MEDCITY

Advancing Clinical Trials

Making the UK a global leader in inclusive and diverse clinical trials

March 2023

Faculty of Pharmaceutical Medicine

NHS Imperial College Healthcare NHS Trust

On Thursday 8th February, MedCity, the Faculty of Pharmaceutical Medicine and the NIHR Clinical Research Network North West London, brought together leading voices from across the pharmaceuticals, life sciences and health sectors to discuss equality, diversity and inclusion (EDI) in clinical trials.

This report builds on that discussion, although the recommendations of this report do not necessarily reflect the views of any individual attendee.

FOREWORD

The UK's life sciences sector has long been recognised as a key area of strength, delivering both health and economic benefits across the country. Clinical trials are integral to this success, enabling the UK to play a leading role in COVID-19 vaccine development [1], and delivering developments in cutting edge therapy areas such as cell and gene therapies [2]. This is unsurprising, given the UK's strong academic research base, rich health data landscape, well-established regulators, and funding ecosystem. Importantly, life sciences have political support; the new Department for Science, Innovation and Technology is committed to promoting a diverse research and innovation system, increasing private research and development, and putting public services at the forefront of innovation [3].

Yet despite these strengths, UK life sciences are increasingly under threat. The number of clinical trials initiated in the UK declined 41% between 2017 and 2021 [4]. and leading pharmaceutical companies are scaling back their UK investments [5]. The reasons for this are complex, from the post-COVID crisis in healthcare, to market access and the challenges of operating in a post-Brexit environment [6], [7]. What is clear is that the UK is at risk of losing its position as a life sciences leader, with clinical trials increasingly being launched in other countries. That's bad for the economy, it's bad for our wider R&D ecosystem, and most importantly, it's bad for patients, making it harder for them to access the latest treatments.

To counter this trend the UK's life sciences ecosystem must set itself apart from its many competitors. This report, which builds on a discussion between leading voices in the pharmaceuticals, life sciences and health sectors, charts a course to establish a diverse and inclusive clinical trial ecosystem as a key unique selling point, to strengthen UK life sciences, and ensure patients continue to benefit from world-leading life sciences research. Now it is up to all of us to deliver on this potential.

Suki Balendra (Director of Strategic Partnerships, Imperial College Healthcare NHS Trust)
Neelam Patel (CEO, MedCity)
Sheuli Porkess (Vice President, Faculty of Pharmaceutical Medicine)

[1] HM Government, *Life Sciences Vision* (July 2021).
[2] Cell and Gene Therapy Catapult, *UK ATMP Clinical Trials Report* (2022).
[3] Department for Science, Innovation and Technology, *About Us* (February 2023).
[4] ABPI, *Rescuing patient access to industry clinical trials in the UK* (October 2022).
[5] The Times, *AstraZeneca: UK losing out on investment in life sciences research* (February 2023).
[6] The Guardian, *UK investment in R&D plunges in blow to 'science superpower' plan* (October 2022).
[7] The Times, *Life sciences at tipping point, warns GSK boss Dame Emma Walmsley* (February 2023).

INTRODUCTION

Equality, diversity, and inclusion (EDI) is increasingly recognised as an essential element of successful clinical trials [8], [9], [10]. The reasons for this are threefold. Firstly, clinicians, companies and healthcare systems all want to improve the health of all our communities. Secondly, diverse trials provide more robust clinical data, demonstrating more clearly either the universal benefit of a drug or treatment, or its differential effect in different communities, enabling better healthcare with wider access to and uptake of new medicines. Thirdly, delivering more clinical trials in more diverse communities creates jobs, boosts local economies, and supports the life sciences sector as a key strategic pillar in the UK economy. In short, EDI is good for everyone.

The UK is a highly diverse nation, particularly in urban centres such as London, Manchester, and Birmingham [11]. In combination with a strong health research infrastructure, this offers a unique opportunity for global investment in diverse clinical trials. Disappointingly however, UK clinical trials all too often fail to reflect the full diversity of the population [12], [13]. Patients may be excluded because of restrictive eligibility criteria and protocol design (e.g., language requirements), practical barriers (such as the financial cost of participation, or the concentration of trials in major teaching hospitals), poor engagement with diverse communities or bias (whether conscious or unconscious) among study teams, while mistrust of medical professionals, fear of potential outcomes or lack of awareness or understanding of opportunities, may also diminish participation among under-represented groups [14].

Understanding these barriers is an essential first step to improving diversity in clinical trials. But as well as understanding, action is also needed at all levels of the life sciences research ecosystem, from funders and regulators, through companies and research teams, to individual researchers and into communities. This report draws out some of these key actions to foster a clinical research culture in which EDI is the default.

[8] Merck, *Diversity in Clinical Trials*.
[9] Pfizer, *Diversity in Clinical Trials*.
[10] Roche, *Representation matters: inclusivity in clinical trials*.
[11] HM Government, *Life Sciences Vision* (July 2021).
[12] NIHR, *NIHR research ethnicity data provides insight on participation in COVID-19 studies* (December 2020).
[13] Lau et al. 'Does Ethnicity Influence Recruitment into Clinical Trials of Parkinson's Disease?', *Journal of Parkinson's Disease* (April 2022).
[14] IFPMA, *Diversity and Inclusion in Clinical Trials: Bioethical Perspective and Principles* (May 2022).

SYSTEM LEADERSHIP

To foster a new culture of research, funders, regulators, and other sector bodies need to lead from the front. In 2022, the US Food and Drug Administration (FDA) published draft guidance for industry on how to improve clinical trial participation among under-represented ethnic groups, which recommends the development of a race and diversity plan for new clinical trials [15]. The full impact of this guidance has yet to be felt, but it seems likely that, if inclusion of under-represented groups is considered from the outset, key barriers such as restrictive eligibility requirements may be identified and addressed before protocols are finalised. Perhaps more importantly, this guidance sets a precedent, recognising diversity as a priority consideration at all levels.

In the UK, the NIHR's INCLUDE project has provided guidance on improving the inclusion of under-served groups in UK clinical trials, particularly reflecting on protocol development [16]. However, the NIHR has no regulatory role; to have the greatest impact in embedding diversity in clinical trials, EDI should be embedded in regulation. The Health Regulatory Authority (HRA) and MHRA are currently developing new EDI guidance, which should be given the strongest basis possible, for example by requiring EDI plans to be submitted as part of the ethics approval process for clinical research (while also seeking to ensure overall requirements remain light touch). Where possible, requirements should be aligned with guidance from other regulators (such as the FDA) to enable international trials to standardised protocols. The FDA or the HRA could further support this process by publishing frameworks for effective EDI plans.

NIHR can also strengthen the role of the INCLUDE guidance, by using it as a basis for EDI criteria for NIHR-funded research. By requiring high-profile, competitive NIHR bids to address the INCLUDE guidance, NIHR could further normalise EDI in trial design. Aligned requirements should be implemented by other funding bodies and research charities.

Another key element of the research ecosystem is played by clinical trial registries, which support rapid recruitment to clinical trials. Where these registries are not diverse, they can undermine diverse recruitment to trials. Registries should therefore be audited to ensure they reflect the diversity of the UK population, and where this is not the case, plans should be established to address these gaps.

---

[15] FDA, *Diversity Plans to Improve Enrollment of Participants from Underrepresented Racial and Ethnic Populations in Clinical Trials Guidance for Industry* (April 2022).
[16] NIHR, *Improving inclusion of under-served groups in clinical research: Guidance from INCLUDE project* (January 2022).

SYSTEM LEADERSHIP RECOMMENDATIONS

The HRA should consider requiring EDI plans as a part of the clinical trial ethics approval process, where possible aligning with international guidance, such as that developed by the FDA.

The NIHR and other research funding bodies and charities should consider strengthening EDI requirements for directly funded research projects.

Clinical trial registries should be audited to ensure they reflect the diversity of the UK population, and where they do not, plans should be established to address gaps.

ALIGNING COMMERCIAL AND CLINICAL PRIORITIES

Diversity in clinical trials makes commercial sense, enabling better clinical data, which supports reimbursement and uptake. Yet often, delivering diversity in trials can conflict with other priorities, such as the drive to deliver trials rapidly, with minimal administrative or regulatory burden. Regulation can help address this mismatch, but a greater recognition of the commercial benefit of diversity in clinical trials is vital in order to fully close the gap.

Pharmaceutical companies should establish internal systems and processes which foster closer working between clinical research and commercial management functions. More tangibly, clinical trial diversity reporting requirements should be strengthened. These two actions would help commercial teams recognise the value of EDI and treat delivering diverse trials as a key success metric which is afforded equal or greater weight than other ESG pillars such as reducing carbon emissions. Ultimately, this will deliver direct financial benefits for companies, and help secure and sustain investment.

ALIGNING COMMERCIAL AND CLINICAL PRIORITIES RECOMMENDATIONS

Pharmaceutical companies should embed internal processes which facilitate greater understanding of the importance of EDI in trials across all functions, including commercial functions.

Clinical trial EDI reporting requirements should be strengthened and standardised, to ensure that EDI is identified as a key metric for commercial success.

DIVERSE LEADERSHIP

Below the system level, individual clinicians and research teams who design and implement studies can have a profound impact on the diversity of those studies.

In the USA, Bristol Myers Squibb (BMS), has established the Diversity in Clinical Trials Career Development Program which provides training to early career researchers from diverse backgrounds, with the aim of creating clinical trials which foster participant diversity [17]. If similar programmes were developed by UK pharmaceutical companies, research institutes and funders, this could deliver a wide range of benefits. Firstly, clinicians from diverse backgrounds may be more conscious of barriers to participation experienced by people from similar backgrounds (for example, participation criteria which exclude participants with poor levels of spoken English, or through ambiguity, lead researcher to favour “easier” groups) and may therefore address such barriers at early stages (rather than struggling to address poor inclusion at later stages of trial recruitment). Secondly, clinicians with similar backgrounds to target participants may be more trusted, helping to boost confidence in both specific trials, and in the broader principle of participation in clinical research. Thirdly, and perhaps most simply, researchers from diverse backgrounds may be more likely to actively encourage participation by diverse communities.

There are also opportunities to embed diverse clinical leadership in study design and implementation, even when lead researchers are not themselves from underserved groups. For example, a broader range of KOLs from more diverse backgrounds could be consulted when developing protocols, to check whether the proposed protocol will enable or undermine participation among key target groups. In addition, by expanding the range of KOLs, awareness of trial activity can be spread beyond larger teaching hospitals into a broader range of communities. Additionally, all clinicians should be encouraged to see signposting to research opportunities as a standard element in the provision of clinical care to all patients.

[17] Bristol Myers Squibb, *The Bristol Myers Squibb Foundation Diversity in Clinical Trials Career Development Program Announces First Group of Physicians to be Trained* (October 2021).

DIVERSE LEADERSHIP RECOMMENDATIONS

Programs should be developed by research institutes, funders, and pharmaceutical companies to train and foster diverse communities of researchers.

Pharmaceutical companies and other research commissioners should ensure that diverse pools of KOLs are developed to review trial designs and protocols, with a view to ensuring diversity in participation.

Clinicians at all levels should be encouraged to present research opportunities to patients as a part of routine care.

CASE STUDY

DELIVERING DIVERSITY IN DIABETIC MACULAR OEDEMA CLINICAL TRIALS IN NORTH WEST LONDON

Diabetic macular oedema (DMO) is a thickening of the central part of the retina and a common cause of sight loss among people with diabetes {i]. Diabetes, in turn, is particularly common among people from black and south Asian ethnic groups [ii]. In particular, type 2 diabetes is 3-5x more common in minority ethnic groups than the white British population [iii], and diabetic macular oedema is 2-3x more common in Black people and South Asians than white Europeans [iv].

Current NICE guidelines for first line treatment of DMO recommend treatment for patients with central retinal thickness of 400 micrometres or more at the start of treatment [v]. However, black and South Asian populations have thinner retinas to begin with on average [vi], meaning such thresholds may result in delays to treatment commencement.

The North West London boroughs of Brent, Harrow and Ealing have highly diverse populations and high rates of diabetes; in Brent, for example, 63.7% of residents identifying as non-white (or ethnic minorities), and diabetes prevalence is 8.91% (compared to the London average of 6.5%) [vii]. However, prior to 2017, large scale ophthalmology clinical trials had not been delivered in Brent.

In July 2016, the DRAKO study, a commercial phase 4 study was launched, which evaluated aflibercept treatment for patients with DMO [viii]. In 2017, the study protocol was altered, removing the requirement for central retinal thickness of 400 micrometres or more at the start of treatment. This enabled a wider patient population to be included in the study.

Following this change, researchers in North West London, led by Christiana Dinah (Department of Ophthalmology, London North West University Healthcare NHS Trust), joined the DRAKO study. The team undertook a programme of targeted outreach to facilitate study participation among patient communities in Brent. The team held patient engagement sessions explaining why research is still needed in diabetic eye diseases, the importance of informed consent, and the regulation of research, in order to normalise participation in ophthalmology research. The study leads allowed interpreters to be involved in the trial, enabling participation by populations with low levels of English fluency, while support from NIHR staff enabled the Brent team to rapidly recruit 64 participants, the most from a single center in the country, from a total study population of 507 across 35 centres. The resulting overall study population was 77% white, compared to 83% and 79% in the earlier VISTA and VIVID trials respectively, underscoring the need for more diverse trial sites and recruitment across a multi-centric study [vii], [viii].

An additional real-world outcomes study, undertaken in London North West University Healthcare NHS, Imperial College Healthcare NHS Trust and Hillingdon Hospital NHS Foundation Trust (which recruited 221 patients), demonstrated the ethnic diversity of patients impacted by diabetic macular oedema in North West London, with just 28% of participants being of white ethnicity [vii]. Notably, this real-world study found a meaningfully lower treatment effectiveness among this diverse population, when compared to the VIVID and VISTA trials, highlighting the importance of ensuring that diverse communities are included in research.

---

[i] Macular Society, *Macular oedema.*
[ii] Public Health England, *Diabetes Prevalence Model* (2016).
[iii] Goff, "Ethnicity and Type 2 diabetes in the UK", *Diabetic medicine* (2019).
[iv] Sivaprasad et al, "Ethnic Variations in the Prevalence of Diabetic Retinopathy in People with Diabetes Attending Screening in the United Kingdom (DRIVE UK)", *PLOS ONE* (2012).
[v] NICE, *Ranibizumab for treating diabetic macular oedema* (2013); *Aflibercept for treating diabetic macular oedema* (2015); *Faricimab for treating diabetic macular oedema* (2022); *Brolucizumab for treating diabetic macular oedema* (2022).
[vi] Kashani et al., "Retinal Thickness Analysis by Race, Gender, and Age Using Stratus OCT™", *American Journal of Ophthalmology* (2020).
[vii] Dinah et al., "Aflibercept for treatment-naïve diabetic macula oedema in a multi-ethnic population: Real-world outcomes from North West London", *PLOS ONE* (2021).
[viii] Sivaprasad et al., "Evaluation of standard of care intravitreal aflibercept treatment of diabetic macular oedema treatment-naive patients in the UK: DRAKO study 12-month outcomes", *Eye* (2022).

DEEP ENGAGEMENT

At the root of many barriers to EDI in clinical trials is a lack of trust or understanding between clinical research communities and the diverse patient populations they want to reach. Where research activity is delivered in under-represented communities over a sustained period, this can enable easier access to trials, improve understanding, reduce mistrust, and normalise both researchers presenting opportunities to patients, and patients accepting those opportunities.

At present, much research activity is centred in major teaching hospitals. This can limit the pool of potential trial participants and lead to the consistent under-representation of certain groups. To address this, pharmaceutical companies should seek to deliver research activities through a wider range of centres and implement programmes to engage diverse and under-represented populations in research, aligning this activity where possible with target populations for products in company pipelines. This engagement should be “culturally competent”, tailored to specific target populations and may entail working with clinicians at all levels, including primary and community care clinicians such as GPs and pharmacists. Such long-term investment in community engagement would increase costs upfront but would bring significant benefits in terms of improved EDI in clinical trials, resulting in better clinical data which supports pipeline priorities. It would also enable more rapid uptake of effective treatments in high-prevalence communities after approval.

The wider system also has a role in enabling this deep community engagement. Funders such as the NIHR already support research into clinical trial methods and practices. Funding opportunities should be expanded to support research which seeks to identify “what works” to address barriers to engagement. Funders, regulators and industry groups (such as the HRA, NIHR and ABPI) can also support engagement by assisting in disseminating good practice guidance to research communities.

Crucially, pharmaceutical companies may be deterred from community outreach to support clinical trials, due to regulations around promoting medicines. The current ABPI code of practice is seen as insufficiently differentiating between engagement to support clinical trials on one hand, and engagement to support uptake of approved medicines on the other. This must change so companies can reach currently disengaged patients.

DEEP ENGAGEMENT RECOMMENDATIONS

Pharmaceutical companies should work with others to support consistent and sustained patient outreach in diverse areas about the importance of research, particularly where populations have a higher-than-average prevalence of diseases in the research pipeline.

Research bodies such as the NIHR should actively fund research into effective models for pre-clinical community engagement which supports diverse participation in research.

Research bodies, regulators, and industry bodies should seek to promote and disseminate good practice in clinical study design, development and community outreach which fosters diverse participation in research.

The ABPI and PMCPA should produce guidance on the ABPI Code of Practice to enable and support patient outreach in relation to research.

CONCLUSION

The UK's clinical trial ecosystem is increasingly under pressure, as pharmaceutical companies critically appraise whether to launch new medicines in a commercially challenging UK environment. A number of challenges, from NHS COVID recovery to the high rebate on innovative new medicines and other market access barriers, have contributed to a 41% decline in the number of clinical trials initiated in the UK between 2017 and 2021 [18]. This shift has potentially huge implications, not only for drug development, but also, crucially, for patient access to more effective treatments.

Nonetheless, the UK market offers unique potential for pharmaceutical research with its strong academic research base and its nationalised, single-payer healthcare system, as well as its role as a global reference market for pricing, and the recognition afforded to NICE decisions. Crucially, the UK is a diverse nation with a well-established clinical research infrastructure and an innovative and collaborative regulatory environment, which offers the potential for pharmaceutical companies to demonstrate the effectiveness of products across a wide range of patient populations.

By fostering a globally competitive research ecosystem in which EDI is the default for clinical trials, the UK can create a new USP for its life sciences research industry, which brings new commercial benefits to pharmaceutical companies while also delivering better patient outcomes. Progress on this front would allow the UK to re-establish global leadership in clinical trials, ultimately ensuring that more patients can access the best treatments.

[18] ABPI, Rescuing patient access to industry clinical trials in the UK (October 2022).

ROUNDTABLE ATTENDEES

- Sheuli Porkess (Faculty of Pharmaceutical Medicine), Chair
- Suki Balendra (Imperial College Healthcare NHS Trust)
- Ben Cottam (Faculty of Pharmaceutical Medicine)
- Mital Desai (Sanofi)
- Christiana Dinah (London North West University Healthcare NHS Trust)
- Kevin Fenton (Faculty of Public Health)
- Marc Fisher (Vertex Pharmaceuticals)
- Shona Fraser (Janssen UK)
- Rachel Lo (Novo Nordisk)
- John Ndikum (Faculty of Pharmaceutical Medicine)
- Neelam Patel (MedCity)
- Marcia Philbin (Faculty of Pharmaceutical Medicine)
- Alex Phipps (AstraZeneca)
- Elizabeth Robertson (Diabetes UK)
- Neha Vohra (MSD)
- Naho Yamazaki (Health Research Authority)
- Jack Fleming (OVID Health)
- Miriam Anorson (OVID Health)

MAKING THE UK A GLOBAL LEADER IN INCLUSIVE AND DIVERSE CLINICAL TRIALS – A CALL TO ACTION

We want to see a UK clinical trials ecosystem which fosters equality, diversity and inclusion, in order to deliver clinical trials which provide richer data, support better patient care, improve the uptake of new medicines, and secure the UK as a leader in life sciences research. We call for action at all levels to embed this culture of diversity by default.

System leadership

- The HRA should consider requiring EDI plans as a part of the clinical trial ethics approval process, where possible aligning with international guidance, such as that developed by the FDA.
- The NIHR and other research funding bodies and charities should consider strengthening EDI requirements for directly funded research projects.
- Clinical trial registries should be audited to ensure they reflect the diversity of the UK population, and where they do not, plans should be established to address gaps.

Aligning commercial and clinical priorities

- Pharmaceutical companies should embed internal processes which facilitate closer working and collaboration between clinical research and commercial management functions.
- Clinical trial EDI reporting requirements should be strengthened and standardised, to ensure that EDI is identified as a key metric for commercial success.

Diverse leadership

- Programs should be developed by research institutes, funders, and pharmaceutical companies to train and foster diverse communities of researchers.
- Pharmaceutical companies and other research commissioners should ensure that diverse pools of KOLs are developed to review trial designs and protocols, with a view to ensuring diversity in participation.
- Clinicians at all levels should be encouraged to present research opportunities to patients as a part of routine care.

Deep engagement

- Pharmaceutical companies should work with others to support a consistent and sustained patient outreach in diverse areas about the importance of research, particularly where populations have a higher-than-average prevalence of diseases in the research pipeline.
- Research bodies such as the NIHR should actively fund research into effective models for pre-clinical community engagement which supports diverse participation in research.
- Research bodies, regulators, and industry bodies should seek to promote and disseminate good practice in clinical study design, development and community outreach which fosters diverse participation in research.
- The ABPI and PMCPA should produce guidance on the ABPI Code of Practice to enable and support patient outreach in relation to research.

ADVANCING CLINICAL TRIALS

Making the UK a global leader in inclusive and diverse clinical trials 2023

MEDCITY

Faculty of Pharmaceutical Medicine

NHS
Imperial College Healthcare
NHS Trust