Ensuring your trial is designed for all who could benefit

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

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

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

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

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

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

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

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

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

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

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

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| **1. Who should my trial results apply to?** |
| **[NB. Completed by Heidi Gardner and Shaun Treweek, University of Aberdeen. The general approach to presenting information was also discussed with two Patient and Public partners, though not the detail of the information provided here. We were not involved in designing 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–** [**http://www.isrctn.com/ISRCTN86534580**](http://www.isrctn.com/ISRCTN86534580)**;** [**https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001209-22/GB#A**](https://www.clinicaltrialsregister.eu/ctr-search/trial/2020-001209-22/GB#A) **and the protocol (V3)** [**https://www.principletrial.org/health-professionals/secondary-and-ambulatory-care**](https://www.principletrial.org/health-professionals/secondary-and-ambulatory-care)**.**  **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 between 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.]**  It is unclear whether different ethnic groups will respond differently to the treatments and comparator being testing in this trial, it is also unclear whether different ethnic groups present with different symptoms.  The current evidence-base suggests that biological differences are unlikely to account for differences observed around the stage at which people access the healthcare system. We know that the overall health status of people from ethnic minority backgrounds is poorer than their White British counterparts, largely due to poor socioeconomic status, poor housing and various other factors that ultimately result from systemic racism.  There is a significant evidence-base to suggest that people from ethnic minority groups are less likely to seek healthcare than their White British counterparts, this means that the health outcomes for people in these groups are likely to be poorer. The response to treatment may therefore differ due to the stage at which people from ethnic minority groups present with symptoms. |

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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 patient partners (from any ethnic group) were involved with the selection or design of the trial interventions or comparator.  The interventions and comparator themselves throw up potential issues for a variety of people. Currently the drugs being tested are azithromycin and doxycycline. These may come in capsule form, the capsule itself can contain animal products, and religious beliefs may therefore prevent certain groups (e.g. Sikhs, Hindus) from taking them. There are vegetarian and vegan alternatives, so it is important that the trial team bears that in mind when explaining the trial drugs to potential participants and also when they are sourcing the drugs for the trial.  The interventions and comparator are all delivered to the participant’s home through the post, which could be a positive or a negative for potential participants – the lack of health professional involvement could improve participation of people from ethnic minority backgrounds (explained previously). The commitment needed for treatment adherence seems fairly limited and is unlikely to limit participation of people from any ethnic group. | |
| 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 first trial feature that may make it harder for groups from ethnic minorities to take part is the short online form (presented in English only) that potential participants complete to see if they are eligible to take part. This can be done by telephone, but the focus is definitely on the trial website. This makes it difficult for people that do not have internet access, are not computer literate, and/or are unable to read written English to a high level. This online questionnaire is the main way that people come to the trial, which again means that the trial team are reducing the potential participant pool available to them. This use of written English is commonplace throughout the trial – there is no evidence of consent forms or the text messages that are used to collect data being translated or available in languages other than English. The participant information sheet is available in various languages (Bengali, French, Polish, Portuguese, Punjabi, Urdu and Welsh), which highlights that the trial team anticipate that these resources will be required.  As well as collecting data using text messages, the trial team is also using data from routine medical records. This is a potential issue for some ethnic groups that distrust healthcare, medical and/or research professions (e.g. Black African, Arabic, Black Caribbean) and which are crucial for the trial.  Participation of people from ethnic minority backgrounds, particularly from the older age demographic (i.e. the group that PRINCIPLE is aimed at), is therefore likely to be limited as a result of linguistic limitations and distrust of medical and research professionals. |

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 affects the whole community, but some ethnic groups are affected disproportionately.  Highest age standardised [diagnosis rates of COVID-19](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) 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). Causes appear to be multiple – lower socio-economic groups, multi-family and multi-generational households, disproportionate employment in lower-band key worker roles, and co-morbidities (especially cardiovascular, diabetes, renal and complex multi-morbidities).  (**NB**: The above was less clear in Mar 2020 when PRINCIPLE 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. People of Chinese, Indian, Pakistani, other Asian, Caribbean and other Black ethnicity had between [10 and 50% higher risk](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) of death when compared to White British during the period 21/3/2020 – 8/5/2020.  Comparing to previous years, all-cause mortality was almost 4 times higher than expected among Black males for this period, almost 3 times higher in Asian males and almost 2 times higher in White males. Among females, deaths were almost 3 times higher in this period in Black, Mixed and other females, and 2.4 times higher in Asian females compared with 1.6 times in White females.  (**NB**: The above was less clear in Jan 2020 when PRINCIPLE 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.  The key difference is that Black, Asian and minority ethnic individuals may well present with more severe disease, because of e.g. higher incidence of chronic diseases and multiple long-term conditions such as diabetes. | |
| 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. PRINCIPAL needs to include areas with large Black, Asian and minority ethnic communities – big English cities such as London, Birmingham, Bradford, Manchester and Leicester would be obvious starting points. The trial is national so geography should not be a problem.  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: Socio-economic factors are likely to be the root cause of the disparity rather than ethnicity itself; systemic racism contributing to the socio-economic factors. | | |
| **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. Some [UK politicians](https://www.bbc.co.uk/news/uk-politics-53612230) have made remarks likely to stigmatise minority groups in [Leicester](https://theconversation.com/leicester-lockdown-blame-on-minority-communities-needs-to-be-challenged-142418) and Manchester.  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) stemming from a history of systemic racism within the medical and research worlds. 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 important that the trial team provide clear, transparent information about the trial – why it is being done, what any potential participant may be asked to do, and clarity around potential benefits and harms. | |
| 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.  The trial is testing a variety of drugs that are readily used within the NHS already – currently the drugs being tested are azithromycin and doxycycline. These may come in capsule form, the capsule itself can contain animal products, religious beliefs may therefore [prevent certain groups](https://www.demanddiversity.co/resources) (e.g. Sikhs, Hindus) from taking them. There are vegetarian and vegan alternatives, so it is important that the trial team bears that in mind when explaining the trial drugs to potential participants and also when they are sourcing the drugs for the trial.  More generally, several ethnic minority groups essential for the trial (e.g. Black Africans) have a deep mistrust of medical research (see above). | |
| 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. This means that individuals from ethnic minority communities may present at hospital later than their White counterparts, which is likely to lead to increased complications and poorer health outcomes. | |
| 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.  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 whether any members of the public from any ethnic group were involved in the selection of interventions or comparator. There are two patient and public members on the Trial Steering Committee.  Part of the study is a blood test, which though optional may be perceived as more of a concern for some participants, especially those with a distrust of state systems such as the NHS (e.g. Black Caribbean). |
| 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 interventions/comparators are delivered to the participant’s home through the post. It is not clear whether this will have any impact on the trial with regard to participation of different ethnic groups.  It would likely be helpful if the parcel that the trial materials are sent in is discretely labelled so that the postal workers, other members of the household etc do not immediately know what it inside – this may not make a difference, but it seems like a good idea as it wouldn’t cost more than branded packaging and may help the participant to maintain privacy should they want it. |
| 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:** All interventions/comparators are delivered to the participant’s home through the post. It is not clear whether this will have any impact on the trial with regard to participation of different ethnic groups.  The trial asks for the participant to name a Trial Partner that can be contacted in the event that the trial participant themselves cannot be contacted, again it is not clear if this will have a positive or negative impact on the trial.  The lack of healthcare professional involvement may be a positive for people from ethnic minority communities due to the distrust discussed earlier, but it could also make people feel less comfortable about taking part in the trial –people that trust the healthcare system and readily use it may be less likely to participate. |
| 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 interventions/comparators are delivered to the participant’s home through the post. It is not clear whether this will have any impact on the trial with regard to participation of different ethnic groups.  Assuming an individual does not think the lack of a healthcare professional is a minus (see above), delivery at home may help participation across all or many ethnic groups. |
| 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:** All trial participants will be isolating at home, and with a modest commitment of taking drugs a few times a day, this doesn’t seem like it will limit participation of people from ethnic minority groups. |
| 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 first barrier is a short online form that potential participants must complete to see if they are eligible for the trial. This can be done by telephone too, but the preferred route appears to be to the online format – difficult for those of all ethnic groups who don’t have internet access at home, or who are not computer literate. [UK Gov data](https://www.ethnicity-facts-figures.service.gov.uk/culture-and-community/digital/internet-use/latest#by-ethnicity-and-age-group) suggest that internet access by 65-74 is 20% lower for Asians (around 65%) than for White British population; data for Black and mixed ethnic background are withheld because of low numbers. Access for age 50-64 is high for all ethnic groups.  The criteria themselves are:   * Have had COVID symptoms for fewer than 15 days, or had a positive test for COVID which was taken fewer than 15 days ago, AND have been unwell with symptoms for fewer than 15 days. * Aged 50-64 with at least one of the following symptoms: weakened immune system, heart disease or high blood pressure, asthma or lung disease, liver disease, diabetes not treated with insulin, stroke or neurological problem. Or if you are aged 65 or over and have symptoms of COVID.   Those two points do not appear to limit participation by ethnic groups. The two other inclusion criteria are being able to consent, and being willing and able to comply with the trial protocol, which may limit participation of some. The participant information leaflets are available in various languages (Bengali, French, Polish, Portuguese, Punjabi, Urdu and Welsh) alongside the standard English version, but the consent form only appears to be available in English, which could be problematic.  Trial procedures are centred around text messages and online questionnaires. Telephone contact with the trial team is mentioned but as a last resort rather than the normal process for the trial, which could be an issue. There is also no information on whether the trial materials themselves (content of text messages etc.) is available in languages other than English, which could easily disadvantage the people that have understood the study using one of the participant information leaflets in a language other than English. |
| 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:** Potential participants can primarily either join the trial directly by going to the study website or are signposted to the trial team and website by their GP practice. Posters in clinics, social media, and website news items can also all signpost potential participants towards the trial website. It looks like all/most of this information is only available in English, which may limit awareness among some ethnic groups. Eligible participants of all ethnic groups are likely to have been isolating so are unlikely to see posters in clinics.  The first point of contact seems to be a short online form that potential participants must complete to see if they are eligible for the trial. This may limit participation of some groups– see above.  Self-referral is likely to be the primary way that potential participants will have come to the trial, and written materials are the focus here – the website, written information leaflet etc. The participant information sheet is available in various languages (mentioned above), but there is nothing on the website to suggest that any of trial materials have been translated. This will be an issue for people from various ethnic minority backgrounds, particularly those that are older (which are the target group for this trial).  The opportunity to participate is largely self-led, which means those who have a general distrust of medical research (e.g. Arabic, Black Caribbean, Black African) may be unlikely to join. |
| How might the information that tells potential participants about the trial (e.g. participant information leaflet) limit the participation of each ethnic group? | **Response:** Written materials are the focus here – the website, written information leaflet, text messaging etc. The participant information sheet is available in various languages, but there is nothing on the website to suggest that any of written materials have been translated– see above.  The telephone option that is mentioned on the PIS may be useful to try and mitigate the impact of lack of translated written materials, but that relies heavily on having trial staff that can speak the same language as potential participants. There is no mention of availability of translators or staff that can speak specific languages, so it appears that the emphasis is on written materials which may limit participation.  For those that can read English (older people may be able to speak it but can’t read it), the written materials are presented in such a way that they exclude people with low literacy levels - the Flesch-Kincaid Grade Level score of the participant information sheet is >10, which is higher than the recommended score of 7 – 8. This not only excludes people of various ethnic groups, but it also excludes fluent English speakers that have poor literacy levels.  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:** Issues such as health literacy, involvement in health research, and ingredients of the drugs that are being tested should all be covered in the written materials that are provided. These are not covered in the English version but may be covered in the translated information leaflets, but we were unable to check. Translations need to include cultural translations to encompass the issues mentioned above as well as linguistic translation. |
| 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 if 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. It is not clear if the consent documents have been translated into multiple languages, which may be a significant issue for potential participants who needed to use a participant leaflet in a language other than English.  For those who can read English (older people may be able to speak it but can’t read it), the written materials are presented in such a way that they exclude people with low literacy levels - the Flesch-Kincaid Grade Level score of the participant information sheet is >10, which is higher than the recommended score of 7 – 8. This not only excludes people of various ethnic groups, but it also excludes fluent English speakers that have poor literacy levels. | |
| How might the way people would like to discuss participation with family before providing consent differ for each ethnic group? | **Response:** People from some ethnic groups – particularly the older members of their communities that this trial focuses on – are likely to want to consult with members of their family, or perhaps other members of their community (religious leaders for example). The consent process is done at the participant’s home so this should be fine. | |
| How might the way the research team can check how well consent information is understood differ for each ethnic group? | **Response:** It is not clear how the research team will understand how well consent information has been understood for any ethnic group as it is done online for most people. Consent is usually done online, but in some cases will be done over the telephone – if this is the case then the staff member may be able to check understanding verbally, but this relies on that staff member being able to speak the same language as the potential participant. | |
| 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 two patient and public members on the Trial Steering Committee.  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 non-academic 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:** Most of the data are collected from routine medical records – the data collection itself, therefore, should not limit the participation of any ethnic group. The recruitment of participants could be a barrier with routinely collected data (see Worksheet 2), but once the participants are in the trial they are not required to do active data collection for the majority of the trial.  The daily diary may limit participation, but this is a method issue rather than a content issue – discussed later. It is not clear what other data are collected. |
| Other factors to consider: | |
| **Who** | How might the people who collect data limit the participation of each ethnic group in the target population? | **Response:** Collection of data will be done through medical records, so no face to face issue. The only issue that may come up is if participants or their families are not comfortable with the trial team (i.e. an unknown group of people) having access to their medical records. This is likely to limit participation of Black individuals, and some Asian individuals as they are known to trust medical and research professionals less. |
| 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 from the medical record, (see above) the data extraction process itself is unlikely to limit participation of any ethnic group.  The other part of data collection is the daily diary which is done through daily text messaging. This may limit participation for communities that don’t have a mobile phone, a contract or top-up facility to enable them to pay for text messages, and some degree of fluency in English (distinction between written and spoken here – some older people from Black, Asian and minority ethnic backgrounds may speak English well but struggle with reading it). |
| 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 most data collection is from routine medical records, and short (up to 28-days post treatment completion) retention is probably less of a problem than recruitment.  The exception is the daily diary– See Worksheet 3a. |
| Other factors to consider: | |
| **Benefits** | How might the benefits of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** It is not clear how the virus impacts ethnic groups biologically in order 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 March 2020 when PRINCIPLE 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.  As with all sub-group analyses, it is unlikely that this trial will be able to fully power these investigations, but if these are built into COVID-19 trials going forward then data could potentially be pooled.  (**NB**: The disproportionate effect of SARS-CoV-2 for Black, Asian and minority ethnic individuals was less clear in March 2020 when PRINCIPLE 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. |
| 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 is not clear whether any patient partners from any ethnic group were involved with the planning of reporting and dissemination of the trial results, and the dissemination activities themselves are not clear as information is not listed on the website, the protocol, or the registration documentation.  There is a news section on the website. |
| 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.  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:** It is not clear what dissemination is planned.  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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