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?

|  |
| --- |
| **1. Who should my trial results apply to?** |
| **[NB. Completed by Sarah Prowse, 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 document used regarding the trial was the registration document –** [**https://www.isrctn.com/ISRCTN11343602**](https://www.isrctn.com/ISRCTN11343602) **and the NHS HRA research summary -** [**https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/the-bhf-senior-rita-trial/**](https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/the-bhf-senior-rita-trial/)**.**  **Given the above, the information in the worksheets may not be a proper reflection of the trial because we did not have access to all the trial materials. The information is therefore intended to be illustrative, not definitive.]**  The SENIOR RITA trial funded by the British Heart Foundation was a UK based study to evaluate the benefit of medical therapy versus angiography and stenting in patients ≥ 75 years of age who were admitted to a participating hospital with cardiac arrest (heart attack).  The aim of the study was to find out whether undergoing a procedure called an angiography (which shows whether there are any blockages in the heart arteries) as well as the latest medications recommended in heart attack is a more effective treatment strategy than medication alone in terms of prolonging life.  The [Office for National Statistics](https://www.ons.gov.uk/aboutus/transparencyandgovernance/freedomofinformationfoi/suddencardiacarrestdeathsbrokendownbyethnicity), which holds mortality data for England and Wales, is unable to provide any bespoke analysis on heart attack which includes ethnicity citing the complex data linkage methods involved. More broadly, research from [The King’s Fund](https://www.kingsfund.org.uk/publications/health-people-ethnic-minority-groups-england#cvd) published in 2023 based within the UK consistently found a higher incidence, prevalence, and mortality rate from heart disease generally in South Asian groups compared with White European groups or the national average.  South Asian groups were found to have the highest mortality from heart disease and develop heart disease at a younger age. This pattern may be associated with a higher clustering in South Asians of risk factors that increase the overall risk of heart disease. In contrast, Black ethnicities in the UK were found to have a significantly lower risk of heart disease compared to much of the population.  Heart disease is the UK’s most common cause of death overall. Cardiovascular disease (CVD) is an umbrella term referring to all diseases of the heart and blood vessels. Coronary heart disease (CHD) is when the coronary arteries that supply the heart muscle with blood become narrowed or blocked due to a gradual build-up of fatty material. CHD is the most common type of CVD and the most common cause of heart attack.  Previous studies suggest that older patients (≥ 75 years of age) are not well represented in clinical research and these patients, particularly those that are frail and those suffering from other conditions, are less likely to receive advanced medications and medical procedures. Observational research presented at the [British Cardiovascular Society annual conference in 2024](https://www.britishcardiovascularsociety.org/conference/home) also found ethnic minority heart failure patients within the UK were 36% more likely to die than White Europeans when following the current standard of care.  [Data from 2004](https://www.bhf.org.uk/~/media/files/research/heart-statistics/hs2010fc_ethnic_differences_in_cardiovascular_disease-full-copy.pdf) show that for the 55+ age group the prevalence of CVD and CHD by ethnicity are as follows:    Given the wide variety of underlying mechanisms that may lead to a heart attack and the inability to find absolute numbers for cases by ethnicity, it is suggest that the proportion of South Asian adults (emphasis on those who are Indian, Pakistani, and Bangladeshi) in the trial should not have been less than 10% given known risk factors and age data. There is a case for over-sampling South Asian individuals to allow greater certainty regarding conclusions drawn from their participation in the trial. The final enrolment number for the trial was 1516. |

|  |
| --- |
| **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.]**  There is [some evidence](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7646689/) from the US that South Asians think heart attacks and heart disease cannot be prevented. Fatalism has been mentioned as a commonly held belief among South Asians.  In [one comparative study of cancer patients](https://bmjopen.bmj.com/content/3/6/e002650.long), British South Asians more frequently used fatalism as a disease coping strategy than British Whites. This might have relevance for attitudes towards heart disease as well.  Perceptions from other ethnic groups are unclear.  More generally, a general distrust in research may reduce the willingness of ethnic minority individuals to take part in a trial. |

|  |  |
| --- | --- |
| **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.]**  If patients agree to participate, they will be randomly allocated to one of two treatment groups. In the first group, patients will receive the latest medications recommended in heart attack. In the second group, in addition to these medications, patients will have coronary angiography. This will show whether they have any blockages in the arteries of the heart.  If appropriate, coronary revascularisation by percutaneous coronary intervention commonly known as coronary angioplasty or coronary artery bypass grafting, sometimes called CABG (a surgical procedure in which a blood vessel from the leg, arm or chest is used to bypass a narrowed section of a coronary artery) will be carried out.  Patients will be invited to attend research clinics for follow-up visits where feasible. Where this is not feasible, alternatives include postal questionnaires, telephone engagement or home visits by the research team to obtain follow-up data from patients.  To what extent the intervention had been developed together with patients from different ethnic groups is unclear. No mention of translation is mentioned, which could be a problem, particularly for an older South Asian demographic. Moreover, the intervention would need cultural tailoring. Surgical interventions require a measure of post-operative care, the perceptions of which may vary by ethnicity.  [In a 2022 study](https://www.magonlinelibrary.com/doi/abs/10.12968/bjca.2021.0109) reporting the experiences of the cardiac rehabilitation journey among South Asian patients in the British Journal of Cardiac Nursing, it was found that the content of cardiac rehabilitation programmes lacked cultural sensitivity, which influenced both adherence and perceived relevance. It would be useful to know to what degree there are differences between ethnic groups in attitudes to the components of the intervention.  There is also no one-size-fits-all approach to the proposed follow-up as related to ethnicity. [The 2022 study from the British Journal of Cardiac Nursing](https://www.magonlinelibrary.com/doi/abs/10.12968/bjca.2021.0109) also found invitations to attend and participate in cardiac rehabilitation must be personalised, accounting for cultural influences on lifestyle and, in this case, the ability to fully participate within the confines of the trial.  This is consistent with earlier findings on the [illness beliefs of patients of South Asian origin living in the United Kingdom](https://www.sciencedirect.com/science/article/pii/S0147956307000799) as related to coronary heart disease which found misconceptions about the cause of CHD and a lack of understanding about appropriate lifestyle changes were evident across ethnic groups (Pakistani-Muslim; Indian-Hindu; Indian-Sikh; White Europeans). Findings from the study suggest that the key to progression is for health care professionals to know when ethnicity makes a difference and mediates a person’s relationship with service support and when it does not. | |
| 1. **Will the way I have planned and designed my trial make it harder for any of the groups identified in Question 1 to consider taking part?** [**( VIEW WORKSHEET )**](#WorksheetTHREEA) |
| **[This question has been answered with a focus on ethnicity for the purposes of this example, though the questions have wider relevance than ethnicity.]**  It is unclear how participants became aware of the trial. One likely route is that a clinician in one of the participating centres invited a person to take part. A patient information sheet is noted on the trial registry as not available in web format and can only be obtained by contacting the trial team directly.  Within the exclusion criteria are scenarios in which neither the patient nor the consultee are able and willing to provide written informed consent. This may lead to some ethnic minority groups being disproportionately affected dependent on the language skills of both potential participants and clinical staff.  No further details on the consent collection process are provided. Assuming consent is written and since translation/interpretation is not mentioned, we can also assume this process is in English. As mentioned above, language issues (both world language and culturally-tailoring) may limit the participation of some ethnic minority individuals.  As seen in Question 3, participants will be invited to attend follow-up research clinics where feasible. This raises practical considerations of accessibility such as site locations, transportation, and appointment times. These concerns are like those [seen in other screening programs](https://doi.org/10.1093/eurpub/ckae073) that may disproportionately affect those from diverse ethnic backgrounds and/or those living in rural/remote communities.  The trial also notes on-site visits can be substituted with telephone or in-person home visits, in addition to the use of questionnaires. Again, the importance of translation if required (or additional social support) should be considered at the outset of the trial as should appropriate cultural tailoring of the questions asked during such engagement.  [Work in the UK on home visits by healthcare professionals](https://onlinelibrary.wiley.com/doi/10.1111/hsc.12233) for new South Asian parents suggested that services were not always perceived to be aligned to participants’ cultural values and beliefs around, for example, sensitivity about revealing personal matters to strangers and involving men in women’s health issues. It is plausible that people from different ethnic groups may have different perspectives on health professionals coming to their homes to conduct similar research following cardiac arrest, and whether this is an acceptable form of follow-up. |

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**

|  |  |  |
| --- | --- | --- |
| **Disease** | How might the prevalence of the disease vary between each ethnic group in the target population? | **Response:** The burden of cardiovascular disease is significant regardless of ethnicity. Studies have shown that 80 per cent of the global burden of CHD can be attributed to [five coronary risk factors](https://raceequalityfoundation.org.uk/wp-content/uploads/2018/03/health-brief16.pdf), all of which are relevant to the UK. Most are potentially modifiable: these are abnormal concentration of cholesterol (and other related substances found in the body), diabetes mellitus, cigarette smoking, hypertension (or high blood pressure) and lack of physical exercise. There is less evidence to explain differences in the potency of individual risk factors across distinct groups, such as individuals from different ethnic groups or younger or older adults.  South Asians living in the UK have a high rate of CVD compared to the majority population. [Work done in the UK in the 1980s](https://www.bhf.org.uk/what-we-do/our-research/research-successes/ethnicity-and-heart-disease) found that first-generation South Asians living in the UK have a higher rate of coronary heart disease (and diabetes) compared to White Europeans. [More recent data show the same pattern](https://raceequalityfoundation.org.uk/wp-content/uploads/2018/03/health-brief16.pdf) (e.g. South Asians living in Scotland have a 60-70 per cent higher incidence of acute myocardial infarction (heart attack) than the general population. Women of South Asian origin do not seem as protected from CVD as women in the general population. Further, young men of South Asian origin experience a high relative risk, at a younger age, compared to those of the majority population.  The [link between heart disease and diabetes is especially strong](https://raceequalityfoundation.org.uk/wp-content/uploads/2018/03/health-brief16.pdf). The prevalence of Type 2 diabetes, for example, shows marked differences among ethnic groups. Almost one in five people of South Asian origin living in the UK develop diabetes, compared to one in twenty-five among the general population. Diabetes onset is earlier in South Asians (46 vs 57 for White individuals), and at a lower BMI than White European individuals.  Although heart disease is common among people of South Asian origin, there is uncertainly as to why. [Four interrelated explanations](https://raceequalityfoundation.org.uk/wp-content/uploads/2018/03/health-brief16.pdf) emerge: people of South Asian origin are more susceptible to established CHD risk factors; they are more likely to experience established CHD risk factors; there are more specific risk factors, which are not known about; and there are fewer competing causes of death in middle-aged people of South Asian origin.  In contrast to South Asian groups, [Black groups in the UK have a significantly lower risk of heart disease compared](https://www.kingsfund.org.uk/publications/health-people-ethnic-minority-groups-england#CVD) to the majority of the population, despite having a high prevalence of hypertension and diabetes (risk factors for heart disease and stroke). Lower cholesterol levels among people of African Caribbean heritage than White Europeans may protect them against heart disease. Heart disease rates are low in sub-Saharan Africa and the Caribbean.  In summary, CHD is more prevalent in South Asians than in the majority UK population, but less prevalent in Black individuals. While this trial focused on treatment for cardiac arrest, there is little data available regarding ethnicity and cardiac arrest within the UK generally. |
| How might the severity of the disease vary between each ethnic group? | **Response:** Broadly, mortality from CVD is decreasing in the UK but remains the leading cause of death. A closer look at data documenting the decline in CVD mortality shows that [the *rate* of decline is inconsistent across different groups within the population](https://raceequalityfoundation.org.uk/wp-content/uploads/2018/03/health-brief16.pdf).  CVD mortality for men aged between twenty and sixty-nine years living in England fell by 29 per cent between 1971 and 1991. For men living in England but born in South Asia, the decline was considerably less (20 per cent).  A similar trend was evident for women. See also the [Kings Fund report](https://www.kingsfund.org.uk/publications/health-people-ethnic-minority-groups-england#CVD), which comes to the same conclusions. [Data published by the UK government](https://www.gov.uk/government/publications/the-report-of-the-commission-on-race-and-ethnic-disparities-supporting-research/ethnic-disparities-in-the-major-causes-of-mortality-and-their-risk-factors-by-dr-raghib-ali-et-al) show that mortality from CHD is significantly worse for South Asians than White individuals but significantly better for Black individuals.  Observational research presented at the [British Cardiovascular Society annual conference in 2024](https://www.britishcardiovascularsociety.org/conference/home) found ethnic minority heart failure patients were 36% more likely to die than White Europeans. This includes ethnic minority patients with atrial fibrillation, who were more than twice as likely to die than White patients. |
| How might the disease present in people from each ethnic group (this may include symptoms, type or pattern or rate of disease progression)? | **Response:** As mentioned above, diabetes is a risk factor for CVD and age at diabetes diagnosis is younger in South Asians by about 10 years (46 vs 57) compared to White individuals, and at lower BMI. The increased risk of diabetes may mean younger South Asians present with CVD than for other ethnic groups.  [There is evidence that CVD risk scores used in the UK do not work well for ethnic minority individuals](https://heart.bmj.com/content/100/1/60). QRISK2 under-predicted risk in South Asian and European men and women, while Framingham under-predicted risk in South Asian women and over-predicted in African Caribbeans. Classification was particularly poor in African Caribbeans. For South Asian women, QRISK2 high risk classification was also poor and would have predicted only one third of events. The study noted that future work should give particular attention to identifying high risk South Asian populations. | |
| How close is the match between each ethnic group living with the disease and the ethnic groups living in the areas where the trial is to be run? | **Response:** The trial was led by the Newcastle Clinical Trials Unit at Newcastle University. The trial registry notes the study will be conducted at the Freeman Hospital (Newcastle upon Tyne) and 24 other NHS hospitals in England, Scotland, and Wales. The majority of participating hospitals were located in England (16/24); followed by Scotland (7/24); and Wales (2/24).  None of the listed centres were within Greater London. According to the 2021 Census, [London was the most ethnically diverse region in England and Wales](https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/national-and-regional-populations/regional-ethnic-diversity/latest) with more people from the black, Asian, mixed and ‘other’ ethnic groups living in London than anywhere else (36.8% White British). The other study areas were much less reflective of ethnic diversity – Wales (90.6% White British); West Midlands (71.8% White British); North East (90.6% White British); and areas in the South East (78.8% White British) and South West (87.8% White British). [Scotland’s Census for 2011](https://www.scotlandscensus.gov.uk/census-results/at-a-glance/ethnicity/) found that Scotland’s population was 96.0% White with 91.8% of people identifying as ‘White: Scottish’ or ‘White: Other British’.  It would be sensible to check local site populations against the overall disease burden but given the importance of South Asians in a trial in which heart disease is a key underpinning factor, these sites may not all be a good match between the ethnic groups needed and where the trial is recruiting. | |
| 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:** There is [some evidence](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7646689/) from the US that South Asians think heart attacks and heart disease cannot be prevented. Fatalism has been mentioned as a commonly held belief among South Asians. In [one comparative study of cancer patients](https://bmjopen.bmj.com/content/3/6/e002650.long), British SAs more frequently used fatalism as a disease coping strategy than British Whites. This might have relevance for attitudes towards heart disease as well.  Perceptions from other ethnic groups are unclear.  In terms of trial participation, generally, trials are known to lack diversity – much of this may be down to lack of trust in the medical and research systems due to historical abuse and exploitation of Black and minority ethnic populations. [Research](https://www.diabetes.org.uk/resources-s3/2017-11/south_asian_report.pdf) has shown that South Asians are often explicitly excluded from research due to perceived cultural and communication difficulties. It has also been shown that many [South Asian people are unwilling to participate](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2571097/) because they accept their illness as an unalterable punishment from God, or have a fear of what research entails. | |
| How might ways of describing the disease be different for each ethnic group? | **Response:** It is uncertain whether terms other than ‘heart disease’, ‘cardiac arrest’, and/or ‘heart attack’ may be used by some ethnic groups. | |
| How might cultural practices, beliefs and traditions influence the acceptability of, and adherence to, the treatment(s) for each ethnic group? | **Response:** [In a 2022 study](https://www.magonlinelibrary.com/doi/abs/10.12968/bjca.2021.0109) reporting the experiences of the cardiac rehabilitation journey among South Asian patients in the British Journal of Cardiac Nursing, it was found that the content of cardiac rehabilitation programmes lacked cultural sensitivity, which influenced both adherence and perceived relevance. It would be useful to know to what degree there are differences between ethnic groups in attitudes to the components of the intervention including potential surgical intervention.  There is also no one-size-fits-all approach to the proposed follow-up as related to ethnicity, which incorporates attending clinics or telephone consultations, or home visits. [The 2022 study from the British Journal of Cardiac Nursing](https://www.magonlinelibrary.com/doi/abs/10.12968/bjca.2021.0109) also found invitations to attend and participate in cardiac rehabilitation must be personalised, accounting for cultural influences on lifestyle and, in this case, the ability to fully participate within the confines of the trial.  This is consistent with earlier findings on the [illness beliefs of patients of South Asian origin living in the United Kingdom](https://www.sciencedirect.com/science/article/pii/S0147956307000799) as related to coronary heart disease which found misconceptions about the cause of CHD and a lack of understanding about appropriate lifestyle changes were evident across ethnic groups (Pakistani-Muslim; Indian-Hindu; Indian-Sikh; White Europeans). Findings from the study suggest that the key to progression is for health care professionals to know when ethnicity makes a difference and mediates a person’s relationship with service support and when it does not. | |
| How or when might people in each ethnic group access healthcare for this disease differently? | **Response:** [Recent evidence](https://www.kingsfund.org.uk/publications/health-people-ethnic-minority-groups-england#CVD) suggests that greater awareness among health care providers of the CVD risk in South Asian populations, earlier diagnosis and improved management of diabetes and CVD, together with second-generation adopting healthier lifestyles than first-generation migrants, have reduced CVD mortality risks relative to white Europeans. Research also indicates that South Asian groups have equitable access to care for heart disease and better survival rates from it. In contrast, Black groups have lower than expected rates of access to and use of cardiovascular care.  [Cultural and social norms](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3588185/) strongly influence health-seeking behaviours – research has shown that health promotion activities tend to be based on assumptions of individualism and self-investment, which may need to be re-thought for South Asian groups in particular where community is often more important. [South Asians](ghttps://www.diabetes.org.uk/resources-s3/2017-11/south_asian_report.pdf) are often explicitly excluded due to perceived cultural and communication difficulties. Language and cultural differences are barriers that impact all minority groups – with people from non-White-European populations seeking healthcare at later stages of their disease than their White counterparts.  [Language and literacy factors](https://www.pcdsociety.org/resources/details/living-with-diabetes-a-qualitative-review-of-minority-ethnic-groups-in-a-deprived-london-borough) are also known factors that impact on overall health literacy. Study participants have reported that both the spoken and written health information provided were sometimes meaningless, even when translated into their own language. Their inability to transform information into action was either due to limited health knowledge or limited linguistic proficiency in either their native language or English and they also felt they were unable to maximise their consultation with their healthcare professional. | |
| Other factors to consider: As data related to cardiac arrest more widely in the UK are limited, the above have been provided in relation to cardiovascular risk, management, and care standards that may be relevant in the context of designing trials related to CVD/CHD. | | |

**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\***

|  |  |  |
| --- | --- | --- |
| **What** | How might the intervention(s) and comparator limit participation of people from each ethnic group in the target population? | **Response:** If patients agree to participate, they will be randomly allocated to one of two treatment groups. In the first group, patients will receive the latest medications recommended in heart attack. In the second group, in addition to these medications, patients will have coronary angiography. This will show whether they have any blockages in heart arteries.  If appropriate, coronary revascularisation by percutaneous coronary intervention commonly known as coronary angioplasty or coronary artery bypass grafting, sometimes called CABG (a surgical procedure in which a blood vessel from the leg, arm or chest is used to bypass a narrowed section of a coronary artery) will be carried out.  Patients will be invited to attend research clinics for follow-up visits where feasible. Where this is not feasible, telephone follow-up will be carried out. If required, home visits by the research team will be organised to obtain follow-up data from patients.  To what extent the intervention had been developed together with patients from different ethnic groups is unclear. No mention of translation is mentioned, which could be a problem, particularly for an older South Asian demographic. Moreover, the intervention would need cultural tailoring. Surgical interventions require a measure of post-operative care, the perceptions of which may vary by ethnicity. See Worksheet 1 (‘Cultural’) for more details.  Material targeting the individual is a strategy that works from a White ethnic group perspective but may be less effective in South Asians (who tend to have more of a sense of community, so appeals to community may be useful) and Black individuals, where appeals to family may be more useful. |
| How, and in what way, were people from each ethnic group involved in selecting or designing the trial intervention/comparator? | **Response:** As only the trial registry documents were available for assessment no further information was available regarding details of the recruitment strategies, the process of consent, PPI, or supplementary materials (including the patient information sheet). |
| Other factors to consider: | |
| **Who** | How might the person delivering the intervention/comparator limit participation of people from each ethnic group in the target population? | **Response:** The trial registry notes the study interventions are standard of care in patients with coronary artery disease and will be performed by interventional cardiologists at local sites with considerable experience in these clinical procedures. The process of recruitment is unclear.  Black and ethnic minority populations are known to distrust the medical and research systems due to historical abuse and exploitation and may remain unconvinced that research participation is something for them. That said, [NHS staff are a more diverse group](https://www.ethnicity-facts-figures.service.gov.uk/workforce-and-business/workforce-diversity/nhs-workforce/latest) than the wider UK population – of NHS staff whose ethnicity is known, 79.2% are White (including White minorities), and 20.7% are from all other ethnic groups. This contrasts to the wider population – the [2011 Census](https://www.ethnicity-facts-figures.service.gov.uk/uk-population-by-ethnicity/national-and-regional-populations/population-of-england-and-wales/latest) showed that 86.0% of the population of England and Wales was White. If the staff conducting research visits with participants are of the same ethnicity, or share a common language, distrust may be reduced.  In general, those tasked with screening and recruitment will need cultural competence training to ensure that people from ethnic groups different to their own are approached, and that both recruiter and potential recruit feel comfortable about the discussion. Depending on the language requirements of target ethnic groups, this may require interpretation and/or translation. |
| 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:** Following intervention in the hospital setting (as above), patients will be invited to attend research clinics for follow-up visits where feasible. Where this is not feasible, telephone follow-up will be carried out. If required, home visits by the research team will be organised to obtain follow-up data from patients.  To what extent the intervention had been developed together with patients from different ethnic groups is unclear. No mention of translation is mentioned, which could be a problem, particularly for an older South Asian demographic. Moreover, all components of the intervention and further follow-up processes would need cultural tailoring. See Worksheet 1 (‘Cultural’) for more details.  The practical considerations of accessibility for on-site follow-up including site locations, transportation, and appointment times should be considered. In previous work on the [uptake of cancer screening services](https://doi.org/10.1093/eurpub/ckae073), those from diverse ethnic backgrounds and those living in rural/remote communities were less likely to take up the offer of screening due to such accessibility concerns. Surgical interventions also require a measure of post-operative care, the perceptions of which may vary by ethnicity.  [In a 2022 study](https://www.magonlinelibrary.com/doi/abs/10.12968/bjca.2021.0109) reporting the experiences of the cardiac rehabilitation journey among South Asian patients in the British Journal of Cardiac Nursing, it was found that the content of cardiac rehabilitation programmes lacked cultural sensitivity, which influenced both adherence and perceived relevance. It would be useful to know to what degree there are differences between ethnic groups in attitudes to the components of the intervention.  In principle a telephone-based exercise or home visits can help to eliminate issues of accessibility based on geographic scope and/or considerations of transportation. However, it is plausible that people from different ethnic groups may have different perspectives on cardiac care, who is best suited to deliver this ongoing care, and how information on care is shared with providers given a lack of culturally tailored resources within the healthcare system.  There is also no one-size-fits-all approach to the proposed follow-up as related to ethnicity. [The 2022 study from the British Journal of Cardiac Nursing](https://www.magonlinelibrary.com/doi/abs/10.12968/bjca.2021.0109) also found invitations to attend and participate in cardiac rehabilitation must be personalised, accounting for cultural influences on lifestyle and, in this case, the ability to fully participate within the confines of the trial. |
| Other factors to consider: | |
| **Where** | How might where the intervention/comparator is delivered (e.g. hospital, general practice, local library) limit the participation of people from each ethnic group in the target population? | **Response:** As above. |
| Other factors to consider: | |
| **When & Intensity** | How might when the intervention/comparator is delivered (e.g. during working hours) or the intensity (e.g. number of times it is delivered, over what period, time commitment for each session and overall) limit participation of people from each ethnic group in the target population? | **Response:** Key data points were noted on the trial registry as collected during research clinic follow-up visits where feasible (e.g., at baseline, 6, and 12 months) with postal questionnaires or in-person home visits to be arrange as alternatives to clinic visits. It is unclear how long face-to-face visits were in the clinic or home setting, and it would be reasonable to assume these were done during standard working hours.  Getting to hospital can be an issue for a variety of reasons including – poor transport links, the timing and length of research visits (i.e. clashing with working hours, childcare or caring responsibilities), financial reasons (time away from work, cost of travel, parking charges). Many of these factors disproportionately impact people from poor socioeconomic backgrounds, which often includes ethnic minority groups. As above, previous work on the [uptake of cancer screening services](https://doi.org/10.1093/eurpub/ckae073) has shown those from diverse ethnic backgrounds and those living in rural/remote communities were less likely to take up the offer of screening due to such accessibility concerns.  Clearly explaining to participants in a culturally appropriate way why attending all visits or arranging the outlined alternatives of questionnaires by post or home visits is important will be key for all ethnic groups. |
| Other factors to consider: | |

**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**

|  |  |  |
| --- | --- | --- |
| **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 list of inclusion and exclusion criteria were as follows:  **INCLUSION** 1. Aged ≥75 years 2. Type 1 NSTEMI during index hospitalisation  **EXCLUSION** 1. Patients presenting with STEMI or unstable angina 2. Patients with cardiogenic shock 3. Patients with known life expectancy 4. Patients in whom neither the patient nor the consultee are able and willing to provide written informed consent 5. Previous inclusion in the BHF SENIOR-RITA trial 6. Inability to undergo invasive coronary angiography, such as no vascular access site, or absolute contraindication to coronary revascularisation  Within the exclusion criteria are patients in whom neither the patient nor the consultee are able and willing to provide written informed consent. This may lead to some ethnic minority groups being disproportionately affected dependent on the language skills of both potential participants and clinical staff.  No further details on the consent collection process are provided. Assuming consent is written and since translation/interpretation is not mentioned, we can also assume this process is in English. As mentioned above, language issues (both world language and culturally-tailoring) may limit the participation of some ethnic minority individuals.  Clinicians with expertise in cardiovascular care will be able to shed more light on whether any specific clinical criterion may disproportionately impact certain ethnic groups. |
| Other factors to consider: The trial specifically targets those who aged ≥75 years. Age extremes (e.g., under 18 and over 75) [are an example of an under-served group](https://www.nihr.ac.uk/documents/improving-inclusion-of-under-served-groups-in-clinical-research-guidance-from-include-project/25435), and even more so among ethnic minority groups. | |
| **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 unclear how participants became aware of the trial. The most likely route is that a clinician in one of the participating hospital centres invited a person to take part.  Eligible patients were given a patient information sheet per the trial registry details; it is unclear who gave the information but probably a member of the clinical team. It is unclear who took consent.  Depending on the language skills of both potential participants and clinical staff, who approaches the potential participant may limit the ability of some ethnic groups (older Pakistani and Bangladeshi women for example) to participate.  It is unclear if the trial team explored who should make the initial approach with an ethnically diverse group of patient and public contributors. |
| How might the information that tells potential participants about the trial (e.g. participant information leaflet) limit the participation of each ethnic group? | **Response:** As some ethnic groups including individuals for whom English may not be their first language are a key required group within the trial (e.g. South Asians, Indian subcontinent) then translation of written and oral material into some languages other than English is likely to be essential (see above).  [Other cultural barriers for South Asians](https://onlinelibrary.wiley.com/doi/epdf/10.1111/dme.13895) (e.g. preference for traditional remedies, see earlier) may be as important, or more important, than linguistic barriers so should not be forgotten. [These beliefs, and linguistic issues, are likely to be more relevant among older generations](https://onlinelibrary.wiley.com/doi/epdf/10.1111/dme.13895).  It is unclear if any material was translated into other languages, or culturally modified. |
| How might cultural practices, beliefs and traditions change the way each ethnic group perceives the information they are given? | **Response:** See earlier comments about sociocultural beliefs, self-management and appeals to individualism rather than community and family. |
| 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:** We can assume consent is written and since translation/interpretation is not mentioned, we can also assume this is in English. As mentioned above, language issues (both world language and culturally-tailoring) may limit the participation of some ethnic minority individuals. The eligibility criteria highlighted above may explicitly exclude some individuals on language grounds linked to consent. | |
| How might the way people would like to discuss participation with family before providing consent differ for each ethnic group? | **Response:** [South Asian women](https://www.researchgate.net/publication/7480322_The_Influence_of_Family_on_Immigrant_South_Asian_Women%27s_Health), particularly older women, are known to make decisions about their healthcare in consultation with members of their community and family. Involvement of family members in the consent process should therefore be considered, including for other genders. Family is also important to people with Black heritage. | |
| How might the way the research team can check how well consent information is understood differ for each ethnic group? | **Response:** There is no information about how understanding is confirmed. | |
| Other factors to consider: | | |

**Worksheet 3b**

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

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

|  |  |  |
| --- | --- | --- |
| **What** | How, and in what way, were people from each ethnic group in the target population involved in selecting the trial outcomes? | **Response:** No information was provided on the trial registry used for assessment regarding patient and public involvement in the SENIOR RITA trial. |
| 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 trial outcomes are scales of one sort of another although there are other measures including accelerometery and mortality. Data were collected from trial participants ideally in the hospital and/or follow-up clinic site visits (to be substituted with questionnaires, telephone, or in-person engagement as needed). It is unclear whether and how the outcomes may limit participation beyond culturally sensitive issues of language. |
| Other factors to consider: | |
| **Who** | How might the people who collect data limit the participation of each ethnic group in the target population? | **Response:** This is unclear because it is unclear who collects data from participants at clinic visits. |
| Other factors to consider: | |
| **How** | How might data collection methods limit the participation of each ethnic group in the target population? | **Response:** See above. |
| Other factors to consider: | |
| **Where** | How might where data are collected limit the participation of each ethnic group in the target population? | **Response:** Getting to hospital can be an issue for a variety of reasons including – poor transport links, the timing and length of research visits (i.e. clashing with working hours, childcare or caring responsibilities), financial reasons (time away from work, cost of travel, parking charges). Many of these factors disproportionately impact people from poor socioeconomic backgrounds, which often includes ethnic minority groups. |
| Other factors to consider: | |

**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:** See Worksheet 3b. |
| Other factors to consider: | |
| **Benefits** | How might the benefits of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** Some outcomes, most noticeably quality of life, could conceivably have a cultural element although this is uncertain. Given the different disease presentation for White and some ethnic minority individuals, especially South Asians it would be reasonable to assume that there could be potential differences due to that, or to acceptance of the multiple forms of intervention as proposed by the trial. |
| Other factors to consider: | |
| **Harms** | How might the possible harms of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** As above. |
| Other factors to consider: | |
| **Subgroup analyses** | How should variation between ethnic groups in the target population be explored– should there be planned subgroup analyses? | **Response:** An exploration of benefits and harms by ethnic group should be pre-planned, especially given the different prevalence for South Asian heritage individuals.  The need for this pre-planned subgroup analysis suggests that over-sampling by ethnicity might be useful. This is unlikely to affect the applicability of the evidence to the majority population but will improve the certainty of conclusions coming from the subgroup analysis. The overall sample size does not need to be changed and it is unlikely to be feasible to fully power any subgroup analyses. |
| Other factors to consider: | |
| **Interim analyses** | How should any interim analysis handle variation between ethnic groups in the target population? | **Response:** Any planned interim analysis should look for signals suggesting that benefits or harms were importantly different in one or more ethnic groups. The certainty available for this will be less than for the majority population, although oversampling may help. |
| Other factors to consider: | |
| **Stopping triggers** | How should any rules to stop the trial early on safety or benefit grounds handle variation between ethnic groups in the target population? | **Response:** Any stopping rules should consider the benefits or harms by ethnic group. The certainty available for this will be less than for the majority population, although oversampling may help. |
| Other factors to consider: | |

**Worksheet 3d**

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

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

|  |  |  |
| --- | --- | --- |
| **What** | How, and in what way, were people from each ethnic group in the target population involved in planning the reporting and dissemination of the trial results? | **Response:** No information was provided on the trial registry used for assessment regarding patient and public involvement in the SENIOR RITA trial. |
| Other factors to consider: | |
| **How** | How might planned reporting and dissemination methods limit engagement with each ethnic group in the target population? | **Response:** The publication and dissemination plan noted on the trial registry indicates the study will be presented at a major cardiovascular scientific session, and for publication in high-impact peer-reviewed journals. Reporting for the trial is largely useful for the charitable funder of the trial, the British Heart Foundation. From the information available, it is unclear how ethnic groups that may benefit most from the intervention can become aware of its presence. |
| 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:** Using publications and scientific clinical meetings as the only forms 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. |
| 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** |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |
|  |  |  |

\*See https://centreforbmehealth.org.uk/resources/toolkits/ for suggestions for how to address factors that affect community-wide involvement.

Acknowledgements

In addition to [Trial Forge](https://www.trialforge.org/) and [NIHR](https://www.nihr.ac.uk/), this work has involved and been supported by the following:

Shape

Description automatically generated with medium confidence [Centre for Ethnic Health Research](https://ethnichealthresearch.org.uk/)

**A close up of a logo

Description automatically generated**

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

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

**A picture containing food, drawing

Description automatically generated**[NIHR-Medical Research Council Trial Methodology](https://www.methodologyhubs.mrc.ac.uk/about/tmrp/)

[Research Partnership](https://www.methodologyhubs.mrc.ac.uk/about/tmrp/)

**A close up of a sign

Description automatically generated**[UK Research and Innovation & Medical Research](https://www.ukri.org/)

[Council](https://www.ukri.org/)

