Nature Environment and Pollution Technology
An International Quarterly Scientific Journal

p-ISSN: 0972-6268
(Print copies up to 2016)
e-ISSN: 2395-3454

Vol. 22 | No. 4 | pp. 2111-2119 | 2023

Original Research Paper

https://doi.org/10.46488/NEPT.2023.v22i04.036

Open Access Journal

Reducing the Carbon Footprint of Clinical Trials: Implementing Sustainable Practices in Clinical Research

Aditi Nidhi†
Gujarat National Law University, Gandhinagar, Gujarat, India
†Corresponding author: Aditi Nidhi; aditinidhirmlnlu@gmail.com

Nat. Env. & Poll. Tech.
Website: www.neptjournal.com

Received: 24-03-2023
Revised: 25-04-2023
Accepted: 30-04-2023

Key Words:
Clinical trials
Environment
Healthcare
Carbon emission

ABSTRACT

Sustainable clinical trials involve conducting trials in a socially conscious and environmentally responsible manner. This involves considering the effects of clinical trials on the environment and the populations engaged in the studies. The pharmaceutical sector, particularly clinical research, is a large contributor to greenhouse gas emissions. The need for a legal framework considering the environmental impact of hundreds of global clinical trials cannot be overstated. Clinical trials' carbon footprint is a complex subject that calls for cooperation from various parties, including researchers, trial sponsors, healthcare providers, and regulatory organizations. The waste generated during clinical trials, including packaging materials, laboratory supplies, and hazardous waste from the disposal of clinical samples, can adversely affect public health and the environment. Therefore, addressing this issue is essential to ensure that clinical trials are conducted in an environmentally and socially responsible manner. The purpose of this study is to discuss potential strategies to cut down on carbon emissions, discuss the challenges in setting up clinical trials in an environmentally sustainable way, and highlight the importance of a precautionary approach during the various phases of conducting clinical trials. Although there is limited research on greenhouse gas emissions generated by clinical trials, it is evident that more work needs to be done in this field.

INTRODUCTION

Clinical trials are an essential component of medical research because they provide evidence that can be used to support the development of novel medicines and treatments to improve healthcare quality (Subbiah 2023). However, conducting clinical trials has significant environmental implications, as they generate substantial amounts of waste and carbon emissions. Although the healthcare sector is vital for saving lives, it has a significant ecological footprint (Lenzen et al. 2020). As a result of climate change, it is imperative to reduce carbon emissions and waste generation. It is essential to explore how clinical trials impact the environment and develop solutions to mitigate their environmental impact while continuing to advance medical research (Clark et al. 2019).

It has been established for quite some time that social, biological, and environmental factors can affect or cause diseases, and numerous clinical trials have been conducted to ascertain the impact of environmental factors on a range of outcomes (Manisalidis et al. 2020). Among other topics, these trials investigated the effect of environmental factors on drug efficacy in treating dry-eye syndrome, the relationship between diet and obesity and cardiovascular disease, and the environmental impact on autoimmune diseases (Fugger et al. 2020). Despite the fact that the healthcare business has prevented the loss of millions of lives, it has had a substantial influence on the environment as a result of its operations (Clarke 2014).

The healthcare sector ranks among the most carbon-intensive industries in the developed world, contributing between 4.4 and 4.6 percent of global greenhouse gas emissions and a comparable amount of harmful air pollutants (Parkins 2022). Healthcare must undergo sustainability revamp, including clinical trials, to reach the target of net-zero carbon emissions by 2030 (Singh et al. 2022). In terms of carbon emissions, a recent study found that over 350,000 national and worldwide clinical trials produce 27.5 million tonnes of greenhouse gas emissions (Cuffari 2021). The Declaration of Helsinki calls for research processes to minimize harm to the environment (Halonen et al. 2021). Still, clinical trials have a negative environmental impact due to greenhouse gas emissions from shipping and transport, as well as waste production, which is an underexplored contributor to greenhouse gas emissions (WHO 2005).

Hence, the healthcare industry must address its environmental impact and take a sustainable approach to clinical trials, which are essential for advancing medical research. By reducing carbon emissions and waste production in clinical trials, we can minimize the environmental impact of healthcare while improving public health outcomes. Thus, this paper will examine the environmental impact of clinical trials, including their carbon footprint and waste production, and propose strategies to promote sustainable clinical trials.

ENVIRONMENTAL IMPACT OF CLINICAL TRIALS

Clinical trials are vital for the development of novel pharmaceuticals and medical treatments, thereby contributing to the improvement of global health and well-being (Inan et al. 2020). However, the conduct of clinical trials can also have environmental impacts that need to be carefully considered and addressed.

The environmental impacts of clinical trials can be direct or indirect (Selby 2011). Direct environmental impacts may include energy and water consumption, hazardous waste generation, air and noise pollution, and land use change (Drew et al. 2022). These impacts can be associated with the construction and operation of clinical trial facilities and the transportation of participants, staff, and equipment. Indirect environmental impacts (WHO 2021) may include the production and transportation of pharmaceuticals and medical devices, as well as impacts on local communities, global health, and animal welfare.

Given the potential negative environmental impacts of clinical trials, it is important for researchers and sponsors to incorporate sustainable practices into clinical trial design and implementation (Alemayehu et al. 2018). This can include strategies such as reducing energy and water consumption, minimizing waste generation, using renewable energy sources, and engaging with local communities to address concerns related to the trial (Edenhofer et al. 2011). By considering the environmental impacts of clinical trials and taking steps to mitigate these impacts, researchers and sponsors can help to ensure that the development of new medical treatments is consistent with environmental sustainability.

Clinical trials can have various environmental impacts, including:

a) Resource consumption: Clinical trials require significant resources such as energy, water, and materials for equipment and supplies, which can contribute to environmental degradation (Rajadhyaksha 2010).

b) Waste generation: Clinical trials generate large amounts of waste, including hazardous waste such as chemicals and biological materials. The disposal of this waste has the potential to have an adverse effect on the surrounding ecosystem.

c) Transportation: Clinical trials often involve the transportation of study participants, clinical staff, and equipment, which can contribute to air pollution and greenhouse gas emissions (Rissman et al. 2020).

d) Land use: Clinical trials may require the use of land for study sites, which can result in habitat destruction, deforestation, or other forms of land use change (OECD 2019).

e) Animal testing: Some clinical trials involve animal testing, which can have ethical implications and contribute to animal welfare concerns.

f) Energy consumption: Clinical trials require the use of energy for powering equipment, heating and cooling facilities, and lighting (De Franco et al. 2017). The energy consumed during clinical trials can contribute to greenhouse gas emissions and other pollutants.

g) Air pollution: The transportation of study participants, clinical staff, and equipment can contribute to air pollution and greenhouse gas emissions. Some medical procedures may also generate air pollutants, such as anesthetic gases.

h) Noise pollution: Clinical trials may generate noise from equipment and machinery used in medical procedures, which can harm the health of humans and wildlife (Belay et al. 2021).

i) Use of non-renewable resources: Clinical trials may require using non-renewable resources, such as fossil fuels, for transportation and electricity generation (Avtar et al. 2019). This can contribute to climate change and other environmental problems associated with the extraction and use of non-renewable resources.

j) Soil contamination: Clinical trials involving hazardous chemicals or biological agents can lead to soil contamination if these substances are not properly disposed of (Ashraf et al. 2014). This can have negative impacts on soil quality and ecosystem health.

k) Landfill waste: Clinical trials may generate large amounts of non-hazardous waste, such as packaging materials and single-use medical supplies, that end up in landfills (Padmanabhan & Barik 2019). This can contribute to the environmental problems associated with landfill waste, such as greenhouse gas emissions and contamination of soil and water.

The magnitude of these direct effects on the environment is highly variable. It is determined by several factors,

including the size and scope of the clinical trial, the location of the study site, and the sort of medical procedures and equipment utilized (Manisalidis et al. 2020). However, by implementing sustainable practices and considering the environmental impacts of their work, researchers and sponsors can help minimize the negative effects of clinical trials on the environment.

Clinical trials may also have indirect environmental impacts, such as the effects of producing and transporting pharmaceuticals or medical devices used in the trials (Boxall 2004). The manufacturing process of these products may require significant amounts of energy, water, and raw materials and may generate greenhouse gas emissions and other pollutants. In addition to this, after the completion of clinical trials, the disposal of unused or expired medicines and medical devices can also have an effect on the surrounding environment (Smale et al. 2021). These products may end up in landfills, where they can leach chemicals and other harmful substances into the soil and water (Salam & Nilza 2021). The indirect environmental impacts of clinical trials may include:

a) Manufacturing and shipping of drugs and medical devices: Significant environmental impacts can be caused by the manufacturing and distribution of drugs and medical devices utilized in clinical trials (Gaw et al. 2014). The production of these items may demand substantial amounts of energy and raw materials and emit greenhouse gases and other pollutants.

b) Impact on local communities: Clinical trials may impact the quality of life of local communities by increasing traffic and noise levels, affecting access to natural resources, and altering the local landscape (Halperin 2014). This can have indirect environmental impacts, such as biodiversity or air quality changes.

c) Impact on global health: The results of clinical trials can have significant impacts on global health, including the treatment and prevention of diseases that may have environmental causes, such as air pollution-related illnesses (Turner et al. 2020). By improving human health, clinical trials can indirectly contribute to environmental sustainability by reducing disease burden and improving quality of life.

d) Use of animal models: Some clinical trials involve the use of animals, which can have indirect environmental impacts related to animal welfare and ethical concerns (Soulsbury et al. 2020). This includes using animal models to study environmental health effects, such as pollution exposure or other environmental stressors.

e) Impact on healthcare systems: The results of clinical trials can impact healthcare systems and healthcare policy, which in turn can affect the environmental sustainability of healthcare (Samuel & Lucassen 2022). For example, developing new medical treatments may increase demand for medical resources and energy use.

Overall, the indirect environmental impacts of clinical trials can be complex and multifaceted. By considering the full range of environmental impacts associated with clinical research, researchers and sponsors can take steps to minimize their negative effects and promote sustainable practices in developing new medical treatments. This includes considering the lifecycle impacts of pharmaceuticals and medical devices, engaging with local communities, and exploring alternative research methods.

Thus, clinical trials can have significant environmental impacts throughout their lifecycle, from developing and manufacturing study drugs to disposing of hazardous waste generated during the study. The main areas of concern include using resources such as water and energy, generating waste and emissions, and impacting ecosystems and biodiversity (Subbiah 2023). To reduce the environmental impact of clinical trials, researchers can implement measures such as using eco-friendly materials and manufacturing processes, reducing waste generation and energy consumption, and selecting study sites with minimal impact on local ecosystems. Collaboration between stakeholders such as pharmaceutical companies, regulators, and research institutions can also help promote sustainable clinical trial practices (Dănescu & Popa 2020). Hence, it is important to consider the environmental impact of clinical trials alongside their scientific and ethical considerations and to strive for more sustainable and responsible practices in clinical research.

CARBON FOOTPRINTS OF CLINICAL TRIALS

The carbon footprint is the total amount of greenhouse gases (GHGs) emitted by human activities like transportation, energy generation, and manufacturing. Clinical trials are a vital component of the process of developing new medicines, and they are also a contributor to the emissions of greenhouse gases (Tennison et al. 2021). The production and transportation of study medications, medical equipment, and supplies, travel of study employees, and energy usage in clinical trial facilities are all examples of activities that contribute to the emission of greenhouse gases (GHGs) during clinical trials. All of these activities have a substantial effect on the carbon footprint of clinical trials.

The carbon footprint of clinical trials has become a growing concern in recent years, as the pharmaceutical industry is one of the major contributors to GHG emissions (Belkhir & Elmeligi 2019). Pharmaceutical companies are

now recognizing the importance of reducing the carbon footprint of clinical trials to reduce their environmental impact and meet sustainability goals. The use of electric vehicles and public transportation, as well as a reduction in air travel and the increased use of remote monitoring equipment, are all part of this effort to lessen the environmental impact of clinical trials (Holmner et al. 2014). In addition, pharmaceutical companies are also exploring the use of sustainable materials in clinical trial supplies, as well as improving energy efficiency in clinical trial facilities. These initiatives not only help to cut emissions of greenhouse gases (GHG), but they also lead to cost savings and an improvement in public health.

Clinical trials are an essential step in the development of new drugs and treatments. They help ensure the safety and efficacy of these products before they are released to the public. However, clinical trials can also have a significant carbon footprint, which can have a negative impact on the environment.

A study by researchers at the University of California, San Francisco, looked at the carbon footprint of a Phase III clinical trial for a cancer drug (Lazar et al. 2018). The trial involved 200 patients from 20 different countries, and the researchers estimated that the trial generated approximately 15,000 metric tons of carbon dioxide equivalents (CO_2e) over a period of three years. Another case study on carbon footprints of clinical trials is the IMPACT (Intensive Management of Patients with Advanced Chronic Kidney Disease) trial, conducted in the United Kingdom (Sanchez et al. 2021). The trial aimed to evaluate the effectiveness of a new treatment approach for patients with advanced chronic kidney disease. The trial involved 2,746 patients from 57 different hospitals across the UK and lasted five years. An analysis of the trial's carbon footprint showed that it generated approximately 4,500 metric tons of CO_2e.

The largest contributor to the trial's carbon footprint was patient travel to and from study visits, which accounted for approximately 80% of the total emissions. Other significant sources of emissions included the production and transportation of study drugs, as well as the energy and resources required to manage and analyze the trial data. To reduce the trial's carbon footprint, the researchers implemented several strategies, including:

a) Using telemedicine and other remote technologies to reduce the need for patient travel.

b) Encouraging patients to use low-carbon modes of transportation, such as public transport or carpooling.

c) Using digital tools to collect and manage study data reduces the need for paper-based records and data transportation.

d) Encouraging hospitals and study sites to implement sustainable practices, such as using renewable energy and minimizing waste.

e) The trial reduced its carbon footprint by approximately 30% by implementing these strategies.

The IMPACT trial is an example of how clinical trials can take steps to reduce their carbon footprint, even when involving a large number of patients and sites. The strategies employed in the trial demonstrate that it is possible to prioritize sustainability without compromising the quality and integrity of the trial data. The total amount of greenhouse gas emissions produced during the lifetime of a clinical trial is referred to as its "carbon footprint." These emissions come from various sources, including the production and transportation of trial materials, the consumption of energy in clinical facilities, and the travel of study participants and staff.

Some case studies from around the world have explored the carbon footprint of clinical trials: The UK Clinical Research Collaboration (UKCRC) conducted a study in 2009 to estimate the carbon footprint of clinical trials in the UK. The study found that clinical trials accounted for approximately 2.5% of the National Health Service's (NHS) carbon footprint. In 2015, researchers at the University of California, San Francisco (UCSF) conducted a case study of a clinical trial for prostate cancer. They found that the trial's carbon footprint was primarily due to participant travel, accounting for 59% of its total emissions. A study conducted in 2017 by researchers at the University of Sydney in Australia found that clinical trials for a new drug to treat hepatitis C had a significant carbon footprint, primarily due to the production and transportation of the drug. In 2018, researchers at the University of Edinburgh in Scotland studied the carbon footprint of clinical trials for five different diseases, including diabetes and heart disease. They found that the carbon footprint varied widely depending on the disease and the trial's design. A 2020 study by researchers at the University of Copenhagen in Denmark estimated the carbon footprint of a phase 3 clinical trial for a new cancer drug. They found that the trial's carbon footprint was primarily due to energy use in clinical facilities and the manufacture and transportation of trial materials. These case studies illustrate that the issue of clinical trials' carbon footprint is a complicated one that varies considerably depending on the trial's design, the trial, the location of the trial, and the ailment being examined. However, they also state that there are chances to lessen the carbon footprint of clinical trials by implementing more environmentally friendly routines, like remote monitoring, virtual participant recruitment, and using renewable energy sources in clinical facilities.

Lowering clinical trials' carbon impact is a significant step toward sustainability and ethical corporate citizenship. As the demand for more sustainable practices continues to grow, clinical trial sponsors will likely increasingly incorporate sustainability criteria into study design and implementation.

CLIMATE CHANGE: A HEALTHCARE CHALLENGE

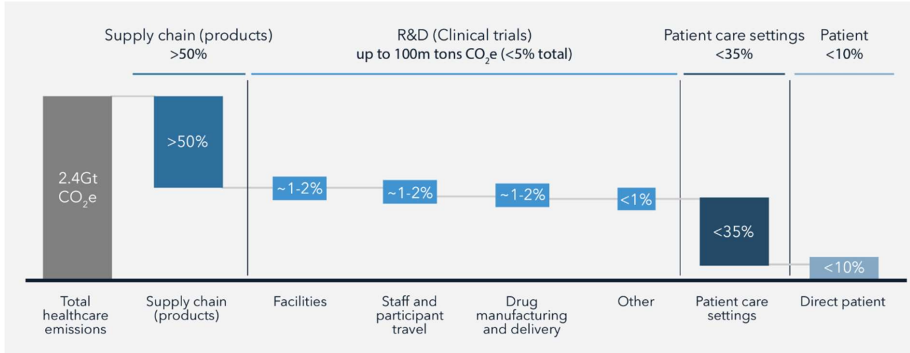
The emissions caused by the healthcare industry account for around 4 to 5 percent of the total emissions made worldwide (Prater 2019), making it the equivalent of the fifth most polluting country in the world behind Russia, India, USA, and China (Evans 2022). Health systems are being tested as they try to keep up with the growing demand for treatment in the face of demographic shifts like an aging population, an increase in chronic non-communicable diseases, and fast urbanization (Jarzebski et al. 2021). All stakeholders must work together to reduce emissions while enhancing health outcomes to reach net zero, including regulatory organizations, legislators, governments, manufacturers, health authorities, and payers.

To successfully decarbonize intricate healthcare systems, cutting emissions at every level of the value chain will be necessary, including research and development, the supply chain, and patient care. While most healthcare sector emissions are created in the upstream supply chain and patient care settings, trial emissions represent up to 100 million tons of CO_2e per year, equivalent to a midsize country like Belgium (Fig. 1).

POSSIBLE SOLUTIONS TO REDUCE CARBON EMISSIONS

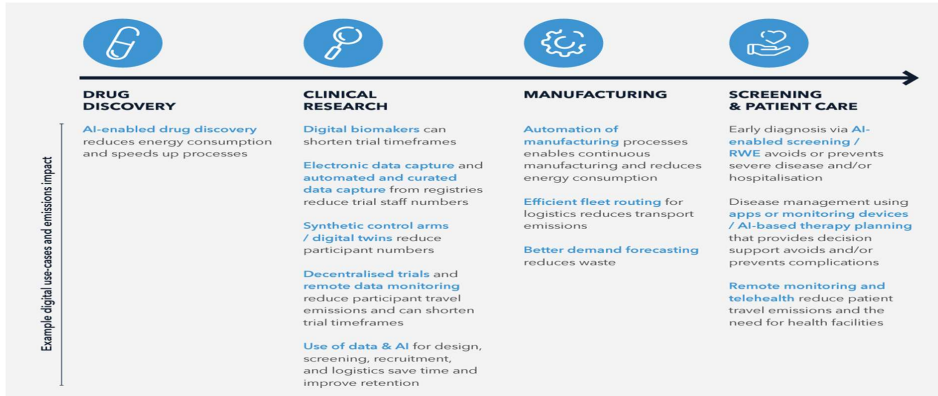
Digital solutions play an increasingly important role throughout the healthcare value chain in driving efficiencies, delivering superior patient outcomes, and reducing costs and emissions (Mondejar et al. 2021) (Fig. 2).

Digital solutions are a key enabler to reduce emissions related to clinical research. Because trials touch upon many aspects of the broader health system (including healthcare facilities, staff and patient travel, drug manufacturing, and delivery), examining how digitalization reduces emissions in



Source: Sustainable Market Initiative 2022

Fig. 1: Clinical trials drive up to ~100 million tons of CO_2e emissions per year.



Note: AI: artificial intelligence; RWE: real-world evidence; Source: Sustainable Market Initiative 2022

Fig. 2: Digital solutions can be used all along the healthcare value chain.

clinical trials provides a good proxy for the benefits of digital in the broader healthcare system. Digitalization refers to using digital technologies to improve the efficiency, effectiveness, and sustainability of various processes, including clinical research. By embracing digitalization, researchers can reduce their reliance on paper-based processes, physical meetings, and travel, all contributing to the carbon emissions associated with clinical research.

For example, electronic data capture (EDC) allows researchers to collect data electronically, reducing the need for paper forms and reducing the carbon footprint associated with paper production and transportation (Mishra 2022). Similarly, virtual clinical trials and remote monitoring allow researchers to conduct studies without requiring participants to travel to clinical trial sites, reducing the carbon emissions associated with transportation.

Cloud computing and electronic communications can also significantly reduce the carbon footprint of clinical research. Cloud computing allows researchers to store and share data without requiring physical servers, which consume much energy. Electronic communications, such as email, video conferencing, and instant messaging, can replace in-person meetings and reduce the carbon emissions associated with travel.

Hence, digitalization has the potential to significantly reduce the carbon footprint of clinical research while still ensuring high-quality studies. By embracing digital technologies, researchers can make clinical research more sustainable and environmentally friendly, helping protect the planet for future generations.

BARRIERS TO DIGITALIZING CLINICAL TRIALS

While COVID-19 accelerated digitalization across clinical trials by limiting options for on-site travel and creating a high unmet need for COVID-19 treatments (Vara 2022), further efforts can be made across four key areas to increase the scale of digital solutions deployed for emissions benefits in clinical trials (Fig. 3).

1. **Regulatory Hurdles**

   In recent years, there have been significant advances in regulatory framework, driven by the COVID-19 pandemic, that have made it possible for clinical trials to make increasing use of digital technology.

   - For example, The US Food and Drug Administration (FDA) has a specific regulatory process to address the use of digital biomarkers (and their components) and is currently piloting a program that further streamlines product-level approvals (Coravos et al. 2019). Meanwhile, the European Medicines Agency (EMA) has a set of qualification criteria companies must follow to use a digital biomarker in a trial (Human Medicines Division 2020).
   - The FDA's 2021 draft guidance details requirements for remote data acquisition from patients in clinical trials, enabling decentralization (CDER 2021).
   - The Digital Health Centre of Excellence at the FDA also offers advice on Software as a Precertification of Digital Health Software, Wireless Medical Devices, Mobile Medical Applications, and Medical Devices (Lievevrouw et al. 2021).

Source: Sustainable Market Initiative 2022

Fig. 3: Four areas where further work is required to scale digital solutions in clinical trials.

- The FDA and EMA published guidelines for good clinical practice that enable greater use of risk-based monitoring principles, paving the way for more remote clinical trial data monitoring. The FDA has also confirmed that sponsors switched to remote monitoring during the pandemic do not need to re-monitor on-site.
- Despite these developments, further guidance and acceptance from regulators are still required for digital solutions to be used widely in clinical trials and drive emissions benefits:

Requirements for digital tools are still evolving: Experts are still debating topics such as using patient-relevant endpoints (in place of clinical outcomes) to indicate efficacy and identify patients that can be included in synthetic control arms. The FDA and EMA do not have official guidance on using digital twins and synthetic control arms in trials. However, the FDA has issued an RWE framework, and the EMA has recently issued a draft qualification on a statistical method (Prognostic Covariate Adjustment) that supports the use of synthetic control arms (Detela et al. 2022).

Guidance on digital tools in clinical trials varies across geographies, limiting the ability of sponsors to implement global approaches: Where clinical trials are intended to produce globally representative results, different regulator guidance on digital tools across geographies can be inefficient for sponsors of multicenter trials. For instance, the European Medicines Agency's (EMA) guidance on electronic consent (eConsent) makes conducting cross-broader trials with digital solutions difficult because it requires the sponsor to clarify legality and compliance with each country's ethics committees and national regulatory authorities (Minisman et al. 2012).

2. **Lack of Interoperability Between Digital Solutions**

   To reap the benefits of digital solutions, they must work seamlessly together (Kerber & Schweitzer 2017). However, digital tools remain complex to set up and are not always interoperable – with data often captured in nonstandard formats using local codes. This increases the difficulty for trial managers and negatively impacts patient user experience. Furthermore, it may include errors that bias assessments, especially when working with the large 19 Sustainable Markets Initiative Health Systems Task Force, in collaboration with BCG, November 2022 data sets, which erodes trust in digital health solutions (Sustainable Markets Initiatives 2020). Although interoperability does not reduce trial emissions, it facilitates adopting and accepting digital solutions that enable emissions savings.

3. **Ingrained Culture, Behavior and Beliefs**

   All those involved in trials—trial sponsors, providers, technology platform providers, CROs, and patients—must learn how to work with new digital systems and devices. Major stumbling blocks in realizing the benefits of these new digital tools include a reluctance to change behaviors and embed digital tools in running clinical trials, concerns about data privacy and security, a lack of access to technology, and insufficient technical literacy (Rosa et al. 2021).

4. **Cost and Range of Digital Solutions**

   Although digital solutions are expected to drive down the cost of clinical trials, technology remains expensive (particularly the initial investment). With so many options, many providers are unsure which to invest in (DiMasi et al. 2022). A survey of 231 clinical trial sites finds that cost, complexity, and the right technology are the key challenges associated with digital adoption (Rosa et al. 2015).

CONCLUSION

In conclusion, clinical trials can have positive and negative consequences on the surrounding ecosystem. It is essential to find a middle ground between medical research's possible benefits and potential costs to the surrounding environment. Researchers and sponsors of clinical trials should consider ways to minimize the environmental impact of their trials by reducing resource use, waste generation, and greenhouse gas emissions. Additionally, they can explore alternative methods to animal testing and promote sustainable practices in clinical trial design and implementation. By doing so, we can ensure that clinical trials continue to advance human health while promoting environmental sustainability for the benefit of current and future generations. In addition to the aforementioned measures, there are additional strategies to minimize the environmental impact of clinical studies. One way is to incorporate sustainability considerations into the study design and protocol development process. For example, researchers can use eco-friendly materials and equipment, choose study locations that minimize transportation and energy use, and use electronic data capture systems to reduce paper usage. Another approach is to use virtual clinical trials, which rely on remote data collection and monitoring, reducing the need for in-person visits and travel. This approach can help minimize the environmental impact of clinical trials while making them more accessible to participants who may have difficulty traveling to a study site.

Lastly, regulatory and policy measures can encourage sustainability in clinical trials. For example, funding agencies and regulatory bodies can require environmental impact assessments to approve the study. They can also incentivize researchers and sponsors who implement sustainable practices in their clinical trials. In conclusion, there are many strategies for lessening the negative effects of clinical trials on the surrounding ecosystem, and sustainability should be factored into every step of the scientific method. By doing so, we can advance medical research while minimizing our impact on the environment and promoting a healthier planet for all.

REFERENCES

Alemayehu, C., Mitchell, G. and Nikles, J. 2018. Barriers for conducting clinical trials in developing countries - a systematic review. Int. J. Equity Health, 17: 37. https://doi.org/10.1186/s12939-018-0748-6

Ashraf, M., Maah, M.J. and Yusoff, I. 2014. Soil contamination, risk assessment, and remediation. Intech eBooks. https://doi.org/10.5772/57287

Avtar, R., Sahu, A., Chakraborty, K., Yunus, D. and Kurniawan, S. 2019. Exploring renewable energy resources using remote sensing and GIS - A review. Resources, 8(3): 149. https://doi.org/10.3390/resources8030149

Belay, S., Giday, M. and Manyazewal, T. 2021. Harnessing clinical trial capacity to mitigate zoonotic diseases: The role of expert scientists in Ethiopia. Front. Public Health, 9: 621433. https://doi.org/10.3389/fpubh.2021.621433

Belkhir, L. and Elmeligi, A. 2019. Carbon footprint of the global pharmaceutical industry and relative impact of its major players. J. Clean Prod., 214: 185-194. https://doi.org/10.1016/j.jclepro.2018.11.204

Boxall, ABA 2004. The environmental side effects of medication. EMBO Rep., 5(12): 1110-1116. https://doi.org/10.1038/sj.embor.7400307

CDER 2021. United States Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research. Digital health technologies for remote data acquisition in clinical investigations. https://www.govinfo.gov/content/pkg/FR-2021-12-23/pdf/2021-27894.pdf (Accessed March 10, 2023)

Clark, L.T., Watkins, L., Piña, I.L., Elmer, M., Akinboboye, O., Gorham, M., Jamerson, B., McCullough, C., Pierre, C., Polis, A.B., Puckrein, G. and Regnante, J.M. 2019. Increasing diversity in clinical trials: Overcoming critical barriers. Curr. Probl. Cardiol., 44(5): 148-172. https://doi.org/10.1016/j.cpcardiol.2018.11.002

Clarke, R.A. 2014. The Challenge of Going Green. Harvard Business Review. Retrieved from https://hbr.org/1994/07/the-challenge-of-going-green (Accessed March 9, 2023)

Coravos, A., Khozin, S. and Mandl, K.D. 2019. Developing and adopting safe and effective digital biomarkers to improve patient outcomes. Digit. Med., 2(1): https://doi.org/10.1038/s41746-019-0090-4

Cuffari, B. 2021. The carbon footprint of clinical trials. News-Medical. https://www.news-medical.net/health/The-Carbon-Footprint-of-Clinical-Trials.aspx (Accessed March 19, 2023)

Dănescu, T. and Popa, M.A. 2020. Public health and corporate social responsibility: Exploratory study on pharmaceutical companies in an emerging market. Glob. Health, 16(1): 117. https://doi.org/10.1186/s12992-020-00646-4

De Franco, A., Shaker, M., Kalubi, D. and Hostettler, S. 2017. A review of sustainable energy access and technologies for healthcare facilities in the Global South. Sustain. Energy Technol. Assess., 22: 92–105. https://doi.org/10.1016/j.seta.2017.02.022

Detela, G., Inacio, P., Saragoussi, D. and Schaumberg, D. 2022. Registries for Regulatory Decision-Making: Comparing EMA and FDA Guidance on Real-World Evidence Insights Hub. https://www.ppd.com/blog/comparing-ema-fda-real-world-evidence-guidance/ (Accessed March 10, 2023).

DiMasi, J.A., Smith, Z., Oakley-Girvan, I., Mackinnon, A., Costello, M., Tenaerts, P. and Getz, K.A. 2023. Assessing the financial value of decentralized clinical trials. Ther. Innov. Regul. Sci., 57(2): 209–219. https://doi.org/10.1007/s43441-022-00454-5

Drew, J., Christie, S.D., Rainham, D. and Rizan, C. 2022. HealthcareLCA: An open-access living database of healthcare environmental impact assessments. Lancet Planet. Health, 6(12): e1000–e1012. https://doi.org/10.1016/S2542-5196(22)00257-1

Edenhofer, O., Pichs-Madruga, R., Sokona, Y., Seyboth, K., Kadner, S., Zwickel, T., Eickemeier, P., Hansen, G., Schlömer, S., von Stechow, C. and Matschoss, P. (eds.) 2011. Renewable energy sources and climate change mitigation: Special report of the intergovernmental panel on climate change. Cambridge University Press.

European Medicines Agency 2020. Questions and answers: qualification of digital technology‐based methodologies to support approval of medicinal products.

Evans, S. 2022. Analysis: which countries are historically responsible for climate change? https://www.carbonbrief.org/analysis-which-countries-are-historically-responsible-for-climate-change/ (Accessed March 29, 2023).

Fugger, L., Jensen, L.T. and Rossjohn, J. 2020. Challenges, progress, and prospects of developing therapies to treat autoimmune diseases. Cell, 181(1): 63-80. https://doi.org/10.1016/j.cell.2020.03.007

Gaw, S., Thomas, K.V. and Hutchinson, T.H. 2014. Sources, impacts, and trends of pharmaceuticals in the marine and coastal environment. Philos. Trans. R. Soc. Lond. B Biol. Sci., 369(1656): 20130572. https://doi.org/10.1098/rstb.2013.0572

Halonen, J.I., Erhola, M., Furman, E., Haahtela, T., Jousilahti, P., Barouki, R., Bergman, Å., Billo, N.E., Fuller, R., Haines, A., Kogevinas, M., Kolossa-Gehring, M., Krauze, K., Lanki, T., Vicente, J.L., Messerli, P., Nieuwenhuijsen, M., Paloniemi, R., Peters, A. and Antó, J.M. 2021. A call for urgent action to safeguard our planet and health in line with the Helsinki Declaration. Environ. Res., 193: 110600. https://doi.org/10.1016/j.envres.2020.110600

Halperin, D. 2014. Environmental noise and sleep disturbances: A threat to health? Sleep Sci., 7(4): 209-212. https://doi.org/10.1016/j.slsci.2014.11.003

Hirsch, I.B., Martinez, J., Dorsey, E.R., Finken, G., Fleming, A., Gropp, C., Home, P., Kaufer, D.I. and Papapetropoulos, S. 2017. Incorporating site-less clinical trials into drug development: A framework for action. Clin. Ther., 39(5): 1064-1076. https://doi.org/10.1016/j.clinthera.2017.03.018

Holmner, A., Ebi, K.L., Lazuardi, L. and Nilsson, M. 2014. The carbon footprint of telemedicine solutions – Unexplored opportunity for reducing carbon emissions in the health sector. PLoS ONE, 9(9): e105040. https://doi.org/10.1371/journal.pone.0105040

Inan, O.T., Tenaerts, P., Prindiville, S.A., Reynolds, H.R., Dizon, D.S., Cooper-Arnold, K., Turakhia, M., Pletcher, M.J., Preston, K.L., Krumholz, H.M., Marlin, B.M., Mandl, K.D., Klasnja, P., Spring, B., Iturriaga, E., Campo, R., Desvigne-Nickens, P., Rosenberg, Y., Steinhubl, S.R. and Califf, R.M. 2020. Digitizing clinical trials. Digit. Med., 3(1): 101. https://doi.org/10.1038/s41746-020-0302-y

Jarzebski, M.P., Elmqvist, T., Gasparatos, A., Fukushi, K., Eckersten, S., Haase, D., Goodness, J., Khoshkar, S., Saito, O., Takeuchi, K., Theorell, T., Dong, N., Kasuga, F., Watanabe, R., Sioen, G.B., Yokohari, M. and Pu, J. 2021. Aging and population shrinking: Implications for sustainability in the urban century. Npj Urban Sustain., 1(1): https://doi.org/10.1038/s42949-021-00023-z

Kerber, W. and Schweitzer, H. 2017. Interoperability in the digital economy. SSRN Electron. J. https://doi.org/10.2139/ssrn.2922515

Lazar, A.A., Schulte, R., Faddegon, B., Blakely, E.A. and Roach, M. 2018. Clinical trials involving carbon□ion radiation therapy and the path forward. Cancer, 124(23): 4467-4476. https://doi.org/10.1002/cncr.31662

Lenzen, M., Malik, A., Li, M., Fry, J., Weisz, H., Pichler, P.P., Chaves, L.S.M., Capon, A. and Pencheon, D. 2020. The environmental footprint of health care: A global assessment. Lancet Planet. Health, 4(7): e271-e279. https://doi.org/10.1016/S2542-5196(20)30121-2

Lievevrouw, E., Marelli, L. and Van Hoyweghen, I. 2022. The FDA's standard-making process for medical digital health technologies: co-producing technological and organizational innovation. BioSocieties, 17(3): 549-576. https://doi.org/10.1057/s41292-021-00232-w

Manisalidis, I., Stavropoulou, E., Stavropoulos, A. and Bezirtzoglou, E. 2020. Environmental and health impacts of air pollution: A review. Front. Public Health, 8: 14. https://doi.org/10.3389/fpubh.2020.00014

Minisman, G. and Bhanushali, M. and Conwit, R. and Wolfe, G.I. and Aban, I. and Kaminski, H.J. and Cutter, G. 2012. Implementing clinical trials on an international platform: Challenges and perspectives. J. Neurol. Sci., 313(1-2), 1-6. https://doi.org/10.1016/j.jns.2011.10.004

Mishra, S.V. 2022. Utilization of digital technology in conduction of clinical trials in India: Issues and perspectives. Int. J. Sci. Res. Pub., 12(5): 93. https://doi.org/10.29322/IJSRP.12.05.2022.p12514

Mondejar, M.E., Avtar, R., Diaz, H.L.B., Dubey, R.K., Esteban, J., Gómez-Morales, A., Hallam, B., Mbungu, N.T., Okolo, C.C., Prasad, K.A., She, Q. and Garcia-Segura, S. 2021. Digitalization to achieve sustainable development goals: Steps towards a Smart Green Planet. Sci. Total Environ., 794: 148539. https://doi.org/10.1016/j.scitotenv.2021.148539

OECD 2019. Biodiversity: Finance and the Economic and Business Case for Action, OECD Publishing, Paris, https://doi.org/10.1787/a3147942-en (Accessed March 6, 2023).

Padmanabhan, K.K. and Barik, D. 2019. Health hazards of medical waste and its disposal, In: Energy from Toxic Organic Waste for Heat and Power Generation. pp. 99-118. https://doi.org/10.1016/b978-0-08-102528-4.00008-0

Parkins, K. 2022. Healthy patients, healthy planet: tackling the carbon footprint of clinical trials. Clinical Trials Arena. https://www.clinicaltrialsarena.com/features/healthy-patients-healthy-planet-tackling-the-carbon-footprint-of-clinical-trials/ (Accessed March 15, 2023).

Prater, T. 2019. Healthcare in world's largest economies 'accounts for 4%' of global emissions. Carbon Brief. https://www.carbonbrief.org/Healthcare-In-Worlds-Largest-Economies-Accounts-For-4-Of-Global-Emissions/ (Accessed March 10, 2023)

Rajadhyaksha, V. 2010. Conducting feasibilities in clinical trials: An investment to ensure a good study. Perspect. Clin. Res., 1(3): 106-109. https://doi.org/10.4103/2229-3485.71767

Rissman, J., Bataille, C., Masanet, E., Aden, N., Morrow, W.R., Zhou, N., Elliott, N., Dell, R., Heeren, N., Huckestein, B., Cresko, J., Miller, S.A., Roy, J., Fennell, P., Cremmins, B., Koch Blank, T., Hone, D., Williams, E.D., de la Rue du Can, S. and Helseth, J. 2020. Technologies and policies to decarbonize global industry: Review and assessment of mitigation drivers through 2070. Appl. Energy, 266: 114848. https://doi.org/10.1016/j.apenergy.2020.114848

Rosa, C., Campbell, A. N. C., Miele, G. M., Brunner, M. and Winstanley, E. L. 2015. Using e-technologies in clinical trials. Contemporary Clinical Trials, 45: 41-54. https://doi.org/10.1016/j.cct.2015.07.007

Rosa, C.B., Narsch, L.A., Winstanley, E.L., Brunner, M. and Campbell, A.N.C. 2021. Using digital technologies in clinical trials: Current and future applications. Contemp. Clin. Trials, 100: 106219. https://doi.org/10.1016/j.cct.2020.106219

Salam, M.D. and Nilza, N.C. 2021. Hazardous components of landfill leachates and its bioremediation. Intechopen, 577: 948. https://doi.org/10.5772/intechopen.94890

Samuel, G. and Lucassen, A.M. 2022. The environmental sustainability of data-driven health research: A scoping review. Dig. Health, 8: 20552076221111297. https://doi.org/10.1177/20552076221111297

Sanchez, J.A. 2021. Treatments for chronic kidney disease: A systematic literature review of randomized controlled trials. Adv. Ther., 39(1): 193-220. https://doi.org/10.1007/s12325-021-02006-z

Selby, P. 2011. The impact of the process of clinical research on health service outcomes. Ann. Oncol., 22(7): 2-4. https://doi.org/10.1093/annonc/mdr418

Singh, H., Eckelman, M., Berwick, D.M. and Sherman, J.D. 2022. Mandatory reporting of emissions to achieve net-zero health care. N. Engl. J. Med., 387(26): 2469-2476. https://doi.org/10.1056/NEJMsb2210022

Smale, E.M. and Egberts, T.C.G. and Heerdink, E.R. and van den Bemt, B.J.F. and Bekker, C.L. 2021. Waste-minimizing measures to achieve sustainable supply and use of medication. Sustain. Chem. Pharm., 20: 100.

Soulsbury, C. D., Gray, H. E., Smith, L. M., Braithwaite, V., Cotter, S. C., Elwood, R. W., Wilkinson, A. and Collins, L. M. 2020. The welfare and ethics of research involving wild animals: A primer. Methods in Ecology and Evolution, 11(10): 1164-1181. https://doi.org/10.1111/2041-210X.13435

Subbiah, V. 2023. The next generation of evidence-based medicine. Nature Medicine, 29(1): 49-58. https://doi.org/10.1038/s41591-022-02160-z

Sustainable Markets Initiative 2022. The digital solution for sustainability in clinical research. Sustainable Markets Initiative Health Systems Task Force, in collaboration with BCG. https://a.storyblok.com/f/109506/x/42119be232/smi-hstf-digital-health-whitepaper.pdf (Accessed March 9, 2023).

Sustainable Markets Initiatives 2020. Health systems task force. https://www.sustainable-markets.org/taskforces/health-systems-taskforce/ (Accessed March 8, 2023).

Tennison, I., Roschnik, S., Ashby, B., Boyd, R., Hamilton, I., Oreszczyn, T., Owen, A., Romanello, M., Ruyssevelt, P., Sherman, J. D., Smith, A. Z. P., Steele, K., Watts, N. and Eckelman, M.J. 2021. Health care's response to climate change: A carbon footprint assessment of the NHS in England. Lancet. Planet. Health, 5(2): e84-e92. https://doi.org/10.1016/S2542-5196(20)30271-0

Turner, M.C., Andersen, Z.J., Baccarelli, A., Diver, W.R., Gapstur, S.M., Pope, C.A., Prada, D., Samet, J., Thurston, G. and Cohen, A. 2020. Outdoor air pollution and cancer: An overview of the current evidence and public health recommendations. Cancer J. Clin., 70(6): 460-479. https://doi.org/10.3322/caac.21632

Vara, V. 2022. Ensuring Data Authenticity, Integrity, And Confidentiality Biggest Barrier to Using Digital Technologies in Clinical Trials: Poll. https://www.clinicaltrialsarena.com/news/ensuring-data-authenticity-integrity-and-confidentiality-barrier-to-digital-technologies-in-clinical-trials/ (Accessed March 1, 2023)

World Health Organization (WHO) 2021. Climate Change and Health. https://www.who.int/news-room/fact-sheets/detail/climate-change-and-health (Accessed February 18, 2023)

World Health Organization (WHO) 2005. Handbook for Good Clinical Research Practice (GCP): Guidance for Implementation. World Health Organization.