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 Seonaidh Cotton and Shaun Treweek, 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 registration document–** [**http://www.isrctn.com/ISRCTN17072692**](http://www.isrctn.com/ISRCTN17072692) **and the study website** [**https://www.imperial.ac.uk/covid-19-vaccine-trial/trial-info/**](https://www.imperial.ac.uk/covid-19-vaccine-trial/trial-info/) **(including the prescreening questionnaire).**  **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.]**  Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a strain of coronavirus that causes respiratory illness. There is [clear evidence](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/892085/disparities_review.pdf) that those most affected are men, older people, people with comorbidity/chronic illness, people with Black, Asian and minority ethnic backgrounds and people living in more deprived areas.  **In summary**  Ideally a vaccine should be suitable for all those at risk from the disease, which for SARS-CoV-2 is essentially the whole population (i.e. different groups at the proportion seen in the community) but particularly those mentioned above.  However, the trial is a Phase I trial, which means extra care is needed with participant selection. Exclusions based on potential contraindications to the vaccine under test and any other known potential safety concerns are appropriate. The population should aim to recruit from across the community but recruit healthy volunteers from within this community where the potential risk is lowest. Later phases of the trial will need to aim for wider community representation, once the safety (and potential efficacy) of the vaccine has been demonstrated. |

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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.]**  The risk of infection is [generally considered higher for minority ethnic groups](https://fullfact.org/health/Covid-19-inequalities-minority-ethnicities/), in large part because of where many individuals from these group live and the jobs they often do. [Local government data for England](https://lginform.local.gov.uk/reports/view/lga-research/covid-19-cases-and-area-characteristics) show that communities with higher proportions of Black, Asian and minority ethnic individuals living there have higher levels of COVID cases. [A study of people involved with the UK Biobank](https://pubmed.ncbi.nlm.nih.gov/32466757/) found Black and south Asian groups were more likely to test positive for COVID, with Pakistani ethnicity at highest risk. Many studies have reported that ethnic minority groups are affected more severely by SARS-CoV-2. [Age-adjusted Office of National Statistics data for July 2020](https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/coronavirusrelateddeathsbyethnicgroupenglandandwales/2march2020to10april2020#ethnic-group-differences-in-deaths-involving-covid-19-adjusted-for-main-socio-demographic-factors) show that the risk of death is much higher in minority ethnic groups than in the White population.  There are many cultural and health belief reasons to consider that some people in some ethnic groups will be less likely to accept a vaccine, particularly Arabic, Black African and Black Caribbean, who have a [deep mistrust of medical research](https://www.demanddiversity.co/resources). There is evidence that uptake of vaccines for other conditions is lower for some ethnic minority groups. A [recent Pew survey in the US](https://www.pewresearch.org/fact-tank/2020/06/04/black-americans-face-higher-covid-19-risks-are-more-hesitant-to-trust-medical-scientists-get-vaccinated/) found that 54% of Black adults said they would definitely or probably get a coronavirus vaccine if one were available today, while 44% say they would not. Hispanic and White adults are far more likely to say they would get the vaccine: 74%. It is likely that [social media stories within some ethnic communities](https://www.reuters.com/article/uk-factcheck-bame-vaccine/fact-check-the-british-government-is-not-targeting-bame-communities-for-coronavirus-vaccine-trials-idUSKBN23V223) will work against participation in vaccine trials by Black, Asian and minority ethnic groups. |

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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.]**  It is not clear whether any members of the public from any ethnic group were involved in the selection of the intervention. See above for some reasons why drug treatments might be problematic for some ethnic groups.  It is unclear who will deliver the vaccine, but it is likely to be a clinical/health professional member of the research team, or a research nurse working within the NHS. NHS staff are ethnically diverse, which may help with engagement with potential participants from those groups. It could potentially harm engagement by some members of the majority population. All treatments are delivered in hospital.  Participants in all three groups of the randomised component of the study will receive a single injection and are then followed up for a year. It is not clear what follow-up entails.  If clinic hours are working hours (i.e. 9am to 5pm in the UK), this is likely to disadvantage those who work during these hours but are unable to take time off to come to the clinic. Ethnic minority groups are more likely to have jobs where this is a problem. | |
| 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.]**  The screening questionnaire asks whether a person is registered with a GP – it is not clear if someone was not registered whether they would fail the initial screening. There are contraceptive requirements (for both men and women participating), which may affect participation by [some ethnic groups more than others](https://pubmed.ncbi.nlm.nih.gov/16904416/). Discussion of HIV (linked to an exclusion criterion) [may be sensitive/carry stigma for some ethnic groups](https://lx.iriss.org.uk/sites/default/files/resources/HIV-related%20stigma%20-and-%20discrimination_racial%20and%20ethnic%20minorities.pdf), especially Black African and Black Caribbean groups.  Potential participants can join the trial directly by going to the study website, or potentially through national NHS/NIHR efforts to raise awareness of SARS-CoV-2 trials such as [Be Part of Research](https://bepartofresearch.nihr.ac.uk/). The recruitment pathway is unclear, but it is likely to have a strong reliance on online written materials in English through the study website. Reliance of written materials in English is likely to limit participation of individuals from any ethnic group with low literacy levels. The opportunity to participate seems largely self-led, which means those who may have a general distrust of medical research (e.g. Arabic, Black Caribbean, Black African) are less likely to join.  It is unclear if the written information has been developed together with people from a range of ethnic groups. It is possible that even for non-White British who read English well, the text may inadvertently limit participation. |

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:** SARS-CoV-2 (COVID-19) affects the whole community but some ethnic groups are affected disproportionately.  The risk of infection is [generally considered higher for minority ethnic groups](https://fullfact.org/health/Covid-19-inequalities-minority-ethnicities/), in large part because of where many individuals from these group live and the jobs they often do. [Local government data for England](https://lginform.local.gov.uk/reports/view/lga-research/covid-19-cases-and-area-characteristics) show that communities with higher proportions of Black, Asian and minority ethnic individuals living there have higher levels of COVID-19 cases. [A study of people involved with the UK Biobank](https://pubmed.ncbi.nlm.nih.gov/32466757/) found Black and south Asian groups were more likely to test positive for COVID-19, with Pakistani ethnicity at highest risk. [Public Health England data for 7th July](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsinthecommunityinengland/july2020#infection-rates-by-age-sex-and-ethnicity-over-the-study-period) conclude that it is too early to say whether COVID-19 infection rates differ between ethnic groups because the number of people testing positive in groups other than the White ethnic group are very small.  In summary, it remains unclear to what extent prevalence varies by ethnic group but it would seem prudent to aim for a trial population that matches the ethnic diversity of the UK population, i.e. [2011 UK census](https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity),:   * 80.5% White British * 7.5% Asian * 3.4% Black * 2.2% Mixed * 5.4% Other White * 1% Other   Depending on recruitment site, these proportions will vary greatly and the aim should be to reflect the local population at these rates. |
| How might the severity of the disease vary between each ethnic group? | **Response:** Many studies have reported that ethnic minority groups are affected more severely by SARS-CoV-2. [Age-adjusted Office of National Statistics data for July 2020](https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/coronavirusrelateddeathsbyethnicgroupenglandandwales/2march2020to10april2020#ethnic-group-differences-in-deaths-involving-covid-19-adjusted-for-main-socio-demographic-factors) show that the risk of death is much higher in minority ethnic groups than in the White population.  This difference became apparent from around March 2020. [After adjusting for region, population density, socio-demographic and household characteristics](https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/articles/coronaviruscovid19relateddeathsbyethnicgroupenglandandwales/2march2020to15may2020), the raised risk of death involving COVID-19 for people of Black ethnic background of all ages together was 2.0 times greater for males and 1.4 times greater for females compared with those of White ethnic background. Males of Bangladeshi, Pakistani and Indian ethnic background also had a significantly higher risk of death involving COVID-19 (1.5 and 1.6 times, respectively) than White males; whilst for females in Bangladeshi or Pakistani, Indian, Chinese and Mixed ethnic groups, the risk of death involving COVID-19 was equivalent to White females. |
| How might the disease present in people from each ethnic group (this may include symptoms, type or pattern or rate of disease progression)? | **Response:** [Clinical presentation in early SARS-CoV-2](https://www.nhs.uk/conditions/coronavirus-covid-19/symptoms/) is one or more of high temperature, new continuous cough and a loss or change to your sense of smell or taste. Symptoms appear similar across ethnic groups.  However, a vaccine trial (especially an early phase one) will aim to recruit individuals who are healthy and without SARS-CoV-2 symptoms. | |
| 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:** To be representative, COVAC1 should include areas where Black, Asian and minority ethnic groups live. The trial will recruit from two sites in London as well as Guildford and Southampton.  The randomised component of the study involving 105 individuals is single-centre; it is not clear which participating centre this will be although it is likely to be London-based.  Recruitment of minority ethnic groups should be monitored to ensure that recruitment of different ethnic groups at least match the levels of each group in the local community. | |
| Other factors to consider: Vaccine trial will target healthy volunteers rather than patients with SARS-CoV-2. | | |
| **Cultural** | How might perceptions of the disease and social stigma around it be different for each ethnic group in the target population? | **Response:** SARS-CoV-2 is a new virus and it is not clear whether it has different degrees of stigma among ethnic groups, or whether it is perceived differently across ethnic groups. In [Feb 2020 WHO highlighted](https://www.who.int/docs/default-source/coronaviruse/covid19-stigma-guide.pdf?sfvrsn=226180f4_2) that terminology used by some to describe the virus (e.g. ‘Chinese virus’) was likely to stigmatise some Asian groups.  Regardless, several ethnic minority groups, particularly Arabic, Black African and Black Caribbean, [have a deep mistrust of medical research](https://www.demanddiversity.co/resources). A [recent survey of over 1200 people](https://www.hra.nhs.uk/documents/1422/HRA_NIHR_general_public_omnibus_survey_2017_FINAL.pdf), 14% of whom were non-White, by the Health Research Authority found more positive attitudes, especially for publicly-funded research. A [recent Pew survey in the US](https://www.pewresearch.org/fact-tank/2020/06/04/black-americans-face-higher-covid-19-risks-are-more-hesitant-to-trust-medical-scientists-get-vaccinated/) found that 54% of Black adults said they would definitely or probably get a coronavirus vaccine if one were available today, while 44% say they would not. Hispanic and White adults are far more likely to say they would get the vaccine: 74%. It is likely that [social media stories within some ethnic communities](https://www.reuters.com/article/uk-factcheck-bame-vaccine/fact-check-the-british-government-is-not-targeting-bame-communities-for-coronavirus-vaccine-trials-idUSKBN23V223) will work against participation in vaccine trials by Black, Asian and minority ethnic groups. | |
| How might ways of describing the disease be different for each ethnic group? | **Response:** It is not clear if SARS-CoV-2 is described differently across different ethnic groups. | |
| How might cultural practices, beliefs and traditions influence the acceptability of, and adherence to, the treatment(s) for each ethnic group? | **Response:** Influenza vaccine uptake in children [has been found to be lower](https://jech.bmj.com/content/71/6/544) in schools with higher proportions of Black, Asian and minority ethnic children. [Other studies](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5484038/) have [found similar results](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/742678/Childhood_flu_vaccination_programme_England_2017_to_2018.pdf).), suggesting that factors related to ethnicity influenced parents’ perceptions about immunisations and secondly, that beliefs about biological ethnic differences altered parents’ perceived susceptibility to disease and vaccine side effects. Individuals across ethnic groups are skeptical of vaccines; [a June 2020 poll done in the UK found 1 in 6 would not get vaccinated for COVID](https://docs.cdn.yougov.com/5mkju0kxbj/CCDH_RESULTS_062620_PR%20%28002%29.pdf) although data on ethnicity was not provided.  [More generally](https://www.demanddiversity.co/resources), some ethnic groups have expressed a preference for traditional, herbal or homeopathic medicine (e.g. Indian, Arabic, Black Caribbean, Black African and Chinese). The contents of medicine are a concern for Black, Pakistani and Arabic Muslims (i.e. that the drug contains ingredients specifically designed to harm them in particular). [Social media stories can play on this concern](https://www.reuters.com/article/uk-factcheck-bame-vaccine/fact-check-the-british-government-is-not-targeting-bame-communities-for-coronavirus-vaccine-trials-idUSKBN23V223).  Religious beliefs may prevent some groups (e.g. Sikhs) taking a drug that includes (or is perceived to contain) ingredients made from pigs; Hindus may have similar problems with ingredients derived from cows. The NIHR “be part of research” website has questions about whether the vaccines contain meat products/or were meat products used to make the vaccine, and if they are Halal/Kosher – the response is that this information is available from the study team. | |
| How or when might people in each ethnic group access healthcare for this disease differently? | **Response:** It is not clear whether healthcare seeking behaviour for SARS-CoV-2 varies across ethnic groups. However, [health literacy is low among some ethnic groups](https://www.england.nhs.uk/wp-content/uploads/2017/07/inequalities-resource-sep-2018.pdf), and this is a known barrier to seeking healthcare support. It is known that [ethnicity affects use of NHS Direct](http://www.equityhealthj.com/content/13/1/99), a telephone-based service though many ethnic minority groups (e.g. mixed) used the service more, not less. The service was used less by Black Africans, Black Caribbean and Asians.  In summary, it is likely that some ethnic groups will seek healthcare differently to the majority population, including access to vaccines. This is particularly likely for Black and Asian groups, and older members of those groups. See also previous section regarding uptake of other vaccines. | |
| 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 a vaccine and there is skepticism about vaccines in some ethnic groups in particular and among some individuals across all ethnic groups (see Worksheet 1).  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. |
| How, and in what way, were people from each ethnic group involved in selecting or designing the trial intervention/comparator? | **Response:** It is not clear whether any members of the public from any ethnic group were involved in the selection of the vaccine, or dosing schedules. The protocol does not appear to be publicly available and the [registration document](http://www.isrctn.com/ISRCTN17072692) and [study website](https://www.imperial.ac.uk/covid-19-vaccine-trial/) do not mention patient and public involvement. |
| 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 unclear who will deliver the vaccine, but it is likely to be delivered in hospital environment by a doctor or nurse working in the NHS. The [ethnic profile of NHS staff is more diverse](https://www.ethnicity-facts-figures.service.gov.uk/workforce-and-business/workforce-diversity/nhs-workforce/latest#by-ethnicity) 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. A [trial video](https://www.imperial.ac.uk/covid-19-vaccine-trial/) shows White doctor/nurse giving the vaccine to volunteer from Black community. Images for large scale trial shows White doctor/nurse giving the vaccine to a White participant.  It is unclear what impact these factors will have in the trial. Clear, culturally sensitive communication between research team, 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 a hospital/clinic environment– see comments above on staff diversity. The vaccine will involve an injection into muscle in the upper arm (deltoid muscle).  It is unclear what impact this might have on the participation of different ethnic 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:** Delivered in hospital by the medical team (intra-muscular injection). Participants need to attend the hospital site for the vaccine and for the follow-up visits.  Health beliefs (see earlier in worksheet) may mean that some ethnic groups’ resistance to seeking health care means they are less likely to attend in a hospital environment. However, for this phase of the vaccine evaluation, hospital-based trial delivery seems appropriate. The research team should be aware of this potential barrier to involvement and perhaps consider alternative environments in later phases. |
| 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:** Participants in all three groups of the randomised component of the study will receive a single injection and are then followed-up for a year. It is not clear what follow-up entails.  It is not clear whether visits are offered outside of normal working hours or what the time commitment is for the visits. If clinic hours are working hours (i.e. 9am to 5pm in the UK), this is likely to disadvantage those who work during these hours but are unable to take time off to come to the clinic. Ethnic minority groups are more likely to have jobs where this is a problem. |
| 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:** There is a long list of eligibility criteria but this is not unexpected for such an early stage vaccine study. The randomised component is being tested on healthy younger individuals (18-45), who are not the group most affected by SARS-CoV-2 but again, this early stage trial is about safety so a low-risk group seem appropriate.  The screening questionnaire asks whether the person is registered with a GP – it is not clear if someone was not registered whether they would fail the initial screening. There are contraceptive requirements (for both men and women participating). Sexually active married Pakistani and Indian women reported the lowest overall use of contraception. Among sexually active single women, Black African and Black Caribbean women reported levels of contraceptive use that were lower than those reported by White women. [Sexually active women from all four minority ethnic groups](https://pubmed.ncbi.nlm.nih.gov/16904416/) were less likely than White women to use reliable methods of contraception. Discussion of HIV (linked to an exclusion criterion) [may be sensitive/carry stigma for some ethnic groups](https://lx.iriss.org.uk/sites/default/files/resources/HIV-related%20stigma%20-and-%20discrimination_racial%20and%20ethnic%20minorities.pdf), especially Black African and Black Caribbean groups.  One criterion refers to access to medical records, which may affect involvement of some ethnic groups: see *Who* in Worksheet 3b. |
| 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:** Pre-screening questionnaire is available online – in English (no translation available). Potential participants are also directed to NIHR [‘Be Part of Research’](https://bepartofresearch.nihr.ac.uk/) (which has specific sign-up for COVID vaccine studies). It is not clear if all participants are identified through these routes, or whether a registry of healthy volunteers or other routes to identify participants are used.  It is not clear if payments are being made to healthy volunteers.  The opportunity to participate seems largely self-led, which means those who have a [general distrust of medical research](https://www.demanddiversity.co/resources) (e.g. Arabic, Black Caribbean, Black African) are unlikely to join. Dependence on written material is likely to exclude others, e.g. South Asians. 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 participant information leaflet was not available for review. Information about the study on both the study website and the NIHR [‘Be Part of Research’](https://bepartofresearch.nihr.ac.uk/) websites is written in English with no translation. This will limit the ability of some members of some ethnic groups to participate, although this may be less of a problem because of the younger age range targeted by this early phase trial. It will be more of an issue for future phases that aim to recruit older people.  Reliance on written materials in English is likely to limit participation of individuals from any ethnic group with low literacy levels. If recruiting staff can speak the same language as the potential participant, this problem may be mitigated. However, the participant has to make that contact first, which relies almost entirely on written material. The pre-screening questionnaire is in English only. The participant information material is not publicly available.  It is unclear if the written information has been developed together with people from a range of ethnic groups. It is possible that even for non-White British who read English well, the text may inadvertently limit participation. Some health belief issues regarding participation that could be addressed in written or verbal information were raised in Worksheet 1. |
| How might cultural practices, beliefs and traditions change the way each ethnic group perceives the information they are given? | **Response:** It is not clear whether members of the public from any ethnic group have been involved in preparing the written materials. As mentioned earlier, differences regarding attitudes to the [benefits/need for health research generally](https://pubmed.ncbi.nlm.nih.gov/27174778/) and purpose and ingredients of the vaccine for Black and some Asian groups may limit their participation unless addressed in writing or verbally (see [this for example](https://www.rsph.org.uk/static/uploaded/3b82db00-a7ef-494c-85451e78ce18a779.pdf) and also *Worksheet 1*). Translation of material needs to consider these issues in addition to simple translation from one language into another. |
| 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:** Consent is likely to be taken in hospital by a doctor or member of the trial team. Consent documents were not publicly available for review. It is unclear if these are available in languages other than English. It is not clear whether members of the public from any ethnic group have been involved in preparing the consent materials, which for reasons given above, may well limit the ability of some ethnic groups to participate. | |
| How might the way people would like to discuss participation with family before providing consent differ for each ethnic group? | **Response:** The study calls for volunteers – so in theory, there is time for volunteers to discuss with family/friends before volunteering. | |
| How might the way the research team can check how well consent information is understood differ for each ethnic group? | **Response:** Detailed information about the consent process is not publicly available for review. | |
| 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:** It is not clear whether any members of the public from any ethnic group were involved in the selection of trial outcomes.  A [core outcome set is being developed for vaccine trials](http://www.comet-initiative.org/Studies/Details/1594) but is not due to complete until Sept 2020. |
| 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:** Outcomes are safety (reactions, SAEs), neutralizing antibodies, vaccine induced serum. For the 105 patient randomised study and the 200 patient open label study it is not clear whether data are collected in the same way as for the 15 patient open label study (online diary daily for 7 days, phone call from team 48 hours post vaccination). It seems likely that there would be a blood sample to assess serum neutralizing antibodies and vaccine induced serum – and likely that these are done in hospital, but it is not clear how frequently. |
| Other factors to consider: | |
| **Who** | How might the people who collect data limit the participation of each ethnic group in the target population? | **Response:** As noted above, it is not clear how the data is collected – or by whom (presumably a member of the research team), and there is a self-completed diary.  Some data may be extracted from medical and general practice records and it is possible that some members of some ethnic groups may not want anyone (at least not an unknown member of NHS staff) going through their own medical record, or that of their family member. This may hinder participation among ethnic groups that have a lower trust in healthcare professionals, or medical research (e.g. Black Caribbean and some Asian groups– see earlier in worksheet). |
| Other factors to consider: | |
| **How** | How might data collection methods limit the participation of each ethnic group in the target population? | **Response:** Online diary will require smartphone/tablet/computer and 4G/internet connection. For those aged 16-44, recent internet users broadly similar across ethnic groups – in older ages, the [proportion in Black, Asian and minority ethnic tends to fall more quickly than in White groups](https://www.ethnicity-facts-figures.service.gov.uk/culture-and-community/digital/internet-use/latest#download-the-data). |
| Other factors to consider: | |
| **Where** | How might where data are collected limit the participation of each ethnic group in the target population? | **Response:** As above. |
| 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:** The follow-up regime is not clear from the information publicly available. |
| Other factors to consider: | |
| **Benefits** | How might the benefits of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** Not clear. These studies are likely to be too small to identify any differences and would need data from phase 3 studies. |
| 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:** These studies are likely to be too small to identify any differences between ethnic groups – particularly in terms of harms. This would need data from phase 3 studies. Differences between groups in terms of serum neutralizing antibodies and vaccine induced serum may be evident from phase 2 studies. |
| Other factors to consider: | |
| **Interim analyses** | How should any interim analysis handle variation between ethnic groups in the target population? | **Response:** As above– probably too small a study. |
| 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:** As above– probably too small a study. |
| 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:** It is not clear what dissemination is planned; information was not provided in the publicly available registration document. It is not clear from other documentation whether people from any ethnic group in the target population were involved in the dissemination plans. |
| Other factors to consider: | |
| **How** | How might planned reporting and dissemination methods limit engagement with each ethnic group in the target population? | **Response:** It is not clear what dissemination is planned; information was not provided at the time of registration.  Different methods are likely to increase engagement with ethnic groups in different ways, so there should be a variety of dissemination methods developed that are tailored to various groups of the public. Patient and public involvement and engagement would inform different approaches to this. |
| 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:** It is not clear what dissemination is planned; information was not provided at the time of registration.  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](https://centreforbmehealth.org.uk/resources/toolkits/), 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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A picture containing flower, drawing

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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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