new focus has emerged. This new area recognises that pharmaceuticals as a product are just one element of a larger care pathway featuring healthcare provider visits, hospitalisation and/or outpatient care.[5–7] A limitation of the recent care pathway approach is that it has focused on typical care pathways in a commercial setting after a drug has received regulatory approval and has often neglected the environmental impact of clinical research required to bring those drugs to market. This research seeks to close that gap by shedding light on the greenhouse gas (GHG) emissions of clinical trials and the key underlying drivers of those emissions in clinical trial designs.

A phase 1 trial represents the first testing of a new drug in humans primarily to assess safety. A drug is given to a small group of healthy volunteers who are then closely monitored. If the safety profile of the drug is favourable, then it may advance to phase 2, where a small group of volunteers with the targeted disease are given the drug to further assess safety, understand how the drug is metabolised, and begin to assess efficacy. If the safety and efficacy profile continue to prove favourable, then a drug may advance to phase 3 where a larger population of volunteers with the targeted disease are exposed to the drug for continued evaluation of safety and efficacy. It is frequently the phase 3 trials that provide the safety and efficacy data required to obtain regulatory approval for the commercial marketing of a new drug; however, overly compelling phase 1 or phase 2 trials can also meet this goal through the breakthrough therapy designation. Phase 4 trials, or postmarketing trials, occur after a drug has received regulatory approval and seek to gather additional data regarding the long-term safety profile of the drug. The common purpose of all phases of clinical trials is to assess safety, but these trials come at a cost as they are carbon intensive. We have little understanding of their magnitude nor the underlying processes that are key drivers behind a trial's overall GHG emissions.

LCA is a standardised method[8 9] for assessing the potential environmental impacts of product systems, taking into consideration all processes related to the product or service life cycle and all relevant environmental impacts.[10] Many companies, business associations and policy-makers use this method as a decision-support tool, providing a quantitative evaluation of environmental sustainability. While LCA methodology allows for the assessment of a broad range of environmental impacts such as land use, water acidification and toxicity, this paper focuses only on measuring the GHG emissions of the clinical trial system. The goals of this project were threefold: to benchmark the GHG emissions across an array of clinical trials spanning multiple trial phases and disease areas, identify primary drivers affecting GHG emissions and inform clinical trial sponsors and those involved in designing clinical trials of potential opportunities to mitigate the impacts of these hotspots.

This new research is intended to complement an earlier publication[11] by expanding our knowledge of clinical trial LCA emissions to include larger clinical trials involving multiple clinical trial sites and countries, and the additional resources and oversight they require.

METHODS

This study uses LCAs to measure the GHG emissions of a set of seven clinical trials sponsored by Johnson & Johnson Innovative Medicine that span all four phases of clinical development as well as multiple disease areas. The LCAs were inclusive of clinical site utilities and other gaps observed in earlier research.

All in-scope clinical trials were conducted between 2018 and 2023. The operational details of the trials are outlined in table 1. The trials were intentionally selected to span different disease areas, trial phases, as well as an attempt to ensure a global representation of clinical site locations (eg, Asia Pacific, Central Asia, Europe, Latin America and North America). All trials were recently completed trials, so that we had a full accounting of all consumables and could ensure access to data such as site personnel travel between their homes and the site which wouldn't be captured in standard trial documentation and risked loss with time.

The LCA boundary conditions excluded overhead functions such as IT services, legal, healthcare compliance and other roles critical to overall clinical research conduct and broader sponsor operations. While these functions are important, they did not directly report the time and resources they expend in support of any one clinical study making it impossible to amortise a portion of their emissions to any one trial. The exclusion of these functions aligns with the boundary conditions of more recently published research.[11 12]

Table 1 Overview of in-scope clinical trials and their specifications

Trial phase	Phase 1	Phase 2		Phase 3		Phase 4	
Clinical trial	TMC114HTX1002	77242113PSO2001	42756493BLC2002	54767414MMY3012	R092670PSY3016	VAC18193RSV3006	28431754DIA4032
Intervention type*	New therapeutic	New therapeutic		New therapeutic		Vaccine	New therapeutic
Disease area	HIV	Psoriasis	Urothelial cancer	Multiple myeloma	Schizophrenia	Respiratory Syncitial Virus	Diabetes
Enrolled patients	39	255	125	517	178	1124	276
Clinical sites	1	76	127	129	30	23	11
Involved countries	1	10	13	18	6	5	1
Drug product kits produced	11	10672	24641	30013	3067	5394	1676
Laboratory samples shipped	3335	56129	46086	120268	1098	35439	0
Sponsor supporting FTEs	2.52	18.2	46.7	115.2	29.3	15.2	2.0
Face-to-face patient visits	357	2103	3841	13789	1404	3369	1661

All data listed as n.
*Intervention defined in alignment with Smith PG, Morrow RH, Ross DA, editors. Field Trials of Health Interventions: A Toolbox. 3rd edition. Oxford (UK): OUP Oxford; 2015 Jun 1. Chapter 2, Types of intervention and their development.
FTE, full-time equivalent; RSV, respiratory syncytial virus.

Included trials

We have previously investigated the GHG emissions of a phase 1 trial, TMC114FD1HTX1002.[11] We include the results of that analysis here to compare to the results with those of phase 2, 3, and 4 trials. This new research is intended to complement the earlier publication by expanding our knowledge of clinical trial LCA emissions to include larger clinical trials involving multiple clinical trial sites and countries, and the additional resources and oversight they require.

We selected trials that we perceived to represent the spectrum of potential GHG emissions, including two phase 2 trials, three phase 3 and two phase 4 trials. Further diversity was introduced by including trials from different disease areas.

VAC18193RSV3006 was a randomised, double-blind, placebo-controlled, phase 3 trial to investigate the safety and immunogenicity of the Ad26.RSV.preF based vaccine in adults 18–59 years of age who are healthy or at risk for severe respiratory syncytial virus (RSV) disease, compared with adults 65 years and above. The trial involved the administration of a single dose of either active or placebo vaccine followed by laboratory assessments at seven or more time points per patient shipped frozen to a central lab.

54767414MMY3012 was a randomised phase 3 trial intended to demonstrate that a subcutaneous administration of investigational drug JNJ-54767414 was non-inferior to intravenous administration terms of the overall response rate and maximum trough concentration. It was a global trial involving clinical sites across North American, European, Asia Pacific and Latin American regions. The average patient visited the site more than 26 times. The trial involved skeletal scans (CT scans, MRI, X-ray per local standard of care) and bone marrow aspirates to monitor disease progression and treatment response. Additionally, it involved frequent laboratory assessments with the shipment of frozen samples to central labs.

R092670PSY3016 was a double-blind, randomised, active-controlled, parallel group, phase 3 trial to assess the long-term safety and tolerability of paliperidone administration via a dose once every 6-month formulation. It was a global trial involving clinical sites in North America, European, Asia Pacific and Latin America regions. Of note to this trial is that it involved a relatively insignificant amount of central laboratory testing, as trial endpoint measures were based on psychiatric assessments and labs that could be performed locally.

77242113PSO2001 was a dose-ranging trial to evaluate the long-term clinical response of investigational drug JNJ-77242113 in participants with moderate-to-severe plaque psoriasis. It involved a broad mix of sites in the Asia Pacific, European and North American regions.

42756493BLC2002 was a phase 2 study to evaluate safety, efficacy, pharmacokinetics and pharmacodynamics of various regimens of investigational drug JNJ-42756493 in subjects with metastatic or locally advanced urothelial cancer. It was a global study with sites in Asia Pacific, Central Asia, European, Latin American and North American regions. Of note is that this trial originally started in January 2018 with trial operations outsourced to a contract research organisation (CRO). The sponsor company decided to take back management of trial operations and bring them in-house. The sponsor assumed full management of trial operations by April 2019, but this left a 14-month gap from January 2018 until April 2019 when it was under the control of the CRO. Because data around staff locations and commuting were not available during the period the CRO was in control, sponsor location and commuting data were substituted to represent how trial conduct would have appeared with the sponsor managing the trial from the beginning.

28431754DIA4032 was an open-label, single-arm, phase 4 trial to evaluate the safety and efficacy of canagliflozin and metformin hydrochloride immediate-release fixed-dose combination as an adjunct to diet and exercise to improve glycaemic control in Indian adult patients with type 2 diabetes mellitus when treatment with both canagliflozin and metformin is appropriate. It was a single-country trial involving sites in India. All laboratory samples were processed locally.

Patient and public involvement

While participants and the public were involved in the 77242113PSO2001 (ClinicalTrials.gov: NCT05364554), 42756493BLC2002 (ClinicalTrials.gov: NCT03473743), 54767414MMY3012 (ClinicalTrials.gov: NCT03277105), VAC18193RSV3006 (ClinicalTrials.gov: NCT05070546), R092670PSY3016 (ClinicalTrials.gov: NCT04072575) and 28431754DIA4032 (ClinicalTrials.gov: NCT04288778) clinical trials, the LCAs were performed as an independent retrospective analysis after the clinical trial was completed. None of the participating trial subjects were involved specifically in the LCA analysis nor was any personal identifying information from the trial subjects collected or shared.

LCA methodology

The LCA was conducted under a dynamic and iterative approach in accordance with ISO 14040/44 standards and peer reviewed by an independent third party. The system boundary of the LCA is summarised in table 2 and visually represented in online supplemental figure A.

Data sources

According to the definitions of the Life Cycle Initiative,[13] the foreground system consists of processes/activities which are under the control of the decision-maker for which an LCA is carried out. The background system consists of processes on which no or, at best indirect, influence can be exercised by the decision-maker. For this LCA, the foreground system is the activities/processes presented in online supplemental figure A. The background system is all supporting activities/processes, including electricity production, energy/heat production, transport operations and incineration processes.

Table 2 System boundary summary

Classification	Category	Activity	Description
Included activities	Drug product	Active pharmaceutical ingredient production	Manufacture of the active components in a pharmaceutical drug that produce the required effect on the body to treat a condition
		Formulation and packaging and labelling	Process in which different chemical substances, including the active pharmaceutical ingredient, are combined to produce a final medicinal product. This is followed by the application of protective packaging and identifying labels in accordance with local regulations.
		Shipment and distribution	Includes distribution and storage of packaged trial drug including emissions from local depots.
		Destruction of waste	End-of-life treatment for unused trial drug. Includes transport from sites to final destination for destruction.
	Site operations	Consumables and trial equipment	Materials consumed by the site in support of trial conduct. This includes exam gloves and other materials used in the clinic as well as equipment such as computers and instruments involved in trial conduct.
		Staff commuting	Travel of trial-related site staff to and from their homes and the clinical site.
		Utilities	Emissions associated with the energy consumed heating, cooling and lighting the site and any impacts from operating site equipment.
	Laboratory samples	Testing kits	Clinical sample collection kits customised to each unique clinical trial protocol and specifically designed to allow for the collection, storage and shipping of different sample types, such as plasma, urine, serum and whole blood.
		Ambient shipments	Shipment of lab samples from the site to the central lab under ambient conditions.
		Frozen shipments	Shipment of lab samples from the site to the central lab under frozen conditions through the use of dry ice.
		Analysis	Analysis of sample at a central lab including materials and energy consumed.
		Storage (biobanking)	Long-term frozen storage of retention samples in biobanks (assumed 7.5 years)
	Patient travel		Patient transport to and from the clinical site based on distance and mode of transport as reported by participating subjects
	Trial meetings		External meetings include investigator meetings and independent review board meetings to review and approve the trial design.
	Sponsor operations	On-site monitoring	Travel by site monitors to and from their homes to trial sites to ensure patient safety and site compliance with the trial protocol and procedures
		Staff commuting	Travel by sponsor staff to and from their homes to sponsor facilities
		Utilities at sponsor facilities	Includes emissions associated with energy consumed heating, cooling and lighting sponsor facilities as well as the impact of equipment provided to sponsor staff such as computers and smartphones
		Staff utilities working from home	Includes emissions associated with energy consumed when sponsor staff work from their homes.
Excluded activities	Patient home utilities		Emissions occurring at the patient's home during at-home administration of the drug product were excluded as participation in the trial had no influence on at-home emissions
	Sponsor land use		Land use associated with Johnson & Johnson Innovative Medicine employees, trial site investigators and patients, due to their expected immateriality
	Capital goods and infrastructure		Capital goods and infrastructure such as sponsor facilities and drug product manufacturing equipment.

For foreground data, certain key parameters (eg, distances, number of visits of participants) are provided as primary data by the case study. Foreground data such as distance and mode of transport for participants, site staff and sponsor staff were based on administered surveys and typical regional behaviour data. Participant responses were anonymised by site staff with only distance and mode of transport provided for analysis.

As no LCAs had previously been performed for any of the drug products included in the clinical trials, proxy

data needed to be used. For non-biological drug products, data from the Association of British Pharmaceutical Industry tools[14] were used as a proxy for the climate change impacts of the active pharmaceutical ingredient (API) (1500 kg carbon dioxide equivalents (CO_2e) per kg). Proxy data from the Ecoinvent v3.8 emissions-factor database were then scaled so that results for all the environmental impact categories could be generated. For biological drug products, data were sourced from Budzinski *et al*[15] to develop a proxy climate change impact for the API of 22.7 t CO_2e per kg.

Other sources of foreground data were based on estimations or calculations, such as utilities consumption at clinical trial sites. While many sites expressed an interest in sustainability, most lacked the bandwidth to support our data collection efforts. For utilities consumption at the trial site and at other sites (eg, clinical management), a time-related allocation was considered where specific activity consumption data were not available. For instance, considering the number of full-time equivalent (FTE) employees working at the specific sites (for the clinical trial) in relation to the total number of FTE at the specific sites.

Background data characterising activities in the background system were drawn from the Ecoinvent Database V.3.8[16] and used as alternative data to represent foreground processes where more reliable primary data (or good estimations) are not available.

All data used in our analysis are publicly available through DRYAD.[17]

LCA Method

The LCA model is created using the SimaPro V.9.5 Software system for life cycle engineering, developed by PRé Consultant BV.[18] The environmental impact of the study, expressed by the global warming potential, was calculated according to the Intergovernmental Panel on Climate Change 100 years method based in kilograms of CO_2e.[19]

RESULTS

The TMC114FD1HTX1002 phase 1 trial was the smallest trial both in terms of number of patients (39) and sites (1) and had the smallest emissions at 17 648 kgCO_2e. The 54767414MMY3012 phase 3 trial was not the largest trial in terms of number of participating patients (517) but had the largest number of participating sites (129) and had the largest emissions at 3,107,436 kg CO_2e. Across all seven trials analysed, the mean emissions per patient were 3260 kg CO_2e. When the overall trial footprints are broken down by phase, the phase 2 mean per patient was 5722 kg CO_2e and the phase 3 mean per patient emissions were 2499 kg CO_2e. The five largest contributors of GHG emissions were drug product (50% mean), patient travel (10% mean), travel for on-site monitoring visits (10% mean), collection and processing of laboratory samples (9% mean) and sponsor staff commuting (6% mean). Patient travel was the only consistent GHG hotspot across all seven trials, as other hotspots appeared intermittently in some trials but not others based on variations in trial design. Across the multisite phase 2, 3 and 4 trials we analysed, a combination of the observed five largest contributors to GHG emissions was responsible for no less than 79% of GHG emissions for any one trial. Online supplemental tables 3 and 4 provide a breakdown of the major sources of GHG emissions across the trials from both total emissions and per-patient emissions perspectives, while online supplemental figure B provides a graphical representation of the primary contributors to the overall GHG emissions for the trial.

DISCUSSION

The goal of this research is to provide a better understanding of the scale of GHG emissions from industry-sponsored clinical trials and the key drivers of those emissions. In our analysis, we observed two significant sources of GHG emissions which until recently were largely absent from previous research[20] . These were patient travel, which contributed to 10% of emissions on average in our sample with a maximum observed contribution of 29%, and clinical site operations, which contributed to 5% of emissions on average in our sample with a maximum observed contribution of 25%. Until recently, previous research has fallen into two categories: those that underestimated the GHG emissions of patient travel or those that neglected or underestimated the impact of GHG emissions from clinical trial sites.

In the former category, Lyle *et al*[21] assumed that participant travel to and from the site was like that of a typical general practice in the UK, with travel of 2.4 km for primary care and 17.4 km for secondary care visits. This contradicts other research[22 23] where average patient travel for clinical site visits averaged between 80 km and 83 km, a near fivefold increase in distance.

The second category of publications[24 25] excludes GHG emissions at the clinical sites under the rationale that hospitals or clinics would exist and continue to operate without the clinical trial in question, and any incremental increase in emissions from the clinical trial would be negligible. During the conduct of our research, we observed that many hospitals have dedicated clinical trial units that have separate operations from the main hospital and are dedicated to clinical trial conduct. The GHG emissions of such clinical trial units should therefore be considered very distinct and separate from the normal operations of the hospitals, as they would not exist in the absence of clinical trials.

The most comprehensive analysis found to date has been that of MacKillop *et al*[12] and the previous publication of the TMC114FD1HTX1002 trial.[11] MacKillop *et al* examined the GHG emissions of three phase 3 clinical trials sponsored by Astra Zeneca. Both analyses thoroughly assessed patient travel and clinical site utilities and sought to create a comprehensive approach that would

be replicated in future clinical trial LCAs. Our research aligns with the scope and depth of these analyses.

Across the phase 2, 3, and 4 studies in our samples, we saw a common set of five activities that contributed to no less than 79% of trial emissions. Patient travel was the only consistent GHG hotspot across all seven trials, as other hotspots appeared intermittently in some trials but not others based on variations in trial design. For example, laboratory samples were a negligible source of GHG emissions in the R092670PSY3016 phase 3 schizophrenia trial. The trial was focused on new therapeutic interventions for schizophrenia, a disease that lacks any blood-based biomarkers, so the use of laboratory samples was limited to pregnancy tests and other simple laboratory measures involved assessing patient eligibility to participate in the trial and none during the actual patient treatment phase.

Comparing the LCA results of the phase 2, 3 and 4 studies in our sample to the previously published LCA results for the TMC114FD1HTX1002 phase 1 HIV trial, we see some more significant differences in the key sources of emissions. These are explained by two important differences in the design and execution of the TMC114FD1HTX1002 trial compared with the others. First, the TMC114FD1HTX1002 trial involved only a single clinical trial site, and the trial timelines for recruitment and treatment of the trial participants were well within the shelf-life of the drug products used. This provided the trial sponsor with near certainty of the amount of drug product required for the trial, and they were able to supply the drug product needs of the trial with negligible waste. In our sample of phase 2, 3, and 4 trials, all trials involved multiple clinical trial sites; and for many of the trials, the overall timelines for trial execution extended well beyond the shelf-life of the involved drug products. When clinical trials involve multiple clinical trial sites, it poses a forecasting challenge in predicting how many patients will be enrolled into the trial at each clinical trial site and the timing of that enrolment. This forces trial sponsors to maintain high levels of safety-stock inventory to counter variability, and that poses a high risk of obsolescence when actual enrolment comes in below forecast. As a result of these challenges, it has been estimated that industry-wide obsolescence is as high as 50%[26] and in some of the trials in our sample, we saw obsolescence rates in this range. The second significant difference between the TMC114FD1HTX1002 trial and the phase 2, 3 and 4 trials in our sample was that the TMC114FD1HTX1002 trial involved a dedicated phase 1 clinical trial site, with oversight provided by monitors already located on-site. This avoided the need for travel associated with on-site monitoring visits. These design differences between the TMC114FD1HTX1002 trial and the other trials in our sample allowed it to avoid the strong influence of drug product (mean 50% of GHG emissions) and on-site monitoring visit travel (mean 10% of GHG emissions) seen in the phase 2, 3 and 4 trials.

While this is the first study detailing the emissions of several different trial types, these trials were selected to show diversity and may not be representative of all trials of their type. Due to resource limitations, the number of trials analysed does not represent a statistically relevant sample size, and the LCAs themselves were limited by our data sources. Despite these limitations, for multisite studies, we believe that the five activities of drug product manufacture, packaging and distribution; patient travel; on-site monitoring visit travel; the collection, transport and processing of laboratory samples; and sponsor staff commuting between their homes and the office; reflect the primary sources of GHG emissions. Addressing these hotspot activities in both the design of new clinical trials and through targeted action to reduce their emissions presents the strongest levers for reducing the GHG emissions of clinical trials.

CONCLUSION

Based on our LCAs of seven clinical trials spanning all four phases of development and multiple disease areas, there are five activities that drive no less than 79% of the average clinical trial's GHG footprint. These are drug product manufacture, packaging and distribution; patient travel; on-site monitoring visit travel; the collection, transport and processing of laboratory samples; and sponsor staff commuting between their homes and the office. Understanding the activities that drive GHG emissions in clinical trials can both guide trial designers in avoiding or minimising reliance on these activities when designing new trials and guide trial sponsors in taking targeted actions to reduce GHG emissions from these activities where their use cannot be avoided.

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Contributors JKL, WDS and KR conceived of and presented the idea. All authors contributed to study design. JKL and JL selected the clinical trial from the larger Johnson and Johnson Innovative Medicine clinical trial portfolio for analysis. JKL, JL, MC, TC, WDS, AC and KR contributed to acquisition of data. TC, MC and HW created the data models for the analysis, while all authors contributed to the analysis and interpretation of data. All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. JKL serves as both submitting and corresponding author. JKL is a guarantor.

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Competing interests JKL is an employee of Johnson & Johnson Innovative Medicine, LLC, and a member of the faculty at Delft University of Technology. JL is an employee of Johnson & Johnson Innovative Medicine, LLC. RA is an employee of Environmental Resource Management, LLC. MC is an employee of Environmental Resource Management, LLC. TC is an employee of Environmental Resource Management, LLC. HW is an employee of Environmental Resource Management, LLC. AC is an employee of ICON, PLC. WDS is an employee of Johnson & Johnson

Innovative Medicine, LLC. JF is a faculty member at Delft University of Technology. KR is an employee of Johnson & Johnson Innovative Medicine, LLC.

Patient and public involvement While participants and the public were involved in the 77242113PSO2001 (ClinicalTrials.gov: NCT05364554), 42756493BLC2002 (ClinicalTrials.gov: NCT03473743), 54767414MMY3012 (ClinicalTrials.gov: NCT03277105), VAC18193RSV3006 (ClinicalTrials.gov: NCT05070546), R092670PSY3016 (ClinicalTrials.gov: NCT04072575), 28431754DIA4032 (ClinicalTrials.gov: NCT04288778) clinical trials, the life cycle assessment was performed as an independent retrospective analysis after the clinical trial was completed. None of the participating trial subjects were involved specifically in the LCA analysis nor was any personal identifying information from the trial subjects collected or shared.

Patient consent for publication Not applicable.

Ethics approval The underlying clinical trials were performed in accordance with the Declaration of Helsinki and Guidelines for Good Pharmacoepidemiology Practice. All participating investigators were required to obtain full governing board approval for conducting research involving humans. Sponsor approval and continuing review were obtained through the appropriate Institutional Review Board/Ethics Committee and Health Authority channels. For academic investigative sites that did not receive authorisation to use the central IRB, full board approval was obtained from their respective governing IRBs, and documentation of approval was submitted to Johnson & Johnson Innovative Medicine, LLC before the site's participation and initiation of any trial procedures. All registry participants provided written informed consent and authorisation before participating.

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Data availability statement Data are available in a public, open access repository. [Dataset] LaRoche, Jason. 'LCA Reports for Janssen-sponsored phase-2, 3, 4 clinical studies'. Dryad, 2025. DOI: 10.5061/dryad.n5tb2rc45.

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