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 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 documents we used regarding the trial were the final report sent to the funder (NIHR) and the registration document -** [**https://www.journalslibrary.nihr.ac.uk/hta/hta25250#/abstract**](https://www.journalslibrary.nihr.ac.uk/hta/hta25250#/abstract) **and** [**https://www.isrctn.com/ISRCTN73485024**](https://www.isrctn.com/ISRCTN73485024)**.**  **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.]**  PARAMEDIC 2 was a UK trial comparing the effects of administering adrenaline with the effects of not administering adrenaline to those experiencing an out-of-hospital cardiac arrest (OHCA). The trial was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment program, which means the findings are intended to be of immediate clinical relevance (i.e., the trial is pragmatic). Participants should therefore be representative of all heart diseases, conditions, and events that may lead to an OHCA. However, this may be challenging given the unpredictable nature of an OHCA.  The [British Heart Foundation](https://www.bhf.org.uk/what-we-do/policy-and-public-affairs/transforming-healthcare/out-of-hospital-cardiac-arrests) states that in the UK there are over 30,000 OHCA a year where emergency medical services attempt to resuscitate the victim. However, the survival rate is low with less than 1 in 10 people in the UK surviving an OHCA. A person may experience an OHCA event or be diagnosed with heart disease, which can lead to a cardiac arrest, at any stage during their lifetime. The [Resuscitation Council UK](https://www.resus.org.uk/library/2021-resuscitation-guidelines/epidemiology-cardiac-arrest-guidelines) note that most cardiac arrests in the UK occur in the home (72%) or a workplace (15%) with 8 out of 10 OHCA due to some form of cardiovascular disease (CVD). Cardiac arrests were found to mostly occur in adults (98%) among whom were aged 15-64 years (33%).  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 and more broadly consistently found a higher incidence, prevalence, and mortality rate from heart disease in South Asian groups compared with white 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, stroke, and diabetes.  In contrast, Black groups in the UK were found to have a significantly lower risk of heart disease compared to much of the population. Lower cholesterol levels among people of African Caribbean heritage than white Europeans may protect them against heart disease.  However, there is little data available regarding ethnicity and an OHCA or cardiac arrest within UK hospitals more generally. Recruitment for the PARAMEDIC 2 trial took place predominantly in England. 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 cardiac arrest which includes ethnicity citing the complex data linkage methods involved. The [Office for Health Improvement & Disparities](https://www.eastsussexjsna.org.uk/media/sablhojn/sex-based-disparity-in-the-survival-of-adult-out-of-hospital-cardiac-arrest-patients-in-england-ohid.pdf) found no difference in survival based on the sex of OHCA victims where resuscitation was attempted by ambulance services.  Given the wide variety of underlying mechanisms that may lead to an OHCA and the inability to find absolute numbers for cases by ethnicity, it is suggest that the proportion of South Asian adults 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. A [recent study from Denmark](https://www.thelancet.com/pdfs/journals/lanepe/PIIS2666-7762(22)00173-9.pdf) in 2022 further noted that most data available on ethnicity and OHCA have been collected in the United States with little research conducted to date in Europe. |

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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.]**  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. |

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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.]**  The intervention compared the effects of administering adrenaline with the effects of not administering adrenaline to those experiencing an OHCA in an ambulatory setting. The trial was randomised to provide equal opportunity of receiving or not receiving adrenaline following an OHCA.  Given the unpredictable nature of an OHCA, the regionality of the five ambulance services undertaking the delivery of the intervention are likely to reflect the various ethnic communities in which they are located. The trial was delivered by the University of Warwick in partnership with Kingston and St George’s University of London and the Welsh, West Midlands, North East, South Central and London Ambulance Services.   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).  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 have all been a good match between the ethnic groups needed and where the trial took place. No data on the ethnicity of participants was presented in the [initial publication of trial results](https://www.nejm.org/doi/full/10.1056/NEJMoa1806842). | |
| 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.]**  In accordance with European legislation, and because of the sudden and life-threatening nature of an OHCA, a process of obtaining written informed consent was deferred until after the emergency had passed. Trial-trained paramedics followed resuscitation protocols as outlined in the European Resuscitation Council Guidelines. If initial attempts at resuscitation, including CPRA and defibrillation, were unsuccessful, the patient was randomly assigned to receive either the intervention or the placebo.  Written informed consent to continue data collection was sought after resuscitation, from either the patient or a legal representative. The PPI members of the PaRAMeDIC trial contributed to the trial design and proposed follow-up processes including the patient information sheet, consent forms, process for information patients or their relatives of their involvement in the trial, the overall trial communications strategy, and issues regarding seeking/obtaining consent. However, the PARAMEDIC 2 report does not specify under PPI details any further information regarding ethnicity (either as a component of the PPI group, or as a wider consideration within PPI factors contributing to the design of the trial).  For patients and legal representatives who did not speak English, patient information sheets and consent forms were translated into some common languages with further language services available if required. As the trial’s outcomes relied on both the administration of the intervention in a life-threatening situation and subsequent follow-up data, it would have been to the advantage of the trial design to consider relevant issues of communication and language in relation to the geographic areas of the five ambulatory services participating. No data on the ethnicity of participants was presented in the [initial publication of trial results](https://www.nejm.org/doi/full/10.1056/NEJMoa1806842). |

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:** The burden of cardiovascular disease is significant regardless of ethnicity. Studies have shown that 80 per cent of the global burden of heart disease 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 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 CVD risk factors; they are more likely to experience established CVD 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, heart disease is more prevalent in South Asians than in the majority UK population, but less prevalent in Black individuals. While this trial focused on OHCA, there is little data available regarding ethnicity and OHCAs or cardiac arrest within UK hospitals more generally. |
| How might the severity of the disease vary between each ethnic group? | **Response:** 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 [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 heart disease is significantly worse for South Asians than White individuals but significantly better for Black individuals. |
| 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 African Caribbeans and South Asian women. | |
| 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 delivered by the University of Warwick in partnership with Kingston and St George’s University of London and the Welsh, West Midlands, North East, South Central and London Ambulance Services.   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).  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: Ethnicity data related specifically to OHCAs has largely only been researched in the context of the United States. [There has been little research conducted in Europe](https://www.thelancet.com/pdfs/journals/lanepe/PIIS2666-7762(22)00173-9.pdf) and due to the variability in heart conditions, diseases, and events that may contribute to an OHCA it follows that South Asian ethnicities should be a focus area for trial recruitment due to risk considerations. | | |
| **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, or the belief that all events are pre-determined and therefore inevitable, 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:** The intervention was a paramedic administered dose of epinephrine (adrenaline) during the onset of a life-threatening OHCA. Consent was deferred until after the emergency had passed.   How acceptable, or useful, such interventions and the process of consent might be considered to be by a wide range of ethnic groups is unclear. It would be useful to know to what degree there are differences between ethnic groups in attitudes to this sort of intervention to preventing or managing heart disease (or other) problems. | |
| 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 OHCA or 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. | | |

**Worksheet 2**

This this worksheet provides some questions **to guide your thinking about ethnic group involvement when answering Question 3** of the INCLUDE Key Questions.

**Intervention and comparator factors that might affect how some groups engage with the intervention and/or comparator\***

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| **What** | How might the intervention(s) and comparator limit participation of people from each ethnic group in the target population? | **Response:** The intervention compared the effects of administering adrenaline with the effects of not administering adrenaline to those experiencing an OHCA in an ambulatory setting. The trial was randomised to provide equal opportunity of receiving or not receiving adrenaline following an OHCA.  To what extent the trial intervention and consent process 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 older South Asian women.  Regarding follow-up data collection where consent was sought, 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 acceptable, or useful such interventions might be considered to be by a wide range of ethnic groups is unclear. It would be useful to know to what degree there are differences between ethnic groups in attitudes to the consent process during a life-threatening cardiac event, and as a way of managing heart disease. |
| How, and in what way, were people from each ethnic group involved in selecting or designing the trial intervention/comparator? | **Response:** The PPI members of the PaRAMeDIC trial contributed to the PARAMEDIC 2 trial design and proposed follow-up processes. However, the PARAMEDIC 2 report does not specify under the PPI details any further information regarding ethnicity (either as a component of the PPI group, or as a wider consideration within PPI factors contributing to the design of the trial). |
| 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 PARAMEDIC 2 trial differs from most in that the intervention is delivered during a life-threatening scenario, where consent is not sought until after the immediate danger to life has resolved. There is also no means to predict who might experience such a cardiac event. Adult patients who had sustained an OHCA for which advanced life support was provided by trial-trained paramedics were eligible for inclusion.  Criteria for exclusion were known or apparent pregnancy, an age of less than 16 years, cardiac arrest from anaphylaxis or asthma, or the administration of epinephrine before the arrival of the trial-trained paramedic.  The person collecting consent for subsequent data collection following the OHCA would require cultural competency training to ensure that people from ethnic groups different to their own have inclusive needs such as interpretation and/or translations considered as part of the process. As a legal representative may be approached during this subsequent consent process, both the recruiter and other invested party must have a level of trust and comfortability surrounding a discussion following a life-threatening event. |
| 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:** See above for details regarding the initial delivery of the intervention.  For subsequent consent processes and collection of data, it is useful to consider that [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.  Participants were appreciative of health advice, but not parenting advice, where family advice carried more weight. It is plausible that people from different ethnic groups may have different perspectives on health professionals coming to their homes to deliver care, and whether this is an acceptable form of health care. |
| 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:** See above for details regarding the initial delivery of the intervention. |
| 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**

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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 list of eligibility criteria was concise given nature of OHCAs:  **Participant inclusion criteria**  1. Cardiac arrest in out of hospital environment 2. Advanced life support initiated and/or continued by ambulance service clinician  The PARAMEDIC 2 trial differs from other trials related to heart disease in that the intervention is delivered during a life-threatening scenario, where consent is not sought until after the immediate danger to life has resolved. There is also no means to predict who might experience such a cardiac event, and as such, the eligibility criteria are likely not to inherently exclude any specific ethnic population. |
| 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:** As above. |
| How might the information that tells potential participants about the trial (e.g. participant information leaflet) limit the participation of each ethnic group? | **Response:** Consent was sought for further data collection follow the resolution of the life-threatening event.   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 self-management, concepts of fatalism, 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:** As above. | |
| 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:** No information was provided in the [initial results](https://www.nejm.org/doi/full/10.1056/NEJMoa1806842) as to how well consent information was understood for each ethnic group, as no ethnic data was provided. | |
| Other factors to consider: | | |

**Worksheet 3b**

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

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

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| **What** | How, and in what way, were people from each ethnic group in the target population involved in selecting the trial outcomes? | **Response:** The PPI members of the PaRAMeDIC trial contributed to the PARAMEDIC 2 trial design and proposed follow-up processes. However, the PARAMEDIC 2 report does not specify under the PPI details any further information regarding ethnicity (either as a component of the PPI group, or as a wider consideration within PPI factors contributing to the design of the 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.  It is unclear whether and how the outcomes may limit participation beyond language issues. |
| Other factors to consider: | |
| **Who** | How might the people who collect data limit the participation of each ethnic group in the target population? | **Response:** Data were collected on a screening log of all cardiac arrests, which were attended by a trial-trained paramedic in the trial areas. These data consisted of the case identifier, the age and sex of the patient and the reason why the patient was not enrolled in the trial. This allowed assessment of the proportion of missed enrolments and the reasons, to ensure that the trial sample was representative of the trial population.   The reasons for missed enrolments were established either from reviewing the patient’s clinical record, or from speaking to the attending clinician. Several strategies were used during the trial to reinforce the message that all eligible patients should be enrolled in the trial, and data on the numbers and reasons for missed enrolments were reviewed throughout the trial and fed back to sites. No data specific to ethnicity appears in the trial reporting. |
| 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:** See above. |
| Other factors to consider: Survivors willing to take part were followed up approximately 3 months and 6 months after their cardiac arrests. The 3-month assessments were typically a home visit but could also be mostly completed by postal questionnaires or via questionnaires over the telephone. At 6 months, questionnaires were distributed for return by post. No data specific to ethnicity appears in the trial reporting, and these additional follow-up measures would need to consider culturally sensitive issues such as language and perceptions surrounding both home and telephone engagement with the wider health system. | |

**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. It would be reasonable to assume there could be perceived differences in quality-of-life following survival of a traumatic, life-threatening event given differing cultural and ethnic backgrounds of participants. |
| 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. |
| 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**

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| --- | --- | --- |
| **What** | How, and in what way, were people from each ethnic group in the target population involved in planning the reporting and dissemination of the trial results? | **Response:** The PPI members of the PaRAMeDIC trial contributed to the trial design and proposed follow-up processes. However, the PARAMEDIC 2 report does not specify under PPI details any further information regarding ethnicity (either as a component of the PPI group, or as a wider consideration within PPI factors contributing to the design of the trial). It was noted that a PPI co-applicant was actively involved in the dissemination of trial results, including public-facing information and relevant conferences and other media presentations. |
| Other factors to consider: | |
| **How** | How might planned reporting and dissemination methods limit engagement with each ethnic group in the target population? | **Response:** Reporting for the trial is largely useful to public funders such as the NIHR, and other mentioned regulatory and guideline bodies including the International Liaison Committee on Resuscitation. While PPI is described as part of the final trial report, it remains unclear how ethnic groups that may benefit most from the intervention can become aware of its presence during ambulatory resuscitation for OHCAs. Some PPI input was noted regarding the trial communication strategy, which may benefit considerations of language among differing ethnic groups. |
| Other factors to consider: | |
| **Where** | How might where trial results are planned to be reported and disseminated limit engagement of each ethnic group in the target population? | **Response:** The [NIHR journal library](https://www.journalslibrary.nihr.ac.uk/hta/JKNZ2003#/abstract) provides the bulk of what is likely to be publicly available on this trial. Results were also initially reported in [the New England Journal of Medicine](https://www.nejm.org/doi/full/10.1056/NEJMoa1806842).  Using publications as the only form of dissemination is not conducive to engaging any ethnic group, or member of the public with the results of this trial. At the very least the publication(s) that come from this trial should be open access.  The development of an infographics leaflet summarizing the results of the trial for patients and members of the public was presented to the trial PPI group for further feedback.  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. The trial communication strategy (including ways in which information about the trial can be shared in relevant communities) is noted in the final trial report as benefitting from the input of members belonging to the wider PPI 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.

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| --- | --- | --- |
| **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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