Trials

METHODOLOGY

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Redesigning trials to be inclusive of people with a learning disability—a practical example

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Abstract

Background People with a learning disability are frequently excluded from clinical trials, with around two thirds of trials either directly or indirectly excluding this group. This contributes to the shocking health inequalities they experience, with people with a learning disability having higher rates of long-term health conditions and dying on average 20 years younger than the general population. Improving inclusion of under-served groups in trials is a priority area for research funders and regulators. A UK-wide collaboration, 'No Research About Us, Without Us', was formed to explore and address the barriers to engaging and involving people with a learning disability in research. The project consisted of a number of intersecting work streams. This paper reports the findings from Working Group 3 which aimed to produce practical examples about how a trial could be redesigned to ensure it is more inclusive of people with a learning disability.

Methods The redesign process consisted of three steps: (1) identifying an appropriate trial using predefined criteria, (2) selecting a tool to systematically review the trial, and (3) identifying barriers to inclusion of people with a learning disability and proposing alternative design approaches that could have widened access to the trial.

Results Following review of a funder's portfolio, we selected a platform trial (PANORAMIC) which had sought to include people with a learning disability as a high-risk group for COVID-19 and yet had only made up 0.01% of those recruited. Using the INCLUDE Impaired Capacity to Consent Framework, our co-produced analysis identified practical strategies that could have ensured greater inclusion of people with a learning disability. This included involving people with a learning disability at the earliest design stage, revisiting eligibility criteria, making reasonable adjustments (e.g. high-quality easy read versions of all documents), and simplifying overly complex study processes.

Conclusion To achieve better health equity and improve the quality of clinical trials, researchers must pay greater attention to accessible study design and ensure appropriate accommodations are in place to enable inclusion of people with a learning disability. We outline some practical strategies that can inform the design and conduct of future trials to improve inclusion.

Keywords Clinical trial, Inclusivity, Accessibility, Learning disabilities, Intellectual disability

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Background

Clinical trials are essential for determining the safety and effectiveness of health and care interventions, enabling meaningful decisions to be made about whether and how these interventions should be used [1]. A major challenge for those who rely on the evidence generated by clinical trials to guide decisions about commissioning services or providing treatment or care is that participants in clinical trials have often lacked diversity, with under-representation of certain populations, resulting in them being under-served by research [1]. Unrepresentative trial populations means that the findings may not be generalisable to the actual clinical population, meaning that clinicians often have to make treatment decisions relying on evidence generated for different populations, and important findings specific to these under-served populations may be missed [2, 3]. As well as being 'bad science', exclusion from research exacerbates health inequalities and can worsen distrust in research [4] and reduce the willingness of people in those under-represented groups to accept treatment recommendations based on trial findings [1].

People with a learning disability (otherwise known as an intellectual disability) have been widely recognised as an under-served group [1, 2, 5] who experience profound disparities in their access to, and outcomes from, health services compared with the rest of the population [6]. A learning disability is defined by the UK Department of Health and Social Care as a significantly reduced ability to understand new or complex information, to learn new skills (impaired intelligence), with a reduced ability to cope independently (impaired social functioning), which started before adulthood [7]. People living with a learning disability have higher rates of long-term health conditions such as cardiovascular disease, respiratory disease, epilepsy, diabetes, and mental illness, and are more likely to be admitted to hospital as an emergency [8, 9]. This contributes to the stark statistic that people with a learning disability in the UK die on average 20 years younger than the general population, with 42% of these deaths considered avoidable compared with 22% of deaths in the general population [10]. The majority of people with a learning disability access routine (i.e. non-specialist) services. Yet, people with a learning disability are frequently excluded from research, which contributes to the health inequalities they experience [11]. For example, few clinical trials into Alzheimer's disease include people with Down syndrome, even though approximately 90% of people with Down syndrome will develop Alzheimer's disease or dementia by the age of 55 [12]. Similarly, even though 25% of people with epilepsy have a learning disability compared with <1% of the general population, people with a learning disability are under-represented in epilepsy studies [13].

Exclusion of people with a learning disability from clinical trials

A review of studies included on the UK National Institute for Health and Care Research (NIHR) portfolio found that only 1.4% of all studies were specifically related to learning disabilities, and 60% excluded people with a learning disability [14]. This picture is repeated internationally. A review of the US National Institute of Health (NIH) funded trials similarly found that three quarters excluded people with a learning disability, with little justification given [15]. However, the authors noted that 65% of studies may have indirectly excluded this group, and half of the studies excluded people based on research teams' perceptions of their inability to complete study procedures or their health status [15]. The most common reason for direct exclusion of people with a learning disability was due to concerns about lacking capacity to consent, with worryingly little explicit provision of modifications to support inclusion [15]. The authors suggested that more thoughtful attention to study design and making appropriate accommodations are critical to promoting equitable inclusion in clinical trials and health equity [15].

Other barriers to inclusion include the role of gatekeepers who decline access to potential research participants with learning disabilities [16], despite evidence that people with learning disabilities generally wish to participate in clinical trials [17]. Researchers report excluding people with a learning disability based on concerns about research ethics committees' views, a lack of confidence when assessing capacity and in communicating with people with a learning disability, and a lack of funding to make reasonable adjustments [13]. Lack of knowledge about the legal frameworks governing research involving adults with impaired capacity to consent also acts as a barrier to inclusion [18]. Researchers and other groups report that merely having concerns that a participant may lack capacity to consent raises fears about opening up the 'black box of horrendousness' of additional regulatory requirements, leading to exclusionary practices [19, 20].

Developing a collaborative partnership to address the barriers to inclusion

An international consensus statement on designing and conducting inclusive health research with people with a learning disability published in 2018 highlighted the need for more work to address the practical challenges, such as models of inclusive research that can be followed [21]. Inclusive research is key to ensuring that research is accessible by design [22]. To design and deliver meaningful and inclusive research, we need to bring together

a diverse range of perspectives from people with a learning disability, academic researchers, funders, and other stakeholder organisations, with self-advocacy groups recognised as being central to building these networks and acting as a catalyst for change [23].

Previous work, such as the NIHR's INCLUDE initiative, found that the way in which trials are designed and delivered is a significant barrier to the inclusion of under-served groups [2]. In response to a call by the NIHR to establish inclusive and collaborative models of partnership working with under-served groups, a group of 25 people including people with lived experience, self-advocacy organisations, community organisations, and academic researchers from across England, Scotland, and Wales formed a partnership to explore and address the barriers to engaging and involving people with a learning disability in research. This collaboration, called 'No Research About Us, Without Us: Removing research barriers for people with learning disabilities', aimed to co-produce new knowledge about how research can be more inclusive of people with a learning disability. Throughout this article, we use the term 'people with a learning disability' as team members with lived experience have selected this as the preferred term to be used in the project.

Further details about the No Research About Us, Without Us project, including information in easy read and video formats, can be found on the Learning Disability England website (https://www.learningdisabilityengland.org.uk/no-research-about-us-without-us). The project consisted of five intersecting work streams: (1) collaborative project design, (2) mapping barriers to inclusion, (3) addressing barriers to inclusion, (4) ensuring research design is inclusive, and (5) evaluating the collaboration.

As decided by the larger project team who collaboratively co-designed the project as a whole, four smaller working groups (see Fig. 1) were formed to facilitate a co-production approach. Members of the project team could choose which of the four working groups to join, depending on their preference and areas of interest.

This paper reports on the findings from Working Group 3 (the 'orange group') which aimed to co-produce practical examples about how a trial could be redesigned to ensure it is more inclusive of people with a learning disability. The core working group consisted of four academic researchers, one member of a national learning disability organisation, and one supporter of people with a learning disability, with further input from two self-advocates with lived experience of a learning disability and one support worker who were part of the wider project team. Together, there were eight female and one male members, drawn from across the UK mainland (Scotland $n=1$, Wales $n=1$, England $n=7$).

Fig. 1 Working groups from the No Research About Us, Without Us project

Methods

The redesign process consisted of three steps: (1) identifying appropriate clinical trial(s) using predefined criteria, (2) selecting a tool that would enable us to review and then redesign the trial, and (3) using the tool to systematically identify areas of the trial where the design was considered to act as a barrier to inclusion for people with a learning disability and propose alternative design approaches that could have widened access to the trial for people with a learning disability.

Identifying a clinical trial to review and redesign

We reviewed trials on the NIHR portfolio that either directly or indirectly excluded people with a learning disability in contexts where they would meet the INCLUDE definition being an under-served group, e.g. as a group they would be likely to need or receive the intervention in practice [2]. Trials were purposively sampled to include pragmatic trials evaluating interventions for general populations (e.g. prevention or management of diabetes), as well as those specifically intended for people with a learning disability (e.g. activity-based interventions), and other relevant trial design/contexts. We also contacted leading academics working in fields identified by the team as most relevant (e.g. epilepsy and intellectual disability) and then discussed and refined their suggestions.

We selected a trial based on our three predefined criteria, that the trial was:

a) Relevant to people with a learning disability, as determined by the researchers who led the study and members of our project team with lived experience. It was considered relevant if the intervention, should it be implemented, would be part of services accessed by people with a learning disability.
b) Should have included people with a learning disability but did not, or included only insufficiently small

numbers, as determined by the researchers who led the study and members of our project team with lived experience. Trials that should have included people with a learning disability were those which related to a condition that has a high prevalence (e.g. epilepsy) in people with a learning disability or is noted to exacerbate health inequalities for people with a learning disability.

c) There was sufficient available information to enable us to reconstruct the trial (e.g. the protocol and study information were publicly available) as determined by our working group.

As a working group, we shortlisted two potential trials that met the criteria and sought consensus from the wider project team members about which to focus on. The working group prepared an easy read presentation outlining the 'pros and cons' of each trial that was presented at a project team meeting for discussion as a group. In line with the co-production approach to the project, a number of practical steps (outlined in our co-produced guide https://www.learningdisabilityengland.org.uk/wp-content/uploads/2025/05/Practical-principles-for-including-people-with-learning-disabilities-in-research-final.pdf) helped ensure the meeting was accessible. No formal definition of consensus was used, but the decision about which trial to select was made using the approach outlined in our co-produced terms of reference (titled 'How we will work together' [24]).

After discussion, we selected a trial that evaluated the effectiveness of antiviral treatments for COVID-19 in the community (PANORAMIC) [25]. Organisations such as MENCAP have highlighted the appalling rate of disproportionate COVID deaths of people with a learning disability compared to the general population in the UK, with 45% of deaths reported to the Learning Disability Mortality Review (LeDeR) being COVID-related [26]. This was exacerbated due to the inequalities in access to COVID vaccines, with only those with a severe or profound learning disability and adults with Down syndrome being on the priority list for vaccines at the time when PANORAMIC was being designed, despite data showing that 68% of those with a learning disability who died from COVID in the first wave in England had a mild or moderate disability [27].

Summary of the clinical trial selected for review and redesign

The trial was a multicentre, UK-based, platform randomised controlled trial involving people aged 50 years or older (or aged 18 years or older with relevant comorbidities) who had been unwell with confirmed COVID for 5 days or fewer in the community [28]. As a platform trial, it was designed to test multiple treatments, with two antiviral treatments (molnupiravir and Paxlovid) selected. It aimed to include adults at increased risk of an adverse outcome from COVID aged 50 years and over, or 18–49 years and considered clinically vulnerable as defined by UK Government guidance at the time. That included people with severe and profound learning disability, Down syndrome, severe mental illness, or who were care home residents.

It was developed at an unprecedented pace due to the COVID pandemic and was designed to be an inclusive trial with a proactive outreach strategy. To maximise recruitment, participants were recruited via General Practice hubs, online, and by telephone via the central trial team. Once recruited, participants were randomly assigned to receive antiviral treatment plus usual care or usual care only, and the adaptive trial design meant that it tested several different antiviral medications during the 3 years it ran for. If randomised to the treatment arm, participants were couriered a pack containing the antiviral medication (along with dosing and safety information) and a pregnancy test (only for use by participants of childbearing potential) [28]. Data were collected through an online daily diary for 28 days, with regular telephone calls if they did not respond, and via their healthcare records. Participants could nominate a trial partner to help provide follow-up data.

PANORAMIC was selected as the focus for this project as it met the three criteria for inclusion:

a) People with a learning disability were identified as a clinically vulnerable group and hence the trial specifically aimed to recruit this group. People with learning disabilities experienced significant impact from COVID [29], and therefore PANORAMIC was considered to be highly relevant by project team members with lived experience.

b) Mortality rates from COVID during the pandemic were 3–6 times higher for people with a learning disability compared to people without a learning disability [30, 31], and people with a learning disability were less likely to receive intensive medical treatment if hospitalised for COVID [32]. However, in PANORAMIC, out of the 26,411 participants recruited to the trial of the first treatment (molnupiravir), only 63 participants were recorded as having a learning disability and 29 as having Down syndrome, making up less than 0.01% of the study population [28].

c) Accurate reporting of the study population, ability to access a wide set of study documents via the study website (https://www.panoramictrial.org/), and the publication of a 'review and learning exercise' reflecting on the lessons learned [33] meant that there was

sufficient information available to enable us to reconstruct the trial to a reasonable degree.

Selecting a tool for reviewing the trial

There are a broad range of approaches and tools that can potentially be used to explore the inclusivity of a trial, including from a disability perspective, such as inclusivity checklists to be used when designing a trial (e.g. a checklist developed by the National Cardiac Surgery Clinical Trials Programme [34]), frameworks to identify and categorise barriers to participation across different dimensions (e.g. Ford framework [35]), and resources to help implement accessibility (e.g. Accessibility By Design toolkit [36]). However, most do not include the issues that were considered by the project team to be particularly relevant to the inclusion of people with a learning disability in this context.

In recent years, the NIHR INCLUDE initiative created a strategic roadmap intended to act as a guide to addressing the needs of under-served groups in research [2]. It provides a structure to address barriers to participation and identifies key points for considering inclusion over the life course of a study with a number of 'check points' for decision-making. Building on this work, a series of INCLUDE frameworks have been developed to support researchers to design and conduct trials involving particular under-served groups, such as the INCLUDE Ethnicity Framework [37]. The working group selected one of these frameworks, the INCLUDE Impaired Capacity to Consent Framework, as it is a structured tool to help identify the key points for considering inclusion of this group [38]. Whilst recognising that having a learning disability should not be conflated with lacking capacity to consent, it covers relevant issues such as accessibility of information and supported decision-making that are key to reducing barriers to involving people with a learning disability in research [13].

The INCLUDE Impaired Capacity to Consent Framework consists of a set of four key questions to help researchers identify who should be included in their trial, and a series of worksheets covering intervention design, recruitment and consent processes, data collection and analysis, and public involvement and dissemination [38]. The final section encourages researchers to summarise the actions and resources needed to ensure their trial is inclusive of people with impaired capacity to consent. The framework is supported by an accompanying website for researchers containing resources on capacity and consent [39].

Identifying barriers to inclusion and alternative designs to support inclusion

The INCLUDE Impaired Capacity to Consent Framework [38] encourages researchers to first consider who the trial results should apply to (Q1), whether those group(s) are likely to respond to the intervention and/or comparator in different ways (Q2), and whether the intervention and/or comparator itself might make it harder for these group(s) to respond to or engage with it (Q3), before considering whether the design of the trial might make it harder for any of the groups to consider taking part and remain in the trial (Q4).

Using the structure of the INCLUDE Impaired Capacity to Consent Framework [38], the members of the working group reviewed a core set of documents from PANORAMIC including the study protocol, easy read and non-easy read versions of participant information sheets, consent forms, information booklet, and other supporting information, supplemented by publications reporting the findings (e.g. [28]) and lessons learnt [33]. Each member then systematically completed their own version of the INCLUDE framework document with the key barriers to inclusion they had identified and proposed where a redesign of these elements may help overcome them. The findings were collated in the form of a shared Excel spreadsheet, with any replications removed, and the text was then refined for clarity and consistency.

Alongside this, the easy read version of the participant information sheet (https://www.panoramictrial.org/files/pis/panoramic_pictorial_pis_v3-0_15nov2022_clean.pdf) was reviewed by three members of the wider project team who are from self-advocacy groups, including two members with lived experience of a learning disability. As the easy read information sheet was describing a clinical trial which involves regulatory aspects and other features less commonly seen when developing easy read documents for other types of studies (e.g. pregnancy testing as a safety requirement, optional clinical procedures, reporting side effects), they reviewed it alongside an easy read information sheet and consent form that had been co-designed by members of the wider project team as part of another trial (https://indd.adobe.com/view/b2985c90-187c-463f-b35a-f9deda03ced4). The feedback from this review was then added to the relevant section in the Excel spreadsheet, which was then summarised.

Findings

The findings from our analysis using Q1–3 of the INCLUDE framework are summarised here.

Who should the trial results have applied to?

The trial website acknowledges that under-served communities, such as those from ethnic minority backgrounds and people with learning disabilities, were disproportionately affected by the COVID pandemic and are traditionally under-represented in medical research. The trial team wanted to ensure that the PANORAMIC trial was accessible to all communities in all four countries of the UK, regardless of background, location, ethnicity, or socioeconomic status. The health inequalities experienced by people with a learning disability are well documented, and people with a learning disability were dying at disproportionately higher rates from COVID compared to people in the general population [30, 31]. Therefore, they were likely to benefit from effective medications to treat COVID. However, eligibility for the trial was restricted to:

- Those living in care homes
- People who have Down syndrome and can consent to take part
- Those who have severe and profound learning disabilities and live in a care home

NHS England data also shows that approximately 11% of people with learning disability have Down syndrome [40]. The protocol states that people who lack capacity to consent for themselves could only be recruited from care homes, which meant that adults who lack capacity to consent but were living elsewhere could not be recruited. This prevented recruitment of the estimated 76% of adults with severe and profound learning disability who are living in a family home [41]. Therefore, the criteria excluded the majority of people with learning disabilities who were not eligible to participate in the trial.

Are people with a learning disability likely to have responded to the intervention and/or comparator in different ways?

The study medication (molnupiravir) consisted of four capsules taken orally twice a day, 12 h apart (example, first daily dose at 8:00 am, second daily dose at 8.00 pm), for 5 days. Participants with a learning disability may have needed additional informational support to adhere to this complex medication schedule; however, information to support participants to take the medication was somewhat limited, and the instructions were not available in easy read or alternative formats. The interaction between the study medication and other medications, such as for epilepsy, which is more common in people with a learning disability, is not clear.

Did the trial intervention and/or comparator make it harder for people with a learning disability to engage with the intervention and/or comparator?

The medication was delivered to the participant directly by courier along with instructions about how to take it and for how long. They were required to confirm receipt of the medication via text or telephone call. If the participant was of childbearing potential and was allocated to an antiviral treatment, the trial pack would also contain a pregnancy test with instructions on how to perform the test. Neither the pregnancy test instructions nor the participant 'card' that was required to be carried as part of the safety arrangements for medication were available in an accessible format. The medication was only available in a tablet format, and it was not clear if it could be crushed or was available in liquid format for those who were unable to take tablets.

Did the trial design make it harder for people with a learning disability to take part, and how could it have been redesigned to be more inclusive?

The findings from Q4 are shown in Table 1. The analysis indicated that there were three key aspects of the design that would have considerably improved the opportunities to include people with a learning disability in larger numbers:

(1) Not restricting eligibility to people with a single named genetic syndrome and one level of learning disability severity, or to people in specific types of accommodation/receiving specific types of care and support such as those living in a care home. This led to the inadvertent exclusion of the majority of people with learning disability.
(2) Ensuring all study information and instructions are available in easy read format. This would have benefited not just the inclusion of people with a learning disability but also larger numbers of other under-served groups (e.g. people with lower literacy levels) or participants with intersectional characteristics.
(3) Ensuring the teams involved in recruiting participants were sensitive to the need to ensure people with a learning disability had opportunities to take part in the trial. For example, being aware that people with a learning disability would often be visiting places that acted as recruitment hubs in the trial (e.g. GP practices) and could have been approached for recruitment. This could also have been facilitated by ensuring that staff have better skills, knowledge, and understanding about the needs of people with a learning disability (e.g. Oliver McGowan

Table 1 INCLUDE Impaired Capacity to Consent Framework questions applied to the design of PANORAMIC to identify barriers to inclusion and the actions required to address them

Section	Question	Response	Actions required
Trial eligibility and participation			
Eligibility criteria	How might the **eligibility criteria** exclude people with a learning disability for reasons other than their clinical eligibility for the trial (e.g. ability to provide consent, availability of family member as consultee/legal representative, requirement to speak English, location, age, internet/mobile telephone access)?	The eligibility criteria (based on Government clinical guidance at the time) only included people with Down syndrome and people with severe-profound learning disabilities living in care homes. This excluded people with differing levels of learning disability who lived in the family home or other residential settings, both with and without capacity to consent. This is likely to be a majority of the learning disability population	The eligibility criteria should have made reference to **learning disability more broadly**, rather than specifying severe-profound learning disability and one syndrome only. **Greater involvement** of people with lived experience of a learning disability and clinicians with expertise in learning disabilities may have enabled this change It is acknowledged that sponsor requirements did not allow for the inclusion of people living outside of care homes without capacity to consent due to risk concerns, and it was developed at pace due to the pandemic. However, future trials should be **more inclusive of people with a learning disability, including those with capacity and those without capacity to consent who live in the community, and should put safety procedures and risk assessments in place to enable this** **Improving the accessibility of information and providing greater support during recruitment** (see 'opportunity to participate' section) may enable more people to be able to make a decision about participation and so widen eligibility for inclusion as the 'threshold' for capacity to consent will be lower
Opportunity to participate	How might the way(s) people with a learning disability are **made aware** of the trial (e.g. posters in a clinic, written letter from a doctor, asked by a nurse) and by whom, limit the participation of people who may not be able to consent for themselves?	There were online videos about the study for other under-served populations which are available on the 'community outreach' page of the website and although the NIHR reported that there were 'videos developed by young advocates with learning disabilities encouraging recruitment to clinical trials during COVID which were shared via the trial website and social media platforms' the website does not include videos for people with a learning disability The registration process was via an online form, and this may be inaccessible to people with a learning disability who may not be able to use a computer and the form may not be in easy read	Researchers should actively consider how to ensure the **opportunity to participate reaches people** with a learning disability. This could include targeted efforts to promote the trial through charities, social media, and networks that are specifically for people with a learning disability More **inclusive resources** should be made available to support inclusion of people with learning disability (e.g. accessible videos, easy read posters) as well as other under-served groups. **Registration** forms should be available in easy read, and via **phone calls** as an alternate option for people who struggle to get online and do not have someone to support them to do this (e.g. adults with a learning disability living at home with elderly parents). A phone helpline was available; however, **information about these options should be provided in accessible formats**. The option for **video calls** (e.g. via Zoom) may also be helpful to enable sharing of visual aids and to help check understanding using non-verbal cues The team providing support, including by phone, should receive **training in best practice in communication and supporting people with a learning disability**
	How might the **information** that tells people with a learning disability about the trial (e.g. format and content of participant information leaflet) limit the participation of people who may not be able to consent for themselves? What accessible information or format may be needed?	Only the information sheet was available in easy read and although this was substantially edited by the public involvement group supporting the trial, in particular by their one public participant with a learning disability and their sister, the quality of the information was viewed as not particularly accessible by our panel of lived experience experts (see comments in the main text). The recruitment letter and other documents (e.g. medication instructions, information booklet) were not available in an accessible format	There is a need for **better quality easy read information** and **easy read versions of all project information**, not just the core information sheet. This includes consent forms, privacy notices, letters, information about taking medication, information booklets, etc. Having easy read information but not equally accessible consent forms is not ethical. Easy read consent forms for clinical trials are rarely available (compared with other types of studies) due to more restrictive regulatory concerns. Given the discriminatory implications, **wider stakeholder engagement, including with the HRA and sponsor organisations, is urgently needed to address this issue further** Similarly, information about the trial medication (molnupiravir) such as dosage and anticipated side effects was not available in accessible formats, neither was the 'information booklet', participant card, or pregnancy test instructions. Not having information about the **study medication in accessible format raises safety concerns. Wider stakeholder engagement, including with the MHRA, HRA, and sponsor organisations**, is urgently needed to address this issue further. Further work is needed to **understand how to make information about medication being used in clinical trials more accessible for people with a learning disability**, using examples from projects looking at information on other medication (e.g. https://www.mmu.ac.uk/research/projects/medication-mental-health)

Table 1 (continued)

Section	Question	Response	Actions required
	How, and in what way, were people with a learning disability (and/or carers) and other stakeholders **involved** in developing the information for potential participants?	There was limited consultation with people with a learning disability prior to the set-up of the trial (the NIHR reports that there was involvement of a public participant with a learning disability and their sister)	A **larger advisory group of people with a learning disability and their carers** could have been consulted at the application phase and throughout the trial A relevant **organisation/charity should be included to help facilitate** advisory group involvement Appropriate expertise should be brought in (i.e. **experts by experience, researchers, accessible design**) when designing the trial
	How might **cultural or language factors** change the way people with a learning disability (and/or carers) perceive the information they are given (e.g. beliefs about consent, language proficiency)? What language(s) should information be provided in?	Videos and other forms of study information were available in other languages People with a learning disability from ethnic minority backgrounds could face additional intersectional barriers (e.g. mistrust, lack of exposure to information, stigma) to signing up to the trial	If easy read versions of all study materials were available, this would also support the inclusion of people who use other languages (i.e. improve accessibility of information more broadly) Consider issues around intersectionality, for example **having easy-read materials available in other languages**. It would also have been helpful to ensure that the advisory group includes **diverse experiences of people with a learning disability who have differing intersectional identities**
Consent procedures	How might the **way consent is sought** (i.e. when, where, by whom, written vs verbal vs electronic, availability of language/translation and access to interpreters) limit the participation of people with a learning disability? What alternative **consent documents and processes** are needed?	The language in the consent form was technical for any reader and could have been made more accessible for all participants Medically qualified professionals, research nurses, nurse prescribers, and prescribing pharmacists provided information about the trial and obtained consent. Those personnel were likely to have limited knowledge and skills about how to use accessible language and recruit people with a learning disability into trials. They may also have biases and could potentially exclude people with a learning disability unnecessarily	The consent form should be amended to use more accessible language (which benefits everyone) and there should be an easy read consent form for people with a learning disability (see comment above) Having **learning disability research nurses** and those with experience working with people with a learning disability would improve this process. Also, **training professionals on how to assess participants' communication needs and to tailor information and support decision-making**, as well as **how to assess capacity to consent**, would be beneficial
	How might the **consent arrangements** differ for people with a learning disability (including those who are able/unable to consent) (e.g. need for assessment of capacity, availability of personal consultees/legal representatives, involvement of professionals as consultees/legal representatives, deferred)? This may differ between acute and chronic conditions, and in emergency situations	It is unclear if and how capacity to consent was assessed It was unclear what support was available to optimise people's ability to make decisions about participating (i.e. what reasonable adjustments were in place), which may have raised the threshold for having capacity to consent (thereby becoming eligible)	There needs to be clear information stated in the protocol about **how/what support will be available to maximise people's ability to understand** the information and make their own decision about taking part. Information is also needed about **how capacity to consent will be assessed** if required The design could be amended so that people who lack capacity to consent could be **recruited from the hubs that were supporting the trial**. For example, recruiting staff could have been trained to identify and support participants who may have impaired capacity, who are likely to have been accompanied by someone who could act as the trial partner/legal representative The design could be amended so that the person accompanying the **people with a learning disability in healthcare settings** can assist with consent and may act as a personal or professional legal representative depending on their relationship. If it is a member of staff, they could be given the option of identifying the **personal legal representative after visiting the hub/healthcare setting** if they do not wish to take on the role of legal representative
	How might the ways in which the research team can check how well consent **information is understood** differ for people with a learning disability (e.g. presence of communication disorders, use of communication aids)?	It was not necessarily clear what checks were made to ensure whether information about the trial was understood, or how the information could have been tailored to meet participants' needs	Some people may need **further resources or adaptations made** to the process to enable them to participate (e.g. talking mats, use of Makaton, alternative communication aids). The **language used may need to be simplified** further and people may need **more time** to be given information about the trial to help them to understand. Further work would be required to ensure these resources are available so that the information giving process can be tailored to suit the person's needs Researchers should use the same processes/adaptations when confirming the potential participant **has understood the information** (e.g. to briefly summarise the study in their own words, asking the person to recall some specific study information)

Table 1 (continued)

Section	Question	Response	Actions required
	How might consent arrangements need to **change over time**? When might consent need to be revisited (e.g. data collection points)? How might the ongoing consent arrangements limit the participation of people who may not be able to consent (e.g. where capacity fluctuates, capacity is lost or regained during the trial)? What **consent documents and processes** are needed?	Capacity to consent is less likely to change over time for this population, particularly where there is a short follow-up period There may be people with (or without) a learning disability who are temporarily unable to consent due to illness related to COVID, so for this group their capacity to consent could change over time	The consent process should be revisited in these cases
Trial design	How might the **design** of the trial (e.g. cluster vs individual randomisation) limit the participation of people with a learning disability?	N/A	N/A
Data collection			
What	How, and in what way, were people with the condition or disability (and/or carers) in the target population **involved** in selecting the trial outcomes? Is there a relevant core outcome set?	It is not clear whether people with a learning disability and their carers were involved in selecting the trial outcomes	An **advisory group** including more people with a learning disability and their carers could have been consulted at the application phase and throughout the trial, including when deciding on the outcome measures
	How might the trial outcomes themselves, or other **data being collected** (e.g. where data is self-reported) limit the participation of people with a learning disability (and may not be able to self-report)?	The research assessments are not accessible or designed for people with a learning disability. For example, it is unclear whether the daily diary is in an accessible format for people with a learning disability and there may be an additional barrier if support is required from someone else to help complete it There could be additional issues for the virology samples cohort; however, it is unclear if this cohort would also include those without capacity to consent. If so, then the legal representative would need to provide consent for these more invasive activities such as nasopharyngeal swabs and finger prick blood samples	The **diaries should have been available in easy read format** (although the option of a phone call was available for data collection) The EuroQOL EQ-5D-5L was used as an outcome measure but there is a more **accessible version** available for people with a learning disability which could have been used instead **Accessible information** could be developed to explain about the additional samples, and further guidance could be developed for legal representatives to support them when making this decision
Who	How might the **people** who collect data limit the participation of people with a learning disability (e.g. the person's role, skills, experiences, or characteristics)?	Data were mostly collected remotely and relied on self-report. People with a learning disability may have needed additional support to do this	The option to have **remote online video meetings** rather than phone calls could provide a more person-centred approach and help to build rapport with person with a learning disability. The **use of pictures/accessible materials could then be shown** to help explain procedures or information. Where possible, the person who is collecting data should remain consistent throughout the participant's time in the study
How	How might data collection **methods** limit the participation of people with a learning disability (e.g. method of data collection such as online)? Are arrangements to access confidential patient information **without consent** (e.g. CAG approval) appropriate or required?	Data were mostly collected remotely	See other comments about alternatives and adaptations
Where	How might **where** data are collected (e.g. hospital, general practice, local library, emergency setting) limit the participation of people with a learning disability?	There is a requirement for those in the intervention group to post samples to the virology processing sites and to return medication and people may require additional help with this or it may not be possible	See other comments about alternatives and adaptations
Analysis			
Retention	How might **follow-up** differ between people with a learning disability and those without capacity? Might re-assessment of capacity be required if someone does not have the capacity to consent? (e.g. ability to remain in the trial if capacity is lost, use of data if unable to obtain retrospective/deferred consent or in event of death or withdrawal, whether consent survives any loss of capacity depending on different legal frameworks)?	Only a small number of people with a learning disability were included in the trial so this information is not known Retention may have been a problem for the trial as a whole Longer-term follow-up data were collected from medical records	May need **extra steps to improve retention for people with a learning disability** which would increase the likelihood of continued participation. Strategies to increase retention would benefit many otherwise excluded groups of participants, not just participants with a learning disability

Table 1 (continued)

Section	Question	Response	Actions required
Benefits	How might the **benefits** of the trial intervention(s) differ between people with a learning disability and those without?	Not known due to the lack of data	**Not known due to the lack of data**. **Planned subgroup analyses** may have been able to investigate possible differential benefits. Evidence generated after the pandemic showed that people with Down syndrome experience a **significantly higher mortality rate** due to COVID [41], therefore it is likely that, as a group, should they have been included in the trial in larger numbers, they **may have benefitted more from effective treatments**
Harms	How might the possible **harms or burdens** of the trial intervention(s) differ between people with a learning disability compared to people without a learning disability?	The potential harms of the trial (outlined in the medication appendices and other documents) were not available in easy read format meaning people with a learning disability were not given the full information and may not be made aware of the potential risks or burdens of participation	**Easy read versions of all project information** should be available, not just the core information sheet to enable people with a learning disability and their advocates to make informed decisions about participation Polypharmacy is more likely amongst people with a learning disability, and likely drug interactions need to be considered
Subgroup analyses	How should **variation** between people with a learning disability and people without a learning disability be explored—should there be planned subgroup analyses?	It will be important to explore how people with a learning disability respond to the treatments. However, the sample size of people in this population was so small that subgroup analyses would be very underpowered	Given evidence of differential susceptibility to COVID, planned subgroup analyses for highly vulnerable groups, such as people with learning disability, should be considered More efforts should be made to be inclusive and recruit people with a learning disability to provide a larger sample size. This would then allow for subgroup analyses to be conducted
Interim analyses	How should any **interim analysis** handle variation between people with a learning disability and people without a learning disability? How might any variations or differences in experiences be explored or known (e.g. through embedded qualitative research)?	Not known due to a lack of data	Not known due to a lack of data
Stopping triggers	How should any **rules to stop** the trial early on safety or benefit grounds handle variation between people with a learning disability and those without a learning disability?	Not known due to a lack of data	Not known due to a lack of data
Reporting and dissemination			
What	How, and in what way, were people with the condition or disability (and/or carers) and other stakeholders **involved** in planning the reporting and dissemination of the trial results?	It is not clear whether people with a learning disability and their carers were involved in planning the reporting and dissemination of trial results	An **advisory group** including more people with a learning disability and their carers could have been consulted in planning and reporting trial results
How	How might planned **reporting and dissemination** methods limit engagement with people who have a learning disability (e.g. accessible versions available)?	The results were published in papers, and infographics were produced	Providing a **summary of the findings in easy read** format to participants, which could also be shared with groups who work with people with learning disabilities and more widely
Where	How might **where** trial results be reported and disseminated limit engagement of people with a learning disability (e.g. online only)?	The results were disseminated via the study website; it is not clear whether or how the results were provided to participants	A summary of the findings should be **shared directly with participants** who are less likely to (or unable to) access them online

Training https://www.olivermcgowantraining.com/), and are trained and encouraged to recruit these groups.

Review of easy read study documents

When reviewed alongside a co-designed easy read information sheet and consent form that was developed for another trial, the members of the project team with lived experience of a learning disability identified a number of issues with the quality of the easy read information sheet that was used for the PANORAMIC trial. They also made several practical recommendations which could inform the development of easy read documents in future trials. The feedback on both sets of documents is summarised in Table 2.

Discussion

Evidence that people with a learning disability are systematically excluded from clinical trials is mounting [13, 15, 43]. The stark inequalities in health outcomes and mortality for people with a learning disability call for including them in the generation of evidence on 'what

Table 2 Summary of feedback on the easy read participant documents and recommendations to improve the quality of documents in future trials

Content area	Issues raised and recommendations for future trials
Language	• Some of the language used was considered to be difficult to understand, for example 'Participant Pictorial Information', 'symptoms', and 'Research Governance Ethics and Assurance Team', and should be reconsidered • Language about the use of randomisation, such as 'randomly' which was explained in one information sheet as being 'like rolling a dice', was considered to need more explanation. This reflects the literature reporting that participants often struggle to understand the concept of randomisation (e.g. [42]) • It was suggested that using 'doctor' instead of 'Dr' or 'GP' and 'worries' instead of 'concerns' would be more accessible • The use of 'study Dr' and 'your Dr' was also found to be confusing
Font	• The font used was not considered to be accessible. It was suggested that Century Gothic (a sans serif font) could be used as an alternative • Use of italics and capital letters in the middle of words was also not considered to be accessible
Content and order	• It was felt that the information about consent was not at the forefront in documents. This led to concerns about whether consent would be in place for the procedures and processes that were described as being part of the study, such as accessing medical records. It was recommended that there should be clear statements about consent at the start of the information sheet • Information about stopping participation during the study was thought to be confusing. For example, it was suggested that if the information which had already been provided by participants was still going to be used as data, then they were still technically 'taking part' in the study • It was suggested that information about what would happen if they decided to stop taking part should be at the beginning of the document alongside information about consent • For study activities that are optional, researchers should make it clear early on in the documents that these are optional and should be aware that some individuals might find specific activities more challenging. For example, some autistic people may find nose swabs and finger pricks more difficult due to their disability and/or fear of tests or blood
Use of images	• The images used did not always show clearly what the text is about. For example, when describing a clinical procedure it may be helpful to show that. In addition, some images were viewed as a bit 'childish'. It was suggested that using real life photos or photosymbols may be preferable to other types of images. The use of photographs of the research team was particularly welcomed
Layout and design	• Having text at the bottom of each page as part of the document footer, which is common in study documents to enable version control, was considered to be inaccessible and distracting • Having multiple statements within a section of the consent form with only one corresponding box in which to confirm agreement was considered confusing • The use of coloured text against different background colours was considered difficult to read, and there were concerns that it was not necessarily accessible for some groups of people. For example, the use of white text against a blue background may be less accessible for people with dyslexia

works' so that treatments and medications are immediately available. In this project, we aimed to support researchers to design more inclusive trials. We analysed a very large trial testing medications for the treatment of COVID and identified aspects of the design that inadvertently excluded (more) people with a learning disability from taking part. A co-produced easy read report of this paper can be found at (https://indd.adobe.com/view/5db07804-c67c-48d0-8f11-f77453385385).

The innovative design of PANORAMIC, conceived and delivered during a pandemic, allowed for remote recruitment of participants from all four UK devolved administrations, irrespective of where people lived or received their health care [28]. Using a pragmatic trial design, PANORAMIC was designed to mirror real-world practice as closely as possible. It strove hard to be a democratic trial, with a proactive outreach strategy led by the trial's national pharmacy and inclusion and diversity lead [28] and its strong commitment to embracing diversity has been described as 'setting a new standard for clinical trials' [44]. Our review was only possible because the trial team made all trial documents publicly accessible on the trial website and, together with the NIHR research delivery team, had engaged in a collective review and learning exercise with the aim of influencing the design and delivery of future studies [33]. However, people with a learning disability—a key population at high risk of adverse outcomes from COVID—were largely excluded from the trial. There were two main phases of the trial that excluded, indirectly, people with a learning disability: the recruitment process and the implementation of study activities.

The recruitment process, albeit initially designed to include people with Down syndrome and people with severe-profound learning disability, inadvertently excluded the majority of people with a learning disability; those with mild or moderate learning disability and those with other genetic syndromes associated with a learning disability.

Indirect exclusion at recruitment was enabled by (a) inclusion criteria that allowed proxy consent only for those in care homes—many people with learning disability live at home with their families, whilst many in residential settings are able to provide independent consent, and (b) by recruitment processes that did not make allowances for people with reduced independence or

cognitive capacity (e.g. online opt-in to the trial, technical language in the consent form, not aiming to recruit people with a learning disability in hubs where face to face recruitment was taking place). These aspects of the design likely resulted in the very small number of people with a learning disability eventually recruited in the trial—just 0.01% of over 26,000 participants [28].

The cohorts that were eligible for PANORAMIC were determined by an independent expert group commissioned by the Department of Health and Social Care and reflected the UK Government guidelines for priority groups eligible for COVID vaccines, which were heavily critiqued at the time by the health research community because of the impact on people with a learning disability [45]. Engagement with other stakeholders with experience of living with/supporting people with a learning disability may have highlighted to policymakers and to the research team that these eligibility criteria would result in an inability to include this key population, thus exacerbating the health inequalities they were (and continue to be) experiencing.

Our co-produced analysis, using the INCLUDE framework which enabled a systematic approach and encompassed all stages of a trial, suggested that including more people with a learning disability and their carers in the advisory group and having easy read information for all study documents could have made a significant difference to numbers of people recruited. Co-production and easy read have been identified as facilitators of inclusion in many other studies [13, 46]. There are several guides on how to carry out co-produced research, and our team recently published a video including top tips for co-production (https://youtu.be/ursIiKPMuV4). Easy read further constitutes 'reasonable adjustments', a legal requirement in the UK under the Equality Act (2010) and the Accessible Information Standard (2016).

Beyond recruitment, trials need to ensure their procedures do not lead to differential drop-out of this group of participants [47]. Our co-produced analysis identified key aspects of the implementation that would have benefitted from adaptation to ensure participants with a learning disability can take their medication and complete the planned assessments. Trials the size of PANORAMIC are designed, by necessity, to minimise research resource needed for delivery and also, crucial during COVID, to minimise contact with participants. These two essential design features can negatively impact retention of participants with a learning disability. However, our analysis identified two adaptations likely to facilitate retention: easy read information for intervention adherence (e.g. how to take the medication) and inclusion of the support person (staff or family carer) to help the participant with a learning disability to self-report or provide a proxy report. There are, of course, limitations with this approach: some assessments that are essential in trials, e.g. health-related quality of life, using standard tools such as EQ-5D are not considered reliable for self-reporting participants with a learning disability [48], whilst they are altogether not possible for those with more severe disability. Accessible versions of the EQ-5D-3L for adults with mild to moderate learning disabilities are available [49]. The reliance on proxy reporters may lead to biases in measurement [50]. In most instances, such obstacles are not insurmountable, and, in all cases, incomplete assessments are preferable to exclusion of large segments of the population where there is an established clinical need to generate evidence on effective interventions. Our co-produced analysis highlighted specific actions (Tables 1 and 2) that could have enabled participation for people with learning disability. Using tools other than the INCLUDE framework, such as an equality impact assessment (e.g. as developed by NIHR Allied Research Collaboration [51]), may have identified other actions to be identified, although they may be more general in nature. Our approach to identifying a suitable trial to review and 're-design' was intended to be pragmatic and so did not use a systematic process. Other trials may have met our criteria, and these may have identified other practical recommendations.

Several of the adaptations proposed here have resource implications for study designers. Co-production and easy read require additional costs in the research budget that are currently missing from funding applications. Adaptations to include carers to support participation have indirect costs in the form of increased research time (e.g. to assess capacity to consent or identify consultees who can provide best interests consent), or occasionally direct costs (e.g. to compensate direct social care costs). Resource implications of including participants with a learning disability are often cited by researchers as reasons for exclusion [13, 43]. The ethical, scientific, and legal imperatives to do more to include under-represented groups, including people with a learning disability, in clinical research suggest the increased resources can be well justified to research funders, who, in turn, are increasingly aware of this inequality: in the UK, the NIHR has funded the development of frameworks to support diverse inclusion (e.g. INCLUDE) and, as a small example, funded our co-produced study and other similar ones actively seeking solutions to this problem. As a funder of the PANORAMIC trial, they also clearly supported its focus on striving to be inclusive and recruit diverse populations.

There are also time implications for co-designing a trial and co-producing components such as participant facing

documents and ensuring that people who may require additional support are able to be recruited. This is particularly relevant to PANORAMIC which was rapidly set up during a pandemic. Whilst early involvement of people with lived experience is strongly encouraged, in time-sensitive situations such as this where it may not be possible at the outset, engaging with under-served communities at the earliest opportunity and incorporating changes via amendments may enable greater inclusion. Importantly, lessons learned from this COVID pandemic will be key to ensuring more inclusive trials in future pandemics. PANORAMIC's successful inclusion of people from minority ethnic backgrounds also demonstrates that it is possible to improve inclusion during a pandemic, given the right resources and focus. We hope that the practical tools and suggestions we have provided can ensure that future trials and collaborations are not 'starting from scratch' when it comes to the inclusion of people with a learning disability. Future work could include co-designing templates for accessible documents that could be co-adapted as needed and developing more accessible versions of standardised text such as statements about data protection regulations.

The appetite for change is further evident in whole system change in health and social care where, as of 2022, all staff are required to complete mandatory training on learning disability (such as the Oliver McGowan Mandatory training on learning disability and autism). These examples are evidence that, at the systems level, attitudes have not only changed but vehicles for practical change are being funded and implemented. Some of these systemic changes (e.g. all staff receiving training on learning disability as part of their clinical role) can support the implementation of our recommendations (staff training on how to recruit people with a learning disability in research), thereby mitigating some of the additional costs. However, this is primarily a workforce capacity issue as we need to improve confidence in our research workforce to recruit people with a learning disability, including becoming more confident in diverse forms of communication. This echoes other study findings such as the recommendation by McDonald et al. that research teams develop the skills necessary to interact appropriately with people with a learning disability, in particular with respect to presumption of capacity, demonstrating respect, fostering choice, and enhancing communication and understanding [52]. These systemic facilitators will no doubt increase awareness outside the learning disability research community and improve skills across a large intersection of staff directly or indirectly involved with research.

Our analysis aimed to provide an example of how a significant trial could be redesigned to achieve greater inclusion of people with a learning disability. We propose that easy read materials, co-production at the design stage, inclusion of carers to support participation, recruitment and participation processes that allow for—legally required—adaptations to enable participation of people with a learning disability are likely to lead to higher numbers of people with a learning disability being included, and retained, in trials. Their continued exclusion is discriminatory and unethical and actively perpetuates the well-established inequalities in health outcomes and mortality. Our study proposes some specific, practical, and feasible adaptations. Whilst only one trial was used to articulate and illustrate the barriers to inclusion, our recommendations have been co-produced with experts by experience. As a multiply disadvantaged group, any steps taken to support inclusion of people with a learning disability in trials will enhance, by extension, participation of other groups of people with reduced independence or cognitive capacity, making our proposed adaptations relevant and justified beyond the world of learning disability research. Although the trial we selected evaluated treatments for COVID-19, we believe the lessons are transferable to trials in other conditions and settings which are relevant to (and therefore should include) people with a learning disability. Arguably, this would be all trials, given that people with a learning disability access general healthcare services and develop health conditions just as people without a learning condition do, yet often experience much poorer outcomes [6, 9].

Conclusions

The exclusion of people with a learning disability from research exacerbates the health inequalities experienced by this group, as demonstrated during the COVID pandemic with devastating consequences. Whilst more research is needed to improve evidence-based care specifically for people with a learning disability, clinical trials that investigate interventions that are relevant to people with a learning disability *must* consider how their trial design will prevent this under-served group from being able to access the trial. Our analysis of a large community-based platform trial has demonstrated how a trial could be redesigned to achieve greater inclusion of people with a learning disability. Involving people with a learning disability (and carers, supporters, and advocates if required) at the earliest design stage will help to ensure that recruitment and participation processes are designed in ways that support people with a learning disability being included and retained in trials.

This 're-design' needs to include fundamental aspects of a trial such as the eligibility criteria which often

directly or indirectly exclude people with a learning disability. This requires greater awareness amongst the wider trials community (not just those who work specifically in learning disability research) about the need to ensure that this under-served population is not excluded from trials, as is the case for all under-served groups. Alongside this, reasonable adjustments, such as having easy read versions of all documents (not just information sheets) and flexible options for taking part (e.g. via 'non-digital' routes), are vital if we are to deliver the person-centred research that policymakers, research funders, and regulators now require. Research inclusion costs must pay attention to this, in addition to the current focus on language translation and other strategies to support the inclusion of under-served groups. In all trials, efforts to improve the accessibility of study information must not solely focus on participant information sheets—requiring participants to sign a consent form or to follow instructions that are not accessible to them is neither ethical nor safe. Research ethics committees, sponsors, and other regulatory organisations also play a key role in supporting inclusivity throughout a participant's time in a trial and not just at the point of recruitment and consent.

Ensuring a trial is accessible for people with a learning disability will help ensure the trial is more accessible for all groups for whom language, literacy, and the (in)ability to navigate overly complex processes currently act as barriers to inclusion, and those for whom intersectionality further compounds their exclusion. A range of tools and resources have been developed to support researchers to design more inclusive trials (e.g. Trial Forge https://www.trialforge.org/improving-trial-diversity/, STEP UP https://step-up-clinical-trials.co.uk/), and public involvement activities and co-production projects such as ours can provide valuable additional learning [53]. We hope that this paper outlining a number of strategies that could have led to a more inclusive trial is a useful contribution for researchers who are seeking practical examples of inclusive trial design when developing future trials.

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Data availability
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Declarations

Ethics approval and consent to participate
Ethical approval was not required for the 'No Research About Us, Without Us' project as it is a co-production project and not a research study. No data were collected for this review of a clinical trial.

Consent for publication
Not applicable.

Competing interests
The authors declare that they have no competing interests.

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