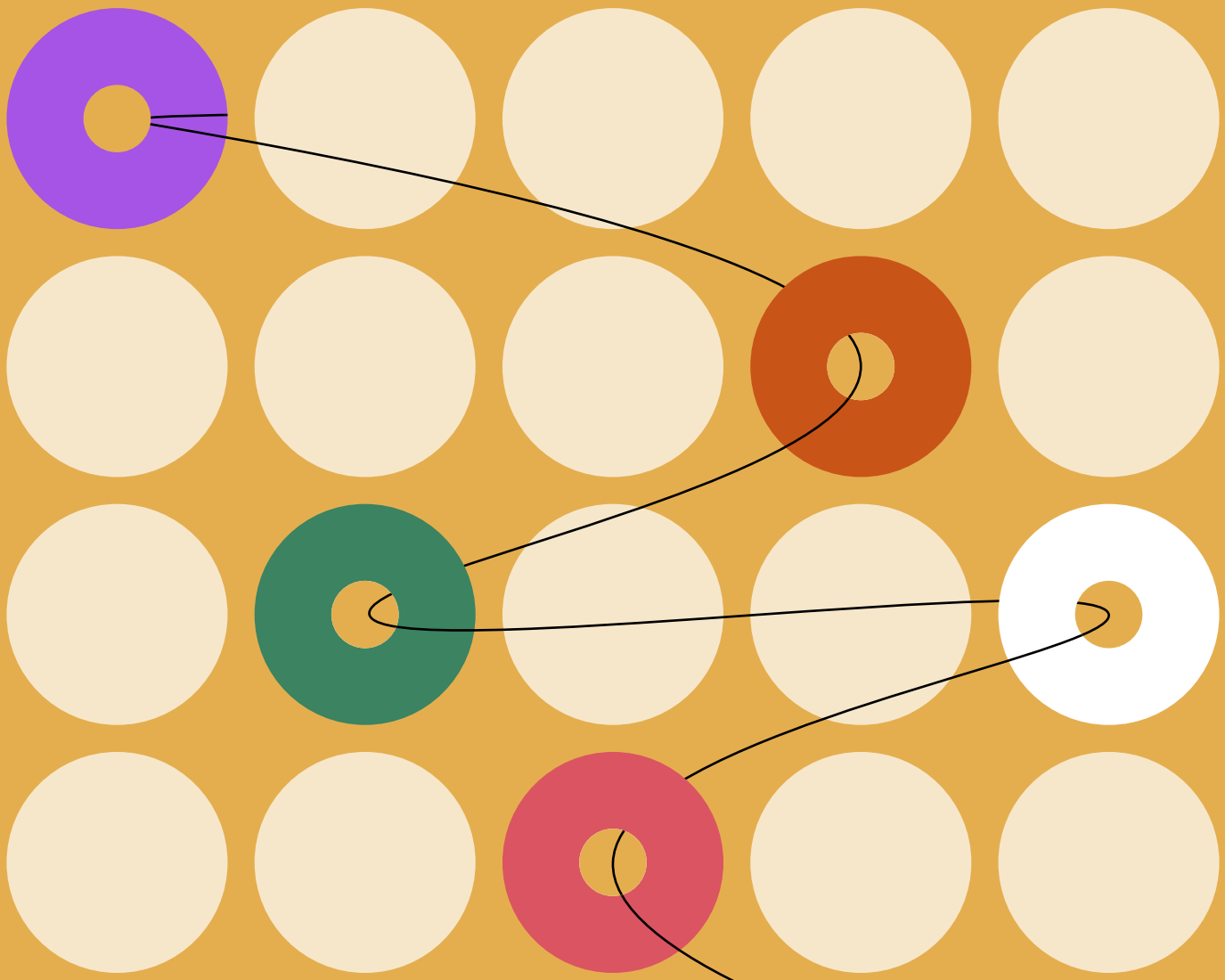

Inclusion by design:

building equity in clinical trials through the lens of metastatic breast cancer

May 2023

The Health Policy Partnership

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About this report

This report was developed to share a vision for improving equity in clinical trials. Through the lens of metastatic breast cancer, it aims to highlight opportunities to improve access to and participation in clinical trials around the world. The report was developed independently by Helena Wilcox, Eleanor Wheeler and Suzanne Wait at The Health Policy Partnership (HPP) under the guidance of a steering committee and in consultation with additional experts.

The steering committee comprises a global collective committed to identifying and addressing unmet needs of people with cancer. Our aim was to provide actionable recommendations on how to achieve equity in cancer clinical trials while prioritising patients' needs and preferences.

HPP is grateful to the steering committee members, who guided the development of this report:

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- **Susannah Stanway**, Medical Oncologist, Co-founder and Board Member, UK Global Cancer Network and London Global Cancer Week

Foreword

Clinical trials are fundamental for people with cancer, representing an important avenue to new, effective treatments. For people with metastatic breast cancer, for which there is currently no cure, clinical trials can be especially important. However, many people with cancer face inequities in access to all aspects of care, including clinical trials. The structures and practices that operate within medicine – and, by extension, in clinical research – systematically exclude those with less power in ways that uphold and mirror inequities across societies.

Around the world, people will experience these power imbalances and inequities in varied ways. It is essential that we recognise those experiences and the associated barriers to receiving best-practice care and outcomes in cancer.

In this report, we discuss some of the most important and widely experienced barriers, centred on research in metastatic breast cancer. We also share examples of best practice and recommendations on approaches to addressing them. It is our hope that the findings will be applicable to cancer clinical trials more broadly.

The terms used have been guided by HPP and the steering committee, taking into account insights shared by the wider metastatic breast cancer community. We recognise that this report will not fully reflect every person's experience of metastatic breast cancer, or of participating in clinical trials. We hope the findings of this work will support the development of more inclusive and representative research, for the benefit of all.

— MEMBERS OF THE STEERING COMMITTEE

Executive summary

There is growing recognition of existing disparities in the incidence and treatment outcomes for many conditions, as well as inequities in access to quality healthcare. Health inequities often mirror broader social and economic inequities, with factors such as economic disadvantage or lower socioeconomic position acting as strong predictors of poorer health outcomes.[1] When taking action on health inequities, it is essential to recognise and address the many complex challenges that lie at their foundation.

People with metastatic breast cancer have significant unmet needs for improved treatments and outcomes. Research demonstrates increased risks and rates of metastatic breast cancer in some populations; for example, data from the US suggest higher rates of metastatic breast cancer among Black women than among White women, even when taking into account their age and the stage of disease at diagnosis.[2] Serious side effects may also be experienced differentially, contributing to wider disparities in experiences of care and overall outcomes.[3-5]

Clinical trials are an important avenue for accessing potentially promising treatments and interventions, yet there are global inequities in where they are conducted and who is able to participate. There are often similarities between barriers to accessing quality healthcare and participating in research.[6 7] This perpetuates existing health inequities, precluding us from broadening our limited understanding of how interventions may affect people with different characteristics.[8 9] This also means interventions may not be designed or delivered appropriately.[5 10]

Action is needed at multiple levels to progress towards health equity, and clinical trials are a key driver for improving health outcomes. Many of the solutions described throughout this report have been presented through the lens of metastatic breast cancer, yet have broader application across cancer clinical trials. This report calls on all those involved in the design and conduct of clinical trials to take action across three priority areas:

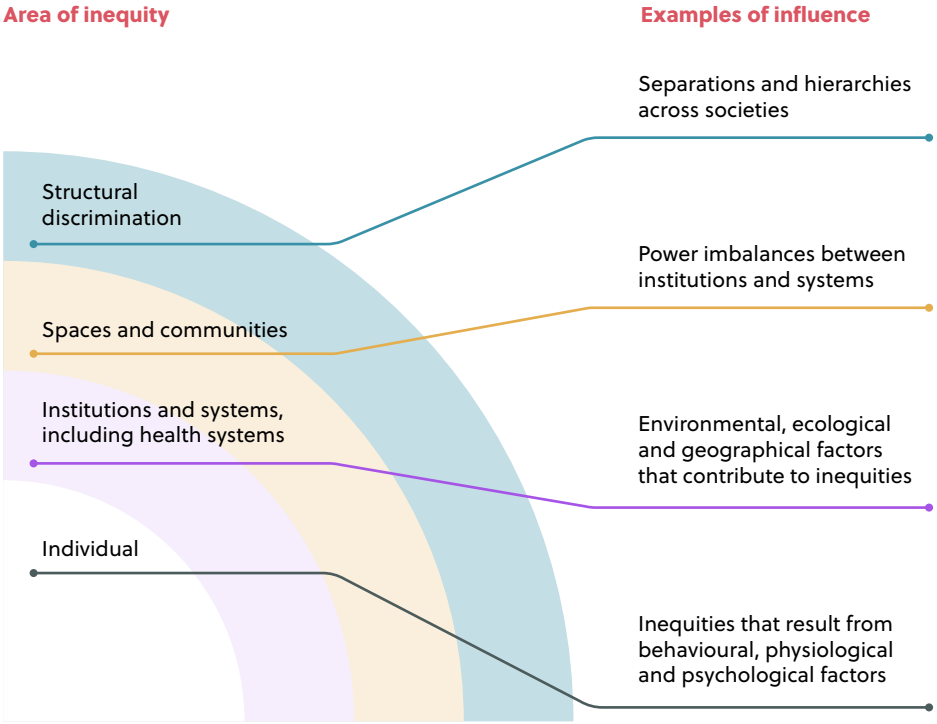
1. **achieving more inclusive data collection, analysis and reporting**
2. **designing more inclusive clinical trials**
3. **embedding more inclusive practices in trial access and participation**

1. How do health inequities affect people and communities?

Global inequities in health

Health inequities continue to persist at both the global and the national level, mirroring broader social and economic inequities. Health inequity affects whether and how people can access healthcare and whether this care is acceptable, affordable and of high quality.[5 11] People who experience greater inequity often have increased rates of certain health conditions and experience worse outcomes.[4 5] Many forms of discrimination in society also prevail in healthcare, and these may lead to certain groups of people being underserved by health systems,[5] and under-represented in clinical trials (*Figure 1*).

Figure 1. Intersections of inequities that may impact health[5 12]



There is strong global evidence that inequities in health manifest in significant variation in access to care and health outcomes. Economic disadvantage or low socioeconomic position are among the strongest predictor of poor health outcomes.[1] However, this often serves as a proxy metric for other characteristics that can affect health equity, particularly race or ethnicity.[5 11 12] As all forms of discrimination can lead to health inequity, it is important to address not only the complex structural challenges affecting whole societies but also the unconscious biases that can exist in healthcare.[5 12 13] These issues may vary considerably by region, country or setting.

'You can never assume that health issues and inequities will be the same in different settings. Globally, we know these inequities do exist and there is an imperative to change the picture.'

SUSANNAH STANWAY, UK GLOBAL CANCER NETWORK

Inequities in metastatic breast cancer

Breast cancer is the most common cancer among women worldwide, and there is a significant unmet need for improved treatments and outcomes, particularly in metastatic breast cancer. There were more than 2.2 million new breast cancer diagnoses globally in 2020.[14] Metastatic breast cancer accounts for 5–10% of initial diagnoses (*Box 1*).[15] In addition, 20–30% of people whose initial breast cancer was diagnosed at an early stage will have a recurrence that manifests as metastatic breast cancer.[15] Improvements in the detection and treatment of breast cancer mean that five-year relative survival rates are as high as 86–99% when cancer is detected early. However, in metastatic breast cancer this rate is much lower, at just 30%.[15 16]

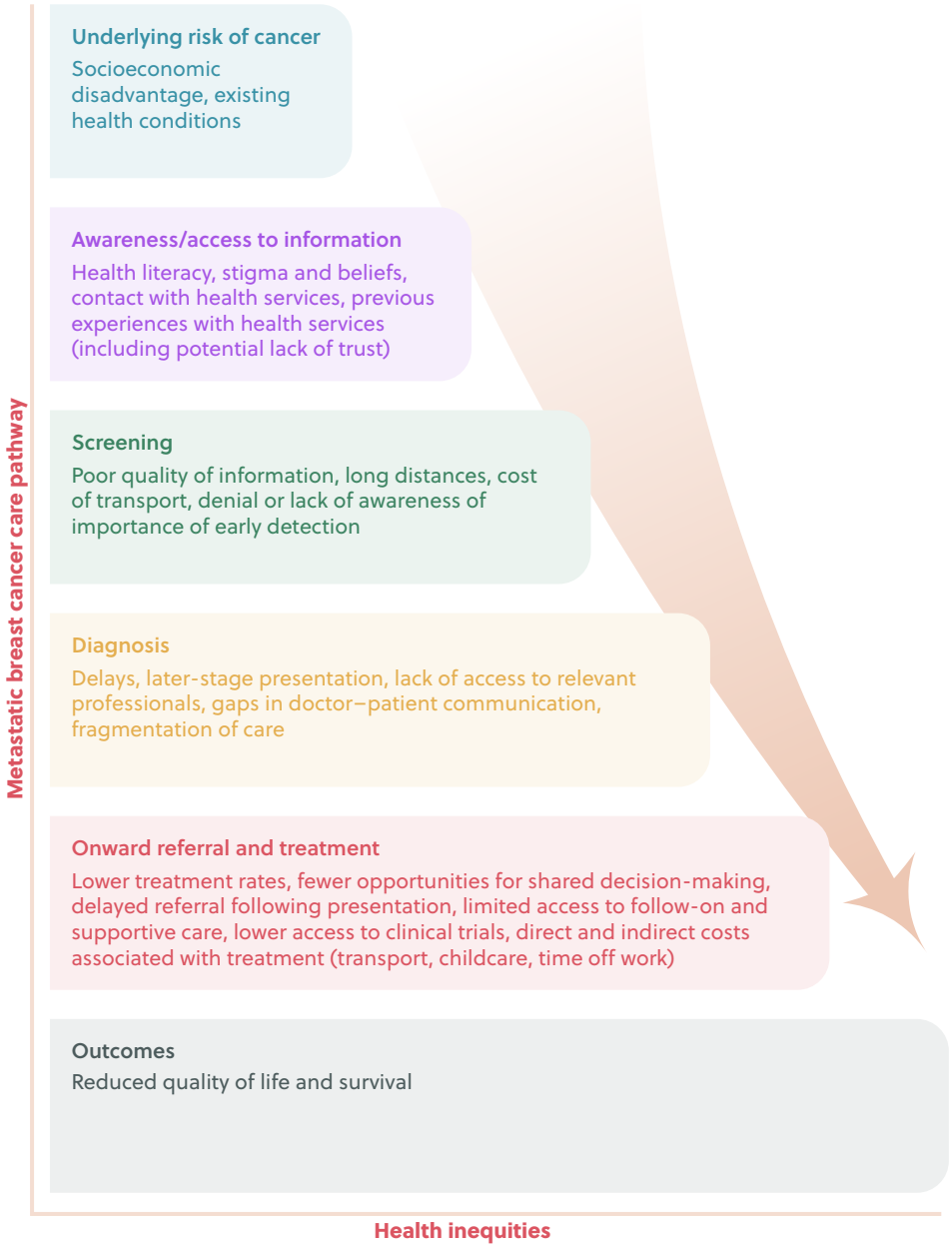
People with metastatic breast cancer also experience inequities in incidence, diagnosis and treatment outcomes. Many factors contribute to these inequities, often reflecting societal power structures (*Figure 2*). For example, research from the US suggests that rates of metastatic breast cancer are higher among Black women than among White women, even when taking into account their age and the stage of disease at diagnosis.[2] A study of women in Australia found that those born outside of Australia whose first language was not English were slightly more likely to be diagnosed with later-stage breast cancer.[18] In addition, people living in low- and middle-income countries are more likely to have metastatic breast cancer at the time of diagnosis, partly because of delays in receiving a diagnosis.[19] Their outcomes are also worse, with research showing a strong association between breast cancer survival and country income.[20 21]

BOX 1

Defining metastatic breast cancer

Metastatic breast cancer refers to cancer that has spread to the lymph nodes and other areas of the body. People may refer to it using various terms, including stage IV breast cancer and advanced breast cancer. Metastatic breast cancer is not the same as 'locally advanced breast cancer', which refers to cancer that has spread to nearby lymph nodes and tissues without reaching other parts of the body.[17]

Figure 2. Cumulative inequities across the metastatic breast cancer care pathway[22]



Despite the growing understanding of some of the causes of disparities in breast cancer, more data are needed, particularly for metastatic breast cancer. Cancer registries – a key data source for cancer diagnoses, treatments and outcomes – are not in place in every country,[23] and they often do not include data on the recurrence of breast cancer, including a later diagnosis of metastatic breast cancer.[15] This lack of complete data can limit the understanding of metastatic breast cancer and lead to an underestimation of how many people it affects.[15] An additional factor is that, in many countries, data are not typically available by race, ethnicity or socioeconomic status. Without outcomes data that reflect different personal characteristics, it is not possible to understand the observed differences in outcomes – information that is necessary to develop targeted efforts to redress existing inequities.[24]

Clinical trials: a driver of inequity in healthcare

Clinical trials are a key pillar of care and represent an important avenue for accessing potentially promising treatments. For conditions such as metastatic breast cancer, for which there are limited effective treatments and no curative treatments, clinical trials provide essential opportunities to develop and provide access to new therapies. One analysis showed that people with metastatic breast cancer who participate in clinical trials may experience improved five-year survival compared with those who do not participate.[25]

> **'So my doctor says, "Okay, you're now metastatic. You have about two years to live. Get your affairs in order; I don't have anything for you." They put me on – back then – an experimental drug for triple-negative breast cancer. And I did a lot more chemo, and I didn't die. And that was 11 years ago in September.'**
>
> RICKI FAIRLEY, TOUCH, THE BLACK BREAST CANCER ALLIANCE

There is strong evidence that participants in clinical trials do not tend to represent the populations of those living with the health condition being investigated. Globally, more than 92% of cancer clinical trials are conducted in high-income countries.[26 27] In breast cancer clinical trials, women over the age of 70 are under-represented, and women with a lower socioeconomic position are less likely to participate.[28-30] There is also limited ethnic or racial diversity within clinical trials. For example, in the US, Black women make up approximately 13% of all women, yet they represented just 1–3% of participants in the clinical trials that led to regulatory approvals for advanced or metastatic breast cancer treatments in 2019.[31 32]

Lower representation in clinical trials perpetuates health inequities because it limits the availability of data showing how interventions may affect different groups. When participants in clinical trials are not representative of the burden of a specific disease in a population, the findings are less generalisable to those living with the disease.[8 9 33] Research in the US found that Black women receiving hormone-based therapies to treat their breast cancer were more likely than White women to experience certain side effects, including serious cardiac issues.[3] However, when data from several clinical trials were reviewed, it transpired that only one clinical trial analysed side effects according to race, and Black women were under-represented in this study.[34] This limits opportunities to provide clear guidance on side effects and may reduce the acceptability of treatments, as evidenced by the fact that Black women who experienced cardiac side effects in trials were less likely to complete the course of treatment.[34]

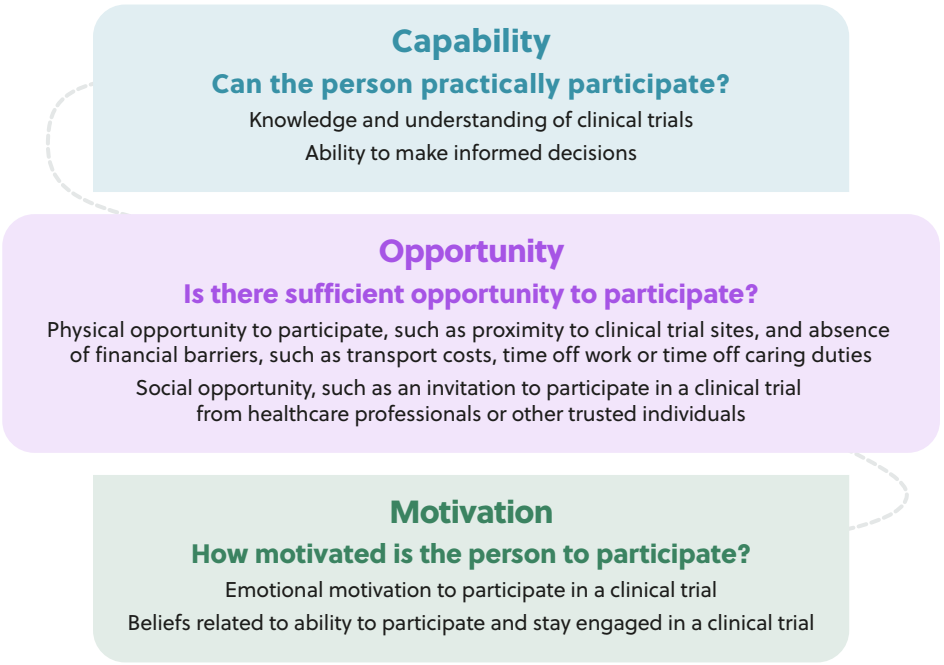
Cultural and behavioural factors influence how people seek care and may also affect their outcomes. A study assessing unmet needs of women following breast cancer treatment in the UK, Ghana and Tanzania highlighted the importance of developing adapted and culturally sensitive approaches to care, such as by reflecting cultural beliefs and practices in the provision of care.[35] Interestingly, the researchers found significant differences in how women in each country described their symptoms, which led to nurse training plans being adapted to reflect such differences.[36] Engagement with refugee communities in Australia also highlights how beliefs around cancer treatments and clinical trials can represent a barrier to treatment uptake.[6]

> **'I listened to one woman explaining how she would discuss symptoms and side effects with her doctor during breast cancer treatment. Her doctor brushed off certain symptoms as they weren't reflected in the literature, but when she talked with other Black women, they were experiencing the same symptoms and side effects. Their experience was just not acknowledged because Black women weren't adequately represented in the research.'**
>
> **IRIS KARRY, COLORECTAL CANCER CANADA**

People with reduced access to quality healthcare face complex barriers to participating in research. Medical and research institutions can, often inadvertently, act in ways that create barriers for some groups to participate in clinical trials, particularly those experiencing other forms of inequity.[6 7] Willingness to participate is often similar across different groups, suggesting that there are many complex reasons that impact the opportunity and decision to participate in a clinical trial.[37] These barriers can be looked at in terms of people's capability, opportunity and motivation to participate (*Figure 3*):

- **Capability:** many trials have a complex informed consent process that may make it difficult for people to decide in a truly informed way whether to participate.[38]
- **Opportunity:** physical barriers include proximity to clinical trial sites, limited financial support related to childcare or other caring responsibilities, time off from employment,[39 40] and unavailability of medical interpreters to address language or cultural barriers.[41-43]
- **Motivation:** cultural beliefs and documented historical abuses related to clinical trials may contribute to negative perceptions that reduce people's motivation to participate.[44-46] Erosion of trust in medical institutions and experiencing barriers when engaging with health services more generally can have a similar effect.[39 42] For example, the BECOME research project in the US found that trust in clinical trials was approximately 40% lower among Black people than people from other communities.[39]

Figure 3. Factors contributing to decisions to participate in a clinical trial[44-46]



A key starting point to improving equity in research is to understand who may be underserved by the health system. The INCLUDE guidelines, which were published by the National Institute of Health Research (NIHR) in the UK, provide a useful starting point to define people and communities underserved within health research. The guidelines explicitly acknowledge the need to adapt the actions necessary to improve equity in ways that are attuned to the specific context (*Box 2*).[47]

While global discourse on equity, diversity and inclusion has tended to focus on race and ethnicity, discussions are broadening to include all aspects of diversity. Research and policy initiatives, such as those identified in the *Appendix*, highlight the momentum to improve equity in cancer care and clinical trials, yet gaps remain. Progress can be seen particularly in improving equity for underserved racial and ethnic groups. However, there is scope for more research on other characteristics, such as gender, age or disability.

BOX 2

NIHR-INCLUDE guidelines

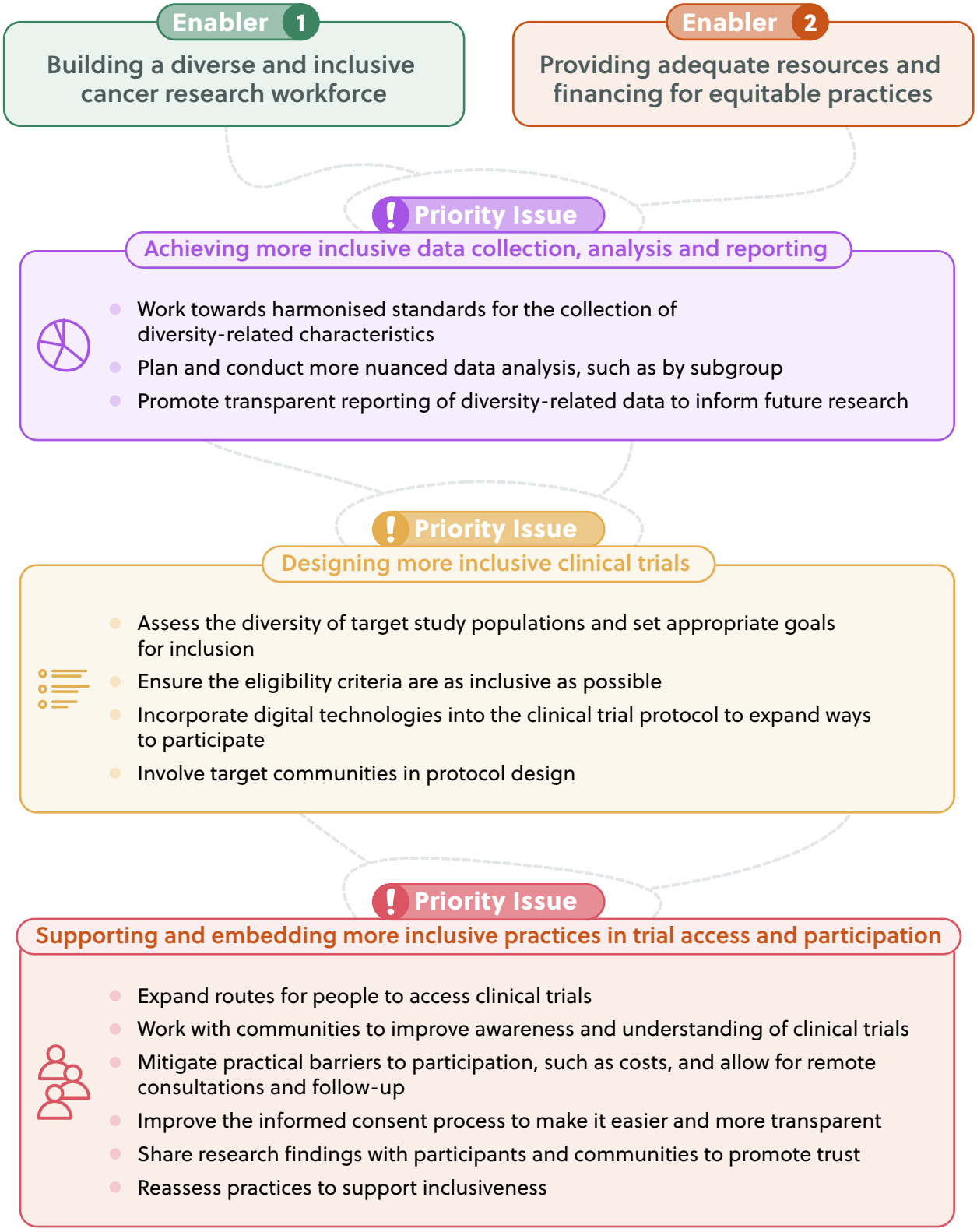
The NIHR-INCLUDE guidelines define the common characteristics of underserved groups in health research:[47]

1. Lower inclusion in research than one would expect from population estimates.
2. High healthcare burden that is not matched by the volume of research designed for the group.
3. Important differences in how a group responds to or engages with healthcare interventions compared with other groups, with research neglecting to address these factors.

2. How can clinical trials be more equitable?

Equity can be improved across the entire clinical trial pathway (*Figure 4*), not just during recruitment and participation phases.

Figure 4. Key opportunities to embed equitable practices in clinical trials



Enabler 1: Building a diverse and inclusive cancer research workforce

A diverse cancer research workforce can help foster a more inclusive clinical trials environment for potential participants. Much like clinical trial populations, the cancer research and clinical workforce does not always adequately represent the people and communities under its care.[48 49] Diverse and representative research teams can help strengthen recruitment and retention, as well as increasing comfort and trust.[49-51]

Where achieving a representative cancer research workforce may not be possible, there are ways to promote inclusive practice for healthcare professionals. Improving the diversity of the cancer research workforce may be affected by challenges such as the global shortage of health workers. At the same time, research shows that 80% of clinicians find it more difficult to engage with people from a different culture to their own.[52] Supporting research teams to complete cross-cultural communication training and implement it in practice can lead to improved participation in research.[6 33 48]

WHAT CAN BE DONE?

Recommendations for a diverse and inclusive workforce

- Seek to establish more diverse and inclusive research teams.
- Provide adequate training to clinicians and researchers on inclusive clinical trial design and inclusive practice.

Enabler 2: Providing adequate resources and financing for equitable practices

A stronger commitment to working towards equitable clinical trials will be needed to enable and realise improvements. Some of the practices described in this report will likely require increased workforce capacity, whether to accommodate additional roles, such as navigators, or to provide training for existing professionals. In addition, adaptations to the design, structure and protocols of clinical trials, such as larger study populations and dedicated support for participants, will likely be needed. There is clear evidence of the benefits of diversity in clinical trials, yet specific resource needs will be context dependent. It is increasingly important that organisations sponsoring clinical trials make resources available to enable more inclusive practice to be embedded.[53-55]

WHAT CAN BE DONE?

Recommendations for resources and financing

- Provide adequate funding for initiatives that seek to improve the recruitment and retention of underserved populations, such as:
  - additional roles e.g. navigators or interpreters
  - training for study teams
  - financial support to cover appropriate participant expenses
  - adapted study materials.

Achieving more inclusive data collection, analysis and reporting

Standardised recording and reporting of diversity data in clinical trials may help drive innovations and improvements in care that reduce inequities.

Work towards harmonised standards for the collection of diversity-related characteristics

Developing overarching standards for the collection of relevant diversity-related characteristics could underpin more robust assessments of disparities. Data collection on demographic and non-demographic variables, such as ethnicity or socioeconomic position, are often lacking or inconsistent across different clinical trials.[56] For example, one analysis found that ethnicity data were missing for 66% of participants in a sample of cancer clinical trials, including breast cancer.[57] There are no standardised requirements for the routine collection of data on social determinants of health, despite this being considered feasible and acceptable.[58] Social determinants of health, which include education and income, are a strong predictor of cancer outcomes.[1]

Standardising the collection and analysis of data on the diversity of participants to inform findings and future clinical trial practice can help accelerate progress towards health equity. Even where data are collected, the lack of consistent standards or collection practices can affect their usefulness. This is particularly limiting when aggregating data from different trials.[56] Requirements for the standardised collection of data on age, sex and ethnicity are starting to be implemented, and there is opportunity for those planning and delivering individual trials to consider how these types of data are built into their trial design and for regulators to establish data standards and requirements.[56 59 60]

Plan and conduct more nuanced data analysis, such as by subgroup

Where data are collected, especially those related to diversity characteristics, it is important to use them to their full potential, such as through performing subgroup analyses. Subgroup analyses can enhance the understanding of the disparities that exist among different groups. Without specific subgroup analyses, researchers cannot accurately state whether their findings are generalisable to the wider patient population. For example, considering ethnicity and socioeconomic position alongside one another may reveal where similarities and differences in responses and outcomes exist between groups, which can provide insights into the causes.[8 61] It is also vital to report subgroup analyses when they do take place.[56 62] These data may help ensure that new interventions or treatments are designed to meet the needs of a wider range of the population, for example, by making a range of dosages available.

Promote transparent reporting of diversity-related data to inform future research

Increased reporting of diversity data and findings from clinical trials could help inform future research, guidelines and policy. More consistent and extensive reporting requirements are needed from research funders, publishers and regulators.[61] Even when data on diversity characteristics are collected, their reporting is limited. Less than 50% of industry-sponsored trials and only about 10% of academic trials publicly report participant race or ethnicity data,[61] which further limits the generalisability of research to people of different backgrounds.[9]

WHAT CAN BE DONE?

Recommendations for inclusive data

- Promote harmonised standards for collection and reporting of relevant diversity data, setting minimum requirements where possible.
- Collect and analyse data on relevant characteristics that may affect outcomes. These practices should meet accepted standards or, where such standards do not yet exist, be in line with accepted ethical norms.
- Establish clear standards for reporting of data and subgroup analyses. These should ensure that full use is made of the data generated from the clinical trial, including an evaluation of diversity-related characteristics.

Designing more inclusive clinical trials

A central goal should be to ensure that clinical trial cohorts appropriately represent the range of people most affected by the health condition in question.

Assess the diversity of target study populations and set appropriate goals for inclusion

Careful consideration is necessary when recruiting for clinical trials to weigh the balance between diversity and internal validity. Clinical trials must be designed and conducted to preserve internal validity so that it is clear whether the intervention is causing the observed effects.[56] For example, recruiting only a small number of participants from a particular group means that the statistical power of the resulting analysis may be insufficient to draw robust conclusions.[56] Larger sample sizes, comprising participants with different characteristics, can address this; however, practical implications such as longer study duration and increased costs must also be considered (see *Enabler 2*).[63] Trials should also aim beyond representation: if a certain group is known to experience higher rates of a particular condition or worse outcomes from it, researchers may wish to consider the benefits of over-enrolling some groups above a level that is representative.[64]

> **'We need to consider strategies for over-enrolment where there is evidence of some groups being disproportionately affected, whether that be [in terms of] incidence, prevalence or severity. Rates of triple-negative breast cancer are 40% higher in Black women, so shouldn't we be striving for a trial that appropriately represents Black women, precisely because they are at greater risk?'**
>
> OLUWADAMILOLA 'LOLA' FAYANJU, UNIVERSITY OF PENNSYLVANIA

Ensure the eligibility criteria are as inclusive as possible

Inclusion and exclusion criteria need to be scrutinised at the design phase, and the rationale behind them clearly communicated. The way a clinical trial is designed sometimes leads to the exclusion of the people or groups that could most benefit from the findings, without clear justification. Although strict eligibility criteria are intended to protect participants and preserve the internal validity of the trial, these protocols may sometimes mean that the exclusion criteria are inappropriate for the specific study.[59 65 66] An analysis of breast cancer clinical trials in the US uncovered that 92.5% of trials prevent people with prior cancer from participating, which excludes up to 30% of people with metastatic breast cancer.[59 67] There is also evidence that clinical trials may exclude certain groups on the basis of perceived vulnerability, such as ethnicity or capacity for decision-making.[59 65 68] However, this is not always accompanied by a clear rationale, despite increasing emphasis from funders and publishers of the need to provide justification.[69]

'You have to be very careful to keep the population more or less homogeneous but not to exclude patients for no good scientific reason, and that includes age or gender, for example. Often the main exclusion criteria are included in the trial just because they have been in previous trials.'

FATIMA CARDOSO, ABC GLOBAL ALLIANCE AND CHAMPALIMAUD CLINICAL CENTRE

Incorporate digital technologies into the clinical trial protocol to expand ways to participate

The remote or hybrid delivery of clinical trials using digital technology may increase inclusivity. During the COVID-19 pandemic, cancer clinical trials were able to continue despite restrictions around using trial sites in hospitals. This was because they successfully implemented the use of digital technologies, such as wearable monitors and electronic consent forms, and made adaptations to accommodate home-based treatment delivery, such as through a tablet rather than an injection.[70] Such adaptations reduce the need for frequent visits to a hospital clinic, addressing practical barriers that often reduce people's willingness and ability to participate.[71] They may be particularly beneficial for improving the participation of people who live in rural communities or those who have work or caring responsibilities.[40 51 72 73]

It is, however, vital to ensure that the use of digital technologies does not create new barriers to participation related to access or acceptance. A lack of digital access, limited digital literacy or low acceptance of new technologies will disproportionately affect some groups, such as older people, those living in rural areas or refugee communities.[74] For example, in the US, only 65% of households headed by people aged 65 years and older have a computer or laptop.[75] At the same time, research has found that 90% of people with cancer would prefer 'hybrid' clinical trials that allow some aspects of the trial to take place remotely or away from the primary clinical trial site.[76] Making the case that technology can reduce the number of visits to the clinical trial centre may enhance trial participation.[77]

Involve communities in protocol design

When designing and evaluating clinical trial protocols, engaging people and communities who are under-represented in research can result in protocols that better support diverse participation. In addition to some of the practical factors discussed earlier, perceptions and beliefs related to clinical trials can impact participation.[78] Engagement with community representatives can help identify such issues and develop solutions.[6] For example, if there are cultural beliefs that are a barrier to giving blood samples, clinical trial designers could consider adjusting the protocol to reduce the burden of blood sampling.[10] Among communities with historic experiences of mistreatment, a lack of trust can also be a barrier to participation (*Case study 1*).[39 79]

> **'To deliver diverse and inclusive clinical trials, it is important for those running clinical trials to include patient advocates in their design as much as possible.'**
>
> **SONYA NEGLEY, METAVIVOR**

WHAT CAN BE DONE?

Recommendations for inclusive clinical trial design

- Carefully set recruitment targets that reflect the incidence, prevalence and severity of the condition in different populations while maintaining the validity of the clinical trial.
- Ensure eligibility criteria are assessed for every trial, considering possible unintended consequences and providing clear justifications for inclusion and exclusion criteria.
- Incorporate digital technologies into the clinical trial protocol, particularly where they can facilitate participation from underserved communities.
- Leverage engagement practitioners and community representatives to build relationships with communities.

CASE STUDY 1

CASE STUDY 1

The WISDOM trial: working with Black communities to increase enrolment[80-82]

The WISDOM trial in the US aimed to learn more about who gets breast cancer and why, to develop ways to reduce women's risk of developing breast cancer. Despite using an existing breast health network to invite more than 140,000 people to participate, the trial initially struggled to recruit a diverse participant population. Even though the trial took place in a racially diverse part of California, only 1.7% of those who enrolled in the first three years were Black. To identify ways to address this lack of diversity, the research team was expanded to include people who were from the Black community, had expertise in working with diverse communities, or both.

The team identified key aspects of the communication materials that were creating barriers to Black women's participation. They addressed them by:

- creating a 'community advisory board' to inform the language and approaches of the study. The advisory board comprised 'nurse navigators', patient advocates and people who had undergone breast cancer treatment
- holding monthly virtual public meetings to better understand perceptions and concerns related to the trial. These meetings offered an additional discussion space in which to address any questions the community had
- building relationships with community organisations and leaders to build trust. Among other things, this involved sharing personal stories from Black people who had participated in the clinical trial.

After these interventions, the enrolment of Black participants increased to around 10%, which was more representative of the Black Californian population.

Embedding more inclusive practices in trial access and participation

Community engagement can help build an understanding of communities' needs, making it possible to use tailored actions to expand access and promote uptake of clinical trials.

Expand routes for people to access clinical trials

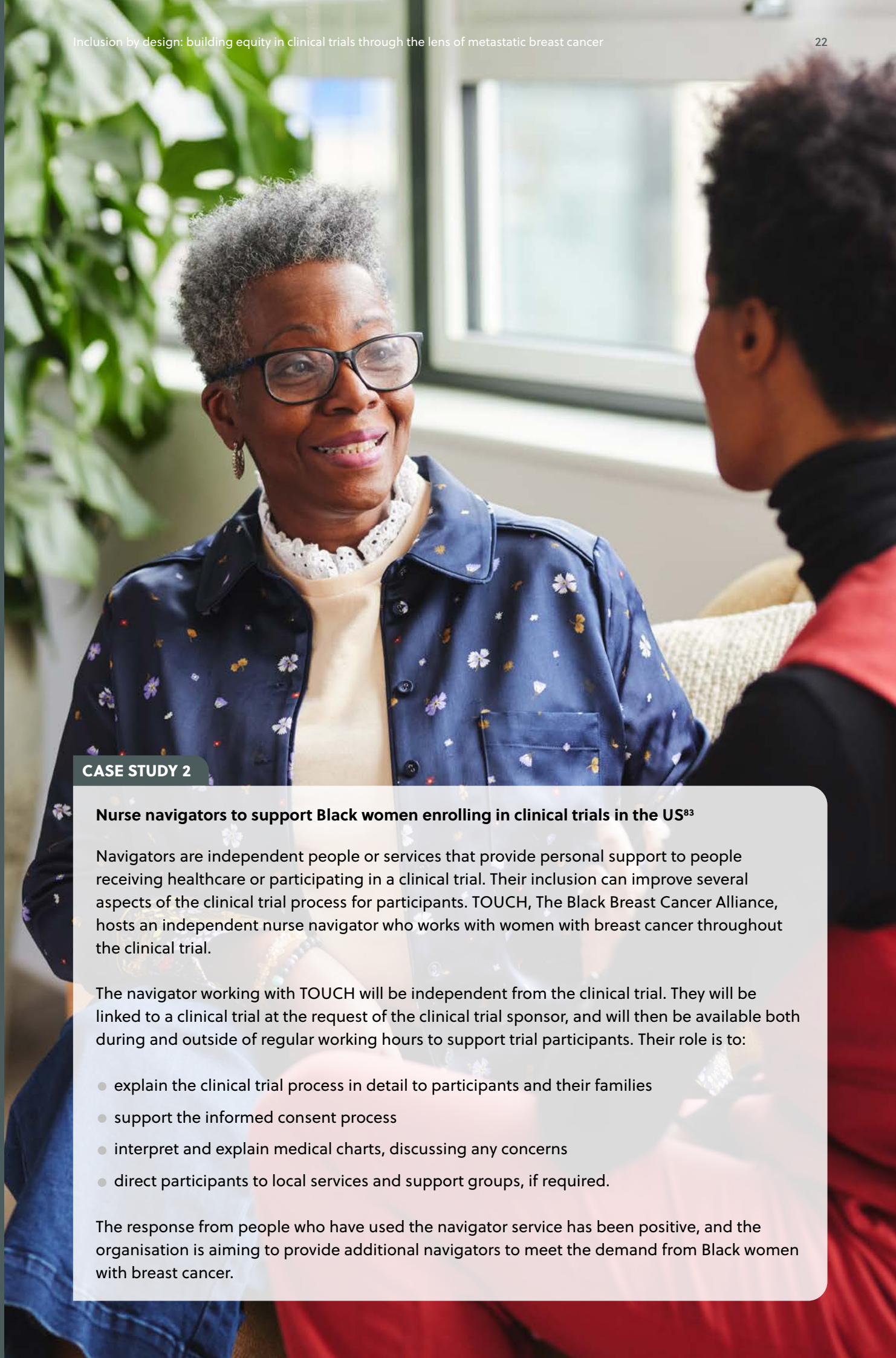
Healthcare professionals should present opportunities to participate in clinical trials to people with metastatic breast cancer more often, and to a more diverse range of people. Healthcare professionals play a key part in giving people access to clinical trials. This is particularly the case in metastatic breast cancer, where an oncologist is a typical point of referral to a clinical trial. Some studies show that some healthcare professionals, whether consciously or unconsciously, may withhold the opportunities to participate in a clinical trial from people from underserved racial and ethnic groups.[41] Alternative approaches, such as invitations being delivered by nurse navigators (*Case study 2*) with whom the patient is perhaps able to relate more closely, can lead to lower rates of refusal and improved retention in the clinical trial.[6 83]

Work with communities to improve awareness and understanding of clinical trials

Collaborating in a tailored way with community organisations can increase awareness of clinical trials and help build trust. Almost 70% of people learn about clinical trials from others with the same health condition, demonstrating the importance of directly engaging with communities.[39] Reaching and collaborating with people from target communities in their own environments or spaces, such as community or religious centres, can make them more open to learning about clinical trials.[44 51 83] It can be achieved in innovative ways, such as the touring 'Mets Mobile' bus in the US, which provides information about breast cancer and clinical trials to the communities it visits. Its successful engagement is attributed to its independence from clinical trial sponsors.[84] Similarly, close collaboration with multicultural communities is a central part of programmes to improve uptake of cancer screening and access to clinical trials in New South Wales, Australia (*Case study 3*).

> **'I learnt pretty quickly that I could convince a Black Breastie [a Black woman who has had a diagnosis of breast cancer] to do a trial in five minutes. Partly because I broke it down in simple language, but also because I'm a voice of trust. Trust the doctors? We don't trust them. Researchers? We don't trust anybody, but we trust each other.'**
>
> RICKI FAIRLEY, TOUCH, THE BLACK BREAST CANCER ALLIANCE

CASE STUDY 2



CASE STUDY 2

Nurse navigators to support Black women enrolling in clinical trials in the US[83]

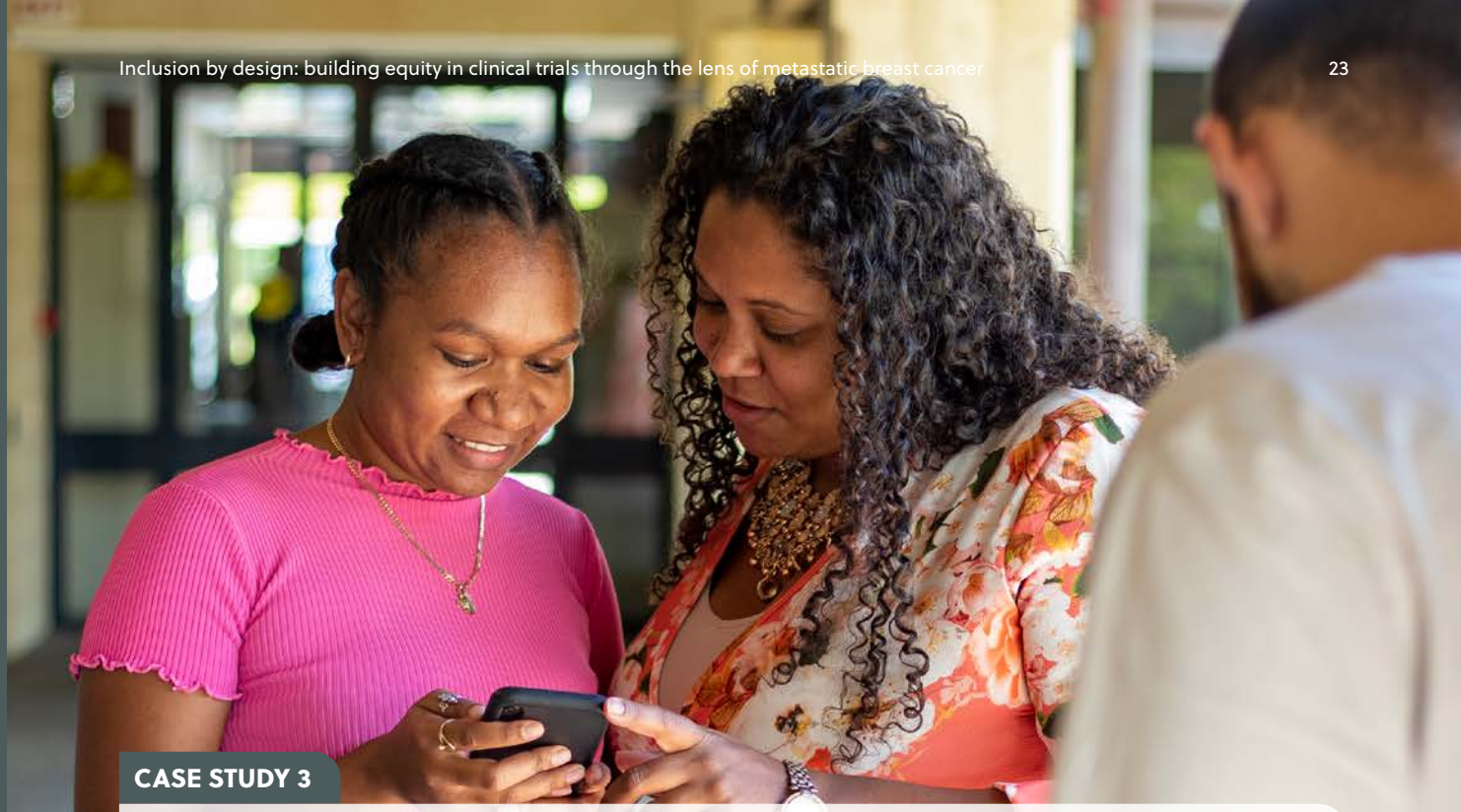
Navigators are independent people or services that provide personal support to people receiving healthcare or participating in a clinical trial. Their inclusion can improve several aspects of the clinical trial process for participants. TOUCH, The Black Breast Cancer Alliance, hosts an independent nurse navigator who works with women with breast cancer throughout the clinical trial.

The navigator working with TOUCH will be independent from the clinical trial. They will be linked to a clinical trial at the request of the clinical trial sponsor, and will then be available both during and outside of regular working hours to support trial participants. Their role is to:

- explain the clinical trial process in detail to participants and their families
- support the informed consent process
- interpret and explain medical charts, discussing any concerns
- direct participants to local services and support groups, if required.

The response from people who have used the navigator service has been positive, and the organisation is aiming to provide additional navigators to meet the demand from Black women with breast cancer.

CASE STUDY 3



CASE STUDY 3

Improving awareness of clinical trials with multicultural communities in New South Wales, Australia[6]

In Australia, where 51% of people were born overseas or have at least one parent born overseas, more than 175 languages are spoken. The Cancer Institute of New South Wales, Australia, connects multicultural communities to the health system to improve cancer literacy, build awareness and address barriers, working in ways that respond to community need.

The Institute's Cancer Plan, launched in 2022, provides a whole-of-sector perspective on cancer control and describes how key stakeholders across the state can work together to deliver better outcomes.[85] Equity of cancer outcomes is at the heart of Institute's work.

The planning and service delivery are underpinned by an understanding of need, using data and guidance through long-term community partnerships and consultative mechanisms, which help inform decisions on priority actions.[86]

Improving awareness of clinical trials was identified as a priority during a co-design workshop. This initiated two surveys, in multiple languages, designed to understand current knowledge of clinical trials among multicultural communities. Some of the key information gaps identified included understanding of placebo, controls, research ethics and informed consent. An additional survey explored perceptions of clinicians around barriers to representation of culturally and linguistically diverse communities. The findings informed the development of audio, video and web resources in multiple languages.[87]

> **'Health literacy is one thing, but cancer literacy is complex. You can safely assume that it needs quite a bit of work. Then you take it to clinical trials, which is another level completely.'**
>
> **SHEETAL CHALLAM, CANCER INSTITUTE OF NEW SOUTH WALES**

Across its initiatives, whether related to clinical trials or cancer screening, the multicultural programme engages with communities at many levels. The programmes are long term and continuously work with each community and with healthcare professionals to iterate and improve approaches.

'If we're serious about inclusion and diversity, we can't just sit in our big cancer hospital waiting for people. We need to think about how we can make it as easy as possible for people to engage with research.'

KATIE ROBB, UNIVERSITY OF GLASGOW

Mitigate practical barriers to participation and allow for remote consultations

Practical accommodations should be implemented to reduce the time and expense burden on participants, especially those with lower incomes. Access concerns such as long or inconvenient travel can create additional logistical and financial barriers for those who live in rural settings[39 40 76] or who have irregular working patterns, a low household income or caring responsibilities.[30 39 77] Research has shown these concerns are shared across many communities.[6 29 39 77] Considering the location of clinical trials sites, removing upfront costs, providing funding for vouchers or travel stipends, or supporting care costs is necessary to promote the participation of underserved people.[44 48 51] Even for decentralised or hybrid clinical trials that can offer a range of flexible or remote participation options, it is essential to assess people's access needs to avoid creating additional barriers.

> **'Something I do every time I evaluate a new trial is to review everything the patient has to do and consider whether it's acceptable. If not, I ask for the justification, but very often there is no specific reason. Asking patients to bear such a high burden, without a clear scientific justification, renders clinical trials unfeasible for many people.'**
>
> FATIMA CARDOSO, ABC GLOBAL ALLIANCE AND CHAMPALIMAUD CLINICAL CENTRE

Improve the informed consent process to make it easier and more transparent

There are well-evidenced approaches to improving engagement with clinical trials, including the consent process, so that it better supports people to make informed decisions on whether to participate. The informed consent process can be a barrier to participation, particularly for multicultural communities.[6 38] The process is not always designed with different languages, reading levels or learning styles in mind, and consent forms may not adhere to health literacy standards.[38] This can hinder someone's ability to make an informed choice on whether to participate in a clinical trial.[88] For people who speak other languages, providing an interpreter and translated materials is one way of supporting them to enrol.[89 90] Beyond this, using different methods of providing information, such as videos or a discussion with a healthcare professional or navigator, can make the informed consent process more accessible.[91] Culturally informed approaches can further help – for example, materials can address specific questions or concerns such as those related to beliefs around tissue samples.[92 93] To ensure both technical and cultural accuracy, materials should be reviewed with community representatives.[10 94]

> **'While it is important to ensure that health literature is easily understood and accessible to all, it is also important to acknowledge that there are individuals who have access to health services and literature, such as for cancer screening, and make an informed decision not to participate. As researchers, our assumptions related to health literacy for those who do and do not have access to care is complex and can have real impact.'**
>
> SHAVEZ JEFFERS, CENTRE FOR ETHNIC HEALTH RESEARCH

Share research findings with participants and communities to promote trust

Sharing research findings can promote trust and accountability with those who participated, helping redress power imbalances in medical research. Providing the opportunity for participants to receive information on the outcomes of clinical trials is increasingly required by regulators and publishers.[95 96] An essential aspect is to ensure that participants understand

how, where and when to expect the results. However, less than half of trials report, or plan to report, their findings to the participants.[96] This is a missed opportunity, as sharing trial results can help increase knowledge of clinical trials among communities and promote accountability, thereby building confidence and trust.[97] It also provides an opportunity to promote equity and address power imbalances in clinical research by recognising the contributions participants have made. In turn, this may also increase the likelihood of recruiting future participants.

Reassess practices to support inclusiveness

It is important that study teams review and reassess participant needs throughout the clinical trial cycle through ongoing engagement with communities, enabling iterative adjustments. Frequent dialogue between communities and healthcare professionals can dispel potentially negative views of research, help build trust and enable the research process to be adapted based on new evidence.[48 76 98] For example, if ongoing reviews reveal that certain groups are under-represented in enrolment or have a higher rate of dropping out, community input can help find ways to address this. Determining the lessons learnt during and after the study, and sharing these broadly, can help mitigate challenges for future studies.[6]

WHAT CAN BE DONE?

Recommendations for inclusive practice

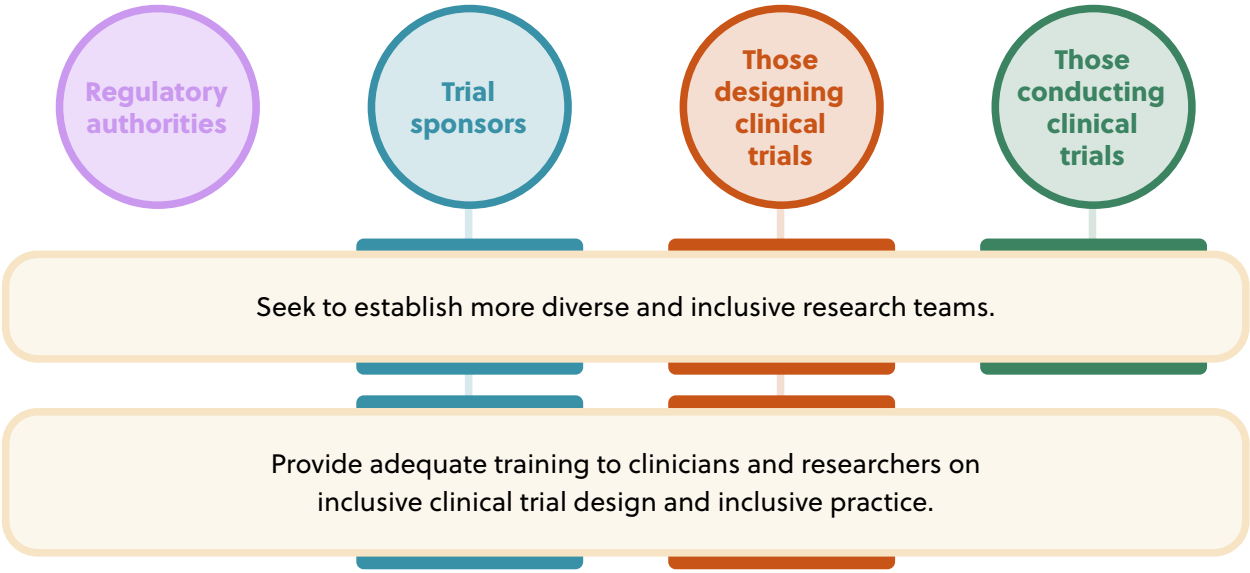
- Expand the routes to participation in clinical trials – for instance, providing communication training to researchers, working with additional members of the clinical trial team or establishing specific roles for outreach.
- Improve awareness and understanding of clinical trials in under-represented communities, such as by working in partnership with community organisations.
- Make appropriate provision to mitigate practical barriers to participation, such as through telemedicine, or providing financial support to travel to clinical trial sites.
- Design informed consent processes and materials with different populations for the trial in mind.
- Proactively share research findings with participants and their communities.
- Embed reflective practice throughout the clinical trial process, providing forums for dialogue with communities as well as mechanisms to implement feedback received.

3. Practical recommendations to realise progress towards inclusion

To drive progress towards more equitable healthcare and outcomes for all, a concerted effort is needed. Bringing together the recommendations outlined in *Chapter 2*, we call on all involved in clinical trials to take action to embed equitable and inclusive practices. Each of the recommendations would bring benefits if implemented in isolation, but significant change could be achieved if they were addressed together, at all levels.

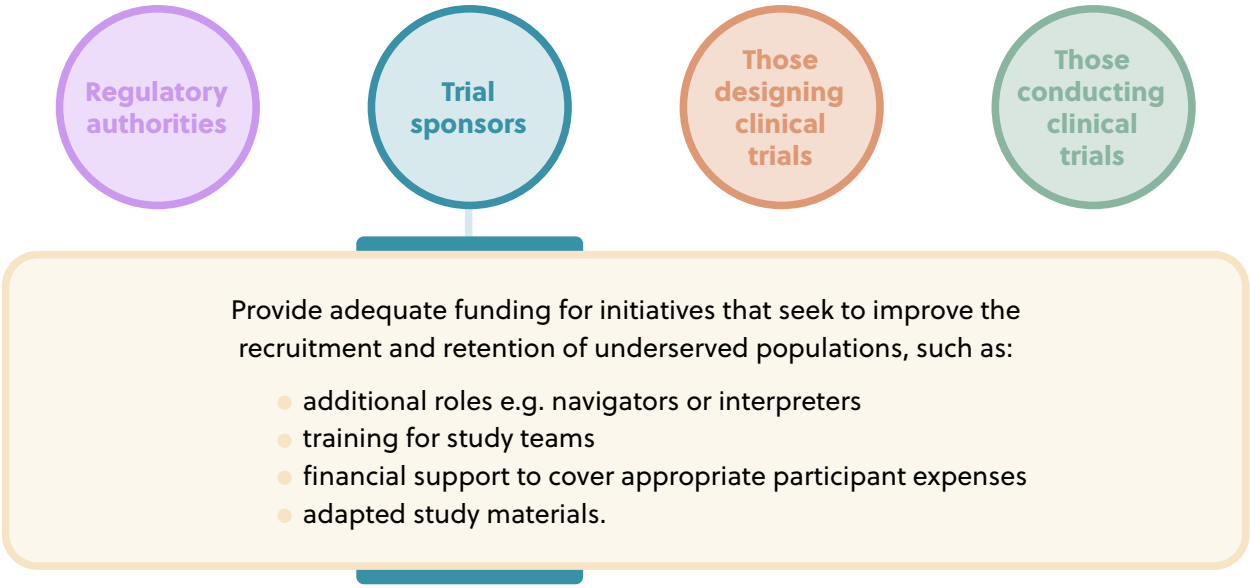
Enabler 1: Building a diverse and inclusive cancer research workforce

Who can take action?



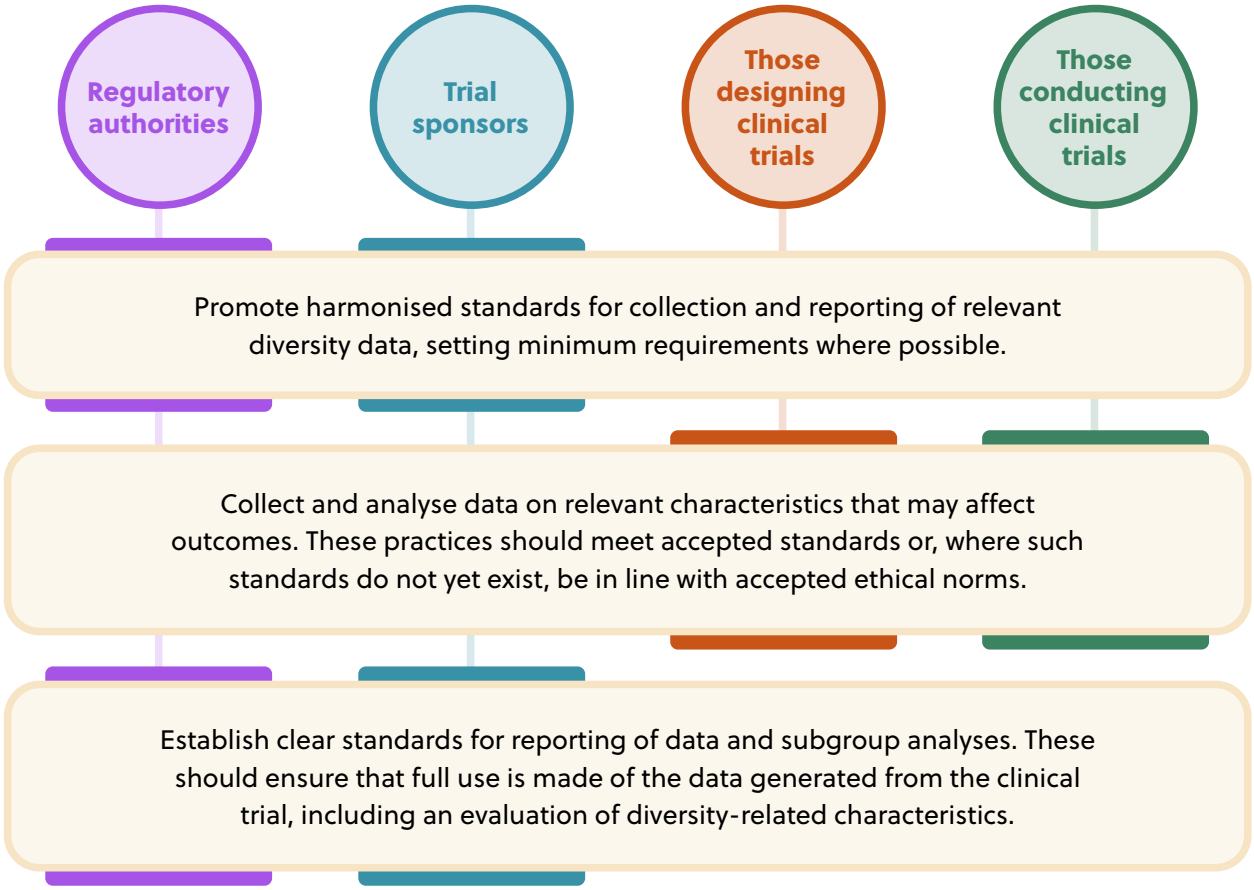
Enabler 2: Providing adequate resources and financing for equitable practices

Who can take action?



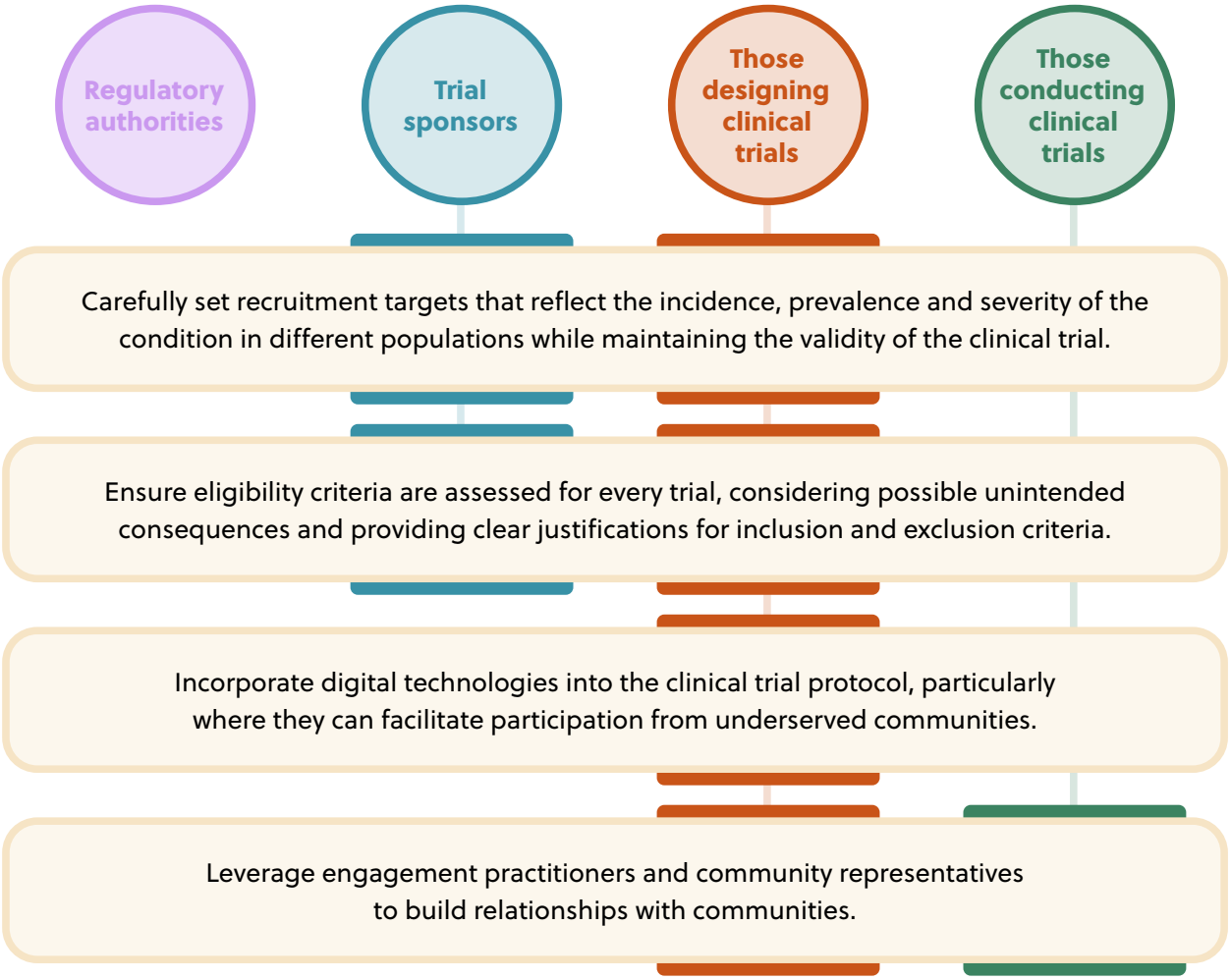
Achieving more inclusive data collection, analysis and reporting

Who can take action?



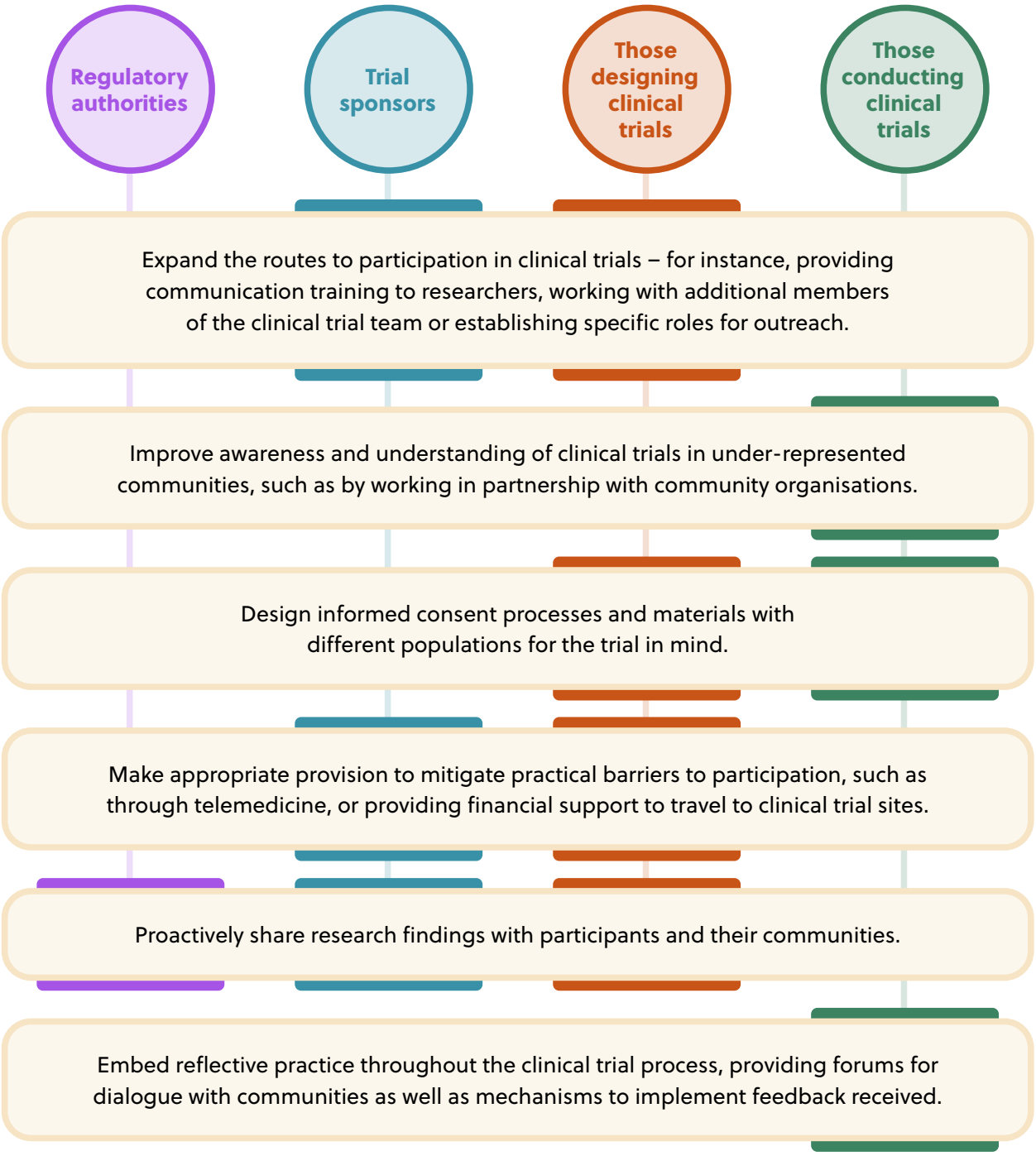
Designing more inclusive clinical trials

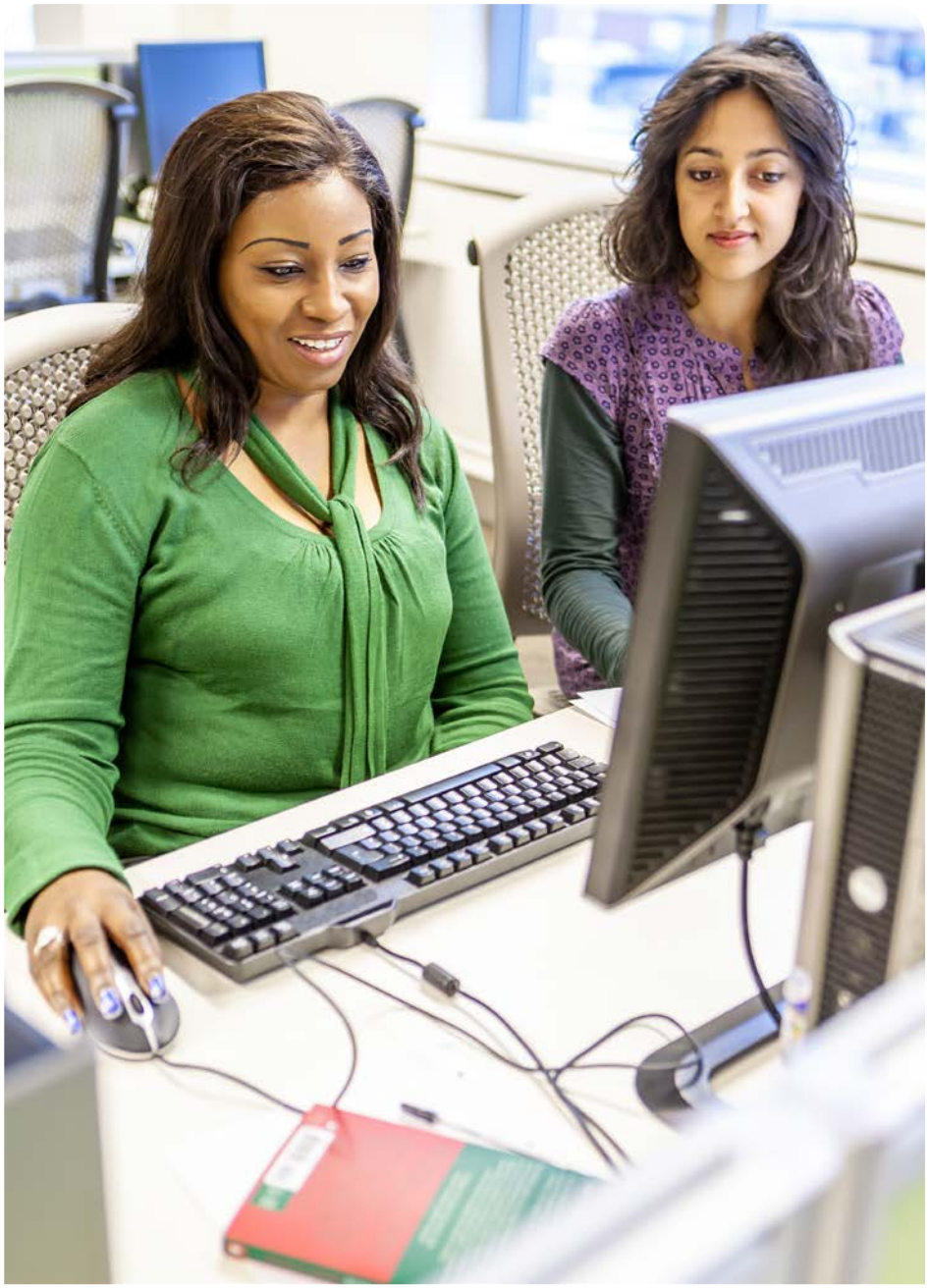
Who can take action?



Supporting and embedding more inclusive practices in trial access and participation

Who can take action?





Appendix: Progress towards more inclusive practice supported by policies

The need to improve diversity among participants of cancer clinical trials is gradually translating into policy, yet more could be done. An increasing number of policies aim to improve equity in cancer outcomes through more inclusive participation in clinical trials (see *Figure A1*). However, there is scope for further improvement, particularly in developing consensus for data collection and inclusive practices. Evolutions in policy to date have tended to focus on the geographical areas outlined in *Figure A1*, but this does not preclude the possibility of additional policy developments arising elsewhere.

PROGRESS TOWARDS MORE INCLUSIVE PRACTICE SUPPORTED BY POLICIES

Figure A1. Key developments in promoting diversity and inclusion in clinical research from around the world

Cancer Australia
National Aboriginal and Torres Strait Islander Cancer Framework[99]
To address disparities and improve outcomes, including through clinical research

European Association of Science Editors
Sex and Gender Equity in Research guidelines[69]
To encourage a more systematic approach to the reporting of sex and gender in research across disciplines

Food and Drug Administration (FDA)
Collection of Race and Ethnicity Data in Clinical Trials[100]
To set out standards for collecting and reporting race and ethnicity data in submissions for clinical trials for FDA-regulated medical products

National Institutes of Health
Inclusion of Women and Minorities as Subjects in Clinical Research[101]
To ensure the inclusion of women and members of racial and ethnic minority groups in a manner that is appropriate to the scientific question under study

Ministry of Health
New Zealand Cancer Action Plan 2019–2029. Te Mahere mō te Mate Pukupuku o Aotearoa 2019–2029[102]
To promote equitable health outcomes by removing barriers to participation in clinical trials for Māori people, Pacific people, people who live in rural and highly deprived areas, and individuals with mental health conditions or physical disabilities

FDA
Enhancing the Diversity of Clinical Trial Populations–Eligibility Criteria, Enrolment Practices, and Trial Designs[103]
To recommend approaches to increase enrolment of under-represented populations in FDA clinical trials

FDA
Male Breast Cancer: Developing Drugs for Treatment[104]
To provide recommendations to industry for the development and labelling of treatments for male breast cancer

American Society of Clinical Oncology
Association of Community Cancer Centers
Increasing Racial and Ethnic Diversity in Cancer Clinical Trials: Joint Research Statement[105]
To enable the research community to improve diversity and inclusion in clinical trials

National Institutes of Health Research (NIHR)
NIHR-INCLUDE[47]
To improve the inclusion of underserved groups in clinical research

FDA
Premenopausal Women with Breast Cancer: Developing Drugs for Treatment[106]
To provide recommendations to industry for the inclusion of pre-menopausal women in breast cancer clinical trials

European Parliament and European Council
No. 536/2014 EU Clinical Trial Regulation[95]
To promote sufficient representation of different genders, races and age groups across clinical trials

New South Wales Government
The NSW Cancer Plan: 2022–2027[85]
To achieve equitable cancer outcomes across New South Wales, with a focus on groups disproportionately affected by cancer

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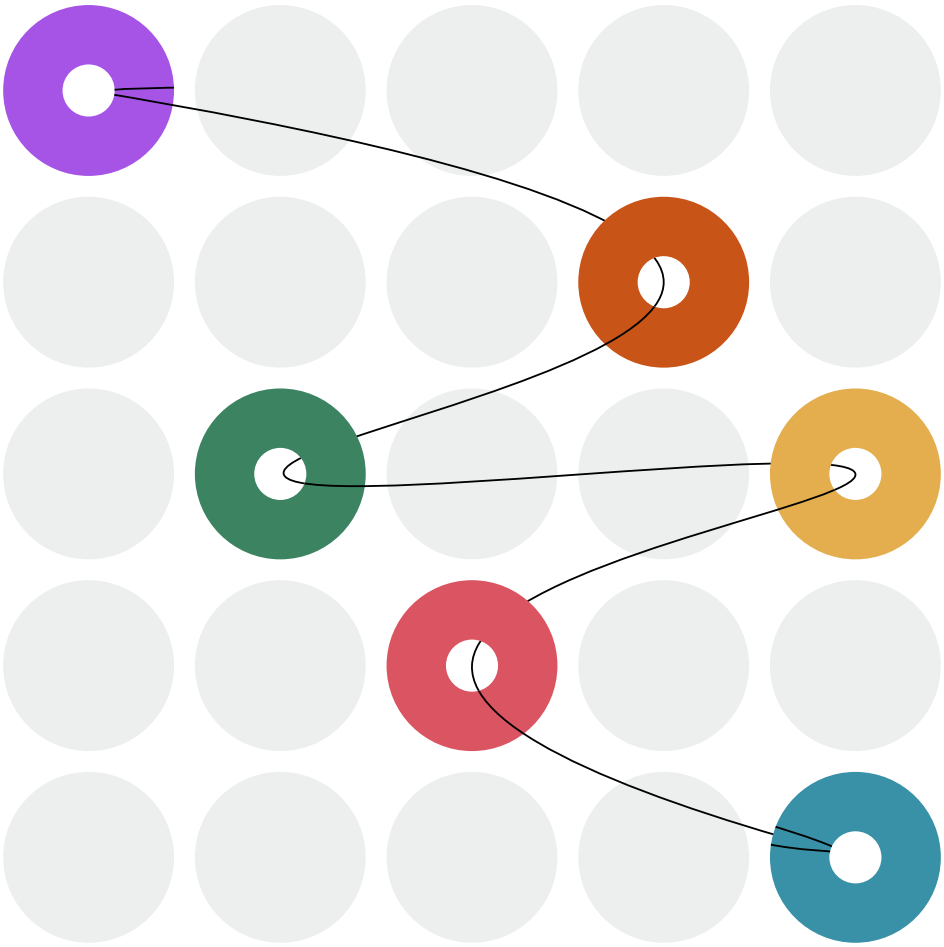

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