OPEN LETTER

Creating equity in health research to drive more and better evidence [version 1; peer review: 1 approved, 2 approved with reservations]

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Abstract

Health research is rapidly changing with evidence being gathered through new agile methods. This evolution is critical but must be globally equitable so the poorest nations do not lose out. We must harness this change to better tackle the daily burden of diseases that affect the most impoverished populations and bring research capabilities to every corner of the world so that rapid and fair responses to new pathogens are possible; anywhere they appear.

We must seize this opportunity to make research easier, better and more equitable. Currently too many nations are unable to generate the evidence or translate it to directly change health outcomes in their own communities. It is essential to act and harness this emerging change in how research data can be generated and shared, so that all nations sustainably gain from this development. There are positive examples to draw on from COVID-19, but we now need to act. Here we present an initiative to develop a new framework that can guide researchers in the design and execution of their studies. This highly agile system will work by adapting to risk and complexity in any given study, whilst generating quality, safe and ethical data.
Keywords
health research, research framework, inequity in health research, LMIC, equity in health research

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The inequity in who benefits from Health Research
We need to support an increase in the quality, volume and diversity of research across all nations and epidemiological settings to improve outcomes through better surveillance and diagnostics, risk factor determination, new prevention, treatment and management strategies and better understanding of the genetic, social and economic drivers of poor health in all settings. One of the fundamental barriers to healthcare practitioners undertaking research is the view that research is something remote and not for them. It is perceived as too difficult or too expensive with a common opinion that getting involved with ‘research’ is about working on clinical trials to evaluate a new regulatory product, and that is something only senior doctors do. However, research should be an integral component function of healthcare delivery and be seen as ‘do-able’ by all actors within hospitals, laboratories, clinics and community health centres. Some health research can be highly pragmatic; about measuring what you see, evaluating new, or improved, interventions and processes and using evidence within decision-making.

Whilst 90% of preventable deaths do occur in resource limited countries, only less than 10% of health research is undertaken in these regions. For example, sub-Saharan Africa contributes only less than 1% of biomedical publications globally; this is not static, with slowings improvements but still far behind. Unfortunately, a common situation still occurs where impactful studies are conducted by residents of resource limited countries on behalf of western organisation, who then publish results in high impact journals that ironically inaccessible to the same resource limited countries where the data originated.

We believe in finding new ways to enable research to be applicable to every setting. Disease outbreaks, such as Ebola, Lassa fever, Zika and now COVID-19 highlight that all types of health research data are equally important, from epidemiological, clinical, social science to intervention studies and implementation research, and that research needs to be guided and supported so that it is always scientifically sound, safe, ethical and accurate.

Zika was a good case to consider; because of the paucity of our knowledge, epidemiological data was critical in to the understanding of the scale and situation, sampling studies were required to understand the disease morphology, and social science to explain the context and perceptions, all required to guide acceptable study designs and possible interventions. Clinical trials were not undertaken within the Zika outbreak, as there were no products to test. Had there been a vaccine however, all these data would have been vital to the design and execution of a successful regulatory trial programme. This story has repeated with COVID-19, where we needed rapid, quality data to understand the virus and characterise the disease in order to determine its clinical impact and find potential preventive and therapeutic interventions, and design the right trials on the right individuals.

Outbreaks are a clear example of why the ability to undertake health research is needed in all countries. Research must be done firstly in the originating country to address the unknowns in those first crucially important cases and then everywhere there is transmission so that data is captured during that all-important unknown window where there are enough cases to answer the questions.

The WHO Research and Development (R&D) Blueprint was put in place after the Ebola crisis to address these gaps by enabling cross-cutting preparedness for research in epidemics. This has made strong impact within the COVID-19 pandemic with studies being coordinated, promoted and supported across the globe, including in many LMICs. The generation of core protocols, standard outcome measures, a global safety review committees and ensuring data sharing has all enabled the generation of faster, high quality evidence.

The pandemic has shaken the globe and created such devastating impact. Meanwhile, day-to-day diseases of course remain, and still need to be tackled. It is also important to understand the interaction between communicable and non-communicable diseases (NCDs). NCDs are becoming the commonest causes of death and disability in developing countries, yet WHO’s Global Observatory on Health R&D highlights the marked lack of research focusing on NCDs in these settings; gaps include product formulations tailored to developing country needs and research on risk factors, how to deliver NCD screening and management in resource poor settings. The same applies to research needs for injury prevention in developing countries.

Looking across Sustainable Development Goal (SDG) 3 it is difficult to find SDG targets that would not benefit from targeted research to increase progress development.

Alongside this universal need for more and better research, we are on the edge of a transformation in how research is undertaken. Digital health records are a significant driver in this; alongside adaptive design approaches and international recognition, there needs to be some fundamental changes to enable clinical trials to be less administratively restrictive, unduly expensive and cumbersome. It is predicted that within a decade we will no longer be undertaking research in the stop-start and highly fragmented way that it is now performed. Currently, we move in disjointed steps from epidemiology to observational sampling studies and into clinical trials, then differentiation into phase I, II, III and IV clinical trials for the evaluation of investigational products. However, this is with the exclusion of non-phased evaluation of diagnostics and prognostics, where we too need better and faster research approaches. We have been working to this step-wise process for over 50 years; our funding systems, guidelines and regulations are set-up around these norms, largely having been developed around product development using paper-based
technology. The changes already happening consider research in a wider sense than just trials, in that the whole ecosystem of health research is now recognised.

Whatever design or approach used, all data should be collected to high quality, ethics and safety standards and all should be shared, in order that others could take part and contribute or run their own studies using these informative datasets. Such an agile and adaptive approach must be designed to be both ethically and regulatory compliant, working from the best available information to ensure the safety of participants while ensuring that important investigations are continued and the social context is considered. Study designs could be better and safer because real-time data monitoring can be more responsive, both to assess, safety and to determine whether a research question has been adequately answered.

Any activity which is beyond standard care and where information is being collected as data for research requires fully informed consent, carefully considered and designed around the risk, complexity and nature of the study. Therefore, a protocol and all the necessary review, approvals and regulations also then become a necessity. If the specific questions set within the protocol could pull data from health records, rather than having separate databases it would increase efficiency, standardisation and enable faster progress, and more information on the participant would be available. This is not so far away, and indeed happening already in terms of studies that analyse real world data. Adaptive design is a commonplace and it is considered a given that all studies will extract data from health records in the future. This evolution could transform our ability to understand diseases and find better ways to tackle the burdens that they bring much faster than is currently possible. Indeed, this evolution from collecting data specifically for research, towards the collection of research data being an embedded element of healthcare would create a more fluid, learning environment. Phase I and challenge trials create different challenges and there are other situations where research questions would set the situations apart from participant records, or that patient records may not exist. The point is the need for agility and approaches designed to the question and clinical, social and epidemiological setting, all focusing on the goal of safe, ethical, accurate and cost effective, rational research.

Surely we need to be ready for this change? And if so, we have some progress to make, since currently our stop-start design, regulatory, review and funding processes are not fully geared to work outside of the old norms of phase I-IV clinical trials, even though that shift is already happening in some parts of the world. If we miss this opportunity we risk impeding progress by having systems in place that stifle rather than facilitate better research to tackle health challenges. Rather than being late recipients in these advances, countries with the greatest burdens on health should be ahead of this curve and be part of this evolution in generating new processes and guidance to encourage good research and make sure all data is collected accurately, safely and ethically. While researchers may be ready and willing in resource-limited nations to move forward with changing how research is designed and done, medical research is not easily trusted, particularly when there is industry engagement. Building trust is not simple, but preparing for and ensuring discussions and a strategy to work with political leadership, media and society is essential to make sure that all nations gain from this progress, and resource limited nations (those in fact who have the most to gain), are not left behind.

What is Health Research?
We know that addressing this first fundamental question will support more research, as currently there is confusion over what is research and what is an audit, or public health implementation. We know that the perceived difficulties of stepping over the ‘line’ into undertaking ‘research’ is preventing many healthcare providers from engaging in research in the first instance.

Here we suggest a viable definition of research that works for any capture of data where informed consent would be required, and therefore a protocol and ethical approval are ensured. This is the point where the caregiver becomes a researcher; and so, this point needs to be easily defined. We think this definition is practical and clear. It would be useful to have a globally accepted definition and as such, we present this for comment:

**Health Research is the assessment of biomedical or health-related outcomes that are either observational or interventional with and where the intention of collecting these data is to derive generalisable new knowledge.**

Creating parity
As a decisive issue in bringing health research closer to the needs of the populations of developing countries and regions, it is important to have a greater democratisation in the generation of scientific knowledge in these countries. One should not accept a situation in which a few countries and research groups direct global research on health even with merit and social commitment. There is a pressing need for research networks to be more symmetrical and equitable in defining problems, objects, research protocols and their translation to the society. Strengthening and reducing the global imbalance in health research is a prerequisite for narrowing the gap between knowledge and the needs of the people and territories in which they live. To this end, it is necessary to support the entry of the developing countries in precision public health that uses health knowledge in the digital age for the social needs, leaving no regions or no people behind. Having a research base, industrial production and high-density knowledge services is vital to the equity and democratisation of health research.

To be ahead of these changes we need a universal research-enabling framework, by which research teams could be guided in the design and operational delivery of their study. A highly agile, adaptable and easy to use system would allow teams to design and deliver studies that would collect quality data, protect the safety of the participants and be conducted to high scientific and ethical standards. All of which would encourage the
delivery of more and better, rational and high-quality health research.

Such a framework needs to align appropriately with the declaration of Helsinki, and be easy to apply to all types of research. It is not true to say that only clinical trials need research guidelines, such as the International Committee for Harmonization - Good Clinical Practice (ICH-GCP). All types of study risk inaccurate data, unethical processes, or procedures that could cause harm. It is important to have quality, reliable data from all types of studies, if we are to generate evidence to improve health outcomes and, equally important, to mitigate harm from all these studies in all disease areas. There should not be different standards, whether research is being conducted for commercial goals, product registration or specific diseases or locations. We need a highly adaptable framework that is designed to work for all research.

This framework would provide guidance relative to the risk and complexity of a specific study and would guide relevant, appropriate and proportionate application of regulations and guidelines, such as ICH-GCP, where needed. However, this would work to assure the accuracy, safety and ethics of all types of study, which are the basic principles behind ICH-GCP but difficult to apply to other types of research, which this would solve. In addition, it would contain new elements, such as community engagement, good participatory practice and assuring quality, safety and ethical standards within qualitative data. Health research studies can involve the giving of an intervention, sample-taking or qualitative elements, or any combination, and this framework should guide the accuracy, safety and ethics for operations and data capture in any or all of these.

**WHO: Taking the lead and working with others**
The World Health Organization (WHO) have a new focus on embedding research into healthcare. Research is transitioning fast in terms of new adaptive designs, fluidity of study types and using digital health records. We think that an accessible and highly adaptable research framework could be developed relatively easily. This tool could guide researchers in setting up high-quality health research studies in context, where the design and conduct will mitigate, or identify and then resolve, any potential risks to the study reliability, data quality, patient safety and ethical standards.

There is a need to be ready for, or even better, be ahead of this change. This is important, as this is an opportunity to harness this evolution and ensure it brings global benefit and increases the collection of better and faster evidence to drive change. Doing nothing is risking widening the inequity gap between those experiencing benefits from health research and those missing the opportunity. We already see areas such as oncology and cardiology leading the way with these changes; it is important that low-resourced regions, neglected diseases and vulnerable populations benefit from these changes too.

The WHO intend to act to address this gap and will be working with a wide body of partners to develop this new framework for health research. The overall goal is to drive the capture of more and better health research data within every healthcare setting across the globe that can bring benefit to all.

**Data availability**
No data are associated with this article.

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In this open letter, the authors provide a rationale for developing a research framework that can be used to inform equitable and responsive health research. Specifically, the authors discuss how the current practices used to collect, analyze and distribute health research and its findings are inefficient, inaccessible, inequitable, and lack a comprehensive framework that could be used to guide research. In addition to arguing for the need for a research framework, the authors provide a compelling rationale for using digital health records as a potential data source for research, which would allow clinical trails to to be "less administratively restrictive, unduly expensive and cumbersome." Finally, the authors discuss work engaged by the WHO to develop protocols, standard outcome measures and a global safety review that articulates the need to develop consistent protocols for equitable and accessible global research.

Overall, the authors provide a solid rationale for the need to develop a research framework and protocols to inform global research and provides compelling support for the claims made in the article, specifically for the need to expand the equitable and ethical use of digital health records to support better and more timely health research. This definition I found concise, clear and consistent with the current understandings of research in health settings.

Although the argument for the need for a comprehensive research framework, protocols, expanded use of digital health records and more equitable access to research is inherently compelling, I am not sure the contribution that this open letter will have in the development of such a framework and subsequent protocols. There is little discussion of a draft of this framework nor is there a clear discussion of the key dimensions of this emerging framework. What would have made it a stronger piece is by providing some details of the emerging framework and using the rationale provided as a introduction to the emerging health research framework. Also, there is little discussion as to how this framework should be developed and by whom and whether or not the framework would address the issues raised to support its development. It is implied that a framework would address the issues of inefficiency, lack of equity, and forwarding a global standard for health research (I suppose using digital health records, however I was not clear of the connection between the two based on my reading of the document), it is unclear how it would
do so and whether or not this can be achieved given some of the challenges discussed in the article. It seems as if the authors spend much of their time articulating the need for equity and a new framework, they do not provide a process through which this can be done equitably and make a case for how this framework would be developed. This seems like an important component of the open letter that has not be discussed adequately.

In addition, there is an implication that using digital health records for the purpose of research would assist in timely and equitable global research. However, it is not well argued as to how these digital health records could be used to foster research or how they would fit into the overall framework proposed. This may not be doable given the focus and purpose of health records and how this can lead to many other ethical issues that are not discussed in the article.

There needs to some thoughtful discussion as to how data collected for the purpose of individual's health could be ethically used in research given that the authors themselves point out the current challenges of getting data for research purpose (since much of these challenges are generally put in place to mitigate unethical uses of data).

I found the writing of the article someone confusing and requires editing. I would recommend that the authors get this piece edited for clarity, word choice and flow so that is would read better to the audience. Also the words research and data were used interchangeably in the article and they are not synonymous. Also there are paragraphs for which the main idea is not clear and the organization of the paragraph fails to support the main idea of the paragraph. This makes the piece hard to read and cumbersome. Editing the document for clarity would help make the argument clear and coherent.

Overall, I think the authors do a solid job of arguing for a framework to inform global health research; however, the authors fail to make a compelling case for how this should be done, who would be involved, how the framework would foster efficiency and equity in health research, and what would be some key elements of the framework that would address the issues raised in the article. Further, the use of digital health records for research is compelling and has potential to streamline health research, the ethical and technical issues inherent in this suggestion must be teased out to make for a compelling case for not only the use of these data but how they should be integrated in this research framework and protocols

**Is the rationale for the Open Letter provided in sufficient detail?**
Yes

**Does the article adequately reference differing views and opinions?**
Partly

**Are all factual statements correct, and are statements and arguments made adequately supported by citations?**
Yes

**Is the Open Letter written in accessible language?**
Partly

**Where applicable, are recommendations and next steps explained clearly for others to**
follow?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Evaluation and Health Equity research

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 02 November 2023

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The Open Letter by Prof Lang and colleagues highlights the need for systematic improvement in research-enabling practices for evidence generation globally. They ground this goal in a call for a framework that supports equitable participation in health research that is at once responsive and forward looking. This timely call is rooted, in part, in a recognition that without deliberate and dedicated attention to the pervasive inequities in health research, including in capacity, funding, and publication and career progression opportunities, the logical trajectory will be the widening of the inequity gap, particularly in terms of benefits gained and responsiveness of research to global needs and contours. This call for a research-enabling framework that serves both short term and long term needs and goals carries with it multiple challenges attendant to the various dimensions of what such a framework must do, how it should be applied to achieve designated goals, and by what process such a framework should be developed. While it is central to clarify and foreground the core objectives of the call, it is also necessary to consider collateral effects, structural limitations, and the possibility of enhanced risks. The Open Letter considers some of these and presumably sees them as surmountable. This is a bold call in that it invites the development of a new way of doing things that centres equity (now and in the future) and requires the global research community to systematically build capacities accordingly. While stressing the essentiality of equity, the authors identify the need for “a highly adaptable framework that is designed to work for all research”, specifically challenging current norms regarding clinical trials, including their centrality in health research as well as the systems that favour the already well established.

There are many critical aspects of a call for an equity creating framework, three of which are 1) requirements of a research-enabling framework for equity in health research 2) the need to accompany the pursuit of broader benefits with careful regard for the emergence of known and novel risks and the need for the development of appropriate protections and 3) the process of framework development and implementation.
1. A research-enabling framework

A core motivation for this call for an equity-grounded, research-enabling framework is the need for research to be more responsive globally. Lang and colleagues refer to examples that highlight the rapid response needed in cases of disease outbreak as well as the relative paucity of research on non-communicable diseases (NCD) that occupy an increasing share of the burden of disease in LMIC. Thus, the proposed framework must address issues of symmetry between the incidence, types, and burden of disease and response capacity, enabling timely response to public health needs wherever they arise. To do this the framework must facilitate the capacity to execute research in a variety of settings around the world such that deployment of effective response does not rely on the presence and expertise of foreign researchers for the necessary research to be conducted. Lang and colleagues appreciate the complexity of achieving this goal, acknowledging challenges at the local, national, regional, and international levels. Such a framework must be future-orienting as well as indicate what must be done today to build and maintain capacity in the short and long term. As the letter acknowledges, there are many challenges of and dimensions to building sustainable capacity, including patterns of hierarchy in the conduct of research in LMIC, (over-) reliance on clinical trials as the most valued form of evidence, funding patterns and trajectories, as well as the absence of career incentives. As Prof. Lang and colleagues have noted, questions regarding selection of research targets (data collection) and other possibly outcome-affecting phenomena require input by local researchers. Identifying the reasons for the current inequity gap in health services research in LMIC, why 90% of research helps less than 10% of the global population, and what will make a difference in increasing capacity in various LMIC countries, for example, are integral to the successful development of a framework.

Given the centrality of equity in the call for a framework, it seems important to stress the multilayered nature of the underlying causes of inequity and, therefore, the nature of interventions that will be needed to ensure that the framework can achieve what it is developed to do. Many questions will need to be addressed in order to get at the multifactorial causes of inequity. For example, to what extent will the framework be designed to accommodate or address structural inequities? How should the framework approach the enduring inequitable effects of past hierarchies on research skills and capacity both within local teams as well as between foreign and local partners?

2. Pursuit of benefit through more and better evidence

Prof. Lang and colleagues emphasize the need for more and better evidence and refer to different types of evidence that could enhance research, ultimately serving to yield better outcomes. The authors suggest that a new framework could systematically facilitate not only new research practices but also new research targets. Responsive to local knowledge of issues, challenges, barriers, intersecting practices, incorporating additional types of data could be significant to crafting effective interventions in the short and long term as well as in crisis situations. As such, the framework that Lang and colleagues call will shift practices to facilitate the collection of data on a range of potentially outcome-affecting phenomena that may be solely within the gaze of local teams but are currently neither collected nor acknowledged as possibly impactful. Underscoring this, the authors assert that clinical trials may not be the optimal form of evidence generation, and certainly not in all situations and for all health issues. They specifically point to
the value of embedding data collection into healthcare delivery. The potential significance of electronic health records and other digital forms of measuring, storing, and generating health information cannot be ignored in the development of the proposed framework. The increased recognition of the value of real-world evidence offers another example of rapid evidence generation needed to respond to crisis. Nevertheless, the monitoring and surveillance that these practices require is not insignificant. Along with the benefits of introducing or expanding the use of these modes of data collection, increased, altered, or novel risks must be considered. That is, with new forms or types of data collection, there will be a need to ensure that protections track these data processing practices. This requires, among other things, consideration of the risks locally for data breaches affecting vulnerable members of populations. In the case of embedding data collection in healthcare delivery, we must query whether data collection of sensitive information will have an adverse effect on healthcare seeking in certain cultural environments.

The emergence and pervasiveness of digital technologies forming some component of health research deserves attention in this framework, not least because of the inequitable uptake or access of digital technologies and the potential resulting impact on health research and outcomes. The increasingly important need for adequate cybersecurity measures worldwide should obviously also be observed in the context of research in LMIC. Dedicated attention to protections against known, emerging, and novel risks including and beyond data protection and privacy, will need to accompany this progressive step toward creating equity in health research. It will be essential to acknowledge the changing risk landscape brought about by implementation of the framework and facilitate the development of effective protections.

3. Process

The Open Letter makes several critical observations about the need for a framework to move toward equitable evidence generation globally. This initiative that aims to create equity in health research through a research–enabling framework comes at a critical time in which timely response to public health needs is essential, with impacts often felt worldwide if not adequately dealt with locally. Nevertheless, the development of such a framework may be as much about process as about outcomes. While we urgently need to prioritize and centre equity in health research, the process by which this is done is likely to be critical to its success. Lang and colleagues rightly suggest that the framework will contain “new elements” in research” such as participatory research. But it may be worth considering which elements may be integral to the process of developing the framework. How and to what extent participatory elements should be adopted in the development of the framework itself. If part of the goal is to develop new guidelines in recognition of the new types and modes of research, then the various levels of impact on local persons and communities will form important input into the framework, for example. Once developed, how will the framework adapt and conform to new insights, knowledge, and evidence? In some ways, it would seem to necessarily be an evolving document in order to meet the task that the authors have assigned to it. The authors could offer some early thoughts on the nature of the framework as a “living” document.

This call for an equity-creating framework is quite ambitious. Thinking through the multiple types and levels of changes that such a framework would necessarily encourage, a critical piece will be how such a framework would be evaluated and assessed. And, if necessary, revised to reflect new insights. Just as researchers and oversight bodies came to recognise the need for a revision of the longstanding Helsinki Declaration⁴, various developments, including the rapid evolution and introduction of technologies used to conduct research point to a reality that consists of the
presentation of continually new challenges. Procedures for amendments, updates, and significant revision could be helpful to timely response to unanticipated challenges.

Additionally, there is substantial complexity in widening the scope data collection in terms of cultural, legal, and other norms. Explicit consideration of the implications of expanding data collection and what would be needed to ensure responsible data collection should accompany the pursuit of the benefits of more data. Moreover, an increase in the scope of data collection may require consideration of infrastructural capacity to provide adequate protections, particularly given the increasingly critical role of cybersecurity.

Finally, the role of process seems fundamental given the motivation, objectives, rationale of the call for such a framework. Some have argued that process is integral to the pursuit of equity. The role of process can rightly be expected to occupy a significant place in the development of this framework. Even before its development, highlighting the role of process could be valuable in grounding this ambitious work in its equity objectives. The call for a framework for creating equity in health research is both timely and urgent as the impact of the Covid pandemic has made clear. Recognition by the World Health Organisation and others of the broad need for equity in health research is an important step toward bringing this call forward.

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Is the rationale for the Open Letter provided in sufficient detail?
Yes

Does the article adequately reference differing views and opinions?
Partly

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Yes

Is the Open Letter written in accessible language?
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Health Policy, Health Technology Innovation, Regulation of Technology, Research Ethics, Translational Digital Health, AI in Healthcare

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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This Open Letter summarises issues of inequity in health research, highlights the ongoing transformation of health research by the integration of digital health records, and makes the case for a universal framework to guide research design (presumably for research involving digital health data) for all researchers, but especially to bridge the gap for clinicians aiming to carry out health research in LMICs.

In my opinion, the greatest contribution made by this Open Letter is the proposed definition of "health research", which I found to be concise and widely applicable.

Beyond this definition, I struggle to identify precisely the contribution made by this Open Letter. The authors make a compelling case for developing a universal research framework to guide all health-related research and provide some features that they think such a framework should have. I think developing such a framework is an ambitious (but important) undertaking, even though the authors suggest that it could be achieved "relatively easily". However, this article does not in fact describe a developed (or even in-progress) version of this framework. As such, I wonder if this Open Letter would not have been more suitable, in a more condensed form, to serve as the background and rationale for this framework once it has been developed and is being shared with the research community, rather than as a stand-alone piece referring to a hypothetical framework which may be developed and shared in future.

I also find there is a misalignment between the emphasis on creating equity in this Open Letter and the purpose of this proposed framework. As it stands, the title and abstract of the Open Letter suggest that this framework will be specifically focused on creating equity, with no specific reference to digital health data. Upon closer inspection, I understood this framework to guide all health-related research, with a focus on research which involves digital health data, thereby implicitly creating greater equity between researchers in the Global North and the Global South. I
would recommend re-working the title and abstract of this Open Letter at least to clarify that the purpose of this framework is to guide the design and delivery of research anywhere in the world which involves digital health data, and this framework may in turn contribute to greater equity in health research. (Unless I have misunderstood the purpose of the framework – see below.)

There are two specific statements in the article which require further support for the authors’ arguments. First, the authors say “it is considered a given that all studies will extract data from health records in the future”. I am not convinced that this is a given. Accessing health records may not be relevant or appropriate for all health-related research. Could the authors either provide some citations for this claim, or present a more detailed argument? Second, the authors argue that “There should not be different standards, whether research is being conducted for commercial goals, product registration or specific diseases or locations.” Again, I am not convinced that this is true. While I appreciate the authors’ case for a universal research framework which can guide researchers anywhere in the world and set a global standard for health research, I am unsure whether a “grand unified framework” for health research – highly adaptable though it may be – can truly replace the need for different levels of regulatory and ethical considerations for research depending on the anticipated outcomes. Could the authors clarify their phrasing, or present a more detailed argument as to why they believe that a single research framework could/should replace more tailored research guidelines for different types of health research?

Beyond these substantive critiques, I believe this article requires comprehensive editing. As a researcher from the Global South and second-language English speaker myself, I am deeply apprehensive about suggesting this (as critique of language is unfortunately all too common in peer reviews, and often driven by bias). However, I found that the issues in writing in several places of the article actively hinder the reader’s understanding of the authors’ arguments, and therefore need to be rectified. While I won't provide a comprehensive list of editing suggestions, some observations are noted below:

- Some extremely long sentences which are very difficult to follow (see, for instance, the first sentence of the main text).
- Some unclear phrasing (e.g. “so that data is captured during that all-important unknown window where there are enough cases to answer the questions” / “direct global research on health even with merit and social commitment” – unclear what these phrases mean).
- Some overly general sentences, which do not necessarily contribute to the authors’ arguments and detract from the academic tone of the article (e.g. “The pandemic has shaken the globe and created such devastating impact. Meanwhile, day-to-day diseases of course remain, and still need to be tackled.”)
- Some contradictory phrasing (e.g. “Strengthening and reducing the global imbalance in health research”).

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Partly

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Is the Open Letter written in accessible language?
Partly

Where applicable, are recommendations and next steps explained clearly for others to follow?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: HIV mental health

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.