Ensuring your trial is designed for all who could benefit

Trial teams need to do everything possible to make their trial relevant to the people to whom the results are intended to apply (often patients) and those expected to apply them (often healthcare professionals). The four questions below are intended to prompt trial teams to think about who should be involved as participants, and how to facilitate their involvement as much as possible. These questions should be considered by trial teams in partnership with patient and public partners, including individuals from, or representing, groups identified in Question 1. Note that:

* *‘Intervention*’ means the treatment, initiative or service being evaluated.
* ‘*Comparator*’ means the what the intervention is being compared to.
* ‘*Effective*’ means the intervention provides important benefits for people with the disease or condition that is the focus of the trial.

We recommend that trial teams use the worksheets to help them think through their answers to the four key questions.

**1.** Who should my trial results apply to?

Which groups in the community could benefit from the intervention if it was found effective, or benefit from not having it if it was found ineffective and/or harmful?

**2.** Are the groups identified in Question 1 likely to respond to the treatment in different ways?

How might the disease or cultural factors mean that some groups in the community respond to, or engage with, the treatment(s) being tested in different ways?

**3.** Will my trial intervention and/or comparator make it harder for any of the groups identified in Question 1 to engage with the intervention and/or comparator?

How might the intervention and/or comparator, including how they are provided, make it harder for some groups in the community to take part in the trial?

**4.** Will the way I have planned and designed my trial make it harder for any of the groups identified in Question 1 to consider taking part?

How might elements of trial design, such as eligibility criteria or the recruitment and consent process, make it harder for some groups in the community to take part?

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| **1. Who should my trial results apply to?** |
| **[NB. Completed by Heidi Gardner (University of Aberdeen) and SOMEONE ELSE (University of SOMEWHERE). We were not involved in this trial,** **we did not discuss the information on the worksheets with the trial team, and the worksheets were completed retrospectively rather than at trial design, none of which is ideal.**  **The key documents we used regarding the trial were trial report:** [**https://doi.org/10.3310/eme05050**](https://doi.org/10.3310/eme05050) **and the trial registration document:** [**https://www.isrctn.com/ISRCTN32207582**](https://www.isrctn.com/ISRCTN32207582)**.**  **Given the above, the information in the worksheets may not be a proper reflection of the trial because we did not have access to all the trial materials. The information is therefore intended to be illustrative, not definitive.]**  The disease being studied is diabetic retinopathy. In its most severe form, proliferative diabetic retinopathy (PDR) can cause severe visual loss due to bleeding and scarring of the retina from the abnormal growth of new blood vessels. Diabetic retinopathy is the most common complication of diabetes and the leading cause of blindness among working-age populations in the Western world.  A community-based cross-sectional study in the UK found that patients of South Asian heritage had significantly higher systolic and diastolic blood pressure, and total cholesterol levels, than white European patients. This resulted in a significantly higher prevalence of diabetic retinopathy and maculopathy. Another study involving people with diabetes attending screening in the UK, found that people with African and African-Caribbean heritage and South Asian heritage were more prone to diabetic retinopathy compared to white Europeans.  South Asians experience significant morbidity and mortality from complications of diabetes – including diabetic retinopathy, coronary artery disease, cerebrovascular disease, and chronic kidney disease. Kidney disease is also known to progress faster in people of South Asian descent in comparison to people of European descent. There is also evidence that African-Caribbean people with diabetes have poorer outcomes than the general population. The prevalence of stroke and chronic kidney disease is higher in African-Caribbean people than in the general population of the UK.  Diabetes risk increases with age in all groups, but onset is much earlier in those of non-European heritage. People from Black African, African-Caribbean, and South Asian backgrounds are at risk of developing type 2 diabetes from the age of 25. This is much younger than the white population where risk increases from age 40. Black Africans, African-Caribbeans and white Europeans tend to be diagnosed at around the same age (66-67 years), whereas South Asian men were 5 years younger on average when diabetes was diagnosed at an even greater risk of related complications.  These patterns and variations in disease presentation of type 2 diabetes translates to younger ages in the presentation of complications such as diabetic retinopathy.  The prevalence of diabetes means that people from South Asian backgrounds and Black Africans and/or African-Caribbeans should be represented in this trial as well as white British people. The trial has 22 NHS recruiting sites across England, including Birmingham, London, Leicester, Manchester, Liverpool, Leeds, and Wolverhampton, and should therefore be able to recruit a diverse trial population. |

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| **2. Are the groups identified in Question 1 likely to respond to the treatment in different ways?** [**( VIEW WORKSHEET )**](#WorksheetONE) |
| **[This question has been answered with a focus on ethnicity for the purposes of this example, though the questions have wider relevance than ethnicity.]**  As discussed in question 1, prevalence of obesity, and complications as a result the condition are increased, and age of onset is younger in diabetes in Black and Asian communities in comparison to white-British populations. Due to the increased health demands of these minority groups, they may stand to benefit more to the treatment. It is not clear whether the root cause of these differences is genetic, social, cultural, or a mix of factors, so it is difficult to suggest whether these groups will respond to the treatment in different ways.  Generally, several ethnic minority groups essential for the trial have a deep mistrust of medical research. In other regards it is unclear to what extent beliefs and traditions might affect acceptability of the surgical interventions in the trial.  Many South Asian people are unwilling to participate in trials because they accept their illness as an unalterable punishment from God, or have a fear of what research entails. This thought process also applies to accepting surgical treatments, with people believing that a trial is not necessary because faith in God is needed more than medicine. |

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| **3. Will my trial intervention and/or comparator make it harder for any of the groups identified in Question 1 to engage with the intervention and/or comparator?** [**( VIEW WORKSHEET )**](#WorksheetTWO) | |
| **[This question has been answered with a focus on ethnicity for the purposes of this example, though the questions have wider relevance than ethnicity.]**  The intervention is intravitreal aflibercept injections, an anti-vascular endothelial growth factor, that prevents growth of new retinal blood vessels, which can result in severe loss of eyesight. The comparator is standard care; panretinal photocoagulation (PRP), a laser treatment used to create thermal burns in the peripheral retina leading to tissue coagulation, the overall consequence of which is improve oxygenation. This prevent severe visual loss but is associated with adverse effects on visual functions. It is unclear how the interventions may limit participation.  After participants are in the laser treatment group, they are reviewed after 8 weeks to assess their regression pattern and therefore the course of action for treatment going forward (i.e., continue with their allocated group, or wait and review until the next block of time). For participants in the injection group, they are reviewed after 4 weeks. This occurs from week 16 of the trial to week 48. The difference in review periods means that people allocated to the injection group may require more treatments than the laser group depending on their regression pattern, increasing the time commitment that the trial requires. This has the potential to disproportionately impact people in full-time work, caring responsibilities, and those experiencing socioeconomic disadvantage. People from ethnic minority groups are known to experience socioeconomic disadvantage at increased rather than the white British majority. It is not clear whether the trial team are able to offer flexible appointment times to accommodate people.  The detail about who will deliver the intervention and comparator are not clearly described in the trial report, but it is fair to assume that as the recruiting sites are NHS sites, both treatments will be delivered staff working within the NHS. The ethnic profile of doctors in the NHS is more diverse than the wider population, with around 40% coming from ethnic minority backgrounds. Asians represent almost 30% of NHS medical staff. This may help with recruitment of some ethnic groups, although racism and prejudice among some members of the majority population could have the opposite effect.  Ethnic minority patients report lower satisfaction and less positive experiences of care overall and ethnic minority patients remained less positive than those in the white British group, after statistical adjustment. Ethnic minority patients also reported lower confidence in, and less understanding of, healthcare professionals, including clinical nurse specialists, doctors, and ward nurses.  Evidence around social stigma due to diabetic retinopathy is not conclusive, but there is evidence to suggest that there is a stigma associated with both type 1 and type 2 diabetes, which are the causal diseases for this type of retinopathy.  Research based in the US has shown the people living with type 1 diabetes do experience stigma associated with the condition, which may make it harder for ethnic minority groups to engage with the intervention and/or comparator. In an online survey sent to 12,000 people with diabetes, perceptions of stigma were significantly higher among respondents with type 1 diabetes than those with type 2 diabetes. The highest rates of stigma were reported by parents of children with type 1 diabetes, with reports of ‘looks of contempt’ when injecting insulin in public, workplace discrimination, and limitations in traveling, maintaining friendships, and adopting children. The experience of stigma disproportionately affects those with a higher BMI, higher A1C, and poorer self-reported blood glucose control, suggesting that those who need the most help are also the most negatively impacted by social stigma. None of this research linked stigma with specific ethnic groups, but it is feasible that these experiences with stigma are more widespread in communities that are known to mistrust and/or distrust medical and healthcare professionals. | |
| 1. **Will the way I have planned and designed my trial make it harder for any of the groups identified in Question 1 to consider taking part?** [**( VIEW WORKSHEET )**](#WorksheetTHREEA) |
| **[This question has been answered with a focus on ethnicity for the purposes of this example, though the questions have wider relevance than ethnicity.]**  It is not clear how potential participants will be made aware of the trial, the report states that participants were recruited from the involved sites. The sites were chosen based on previous clinical trial experience or by estimated volume of potential eligible patients. Interested sites completed a site feasibility questionnaire, and some sites required support from the UK Clinical Research Network. It seems that awareness of the trial is therefore at the recruiter’s discretion unless there were other ways used that have not been described in the trial report.  Depending on the language skills of both staff member and potential participant/family members, and the difficulties of making that approach as perceived by the recruiter, a direct recruiter approach may limit the ability of some members of some ethnic groups (e.g., older South Asians, especially women; some white non-British) to take part.  The eligibility criteria are clinically focussed and do not give cause for concern with regards to limiting participation of any ethnic groups. A more in-depth assessment from an expert in this area would be beneficial to confirm this clinical focus. The inclusion criteria ‘ability to give informed consent’ has the potential to disproportionately impact people that have learning disabilities, neurodegenerative disorders and/or other conditions or situations that limit their ability to provide informed consent for themselves. This is unlikely to impact the population of patients living with diabetic retinopathy.  Data were collected on diabetic history and management, ocular history, treatment, other clinically relevant medical history and their management in the last 12 months, and concomitant medication. This information was retrieved from the participant, hospital medical records, or the general practitioner. As discussed earlier, in general, ethnic minority communities are less trusting of healthcare professionals, and they may be hesitant of research teams accessing their medical records.  The trial’s primary outcome was the mean change in BCVA (best corrected visual acuity), measured by ETDRS letter score at 4 metres. Secondary outcomes are measured with a variety of visual function and quality-of-life outcomes. There is no reason to believe that the trial’s outcomes or other data being collected will limit the participation of any ethnic group.  Data are likely to be collected in hospital. The main issue is likely to be getting to the hospital (e.g., use of public transport) and the time needed to complete the measures (e.g., leaving work or getting away from caring responsibilities to attend appointments). These issues may disadvantage people experiencing socioeconomic disadvantage. People from ethnic minority communities are at higher risk of socioeconomic disadvantage, and participation could therefore be limited.  The application had a lay co-applicant, Richard Lane OBE, who helped design the study and contributed to the grant application. Three lay members of the North East London Lay Member panel of the diabetes research network also contributed to the design of the study. The ethnicities of these individuals are not clear from the trial report, and the specifics of their involvement is unclear also. |

Worksheets for thinking through factors that might affect ethnic group involvement in a trial

These worksheets are intended to be used by trial teams in partnership with patient and public partners to ensure that ethnic group involvement is considered at the trial design stage.Before completing the worksheets, the trial team **should have answered Question 1** **of the INCLUDE Key Questions with regard to ethnic group involvement**.

The worksheet may cover issues that some trial teams already think about. The intention is that the worksheet will help to highlight issues consistently across trials for all trial teams, as well as raising some questions that may not be routinely considered at present.

Finally, while the worksheet asks trial teams to think about possible differences between ethnic groups, it is important to remember that there are also differences *within* ethnic groups, especially between generations and between men and women. No ethnic group is homogenous. See [Appendix 1](https://www.trialforge.org/trial-forge-centre/include/) for more on our definition of ethnicity.

**Worksheet 1**

This worksheet provides some questions **to guide your thinking about ethnic group involvement when answering Question 2** of the INCLUDE Key Questions.

**Disease and cultural factors that might influence the effect of treatment for some ethnic groups**

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| **Disease** | How might the prevalence of the disease vary between each ethnic group in the target population? | **Response:** The disease being studied is diabetic retinopathy. Diabetes can affect many parts of the body, including the eye where it typically affects the light-sending tissues, the retina. In its most severe form, proliferative diabetic retinopathy (PDR) can cause severe visual loss due to bleeding and scarring of the retina from the abnormal growth of new blood vessels. Diabetic retinopathy is the most common complication of diabetes and the leading cause of blindness among working-age populations in the Western world.  [A study](https://pubmed.ncbi.nlm.nih.gov/22542913/) led by researchers in the UK found the prevalence of diabetic retinopathy, sight-threatening diabetic retinopathy, and clinically significant macular edema are higher in people of South Asian, African, Latin American, and Indigenous tribal descent compared to the white population.  A [community-based cross-sectional study](https://pubmed.ncbi.nlm.nih.gov/19074992/) in the UK found that patients of South Asian heritage had significantly higher systolic and diastolic blood pressure, and total cholesterol levels, than white European patients. This resulted in a significantly higher prevalence of diabetic retinopathy and maculopathy. [Another study](https://pubmed.ncbi.nlm.nih.gov/22412857/) involving people with diabetes attending screening in the UK, found that people with African and African-Caribbean heritage and South Asian heritage were more prone to diabetic retinopathy compared to white Europeans. |
| How might the severity of the disease vary between each ethnic group? | **Response:** South Asians experience significant morbidity and mortality from complications of diabetes – including [diabetic retinopathy](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2646018/), [coronary artery disease, cerebrovascular disease](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4026332/), and [chronic kidney disease](https://care.diabetesjournals.org/content/29/6/1383). Kidney disease is also known to [progress faster](https://care.diabetesjournals.org/content/29/6/1383) in people of South Asian descent in comparison to people of European descent.  There is also evidence that African-Caribbean people with diabetes have poorer outcomes than the general population. The [prevalence](https://pubmed.ncbi.nlm.nih.gov/8762376/) of stroke and chronic kidney disease is higher in African-Caribbean people than in the general population of the UK. |
| How might the disease present in people from each ethnic group (this may include symptoms, type or pattern or rate of disease progression)? | **Response:** Diabetes risk increases with age in all groups, but onset is much earlier in those of non-European heritage. People from Black African, African-Caribbean and South Asian backgrounds are at risk of developing type 2 diabetes [from the age of 25](https://www.diabetes.org.uk/preventing-type-2-diabetes/diabetes-risk-factors). This is much younger than the white population where risk increases from age 40.  Black Africans, African-Caribbeans and white Europeans tend to be diagnosed at around the same age (66-67 years), whereas South Asian men were [5 years younger on average](https://care.diabetesjournals.org/content/early/2012/09/06/dc12-0544.abstract) when diabetes was diagnosed at an even greater risk of related complications.  These patterns and variations in disease presentation of type 2 diabetes translates to younger ages in the presentation of complications such as diabetic retinopathy. | |
| How close is the match between each ethnic group living with the disease and the ethnic groups living in the areas where the trial is to be run? | **Response:** The prevalence of diabetes means that people from South Asian backgrounds and Black Africans and/or African-Caribbeans should be represented in this trial as well as white British people. The trial has 22 NHS recruiting sites across England, including Birmingham, London, Leicester, Manchester, Liverpool, Leeds, and Wolverhampton, and should therefore be able to recruit a diverse trial population. | |
| Other factors to consider: | | |
| **Cultural** | How might perceptions of the disease and social stigma around it be different for each ethnic group in the target population? | **Response:** Evidence around social stigma due to diabetic retinopathy is not conclusive, but there is evidence to suggest that there is a stigma associated with both type 1 and type 2 diabetes, which are the causal diseases for this type of retinopathy.  [Research based](https://diabetesjournals.org/clinical/article/35/1/27/35423/Stigma-in-People-With-Type-1-or-Type-2-Diabetes) in the US has shown the people living with type 1 diabetes do experience stigma associated with the condition. In an [online survey](https://diabetesjournals.org/clinical/article/35/1/27/35423/Stigma-in-People-With-Type-1-or-Type-2-Diabetes) sent to 12,000 people with diabetes, perceptions of stigma were significantly higher among respondents with type 1 diabetes than those with type 2 diabetes. The highest rates of stigma were reported by parents of children with type 1 diabetes, with reports of ‘looks of contempt’ when injecting insulin in public, workplace discrimination, and limitations in traveling, maintaining friendships, and adopting children.  The [experience of stigma](https://diabetesjournals.org/clinical/article/35/1/27/35423/Stigma-in-People-With-Type-1-or-Type-2-Diabetes) disproportionately affects those with a higher BMI, higher A1C, and poorer self-reported blood glucose control, suggesting that those who need the most help are also the most negatively impacted by social stigma. None of this research linked stigma with specific ethnic groups, but it is feasible that these experiences with stigma are more widespread in communities that are known to mistrust and/or distrust medical and healthcare professionals.  A [qualitative synthesis](https://bmcendocrdisord.biomedcentral.com/articles/10.1186/s12902-016-0103-0) suggested that non-adherence to medicines could be the cause of poor clinical outcomes for South Asian patients, with the reasons for non-adherence being attributed to 1) beliefs about the need for and efficacy of medicines, 2) toxicity of medicines and polypharmacy, 3) the necessity of traditional remedies versus ‘western medicines’, 4) stigma and social support, and 5) communication. Stigma and social support was found to have a major influence on medicine taking, with South Asian patients being reluctant to disclose their use of insulin to their families and community. This is described in a [2004 publication](https://onlinelibrary.wiley.com/doi/pdf/10.1002/pdi.624) where a young South Asian girl with type 2 diabetes was unwilling to accept treatment as it was felt by both her and her family that acceptance of the diagnosis of diabetes would adversely affect her prospects for an arranged marriage. A [2013 systematic review of studies of barriers to self-management of type 2 diabetes](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5060817/pdf/HEX-18-0625.pdf).) among minority groups found views on stigma mixed, some thinking it was a barrier, others finding that type 2 diabetes being so common meant it was not stigmatized. | |
| How might ways of describing the disease be different for each ethnic group? | **Response:** Diabetes is sometimes called ‘high sugar’, (e.g., some South Asians). Other terms may be used some ethnic groups. Diabetic retinopathy may be referred to by its symptoms, e.g., sight loss, blindness, or simply, eye disease. | |
| How might cultural practices, beliefs and traditions influence the acceptability of, and adherence to, the treatment(s) for each ethnic group? | **Response:** Generally, several ethnic minority groups essential for the trial have a [deep mistrust of medical research](https://www.demanddiversity.co/resources). In other regards it is unclear to what extent beliefs and traditions might affect acceptability of the surgical interventions in the trial.  Many [South Asian people are unwilling to participate](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2571097/) in trials because they accept their illness as an unalterable punishment from God, or have a fear of what research entails. This thought process also applies to accepting surgical treatments, with people believing that a trial is not necessary because faith in God is needed more than medicine. | |
| How or when might people in each ethnic group access healthcare for this disease differently? | **Response:** In general terms, [health literacy is low among some ethnic groups, and this is a known barrier to seeking healthcare support](https://www.england.nhs.uk/wp-content/uploads/2017/07/inequalities-resource-sep-2018.pdf). This means that individuals from ethnic minority communities may present later than their white counterparts, which is likely to lead to increased complications and poorer health outcomes.  A [2014 systematic review](https://diversityhealthcare.imedpub.com/cultural-barriers-impeding-ethnic-minority-groups-from-accessing-effective-diabetes-care-services-a-systematic-review-of-observational-studies.php?aid=1595) assessed cultural barriers that impede ethnic minority groups from accessing effective diabetes care services. Eight key cultural issues emerged, namely participants’ strong adherence to cultural norms, religious beliefs, linguistic diversity, low health literacy levels, different beliefs about health and illness, belief in expert and professional support, low accessibility of culturally-appropriate services/information, and low concordance with western professional advice.  [Cultural and social norms](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3588185/) strongly influence health-seeking behaviours – research has shown that health promotion activities tend to be based on assumptions of individualism and self-investment, which may need to be re-thought for South Asian groups in particular. As mentioned earlier, [South Asians](ghttps://www.diabetes.org.uk/resources-s3/2017-11/south_asian_report.pdf) are often explicitly excluded due to perceived cultural and communication difficulties. Language and cultural differences are barriers that impact all minority groups – with people from non-white-European populations seeking healthcare at later stages of their disease than their white counterparts. [Language and literacy factors](https://www.pcdsociety.org/resources/details/living-with-diabetes-a-qualitative-review-of-minority-ethnic-groups-in-a-deprived-london-borough) are also known factors that impact on overall health literacy. Study participants have reported that both the spoken and written health information provided were sometimes meaningless, even when translated into their own language. Their inability to transform information into action was either due to limited health knowledge or limited linguistic proficiency in either their native language or English and they also felt they were unable to maximise their consultation with their healthcare professional. | |
| Other factors to consider: | | |

**Worksheet 2**

This this worksheet provides some questions **to guide your thinking about ethnic group involvement when answering Question 3** of the INCLUDE Key Questions.

**Intervention and comparator factors that might affect how some groups engage with the intervention and/or comparator\***

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| **What** | How might the intervention(s) and comparator limit participation of people from each ethnic group in the target population? | **Response:** The intervention is intravitreal aflibercept injections, an anti-vascular endothelial growth factor, that prevents growth of new retinal blood vessels, which can result in severe loss of eyesight. The comparator is standard care; panretinal photocoagulation (PRP), a laser treatment used to create thermal burns in the peripheral retina leading to tissue coagulation, the overall consequence of which is improve oxygenation. This prevent severe visual loss but is associated with adverse effects on visual functions. It is unclear how the interventions may limit participation. |
| How, and in what way, were people from each ethnic group involved in selecting or designing the trial intervention/comparator? | **Response:** The application had a lay co-applicant, Richard Lane OBE, who helped design the study and contributed to the grant application. Three lay members of the North East London Lay Member panel of the diabetes research network also contributed to the design of the study. The ethnicities of these individuals are not clear from the trial report, and the specifics of their involvement is unclear also. |
| Other factors to consider: | |
| **Who** | How might the person delivering the intervention/comparator limit participation of people from each ethnic group in the target population? | **Response:** The detail about who will deliver the intervention and comparator are not clearly described in the trial report, but it is fair to assume that as the recruiting sites are NHS sites, both treatments will be delivered staff working within the NHS. The ethnic profile of doctors in the NHS is [more diverse than the wider population](https://www.ethnicity-facts-figures.service.gov.uk/workforce-and-business/workforce-diversity/nhs-workforce/latest#by-ethnicity), with around 40% coming from ethnic minority backgrounds. Asians represent almost 30% of NHS medical staff. This may help with recruitment of some ethnic groups, although racism and prejudice among some members of the majority population could have the opposite effect.  [Ethnic minority patients report lower satisfaction and less positive experiences](https://bmjopen.bmj.com/content/bmjopen/6/6/e011938.full.pdf) of care overall and ethnic minority patients remained less positive than those in the white British group, after statistical adjustment. Ethnic minority patients also reported lower confidence in, and less understanding of, healthcare professionals, including clinical nurse specialists, doctors, and ward nurses.  It is unclear what impact these factors will have in the trial. Clear, culturally sensitive communication between doctor, patient and family will, as always, be helpful for both care delivery and the trial. |
| Other factors to consider: | |
| **How** | How might the mode of delivery (e.g. telephone, video-call, face-to-face, in groups) limit participation of people from each of the ethnic groups in the target population? | **Response:** The intervention will be delivered face-to-face in hospital. Mode of delivery is unlikely to be a factor; if injections and laser treatment are both acceptable to an individual, there is no other way to deliver it than face-to-face with a healthcare professional. |
| Other factors to consider: | |
| **Where** | How might where the intervention/comparator is delivered (e.g. hospital, general practice, local library) limit the participation of people from each ethnic group in the target population? | **Response:** As above. |
| Other factors to consider: | |
| **When & Intensity** | How might when the intervention/comparator is delivered (e.g. during working hours) or the intensity (e.g. number of times it is delivered, over what period, time commitment for each session and overall) limit participation of people from each ethnic group in the target population? | **Response:** After participants are in the laser treatment group, they are reviewed after 8 weeks to assess their regression pattern and therefore the course of action for treatment going forward (i.e., continue with their allocated group, or wait and review until the next block of time). If participants are in the injection group, they are reviewed after 4 weeks to assess their regression pattern and course of action going forward. This occurs from week 16 of the trial to week 48.  The difference in review periods means that people allocated to the injection group may require more treatments than the laser group depending on their regression pattern, increasing the time commitment that the trial requires. This has the potential to disproportionately impact people in full-time work, caring responsibilities, and those experiencing socioeconomic disadvantage. People from ethnic minority groups are known to experience socioeconomic disadvantage at increased rather than the white British majority. It is not clear whether the trial team are able to offer flexible appointment times to accommodate people. |
| Other factors to consider: | |

\*These factors are taken from TIDieR ([http://www.equator-network.org/reporting-guidelines/tidier/](about:blank)).

**Worksheet 3a**

This worksheet provides some questions **to guide your thinking about ethnic group involvement when answering Question 4** of the INCLUDE Key Questions.

**Trial eligibility and participation factors that might affect how some groups engage with the trial**

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| **Eligibility** | How might eligibility criteria exclude members of each ethnic group in the target population for reasons other than their clinical eligibility for the trial (e.g. availability of medical history, must speak English, location, gender, age, discussing pregnancy, internet/mobile telephone access)? | **Response:** The eligibility criteria are clinically focussed and do not give cause for concern with regards to limiting participation of any ethnic groups. A more in-depth assessment from an expert in this area would be beneficial to confirm this clinical focus.  The inclusion criteria ‘ability to give informed consent’ has the potential to disproportionately impact people that have learning disabilities, neurodegenerative disorders and/or other conditions or situations that limit their ability to provide informed consent for themselves. This is unlikely to impact the population of patients living with diabetic retinopathy.  Data were collected on diabetic history and management, ocular history, treatment, other clinically relevant medical history and their management in the last 12 months, and concomitant medication. This information was retrieved from the participant, hospital medical records, or the general practitioner. As discussed earlier, in general, ethnic minority communities are less trusting of healthcare professionals, and they may be hesitant of research teams accessing their medical records. |
| Other factors to consider: | |
| **Opportunity to participate** | How might the way(s) (and by whom) potential participants are made aware of the trial (e.g. posters in clinic, written letter from a doctor, asked by a nurse) limit the participation of each ethnic group in the target population? | **Response:** It is not clear how potential participants will be made aware of the trial, the report states that participants were recruited from the involved sites. The sites were chosen based on previous clinical trial experience or by estimated volume of potential eligible patients. Interested sites completed a site feasibility questionnaire, and some sites required support from the UK Clinical Research Network. It seems that awareness of the trial is therefore at the recruiter’s discretion unless there are other ways in which awareness of the trial is raised.  Depending on the language skills of both staff member and potential participant/family members, and the difficulties of making that approach as perceived by the recruiter, a direct recruiter approach may limit the ability of some members of some ethnic groups (e.g., older South Asians, especially women; some white non-British) to take part. See below. |
| How might the information that tells potential participants about the trial (e.g. participant information leaflet) limit the participation of each ethnic group? | **Response:** The trial report does not detail the information that potential participants receive about trial.  As some ethnic groups including individuals for whom English may not be their first language are a key required group within the trial (e.g. South Asians, Indian subcontinent) then translation of written and oral material into some languages other than English is likely to be essential (see above). [Other cultural barriers for South Asians](https://onlinelibrary.wiley.com/doi/epdf/10.1111/dme.13895) (e.g., preference for traditional remedies, see earlier) may be as important, or more important, than linguistic barriers so should not be forgotten. [These beliefs, and linguistic issues, are likely to be more relevant among older generations](https://onlinelibrary.wiley.com/doi/epdf/10.1111/dme.13895).  It is unclear if the written/verbal information has been developed together with people from a range of ethnic groups. |
| How might cultural practices, beliefs and traditions change the way each ethnic group perceives the information they are given? | **Response:** As above. |
| Other factors to consider: | |
| **Consent procedures** | How might the way consent is sought (i.e. where, by whom, written vs verbal, verbal translations/multiple languages, access to interpreters) limit the participation of each ethnic group in the target population? | **Response:** The trial report does not detail the way that consent is sought from participants, only that a consent form needed to be signed.  The application had a lay co-applicant, Richard Lane OBE, who helped design the study and contributed to the grant application. Three lay members of the North East London Lay Member panel of the diabetes research network also contributed to the design of the study, including design and content of the consent form. The ethnicities of these individuals are not clear from the trial report, and the specifics of their involvement is unclear also. | |
| How might the way people would like to discuss participation with family before providing consent differ for each ethnic group? | **Response:** [South Asian women](https://www.researchgate.net/publication/7480322_The_Influence_of_Family_on_Immigrant_South_Asian_Women%27s_Health), particularly older women, are known to make decisions about their healthcare in consultation with members of their family. Involvement of family members in the consent process should therefore be considered. | |
| How might the way the research team can check how well consent information is understood differ for each ethnic group? | **Response:** The trial report does not detail if/how the research team will check how well consent information is understood.  The chief challenge for the research team to understand how well consent information has been understood is around language ability and cultural competence (i.e., an awareness of issues that maybe be important to some ethnic groups but not others, or more to some groups than others). If the research team member is white-British it is unlikely that he/she/they will have this for any ethnic group other than white-British unless he/she/they has received training. | |
| Other factors to consider: | | |

**Worksheet 3b**

This worksheet provides some questions **to guide your thinking about ethnic group involvement when answering Question 4** of the INCLUDE Key Questions.

**Trial data collection factors that might affect how some groups engage with the trial**

|  |  |  |
| --- | --- | --- |
| **What** | How, and in what way, were people from each ethnic group in the target population involved in selecting the trial outcomes? | **Response:** The application had a lay co-applicant, Richard Lane OBE, who helped design the study and contributed to the grant application. Three lay members of the North East London Lay Member panel of the diabetes research network also contributed to the design of the study. The ethnicities of these individuals are not clear from the trial report, and the specifics of their involvement is unclear also. |
| How might the trial outcomes themselves, or other data being collected (e.g. a patient’s background information) limit the participation of each ethnic group? | **Response:** The trial’s primary outcome was the mean change in BCVA (best corrected visual acuity), measured by ETDRS letter score at 4 metres. Secondary outcomes are measured with a variety of visual function and quality-of-life outcomes. There is no reason to believe that the trial’s outcomes or other data being collected will limit the participation of any ethnic group. |
| Other factors to consider: | |
| **Who** | How might the people who collect data limit the participation of each ethnic group in the target population? | **Response:** It is not clear who the people collecting the data are – likely to be NHS staff. Potential issues are discussed in worksheet 2. |
| Other factors to consider: | |
| **How** | How might data collection methods limit the participation of each ethnic group in the target population? | **Response:** See below, under ‘Where’. |
| Other factors to consider: | |
| **Where** | How might where data are collected limit the participation of each ethnic group in the target population? | **Response:** Data are likely to be collected in hospital. The main issue is likely to be getting to the hospital (e.g., use of public transport) and the time needed to complete the measures (e.g., leaving work or getting away from caring responsibilities to attend appointments). These issues may disadvantage people experiencing socioeconomic disadvantage. People from ethnic minority communities are at higher risk of socioeconomic disadvantage, and participation could therefore be limited. |
| Other factors to consider: | |

**Worksheet 3c**

This worksheet provides some questions **to guide your thinking about ethnic group involvement when answering Question 4** of the INCLUDE Key Questions.

**Factors that might affect the planned analysis of trial results**

|  |  |  |
| --- | --- | --- |
| **Retention** | How might the trial data available for participants differ between each ethnic group in the target population? | **Response:** Data are likely to be collected during research visits at hospital sites – see worksheet 3b for discussion of the potential issues with this that may lead to differences in the data available for participants from ethnic minority backgrounds. |
| Other factors to consider: | |
| **Benefits** | How might the benefits of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** The prevalence of the disease may differ for ethnic minority groups, as discussed previously, but there is no reason to believe that the impact(s) of the trial intervention will differ between ethnic groups. |
| Other factors to consider: | |
| **Harms** | How might the possible harms of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** As above. |
| Other factors to consider: | |
| **Subgroup analyses** | How should variation between ethnic groups in the target population be explored– should there be planned subgroup analyses? | **Response:** An exploration of benefits and harms by ethnic group should be pre-planned, especially given the disproportionate effects of diabetes on people with South Asian, African and African-Caribbean heritage.  The need for this pre-planned subgroup analysis suggests that over-sampling by ethnicity might be useful. This is unlikely to affect the applicability of the evidence to the majority population but will improve the certainty of conclusions coming from the subgroup analysis. The overall sample size does not need to be changed and it is unlikely to be feasible to fully power any subgroup analyses. |
| Other factors to consider: | |
| **Interim analyses** | How should any interim analysis handle variation between ethnic groups in the target population? | **Response:** Any planned interim analysis should look for signals suggesting that benefits or harms were importantly different in one or more ethnic groups. The certainty available for this will be less than for the majority population, although oversampling may help. |
| Other factors to consider: | |
| **Stopping triggers** | How should any rules to stop the trial early on safety or benefit grounds handle variation between ethnic groups in the target population? | **Response:** Any stopping rules should consider the benefits or harms by ethnic group. The certainty available for this will be less than for the majority population, although oversampling may help. |
| Other factors to consider: | |

**Worksheet 3d**

This this worksheet provides some questions **to guide your thinking about ethnic group involvement when answering Question 4** of the INCLUDE Key Questions.

**Factors that might affect the planned reporting and dissemination of trial results**

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| --- | --- | --- |
| **What** | How, and in what way, were people from each ethnic group in the target population involved in planning the reporting and dissemination of the trial results? | **Response:** The application had a lay co-applicant, Richard Lane OBE, who helped design the study and contributed to the grant application. Three lay members of the North East London Lay Member panel of the diabetes research network also contributed to the design of the study. The ethnicities of these individuals are not clear from the trial report. The specifics of their involvement is unclear, though the trial report does say that they were involved with contributing to the contents of the letter to the participants informing them of the trial’s results.  Dissemination materials intended for the public should consider the health beliefs, health literacy and languages of the ethnic groups in the community and use channels appropriate for the ethnic group. For example, community radio can be a useful tool for some ethnic groups, as can social media. |
| Other factors to consider: | |
| **How** | How might planned reporting and dissemination methods limit engagement with each ethnic group in the target population? | **Response:** Details about the reporting and dissemination methods are not clear from the trial report. We can assume that the trial team will publish scientific manuscripts from this trial, in which case they should be open access. In addition, public-facing engagement methods such as presentations, activities, newsletters, and other methods, should be designed and developed with people from various ethnic groups to ensure that the trial’s results reach all who may be impacted by them. |
| Other factors to consider: | |
| **Where** | How might where trial results are planned to be reported and disseminated limit engagement of each ethnic group in the target population? | **Response:** As above. |
| Other factors to consider: | |

Worksheet for thinking through measures to address factors that might prevent full community involvement

Use this worksheet to list key factors that might affect the involvement of some ethnic groups in the target population of your trial, along with measures to mitigate the effect of those factors and their cost. Add extra rows as needed.

Please remember that there are also differences *within* ethnic groups, especially between generations and between men and women. No ethnic group is homogenous.

|  |  |  |
| --- | --- | --- |
| **Factors that may prevent full community involvement** | **Proposed measures (several options may be needed)\*** | **Cost of measures** |
|  |  |  |
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\*See https://centreforbmehealth.org.uk/resources/toolkits/ for suggestions for how to address factors that affect community-wide involvement.

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[Centre for Black and Minority Ethnic Health](https://centreforbmehealth.org.uk/)

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[Health Research Board Trial Methodology Research](https://www.hrb-tmrn.ie/)

[Network](https://www.hrb-tmrn.ie/)

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