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COMMENTARY

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The undue burdens of clinical trial participation: implications for equity, diversity, and inclusion

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Abstract

A wide range of factors has detrimental impacts upon equity, diversity, and inclusion in clinical trials, amongst which participant burden can be significant. In addition to the potential physical burdens associated with investigational interventions, participants may face onerous demands related to factors like travel, time commitments, psychological, or logistical challenges. Many of these factors have been shown to create barriers that disproportionately affect certain groups like minoritised ethnic groups, people with caring responsibilities, and older adults. One increasingly problematic aspect of participant burden is associated with an excessive volume of data collection, much of which may lack direct relevance to the study's primary objectives and may never be analysed. Although pragmatic and participant-centred trial methodologies have risen in prominence over the past decade, quantitative evidence demonstrates that trial complexity and data volumes are continuing to rise. The widening gap between the notion of participant-centricity and the realities of current trial practice underscores the need for a shift in approach. Reducing unnecessary burden should be regarded as a moral obligation across all clinical trial designs to avoid the systematic exclusion of certain groups. With a focus on data-related aspects, this paper examines the ethical implications of undue burdens upon participants and proposes measures to help minimise and mitigate these burdens. In addressing this issue, researchers contribute to broader efforts to enhance inclusivity and representation in clinical studies.

Keywords Equality, diversity, and inclusion, Research ethics, Participation burdens, Undue burdens in clinical trials, Trial design

Background

Sound justifications for increasing diversity in clinical trials are well articulated in the literature for purposes such as earning and building trust, promoting fairness, and generating biomedical knowledge [1]. But despite various policy efforts to increase diversity [2–4], minoritised ethnic groups, women, and other marginalised groups remain underrepresented in clinical research. The problem is pervasive; underrepresentation is found in reviews of clinical trials from around the world and across many different conditions [5–9].

Multiple and intersectional barriers to equity, diversity, and inclusion in trials have been identified, such as trust or lack of knowledge [10], amongst which participant burden can be significant.

Randomised controlled clinical trials may be widely accepted as the gold standard for generating reliable evidence of the benefits and harms of a potential treatment [11, 12], but there is growing concern that clinical trials

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are becoming overly complex and burdensome for participants [13–16]. Revision 3 of the International Conference on Harmonisation (ICH) Guideline for Good Clinical Practice (GCP) (hereafter referred to as ICH E6(R3)) includes a new focus on quality-by-design and reducing unnecessary burdens on both participants and investigators, highlighting the importance of designing trials that are accessible to a wide group of participants [17].

Even so, it was reported in the Tufts Center for the Study of Drug Development's 2024 Impact report that overall participation burden in phase II and III non-oncology trials has increased by 39% since 2011. The largest contributors to this increase in participation burdens included an increase in participant reported outcome questionnaires, as well as an increased number of blood samples, physical exams, and other clinical measurements. It was also reported that just over 45% of phase II and III trials have average visit durations of more than 2 h compared to 17% 10 years ago [13].

Ulrich et al. defined participation burden in clinical trials as the subjective perceptions of study participants 'of the psychological, physical, and economic hardships associated with participation in the clinical research process'. [18] From their systematic review of 45 qualitative studies exploring adult patients' experiences with randomised controlled trial (RCT) participation, Naidoo et al. [19] identified such hardships across all phases of the clinical trial. For instance, psychological burdens included anxiety and fears related to feeling like 'a guinea pig' or disappointment, anger, and depression following allocation to the control arm of the trial. Participants might also be required to travel, attend trial visits, undergo medical procedures, complete multiple questionnaires, amongst other obligations which are likely to incur direct and indirect costs for participants. Indirect costs such as travel are usually reimbursable for clinical trial participants, but this can disadvantage participants with less disposable income who are unable to pay for travel upfront. Other indirect costs can include time away from work or caring responsibilities and childcare costs to attend trial appointments [20].

Understanding and addressing the burdens placed on people who volunteer to take part in clinical research is essential not only for effective recruitment and retention, but also for ensuring trials are ethical and accessible to a broad range of participants [10, 21, 22]. Whilst firm evidence of causal relationships between specific types of burdens and reduced enrolment amongst specific groups remains elusive, many studies indicate that participation burdens including travel, time, logistical challenges, and accessibility barriers disproportionately affect minoritised and underserved groups [10, 21–23]. Recognising this, both the US Food and Drug Administration (FDA) [4] and the UK Health Research Authority (HRA) [3] have released draft guidance highlighting the importance of reducing participant burden as a key strategy for improving diversity in clinical trials, recommending that it be explicitly addressed when developing diversity plans for clinical research.

In this short paper, we highlight the pragmatic and ethical implications of participation burdens with a focus upon one significant contributory factor to these burdens that of excessive or undue data collection. We begin by outlining the nature of the data burden problem.

The increasing data burdens in clinical trials

The purpose of any clinical trial is to generate reliable evidence to inform clinical care. The clinical trial protocol outlines the main requirements for the collection of data, which is then operationalised by other trial documentation including standard operating procedures, manuals, and instructions with increasing levels of detail. Data is collected through various methods such as directly from participants during participant interviews, from biological tests and physical exams, and other methods. However, as clinical trials have increased in complexity, the overall number of data elements has risen dramatically. Earlier analyses estimated that many large trials collect over 3 million data elements [15]. More recent evaluations show this trend has continued, with phase III protocols now averaging approximately 5.9 million data points, reflecting an 11% year-on-year increase since 2020 [24]. Research undertaken by Duke-Margolis Health Policy Center [25] found that there has been a 283% increase in data points collected during phase III trials over the past 10 years. Increases in data elements across clinical trials have included an increased number of endpoints and eligibility criteria, an increase in the number of physical examinations, clinical examinations, and participant questionnaires [13, 14].

When considering the implications of excessive data collection, it is relevant to note that the method of data collection is likely to influence the burden on participants more than the number of data points collected. For instance, new technologies such as wearables [26] and advancements in Omic technologies [27] have enabled researchers to collect significant amounts of data with minimal burden on participants. Nevertheless, these same tools often generate continuous, high-volume datasets that create significant informational burdens, including challenges related to data management and standardisation. Recent evidence shows that wearables produce large and complex data streams and that digital platforms more broadly are contributing to vast and

diverse clinical datasets that require advanced analytical approaches [28–30].

The increase in the number of eligibility and exclusion criteria in clinical trials has also been directly linked to greater protocol complexity and corresponding growth in trial data volume [15]. This issue is reportedly of particular concern in oncology whereby the median number of eligibility criteria in thoracic oncology trials has more than doubled since the 1980s [31]. Oncology trials face specific challenges around complexity and data burden due to the inherently intensive scientific and operational requirements of cancer research, including extensive biomarker and molecular profiling, higher volumes of imaging and biopsies, increased frequency of safety and efficacy assessments, and the need to capture multiple clinically meaningful endpoints such as tumour response, progression-free survival, and overall survival. These factors, which have escalated substantially over time, result in oncology protocols demanding significantly more procedures, data points, and follow-up than trials in many other therapeutic areas [32, 33].

Given the associated burdens, it is important to consider whether there are sound scientific reasons for the substantial increase in data collection that has been witnessed over recent years. Afterall, advancements in technologies and innovations have enhanced the researchers' ability to collect rich and informative data, making extensive data collection increasingly attractive to both sponsors and investigators seeking deeper insights into the condition and intervention under investigation [34]. Whilst it is important to acknowledge that there are differing views between stakeholders on the data required and there is often justification to add additional substudies or collect various data points to inform future research [34–36], it appears that the scientific rationale is not always clear.

Getz proposed that the proliferation of data points has occurred due to an expansion of protocol and other document templates without first streamlining the existing requirements, and that 'out of habit, research professionals like to tack on additional studies and even "pet projects" that may not be central to the original protocol' [37].

Regulatory risk aversion has also been identified as a contributory factor as it impacts upon sponsor decision-making regarding the collection of data points [36–38]. In 2023, Tufts Centre for the Study of Drug Development (CSDD) collaborated with the FDA to work with trial sponsors on a case study to help understand the nature of non-core protocol procedures to inform future initiatives around protocol optimisation [38]. As part of the study, trial sponsors and FDA reviewers were asked to classify core and non-core study procedures for 19 pivotal trials. The findings highlighted a misalignment between regulators and trial sponsors: 'FDA reviewers classified a much higher percentage of procedures as non-core (26% vs. 18%) with the largest proportion (50%) of these procedures perceived as core by sponsor companies'. Sponsor organisations involved in the study indicated one out of six non-core procedures were included due to perceived regulatory requirements and expectations [38].

Thus, a substantial portion of the information that is collected might never be analysed. Back in 2013, O'Leary et al. conducted an analysis of data collection practices in cancer clinical trials and reported a median of 599data items collected per participant per trial (range: 186–1035). However, across the associated publications, a median of only 96 data items (approximately 18%) were actually analysed and reported [15]. The authors concluded that a considerable proportion of collected data appeared to go unused and could potentially be excluded from case report forms (CRFs), thereby streamlining data collection and enhancing trial efficiency.

Trial complexity can also affect the reliability of trial results [13–15]. The detrimental impacts of complex and burdensome protocols on clinical trial efficiency are well documented in the literature: protocols with a greater number of endpoints, procedures, and eligibility criteria have been associated with reduced physician referral rates, decreased participant willingness to enrol, lower recruitment and retention rates, and a higher frequency of protocol amendments. These factors collectively contribute to prolonged study timelines and increased overall study costs [39]. There is also evidence to suggest that trials with a large number of data points can result in poorer data quality due to an increased amount of 'missing data' linked to participant dropout and the administrative burden of collecting large amounts of data [40]. As missing data can significantly reduce the reliability and interpretability of data, researchers are advised to take steps to reduce the possibility of missing data during the trial design stage, including ensuring that the number of data points are streamlined and that data collection tools are feasible [41].

High costs are often cited as a barrier to generating evidence for new and existing treatments [16, 42]; the estimated median cost of a phase III randomised, industry-sponsored pivotal drug trial was approximately 45 million US dollars in 2018 (and has risen since) [15]. Although there are many factors linked to the increasing cost of clinical trials, collecting large amounts of data drives up this cost not just in terms of the resources required to collect and process the data, but also in relation to source data verification and trial monitoring [43, 44]. The excessive collection of data adds immense costs and administrative burdens to clinical trials [34–37].

As well as concerns around cost and administrative burden for both researchers and participants, protocols with complex or burdensome requirements can impact the ability to recruit and retain the required number of participants [45–47]. The perceived burden of participation is one of the primary contributory factors to the decision not to participate in a clinical study, as well as one of the top five factors that participants liked the least [39]. Additionally, a link between participant dropout and the complexity of the trial has been identified, with less burdensome protocols in phase II and III trials being associated with a lower dropout rate. Further, more than half of study dropouts are reportedly due to patient choice rather than due to an adverse drug reaction or a clinical decision [13].

Collectively, this demonstrates a consistent pattern of substantial volumes of data being collected without scientific justification, contributing to unnecessary participant and operational burden.

The ethical implications of undue burdens

All clinical trials entail burdens that must be managed ethically to safeguard the rights and the wellbeing of the study participants. However, the aforementioned findings suggest that in many studies there are avoidable burdens, like the excessive collection of data, much of which is unwarranted. We refer to these burdens as *undue* because they impose unjustified burdens on the participants and give rise to a number of ethical concerns as explained below.

The foundations of ethical theory for clinical research were first codified in the Belmont Report [48] as the three principles of beneficence, respect for persons, and justice, which continue to influence ethical decision-making in clinical research globally. The imposition of undue burdens poses challenges for each of these principles.

First, the principle of beneficence concerns the participants' right to freedom from harm and discomfort [49], which in clinical studies requires an assessment of the potential risks and burdens in comparison with the foreseeable benefits to them or others (Declaration of Helsinki, P17) [50]. Hence, the burdens associated with the setting of particular data points, for example, and the processes involved in the collection of all data must be considered within the context of the potential for benefit. Procedures or monitoring activities that do not contribute meaningfully to the study are unethical because they increase burdens without corresponding benefit. Ethics guidelines and ICH E6(R3) are clear on this point: Trial processes should be operationally feasible and avoid unnecessary complexity, procedures, and data collection (ICH E6(R3) 7.4) [17].

Second, the principle of respect for persons obliges researchers to appreciate and uphold the autonomy of participants, a responsibility that is operationalised through the process of obtaining voluntary, fully informed consent from every individual (Declaration of Helsinki, P25) [50]. Accordingly, potential participants must be informed about the expected burdens (and benefits) associated with participation. If the true extent of burdens is not communicated clearly, participants' consent may not be fully informed. However, the informed consent process, which usually involves the provision of lengthy and detailed participant information sheets (PIS), can itself create burdens. Participant information sheets are becoming longer and inappropriately complex [51, 52]. Further, this trend has been amplified by the implementation of the European Union's General Data Protection Regulation [53], which mandates the disclosure of additional information to participants. Evidence indicates that participants frequently misinterpret or fail to retain critical information, thereby compromising the overall quality of consent [54]. Given that a lengthy, detailed PIS may actually reduce participant understanding and recall when compared to a more concise version [55], and that most participants choose not to read all of the details on a longer PIS [56], this poses the challenge of how to respect autonomy via the provision of relevant information without overburdening potential participants. This challenge is yet to be addressed adequately by all research teams and sponsors; research ethics committees have noted that consent procedures are often not tailored to match the actual burdens or risks of a study [57]. But whilst suggestions have been made about how to resolve this challenge, there is limited empirical evidence as to what information potential participants want to help them decide whether or not to participate in research [58].

Rooted in Kantian moral philosophy [59], the principle of respect for persons also obliges researchers to recognise that all individuals be accorded inherent dignity and moral worth. Thus, participants must be treated as 'ends in themselves' and never merely as a means to achieve research objectives. Whether deliberate or unintentional, a failure to consider the full implications of study-related burdens upon participants risks compromising this principle. That is because the imposition of undue burdens can amount to the exploitation of research participants, treating them as a means to achieve research ends. Even in cases where the overall research question is answered, participants receiving additional exams or medical procedures which do not contribute to the overall outcome of the trial poses a risk of exploitation. This risk is especially pronounced when participants are in a state of desperation because

people may volunteer for the most burdensome studies if they are desperate. For instance, the chance to live longer can overwhelm potential hardships [60]. However, the risk is not confined to desperate circumstances. Trial participants often want to feel that they are contributing to the advancement of treatments for their condition even if they believe they will not reap the benefits themselves [34] and the imposition of unjustifiable burdens can be viewed as exploitation of their goodwill.

Third, whilst participation burdens have clear ethical implications associated with beneficence and respect for persons, it is in the area of justice that we see the most obvious impact upon equity, diversity, and inclusion. The principle of justice requires that the selection of participants is equitable, the risks and benefits of research are fairly distributed, and that no persons are unfairly burdened or excluded from the potential benefits of research. Undue burdens in research pose justice-related ethical issues in clinical trials because excessive burdens create participation barriers that affect certain individuals disproportionately, such as those from minoritised ethnic groups, people with caring responsibilities, and older adults [10, 21, 22]. For example, two main barriers to the recruitment of diverse populations to early phase clinical trials were identified as the location of research centres and the intensive time commitment required of participants reference [61], which can disproportionately disadvantage those with inflexible employment, caregiving responsibilities, or limited resources.

Some of the key participation barriers for minoritised ethnic populations were identified in a joint statement by the American Society of Clinical Oncology and the Association of Community Cancer Centers on increasing Racial and Ethnic Diversity in Cancer Clinical Trials [62]. For instance, both direct medical costs and indirect costs such as travel, childcare, and time away from work made trial participation impractical or impossible for some potential participants. 'These financial barriers are more likely to affect racial and ethnic minority populations because they often have lower socioeconomic status relative to White populations' [62]. Similarly, it was reported that burdensome participation requirements, including multiple trial visits and frequent lab tests and biopsies, may also create obstacles for individuals from minoritised ethnic groups.

Similar barriers reportedly affect women's participation in clinical trials [63]. With concerns around the logistical aspects of trial participation acting as a barrier to participation, the impact of these barriers is an underrepresentation of women and especially women of colour in clinical trials [64]. Likewise, older adults are also more likely to carry additional logistical burdens when participating in demanding research protocols due to potential comorbidities and/or frailty [65].

Participation barriers that are caused or exacerbated by avoidable burdens contravene the principle of justice because they can lead to unfair exclusion from research. The ways in which clinical trials are conducted can impose a form of justice-based vulnerability, which can affect entire groups [66]. Consequently, minoritised groups and other underrepresented populations can be denied the benefits that arise from the significant advancements we have witnessed in medical and scientific knowledge in recent years [21, 67]. Women's underrepresentation in clinical trials could have both safety and efficacy implications [63], and the exclusion of older adults is of particular concern given their higher disease burden, particularly for cancer, and the rising numbers of older adults diagnosed with cancer year upon year [68].

Restrictive eligibility criteria can also affect various underrepresented groups such as minoritised ethnic groups, women, and older patients disproportionately. Whilst early phase clinical trials aim to recruit younger, fitter participants to demonstrate safety and efficacy, later phase trials should recruit a wide range of participants to reflect the patient population of the disease under investigation. Applying restrictive eligibility criteria for late phase clinical trials risks excluding participants with lower performance or functional status and/or pre-existing health conditions which are characteristics more typical of minoritised ethnic and older patient populations [62, 65, 69].

As well as becoming more burdensome for participants, many researchers believe that clinical trials are moving further away from the needs of patients [15, 70]. Treweek et al. identified a significant divergence between the end points selected by trialists and the endpoints that matter the most to patients and the healthcare professionals who treat them. In a sample of 44mostly phase III trials with 46 primary outcomes, a participating group of patients and healthcare professionals agreed that the primary endpoint of the trial was correct only 28% of the time. As the primary endpoint sets the most important result of a clinical trial, this study highlights the importance of engaging people with lived experience of the condition under investigation in clinical trial design. The participants in this study asserted that 'trial teams got the choice of primary outcome wrong more often than they got it right' [70].

Towards participant-centric data collection

Since the COVID-19 pandemic, there has been greater focus on optimising trial design to be more participant-centric whilst also improving efficiency [71, 72]. For instance, decentralised trials offer a unique opportunity

to reduce participation burden and ensure clinical trials are accessible to a wider range of participants [73]. Nevertheless, participant preferences cannot simply be assumed; it is reported that participants sometimes prefer the option of an in-person visit in a decentralised trial model [74]. It is essential that potential participant perspectives are integrated during the design process to ensure that a realistic assessment of participant burdens and preferences is factored into the trial design [75].

The importance of reducing burden and making trials more accessible to a wider group of participants has been recognised in ICH E6(R3) [17], which was adopted in January 2025, and specifies the need to focus upon the key data required to answer the main trial outcomes as well as to ensure participant safety.

ICH E6(R3) included significant changes to both its structure and content in response to concerns that the clinical trial ecosystem is rapidly evolving and that the guidance should acknowledge there is no 'one size fits all' approach to clinical trials. The structure of the guidance has changed to focus on the principles of GCP, which should apply to all clinical trials, along with Annex 1 to be applied to interventional clinical trials and Annex 2 (currently in draft) for pragmatic clinical trials. The revised principles of GCP includes a focus on reducing trial burdens, as outlined in the newly added principle 7 'Clinical trial processes, measures and approaches should be implemented in a way that is proportionate to the risks to participants and to the importance of the data collected and that avoids unnecessary burden on participants and investigators' [17]. ICH E6(R3) also includes additional responsibilities for the sponsor around the design of the trial not limited to the scientific design, incorporating 'quality-by-design' methodologies, ensuring that the trial, its documentation, and data collection tools are fit for purpose [17].

This shift in approach reflects the rapid expansion and increasing prominence of pragmatic clinical trial (PCT) methodology over the past decade; more than 80% of National Library of Medicine citations of PCTs were published in the past 10 years [76]. PCTs bridge the gap between tightly controlled RCTs and real-world clinical practice, improving applicability for diverse patients and care environments [77]. The PRECIS-2 tool has gained significant prominence in the pragmatic trials landscape, becoming a central resource for researchers seeking to design studies that better reflect real-world clinical practice. Since its publication in 2015, it has been cited almost 700 times, underscoring its widespread adoption as a framework for assessing and communicating the degree of pragmatism in trial design [76].

Despite the increasing prominence of PCTs and tools such as PRECIS-2, there remains a need for clinical trials to optimise and reduce the amount of data collected. Accordingly, data optimisation for clinical trials has been recognised as a key initiative by TranCelerate Biopharma with the objective to 'motivate sponsors to take action to support initiatives that optimize data collection via simplified protocol design' [78]. One possible approach to optimising data collection and reducing participant burden lies in the use of centralised healthcare data [79]. In the UK, for example, there are several initiatives to try to promote and govern the use of healthcare data in clinical research to reduce burden and improve clinical trial efficiency [80, 81]. However, as highlighted by a UK government review, further policy initiatives are needed to ensure the full potential of healthcare data can be realised via clinical studied to improve public health [82].

Still, there are some design choices that can be implemented relatively easily by sponsors and researchers to reduce participation burdens and the overcollection of data, regardless of whether the trial leverages PCT or traditional design methodologies. For example, consideration of the four protocol-specific dimensions associated with participation burdens defined by Getz et al. (below) might help to reduce participation burden and help to make trials accessible to a wider range of participants. [39] These include:

1. Procedural—including time, effort, commitment, and pain associated with each trial procedure.
2. Convenience—focused on logistical issues such as number of visits, distance and travel, days of work missed, and childcare needs.
3. Lifestyle—such as restrictions associated with diet, alcohol consumption, exercise, and smoking.
4. Caregiver involvement, e.g. if a caregiver is required to help with enrolling in the study, record data or notes, administer study drug, and provide transportation or childcare.

Excessive data collection—what is the solution?

The use of pragmatic and participant-centred trial designs is now well established, but they are often regarded as optional design preferences rather than approaches grounded in ethical responsibility. Further, despite growing interest in participant-centred methods, we know that clinical trials continue to increase in complexity and in the volume of data collected [24, 36–38]. The widening gap between the notion of participant-centricity and the realities of current trial practice underscores the need for a shift in approach. Reducing participation burden should not be limited to pragmatic designs. Rather, we maintain that there is a moral obligation to minimise unnecessary burdens across all clinical

trials and that this will help to ensure that no group is systematically excluded or left behind in research. The leveraging of established approaches such as PCTs [76, 83] and quality-by-design [84], and alignment with the World Health Organization guidance on clinical trial design [1] may help to address this moral obligation and have been incorporated into our recommendations. However, the reduction of participant burdens should be a central consideration in any and every trial design.

To this end, we have developed a set of recommendations (Table 1) to assist sponsors and researchers in taking a holistic approach to reducing unnecessary data and

Table 1 Reducing undue participation burdens in clinical trials

Protocol dimension	Consideration	Operationalised by
Ethical matters	Identify the potential participant burdens	Include relevant stakeholders (e.g. patients) in the identification of potential burdens, how they might impact upon different populations and how they should be factored into trail design
	Weigh the burdens and benefits	For the identified burdens, ensure that there are corresponding realistic potential benefits
	Potential for exploitation	Prioritise participant wellbeing over research aims and objectives
	Appropriate informed consent procedures	Design and implement participant-focused consent procedures that are proportionate to the potential burdens and risks
Logistical matters	Selection of research sites	Establish research sites in locations that are accessible and acceptable to the intended participants
	Reduce the number of in-person visits	Consider whether any part of the trial can be conducted in a decentralised manner. Provide options that support participant preferences
	Quality of data collection	Where possible, utilise data collection tools that maximise the chances of data being correct at the point of entry
	Caregiver involvement	Any additional complexity associated with caregiver involvement should be weighed against the potential for widening participation
Trial design	Setting the primary and secondary endpoints	Ensure the endpoints matter to patients and other relevant stakeholders by including them during design stages
	Applicability to a broad and varied group of trial participants	Eligibility and exclusion criteria should be scientifically justified to avoid unnecessarily restrictive eligibility criteria and additional burdens (including tests and/or physical exams associated with assessment of eligibility)
	Lifestyle modifications	Restrictive lifestyle changes such as dietary, alcohol consumption, exercise, smoking, and limitation of background medication must be scientifically justified and relevant to the research question
	Protocol required procedures and data collection	Reduce the number of trial procedures or questionnaires to match the research question Trial procedures and patient-reported outcomes should only be included if they are linked to the specified trial outcomes Consider the potential burdens on participants when determining the methods of data collection. The importance of the data to the trial outcomes should be weighed against the burden on participants
	Principle of data minimisation	Process the minimum amount of personal data required to answer the research question. Never collect any type of personal data unnecessarily
	Data sources	Minimise the number of trial procedures or data points through the use of central healthcare data or other data sources
Informing future trial design	The participant experience	Include questions about participation burdens (as well as benefits) in participant satisfaction/feedback tools at appropriate intervals during the trial to inform the design of future studies. Participant satisfaction tools should be short and easy for participants to complete

other participation burdens. Our recommendations are designed to be internationally applicable and suitable for integration into any trial design. The recommendations are based around the protocol-specific dimensions identified by Getz et al., [39] as well as other factors associated with undue data burdens in clinical trials that are identified in this paper [37, 41, 70, 73, 82, 85]. Our recommendations align with draft FDA [4] and HRA [3] guidance, which underscore the importance of minimising participation burdens to facilitate the recruitment and retention of diverse participant populations.

These recommendations are directed primarily at sponsors and researchers responsible for trial design, but we hope they might also inform other stakeholders such as regulators, ethics committees, and funders about the ethical implications of imposing unnecessary data burdens and support broader adoption and implementation of more participant-centred approaches.

Although the revisions in ICH E6(R3) are an encouraging step forward, overcoming the challenges of regulatory risk aversion in the pharmaceutical industry [25, 36–38] will require support from regulators to enable confident implementation by trial sponsors. Regulatory leadership is essential to shift industry practice through guidance and inspection frameworks signalling that proportionate and burden-reducing trial designs are not only compliant with ICH E6(R3) but set an expected standard.

We recognise that these recommendations are not sufficient on their own to resolve challenges to equity, diversity, and inclusion in clinical trials. In order to fully support widespread implementation, additional policy initiatives are required at the national level to align guidance for regulators, sponsors, research ethics committees, and patient advisory groups.

Conclusion

There are undoubtedly multiple, intersectional factors that can have detrimental impacts upon equality, diversity, and inclusion in clinical trials [86], but in this paper, we have focused upon the potential impacts of undue participation burdens, specifically those that are associated with data collection.

Undue burdens in clinical trials, particularly those arising from excessive and non-essential data collection, pose both moral and scientific challenges. As outlined in this article, such burdens compromise the well-known ethical principles of beneficence, respect for persons, and justice; they can add burdens without corresponding benefits, pose challenges for informed consent, risk the exploitation of participants, and risk exacerbating inequities in trial participation by disproportionately excluding already underrepresented groups. The consequences of undue burdens extend beyond the wellbeing of trial participants; burdensome trial designs can pose barriers to recruitment and retention as well as threatening data quality.

Worryingly, evidence indicates that the burdens associated with the collection of data are increasing; as clinical trials have increased in complexity, so too has the overall number of associated data elements [13, 14, 25].

Given the potential consequences, we suggest that there is a moral imperative for researchers and sponsors to minimise and mitigate all participation burdens, to help ensure that no one is left behind in research [87]. We also propose that reversing the trend for ever-increasing data burdens will require a deliberate, participant-centred approach to trial design (Table 1) in which data collection is proportionate, endpoints are relevant to patients, and logistical requirements are minimised without compromising scientific integrity. Recent developments, such as ICH E6 (R3)'s emphasis on proportionality and avoidance of unnecessary burden, the quality-by-design framework, and our recommendations offer a pathway forward.

Abbreviations

CRF	Case report form
CSDD	Centre for the Study of Drug Development
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonisation
ICH E6(R3)	Revision 3 of ICH GCP
PCT	Pragmatic clinical trials
PIS	Participant information sheet
RCT	Randomised controlled trial

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EL conceived the initial concept, conducted the literature review, and was the primary author of the manuscript. KC was a major contributor, particularly to the research ethics-related sections. Both authors (EL and KC) read and approved the final manuscript.

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