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 Shaun Treweek and Heidi Gardner, University of Aberdeen. 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 the two registration documents–** [**https://clinicaltrials.gov/ct2/show/NCT02653209**](https://clinicaltrials.gov/ct2/show/NCT02653209) **and** [**http://www.isrctn.com/ISRCTN12039221**](http://www.isrctn.com/ISRCTN12039221)**.**  **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.]**  TriMaster is a research study to help improve the treatment of type 2 diabetes, by learning how individuals respond to different blood sugar lowering drugs, so participants should be people with type 2 diabetes that struggle to control their blood sugar levels. In the UK there are 2.5 million people who have been diagnosed with diabetes – an estimated 90% of those have type 2 diabetes. Half of all people from South-Asian, African and African-Caribbean descent will develop type 2 diabetes by age 80, compared with a fifth of people with European descent. The age of onset of type 2 diabetes is also significantly lower in ethnic minority populations compared with White-British populations, and diabetes associated complications are more common in South Asians, Africans and African-Caribbeans too. Public Health England 2018/19 data suggest that 21% of people in England with type 2 diabetes are of minority ethnic origin. The trial team should work to include South Asians, Africans and African-Caribbeans, particularly younger members of these communities, in this trial.  The trial population should look like the UK type 2 diabetes population. This means that it needs to involve ethnic minority individuals, especially South Asians and Black Caribbeans, at higher levels than in the general population. The proportion of minority ethnic individuals in the trial population as a whole needs to be at least 20%. |

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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, disease severity and age of onset differs in South Asian, African and African-Caribbean populations in comparison to White-British populations. Evidence for the root of these differences is limited, but genetics are thought to play a part.  In addition to genetics, it is likely that cultural differences may play a role in how participants from South Asian, African and African-Caribbean populations respond. Research has suggested that poor clinical outcomes for South Asian patients could be worsened by non-adherence to medication. This has been 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. Linking in with non-adherence, 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.  The drugs being tested in the trial may contain ingredients from animal origins – limiting participation of potential participants practicing Judaism, Islam or Hinduism. Sitagliptin, pioglitazone, and canagliflozin all contain magnesium stearate which is normally pork-derived but can also be found in butter, chicken, beef, fish and milk. Vegan and vegetarian-friendly sources are available, so it is important that the trial team consider this.  The drugs are in over-encapsulated capsule form – capsules commonly contain gelatine which again, could limit participation due to it being an animal product.  Eight key cultural issues have been identified as factors that impede ethnic minority groups from accessing effective diabetes care services. These are: 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. These can result in blood sugar levels being uncontrolled. The trial team should pay particular attention as participants are people with diabetes that struggle to control their blood sugar levels. |

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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.]**  As the protocol for this trial has not been published and is not publicly available, we are relying on the trial registration documents for this information.  It is not clear if or how any patient partners were involved in the selection of the trial interventions and/or comparator, who delivers the treatments, or where they are delivered. It is clear that there is a screening and consent visit, followed by 5 separate research visits. It is therefore likely that the participants will meet with a clinician or research nurse based at one of the 19 trial sites. Black and minority ethnic populations are known to distrust the medical and research systems due to historical abuse and exploitation, so it may be that attending research visits at an NHS hospital site would limit participation.  The trial requires close to daily medication over 48-54 weeks, drugs are taken at home, so this is unlikely to limit engagement. The trial team should consider that religious celebrations such as Ramadan will take place during the period of the study. Ramadan is a community celebration for practising Muslims – over the month of Ramadan, individuals fast between dawn and sunset. Taking medicine orally is considered breaking the fast. Exceptions are made for people that cannot perform the fasting safely (including those with diabetes). Despite being exempt, many people with diabetes do choose to fast. All of the trial drugs can be taken with or without food, but the trial team should bear in mind that the time that they are taken may differ during Ramadan. | |
| 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.]**  As the protocol for this trial has not been published and is not publicly available, we are relying on the trial registration documents for this information.  It is not clear how participants are made aware of the trial, what information they receive, how consent is taken, or if/how consent information is understood. South Asian women, 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. Translation of at least some trial documentation is likely to be required.  Research visits (5 over the course of a year) at hospital sites are used for outcome data collection, and for the participants to collect medication throughout the trial. Getting to hospital can be an issue for a variety of reasons including – poor transport links, the timing and length of research visits (i.e. clashing with working hours, childcare or caring responsibilities), financial reasons (time away from work, cost of travel, parking charges). Many of these factors disproportionately impact people from poor socioeconomic backgrounds, which often includes ethnic minority groups.  The trial’s outcomes largely rely on a blood sample taken at each of the research visits. Weight, blood pressure and data about patient experience are also collected including perceived side effects, preparedness to remain on therapy, psychological health and health related quality of life. Participation could be limited for those that are scared of needles, but this is not a problem specific to any ethnic group. |

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:** In the UK there are 2.5 million people who have been diagnosed with diabetes – an estimated 90% of those have type 2 diabetes. [Type 2 diabetes is up to 6 times more likely in people of South Asian descent (Indian, Pakistani, Sri Lankan and Bangladeshi heritage)](https://www.diabetes.org.uk/resources-s3/2017-11/south_asian_report.pdf) than in the White population. [South Asians are estimated to be around 11% of the UK type 2 diabetes population minority ethnic individuals were 21% of the type 2 diabetes population in England](https://fingertips.phe.org.uk/profile/diabetes-ft/data#page/0/gid/1938133138/pat/44/par/E40000007/ati/154/are/E38000007/cid/4/tbm/1/page-options/ovw-do-0) in 2018/19.  People of African and African-Caribbean descent are also known to have an increased risk of type 2 diabetes.  [A study](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3304519/) which followed nearly 5000 middle-aged Londoners of European, South Asian, African and African-Caribbean descent for more than 20 years, revealed that half of all people from South-Asian, African and African-Caribbean descent will develop type 2 diabetes by age 80, compared with a fifth of people with European descent. |
| 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. The [response to treatment may vary](https://pubmed.ncbi.nlm.nih.gov/26926478/), with differences seen in studies where the trial population was Asian-dominant compared to non-dominant.  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:** [Children of all ethnic minority backgrounds](https://pubmed.ncbi.nlm.nih.gov/27426206/) are at greater risk for childhood-onset type 2 diabetes, particularly girls. In terms of adult age of onset, 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. | |
| 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 trial is being led by Royal Devon and Exeter Hospital, and is being run across 19 other hospitals in England, Scotland and Wales. These sites include Glasgow, Manchester, London, Sheffield, and Newcastle, which have reasonable populations of both South Asians, Black Africans and/or African-Caribbeans.  Birmingham is the second largest city in the UK and is home to a wide range of Asian communities, so it would have been a good choice too, but the sites included should allow the trial to recruit populations of all ethnic groups. It would be sensible to check local site populations against the overall disease burden, but the national spread of the trial should mean that substantial populations of all ethnic groups are in the recruitment areas of at least some participating sites. | |
| 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 is not conclusive. 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.  In terms of trial participation, generally, trials are known to lack diversity – much of this may be down to lack of trust in the medical and research systems due to historical abuse and exploitation of Black and minority ethnic populations. [Research](https://www.diabetes.org.uk/resources-s3/2017-11/south_asian_report.pdf) has shown that South Asians are often explicitly excluded from research due to perceived cultural and communication difficulties. It has also been shown that many [South Asian people are unwilling to participate](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2571097/) because they accept their illness as an unalterable punishment from God, or have a fear of what research entails. | |
| 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. | |
| How might cultural practices, beliefs and traditions influence the acceptability of, and adherence to, the treatment(s) for each ethnic group? | **Response:** The trial treatments are all drugs - three classes of oral third-line glucose-lowering therapies: i) sitagliptin, a DPP4 inhibitor ii) pioglitazone, a thiazolidinedione and iii) canagliflozin, a SGLT2 inhibitor.  Briefly mentioned in section above –  The necessity of traditional remedies versus ‘western medicines’ – not only are traditional remedies often viewed as necessary, they are viewed as effective. Traditional remedies are also thought to have no side effects, provide balance, contain natural ingredients, and lack the perceived toxicity associated with medicines prescribed by a doctor.  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 taking drug treatments, with people believing that a trial is not necessary because faith in God is needed more than medicine. [South Asian views on diabetes drugs are complex](https://www.diabetes.org.uk/resources-s3/2017-11/south_asian_report.pdf), with some considering them only for symptomatic benefit and tried to reduce the dose at every possible opportunity.  The drugs being tested in the trial may contain ingredients from animal origins – limiting participation of potential participants practicing Judaism, Islam or Hinduism. Sitagliptin, pioglitazone, and canagliflozin all contain magnesium stearate which is normally pork-derived but can also be found in butter, chicken, beef, fish and milk. Vegan and vegetarian-friendly sources are available, so it is important that the trial team consider this.  The drugs are in over-encapsulated capsule form – capsules commonly contain gelatine which again, would limit participation due to it being an animal product. Side note – this is not just a religious/ethnicity issue, vegetarian and vegan lifestyles are rising around the world as a response to the climate crisis. Moving to vegan-friendly capsules and ingredients would prevent barriers to participation for many populations. | |
| How or when might people in each ethnic group access healthcare for this disease differently? | **Response:** 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:** All the interventions are drugs and the [content of medicine is a concern](https://www.demanddiversity.co/resources) for Black, Pakistani and Arabic Muslims (i.e. that the drug contains ingredients specifically designed to harm them in particular). Older people in most minority ethnic groups are more likely to believe that faith in God is needed more than medicine, a theme also recognised by younger members of those communities. Religious beliefs may prevent some groups (e.g. Sikhs) taking drug that include ingredients made from pigs; Hindus may have similar problems with ingredients derived from cows. See Worksheet 1.  In summary, a lack of clarity about drug ingredients is likely to be a barrier to recruitment of many ethnic minority groups, especially older people. |
| How, and in what way, were people from each ethnic group involved in selecting or designing the trial intervention/comparator? | **Response:** \*The protocol for this trial is not publicly available, so the registration documents have been used (<https://clinicaltrials.gov/ct2/show/NCT02653209> and [http://www.isrctn.com/ISRCTN12039221)\*](http://www.isrctn.com/ISRCTN12039221)*)  It is not clear if or how any patient or public partners were involved in this work, neither the protocol nor the membership of the trial steering group are publicly available. |
| 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:** It is not clear who will deliver the interventions/comparator, but it is clear that there is [a screening and consent visit, followed by 5 separate research visits](https://www.diabetesgenes.org/current-research/trimaster/). It is therefore likely that the participants will meet with a clinician or research nurse based at one of the 19 trial sites. As mentioned previously, Black and minority ethnic populations are known to distrust the medical and research systems due to historical abuse and exploitation, so it may be that attending research visits at an NHS hospital site would limit participation.  That said, [NHS staff are a more diverse group](https://www.ethnicity-facts-figures.service.gov.uk/workforce-and-business/workforce-diversity/nhs-workforce/latest) than the wider UK population – of NHS staff whose ethnicity is known, 79.2% are White (including White minorities), and 20.7% are from all other ethnic groups. This contrasts to the wider population – the [2011 Census](https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/national-and-regional-populations/population-of-england-and-wales/latest) showed that 86.0% of the population of England and Wales was White. If the staff conducting research visits with participants are of the same ethnicity, or share a common language, this distrust may be reduced. |
| 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:** As stated above, the mode of delivery of the interventions/comparator is not clear, though it is likely that the research visits will be used for outcome data collection and to provide the participants with the drugs to take over a period of time (i.e. in their own home).  Taking the drugs at home should not be an issue but attending research visits may well be. Getting to hospital can be an issue for a variety of reasons including – poor transport links, the timing and length of research visits (i.e. clashing with working hours, childcare or caring responsibilities), financial reasons (time away from work, cost of travel, parking charges). Many of these factors disproportionately impact people from poor socioeconomic backgrounds, which often includes ethnic minority groups. |
| 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:** The total time commitment is 48-54 weeks (3 x 16 weeks of therapy), with a screening and consent visit at the beginning, followed by 5 research visits. It is not clear how long each research visit will take. Five hospital visits over the course of a year is not a huge commitment, but participants will be required to take medication daily for most of that time too. Clearly explaining to participants in a culturally appropriate way why attending all visits is important will be key for all ethnic groups.  The trial team should bear in mind that religious celebrations such as Ramadan will take place during the period of the study. Ramadan is a community celebration for practising Muslims – over the month of [Ramadan](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5415064/), individuals fast between dawn and sunset. Taking medicine orally is considered breaking the fast. Exceptions are made for people that cannot perform the fasting safely (including those with diabetes). Despite being exempt, [many people with diabetes do choose to fast](https://www.idf.org/our-activities/education/diabetes-and-ramadan.html). All of the trial drugs can be taken with or without food, but the trial team should consider that the time that they are taken may differ during Ramadan. |
| 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. Clinicians with expertise in diabetes management will be able to shed more light on whether specific criterion may disproportionately impact certain ethnic groups – for example, the criterion ‘currently treated with two classes of oral glucose-lowering therapy (given either as separate or combined medications), that do not include a DPP4-inhibitor, a SGLT2-inhibitor or a thiazolidinedione’.  It is not clear what sort of medical history information are taken at baseline (or later).  Consent and language are discussed below. |
| 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:** The protocol for this trial is not publicly available, and the registration documents do not detail how potential participants are made aware of the trial. |
| 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 protocol for this trial is not publicly available, and the registration documents do 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:** The protocol for this trial is not publicly available, and the registration documents do not detail the information that potential participants receive about the trial. |
| 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 protocol for this trial is not publicly available, and the registration documents do not detail how consent is taken. | |
| 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 protocol for this trial is not publicly available, and the registration documents do not detail if/how the research team will check how well consent information is understood. | |
| 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**

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| **What** | How, and in what way, were people from each ethnic group in the target population involved in selecting the trial outcomes? | **Response:** \*The protocol for this trial is not publicly available, so the registration documents have been used (<https://clinicaltrials.gov/ct2/show/NCT02653209> and [http://www.isrctn.com/ISRCTN12039221)\*](http://www.isrctn.com/ISRCTN12039221)*)  It is not clear if or how any patient or public partners were involved in planning the reporting and dissemination of the trial results, neither the protocol nor the membership of the trial steering group are publicly available.  There is a [core outcome set for type 2 diabetes studies](https://drc.bmj.com/content/7/1/e000700.long), although this was published after the TriMaster study started and the ethnicity of public participants in developing the core outcome set is unclear, though the study was international. The TriMaster primary outcome, glycaemic control, is in the core outcome set, as is the secondary outcome of side effects. Another secondary outcome, patient preference, could be a proxy for quality of life, also on the core outcome set. TriMaster has no other outcomes (apart from one on gender differences, which is done with data collected for other outcomes). |
| 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 outcomes largely rely on a blood sample taken at each of the research visits. Weight, blood pressure and data about patient experience are also collected including perceived side effects, preparedness to remain on therapy, psychological health and health related quality of life. Participation could be limited for those that are scared of needles, but this is not a problem specific to any ethnic group.  It is not clear what background information are collected from the patient. |
| 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:** Apart from the potential limitation linked to who does data extraction, (see above re: distrust in medical and research professionals) the data extraction process itself is unlikely to limit participation of any ethnic group. |
| 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 collected during research visits at hospital sites – see worksheet 2 for discussion of the potential issues with this. |
| 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 collected during research visits at hospital sites – see worksheet 2 for discussion of the potential issues with this. |
| Other factors to consider: | |
| **Benefits** | How might the benefits of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** There is [evidence to suggest that genetics](https://www.diabetes.org.uk/resources-s3/2017-11/south_asian_report.pdf) play a part in susceptibility for South Asians, so it is likely that the trial drugs may have different impacts on this population too. |
| 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**

|  |  |  |
| --- | --- | --- |
| **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 protocol for this trial is not publicly available, so the registration documents have been used (<https://clinicaltrials.gov/ct2/show/NCT02653209> and [http://www.isrctn.com/ISRCTN12039221)\*](http://www.isrctn.com/ISRCTN12039221)*)  It is not clear if or how any patient or public partners were involved in planning the reporting and dissemination of the trial results, neither the protocol nor the membership of the trial steering group are publicly available. |
| Other factors to consider: | |
| **How** | How might planned reporting and dissemination methods limit engagement with each ethnic group in the target population? | **Response:** The [registration document](http://www.isrctn.com/ISRCTN12039221) details only scientific publication(s), which limits engagement with all ethnic groups.  Using publications as the only form of dissemination is not conducive to engaging any ethnic group, or member of the public with the results of this trial. At the very least the publication(s) that come from this trial should be open access.  The [registration document](http://www.isrctn.com/ISRCTN12039221) states that data and results related to protocol-derived outcomes will be published by the MASTERMIND consortium and that a lay summary of results will be provided to all participants. It is not clear how the lay summary will be provided, or whether it will be tailored in any way by ethnic group, or whether it will be available in languages other than English. |
| 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:** The [registration document](http://www.isrctn.com/ISRCTN12039221) details only scientific publication(s), which limits engagement with all ethnic groups.  Using publications as the only form of dissemination is not conducive to engaging any ethnic group, or member of the public with the results of this trial. At the very least the publication(s) that come from this trial should be open access.  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 (e.g. Sikhs), as can social media. |
| 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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