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 Katie Banister, Seonaidh Cotton, Heidi Gardner and Shaun Treweek, University of Aberdeen. It was also discussed with three Patient and Public partners. We were not involved in designing this trial,** **we did not discuss the information on this worksheet 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–** [**http://www.isrctn.com/ISRCTN50189673**](http://www.isrctn.com/ISRCTN50189673)  **and** [**https://clinicaltrials.gov/ct2/show/NCT04381936**](https://clinicaltrials.gov/ct2/show/NCT04381936) **– and the protocol (V7), which is publicly available on the study website** [**https://www.recoverytrial.net/for-site-staff**](https://www.recoverytrial.net/for-site-staff)**.**  **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.]**  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 .  After accounting for the effect of sex, age, deprivation and region, people of Bangladeshi ethnicity have around twice the risk of death when compared to people of White British ethnicity. People of Chinese, Indian, Pakistani, other Asian, Caribbean, and other Black ethnicities had been 10 and 50% higher risk of death when compared to White British.  There are clear links between people from ethnic minority backgrounds, and poor socioeconomic status, and the trial team should therefore endeavour to ensure that the trial’s results are applicable to people from ethnic minority backgrounds, as well as people with low socioeconomic status. Men are at higher risk of death than women, older people are at higher risk than younger people, and people with existing underlying health conditions, respiratory illnesses, and diabetes are all at higher risk than people without these health issues.  **In summary**  Ideally treatments should be suitable for all those at risk from the disease, which for SARS-CoV-2 is essentially the whole population but particularly those mentioned above. Overall, the trial population should aim to look similar to UK census data on ethnic group distribution:   * 80.5% White British * 7.5% Asian * 3.4% Black * 2.2% Mixed * 5.4% Other White * 1% Other   A case could be made for over-sampling of groups most at risk. |

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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.]**  SARS-CoV-2 affects the whole community, but some ethnic groups are affected disproportionately.  The risk of infection is generally considered higher for minority ethnic groups, in large part because of where many individuals from these groups live and the jobs they often do. Public Health England data for 7th July 2020 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. Many studies have reported that ethnic minority groups are affected more severely by SARS-CoV-2, including the risk of death.  Generally speaking, several ethnic minority groups, particularly Arabic, Black African and Black Caribbean, have a deep mistrust of medical research. It is likely that some ethnic groups essential for the trial (e.g. Black Caribbean) will need to be reassured about why the research is being done and why they should consider taking part. 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 some (e.g. Black, Pakistani and Arabic Muslims) because of beliefs that a drug contains ingredients specifically designed to harm them in particular. Older people in most minority ethnic groups may 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 taking a drug that include ingredients made from animals. Moreover, health literacy is low among some ethnic groups, and this is a known barrier to seeking healthcare support.  The above means that some members of some ethnic groups essential for the trial may be reluctant to take part in the trial without additional support. |

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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.]**  All treatments will be delivered by a doctor working in the NHS. NHS doctors 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. Health beliefs (see above) may mean that care is not sought, or sought very late. Both may lead to poor outcomes.  The treatment regimens are modest given that participants will be hospitalised and likely to be receiving more intense interventions are part of their care. The treatment regimens are unlikely to play an important role in the ability of some ethnic groups to participate. | |
| 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 list of eligibility criteria is short and only one is open for interpretation (exclude on any ‘medical history’ grounds). It is more likely that recruiters may simply fail to consider some individuals for the trial for reasons of perceived practical difficulty, especially around language and communication. This 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 consent process rests heavily on written materials, which may limit the ability of some ethnic groups to take part. The written materials are available in ten languages, which will help engagement with diverse ethnic groups. The written (English) materials, especially the consent form, may be difficult for some in all ethnic groups. If recruiters cannot speak the same language as a potential participant and/or his or her family members, then the recruiter may choose not to offer participation. This will adversely affect the ability of some ethnic groups to participate. In some Asian groups (e.g. Pakistani) older women may look to their husbands or other male family member for guidance; discussions about participation will need to explicitly consider this.  It is not clear whether any members of the public from any ethnic group were involved in the selection of trial outcomes. There is overlap with a SARS-CoV-2 Core Outcome Set. All trial data are collected from routine hospital records and therefore the outcomes themselves are unlikely to limit participation of any ethnic group. These data are collected from medical records so uncertainty about who may do the data collection may prevent participation among ethnic groups that have a lower trust in healthcare professionals, or medical research (e.g. Black and some Asian groups– see above).  Measures to improve communication with non-White British ethnic groups are likely to improve the ability of people from these groups to take part. |

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:** Response: SARS-CoV-2 affects the whole community, but some ethnic groups are affected disproportionately.  The risk of infection is generally [considered higher](https://fullfact.org/health/Covid-19-inequalities-minority-ethnicities/) for minority ethnic groups, in large part because of where many individuals from these group live and the jobs they often do. [Local government data](https://lginform.local.gov.uk/reports/view/lga-research/covid-19-cases-and-area-characteristics) for England show that communities with higher proportions of Black, Asian and minority ethnic individuals living there have higher levels of COVID cases. [A study](https://pubmed.ncbi.nlm.nih.gov/32466757/) of people involved with the UK Biobank found Black and south Asian groups were more likely to test positive for COVID, with Pakistani ethnicity at highest risk. [Other data](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/908434/Disparities_in_the_risk_and_outcomes_of_COVID_August_2020_update.pdf) show that the highest age standardised diagnosis rates of COVID-19 per 100,000 population were in people of Black ethnic groups (486 in females and 649 in males) and the lowest were in people of White ethnic groups (220 in females and 224 in males).  [Public Health England data](https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/articles/coronaviruscovid19infectionsinthecommunityinengland/july2020" \l "infection-rates-by-age-sex-and-ethnicity-over-the-study-period) for 7th July 2020 did however 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 includes Black, Asian and minority ethnic individuals at the population level.  (**NB**: The above was less clear in Jan 2020 when RECOVERY was designed.) |
| 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](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) for July 2020 show that the risk of death is much higher in minority ethnic groups than in the White population.  The increase varies from an odds ratio of around 1.2 for Chinese women to over 4 for Black men. South Asians are over 3 for both men and women.  (**NB**: The above was less clear in Jan 2020 when RECOVERY was designed although experience from SARS-CoV-1 shows that people with comorbidity/chronic illness will be affected more severely, and Black, Asian and minority ethnic groups generally have greater comorbidity/chronic illness than the majority population). |
| 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 is one or more of fatigue, high temperature, new dry cough and in more severe cases, shortness of breath or difficulty breathing. Symptoms appear similar across ethnic groups. | |
| 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:** Black, Asian and minority ethnic groups are more severely affected by SARS-CoV-2. RECOVERY needs to include areas where Black, Asian and minority ethnic groups live. The trial is a very large, national trial with 176 sites across the UK; it is highly likely to be recruiting in areas with large populations of people with Black, Asian and minority ethnic backgrounds.  Recruitment of all 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: | | |
| **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](https://www.demanddiversity.co/resources), particularly Arabic, Black African and Black Caribbean, have a [deep mistrust of medical research](https://onlinelibrary.wiley.com/doi/epdf/10.1111/dme.13895) ([A recent survey](https://www.hra.nhs.uk/documents/1422/HRA_NIHR_general_public_omnibus_survey_2017_FINAL.pdf) of over 1200 people, 14% of whom were non-White, by the Health Research Authority found more positive attitudes, especially for publicly-funded research.  It is likely that some ethnic groups essential for the trial (e.g. Black African) will need to be reassured about why the research is being done and why they should consider taking part. | |
| 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:** All the trial treatments are drugs, so issues of culture are linked to views around drug treatments (both general and the ones used in the trial) and taking part in health research more generally.  Some ethnic groups have [expressed a preference](https://www.demanddiversity.co/resources) for traditional, herbal or homeopathic medicine (e.g. Indian, Arabic, Black Caribbean, Black African and Chinese).  More generally, several ethnic minority groups essential for the trial (e.g. Black Africans) have a deep mistrust of medical research (see above).  Also see *Worksheet 2*. | |
| 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, and this is a [known barrier](https://www.england.nhs.uk/wp-content/uploads/2017/07/inequalities-resource-sep-2018.pdf) 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 possible that some people in some ethnic groups will seek healthcare later in disease progression although the picture is unclear. | |
| 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. Prednisolone and azithromycin tablets both contain magnesium stearate which may be of animal origin. Convalescent plasma is introduced as part of the main randomisation in part B – Jehovah’s Witnesses will not accept blood products. Lopinavir-ritonavir is an HIV drug, and therefore issues could arise with association with HIV/AIDS in communities where these are still heavily stigmatised.  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 who are those most likely to be affected by SARS-CoV-2. |
| 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 that any members of the public from any ethnic group were involved in the selection of interventions or comparator. There are no Public and Patient partners listed on the Trial Steering Committee membership listed in the protocol (V7.0). The [ISCTRN registration](http://www.isrctn.com/ISRCTN50189673) says ‘The UK New and Emerging Respiratory Virus Threats Advisory Group (NERVTAG) advised that several possible treatments should be evaluated, including lopinavir + ritonavir, low-dose corticosteroids and hydroxychloroquine.‘ [The group](https://www.gov.uk/government/groups/new-and-emerging-respiratory-virus-threats-advisory-group#membership) does not appear to have public/patient members.  The research team may have diverse ethnic representation within it, but this is unclear. |
| 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:** All treatments are likely to be delivered by a doctor 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%](https://www.ethnicity-facts-figures.service.gov.uk/workforce-and-business/workforce-diversity/nhs-workforce/latest#by-ethnicity) 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, although the patient may be unconscious depending on disease severity.  Mode of delivery is unlikely to be a factor for RECOVERY, especially since once consent has been given, trial treatment may be indistinguishable from other procedures participants receive while in hospital. |
| 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:** All participants will be hospitalised when the intervention is delivered; this is an eligibility criterion. It means treatments will be tested in only those who have become very unwell, which seems a sensible choice for a new virus (i.e. target treatment on those most affected).  Health beliefs (see Worksheet 1) may mean that some ethnic groups’ resistance to seeking health care means care is not sought, or sought very late. Both may lead to poor outcomes. However, community-based trial delivery seems neither feasible nor safe at this stage of understanding regarding SARS-CoV-2. Not all the treatments under test are familiar drugs so a hospital environment seems appropriate.  There is a specific issue to bear in mind with regards to SARS-CoV-2 and the trial setting, which may affect RECOVERY and other SARS-CoV-2 trials. The Nightingale Hospital was set up in Newham, which has the most diverse population in Europe – over 70% of the population are Black, Asian and minority ethnic, and it has some of the poorest health outcomes and health inequalities in England. The local community were not consulted about the site of the new hospital, and the fact that it meant potentially bringing people that had the virus from all over London into their at-risk community. This may add to distrust in the NHS regarding the way Black, Asian and minority ethnic communities are viewed. |
| 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 intensity of treatment is modest given that patients are in hospital with a potentially life-threatening illness. For some participants other aspects of the care they receive (e.g. mechanical ventilation) will be far more invasive than the trial treatment regimen. Some will be unaware of the treatment because of their condition, although family members may have greater awareness.  In summary, the trial treatment regimens are considered unlikely to play an important role in the ability of some ethnic groups to participate. |
| 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 are just four eligibility criteria and the first three shouldn’t affect involvement for non-clinical reasons (one is ‘*Aged at least 18 years*’, which for SARS-CoV-2 seems appropriate given the clinical burden of the virus).  The fourth criterion (‘*No medical history that might, in the opinion of the attending clinician, put the patient at significant risk if he/she were to participate in the trial’*) could, in principle, be used consciously or unconsciously to exclude some ethnic groups depending on how broadly ‘medical history’ is interpreted. It could, for example, be used as a proxy to exclude individuals where the next stage of the trial process, consent, is considered likely to be difficult for reasons of language, health literacy or other non-clinical reason. The criterion itself, however, does state the reason should be medical.  Alternatively, recruiters may simply fail to consider some individuals for the trial for reasons of perceived later practical difficulty. See 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:** It is not clear how potential participants become aware of the trial, but it is likely that a member of healthcare or research staff mentions the trial directly to the potential participant, or to a family member. 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 participant information leaflet and consent form are available in ten languages.  The training video on the RECOVERY website makes it clear that written material is a key part of the information provision for the trial. This 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. For the English materials, the written information is not particularly easy to read; the Flesch-Kincaid Grade Level score of the basic participant information sheet is >10, which is higher than recommended for public-facing materials (7 – 8). Even with translation, older people from some ethnic groups do not read the language they speak.  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 (See 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 that members of the public from any ethnic group have been involved in preparing the written materials, or influenced what staff tell potential participants. Differences regarding attitudes to the benefits/need for health research generally and concerns about drugs ingredients for some (e.g. Black and some Asian groups, see Worksheet 1) will probably limit their participation unless addressed in writing or verbally. Translation of material needs to consider these issues in addition to simple translation from one language into another.  In [some Asian groups](https://www.demanddiversity.co/resources) (e.g. Pakistani) older women may look to their husbands or other male family member for guidance; discussions about participation will need to explicitly consider this. |
| 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:** It is not clear that 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. For the English version, the consent form is not easy to read: the Flesch-Kincaid Grade Level score of the basic consent form is >17, higher than the participant information leaflet and much higher than recommended for public-facing materials (7 – 8). Written consent may limit participation of some groups (e.g. South Asians) who may prefer verbal discussion to written documents. | |
| How might the way people would like to discuss participation with family before providing consent differ for each ethnic group? | **Response:** Some ethnic groups (e.g. South Asians) are more likely to want to involve family in decisions and this may limit their ability to take part if this cannot happen (which may be the case for potential participants who are very ill and for whom consent needs to be given quite quickly, or with social distancing measures seen with SARS-CoV-2). An awareness of the likely need to explicitly involve other family members, especially for older South Asian women and Arabic women, would help recruitment of individuals from these groups. | |
| How might the way the research team can check how well consent information is understood differ for each ethnic group? | **Response:** 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**

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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. There are no patient and public contributors listed on the Trial Steering Committee membership listed in the protocol (V7.0). Some of the outcome data collected match those recommended by the [SARS-CoV-2 trial Core Outcome Set](https://pubmed.ncbi.nlm.nih.gov/32292626/) available in Jan 2020 although that study did not involve the public or patients (or health professionals). |
| 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:** All trial data are collected from routine hospital records and therefore the outcomes themselves are unlikely to limit participation of any ethnic group as the data are being collected anyway as part of care delivery. |
| Other factors to consider: | |
| **Who** | How might the people who collect data limit the participation of each ethnic group in the target population? | **Response:** Having consented to take part, participants will be unaware of who is collecting their data as it extracted from their medical record. It is possible that some members of all ethnic groups may not want anyone (at least not an unknown member of NHS staff) going through their medical record, or that of their family member.  The uncertainty of who may do the data collection may prevent participation among ethnic groups that have a lower trust in healthcare professionals, or medical research (e.g. Black and some Asian groups– see Worksheet 1). |
| Other factors to consider: The cultural awareness of the person extracting data may limit a person’s ability to interpret data as being relevant in the medical record, depending on what is to be extracted. For the objective data collected in RECOVERY this may not be an issue. | |
| **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 from the medical record, (see above) 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:** 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**

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| **Retention** | How might the trial data available for participants differ between each ethnic group in the target population? | **Response:** As data collection is from routine medical records, and short (up to 28-days post randomisation) retention is probably less of a problem than recruitment. Once in the trial, data collection ought to be as good (or bad) as routine medical record keeping. |
| Other factors to consider: | |
| **Benefits** | How might the benefits of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** We do not have enough information about how the virus impacts ethnic groups biologically to understand how the effect of trial drugs may differ between ethnic groups. From what is currently known, it appears that structural/social/cultural factors are more likely to be the root of why Black, Asian and minority ethnic communities are being disproportionately affected by SARS-CoV-2, which suggests that the drugs would not differ based on biology.  (**NB**: The above was less clear in Jan 2020 when RECOVERY was designed.) |
| 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 disproportionate effects of SARS-CoV-2 on Black, Asian and minority ethnic groups.  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 there is no set sample size for RECOVERY), and it is unlikely to be feasible to fully power any subgroup analyses.  (**NB**: The disproportionate effect of SARS-CoV-2 for Black, Asian and minority ethnic individuals was less clear in Jan 2020 when RECOVERY was designed.) |
| 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:** It doesn’t look like patient and public partners from any ethnic group were involved with the planning of reporting and dissemination of the trial results. There are no patient and public contributors listed on the Trial Steering Committee membership listed in the protocol (V7.0). |
| Other factors to consider: | |
| **How** | How might planned reporting and dissemination methods limit engagement with each ethnic group in the target population? | **Response:** The protocol (V7.0) details only scientific publications, which limits engagement with all ethnic groups. It is likely that the mainstream media will pick up on these results quickly, but other dissemination and reporting methods should be planned to ensure that specific ethnic groups (i.e. those that are being disproportionately impacted by SARS-CoV-2) have access to the results in a way that suits them.  The reporting and dissemination methods described in the protocol also appear to be largely one-way communication methods. As the trial focuses on a public health emergency, two-way communication methods would be the preferred method – allowing members of all ethnic groups to engage with the trial results, rather than just be told about them. 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. |
| 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:** Similar to the points made above – 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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