Ensuring your trial is designed for all who could benefit

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

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

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

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

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

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

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

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

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

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

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

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| **1. Who should my trial results apply to?** |
| **[NB. Completed by Heidi Gardner (University of Aberdeen) and SOMEONE ELSE (University of SOMEWHERE). 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 trial report:** [**https://doi.org/10.3310/hta21200**](https://doi.org/10.3310/hta21200) **and the trial registration document:** [**https://www.isrctn.com/ISRCTN61215213**](https://www.isrctn.com/ISRCTN61215213)**.**  **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 disease being studied is type 1 diabetes. In type 1 diabetes glucose levels in the blood are too high because the body cannot make the insulin hormone. Type 1 is less common than type 2 diabetes; approximately 90% of people with diabetes have type 2, approximately 8% of diabetics have type 1, and around 2% of people with diabetes have rarer types of diabetes such as monogenic diabetes, cystic fibrosis-related diabetes, and other diabetes caused by rare syndromes. The UK has one of the highest rates of type 1 diabetes in the world, for reasons which are currently unknown. The incidence of type 1 diabetes is highest in the temperate regions and declines progressively towards the equator.  There is no conclusive evidence to suggest that prevalence of the disease varies between ethnic groups, though there is some research based in the US that suggests that non-Hispanic white populations have consistently higher type 1 diabetes incidence and prevalence rates than Hispanics.  Type 1 diabetes can cause long-term complications such as heart disease, stroke, retinopathy, kidney disease, and neuropathy which can cause leg, foot, or toe amputations. A UK based-study found no ethnic differences in diabetes related amputation in women, in men, the amputation risk in African-Caribbeans was one-third that of Europeans. South Asians experience significant morbidity and mortality from complications of diabetes – including diabetic retinopathy, coronary artery disease, cerebrovascular disease, and chronic kidney disease. Kidney disease is also known to progress faster in people of South Asian descent in comparison to people of European descent. There is also evidence that African-Caribbean people with diabetes have poorer outcomes than the general population. The prevalence of stroke and chronic kidney disease is higher in African-Caribbean people than in the general population of the UK.  In about 5-15% of cases, type 1 diabetes is associated with other autoimmune conditions, but ethnic differences between these incidences have not been reported.  Research based in the US has shown the people living with type 1 diabetes do experience stigma associated with the condition. The highest rates of stigma were reported by parents of children with type 1 diabetes, with reports of ‘looks of contempt’ when injecting insulin in public, workplace discrimination, and limitations in traveling, maintaining friendships, and adopting children. The experience of stigma disproportionately affects those with a higher BMI, higher HbA1c, and poorer self-reported blood glucose control, suggesting that those who need the most help are also the most negatively impacted by social stigma. None of this research linked stigma with specific ethnic groups, but it is feasible that these experiences with stigma are more widespread in communities that are known to mistrust and/or distrust medical and healthcare professionals.  The prevalence of the disease does not show variation within ethnicities, but the potential complications from the disease do have the potential to disproportionately impact people with South Asian heritage, and people with African-Caribbean heritage. For that reason, it is important to include these groups in the trial. |

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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.]**  As discussed in question 1, the prevalence of the condition does not appear to vary by ethnicity, but complications as a result the condition are increased in ethnic minority communities in comparison to white-British populations. Due to the increased health demands of these minority groups, they may stand to benefit more to the treatment. It is not clear whether the root cause of these differences is genetic, social, cultural, or a mix of factors, so it is difficult to suggest whether these groups will respond to the treatment in different ways.  The fact that the REPOSE trial includes people with type 1 diabetes may alleviate fears around research that are usually due to the need to ingest medicines, because type 1 diabetes will have been ingesting insulin (via insulin pens or a pump) before the trial. REPOSE is simply looking at different ways of delivering insulin – continuous subcutaneous insulin infusion (CSII) or multiple daily injections (MDI). |

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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 interventions are different methods of delivering insulin, pump or multiple daily injections.  Participants in the multiple daily injection arm attended a standard DAFNE (dose adjustment for normal eating) structured education course. Courses are conducted over 5 consecutive days, providing an average of 38 hours of structured education, delivered to groups of 5-8 adults, aged 18 years or older, in an outpatient setting. Courses are delivered by diabetes specialist nurses and dietitians who attend an educator training course, the DAFNE education programme, a seven-part programme consisting of 105 hours of structured training. Participants on the insulin pump arm attended a modified DAFNE course. The 5-day structure was maintained while incorporating the additional skills and learning outcomes that were considered necessary to use pumps successfully. The need to introduce ‘pump skills’ required the addition of a pre-course group session, delivered 1-3 weeks before the DAFNE course.  After course attendance, participants received the trial treatment for 2 years from the secondary care service. All participants in both groups were invited to an additional DAFNE follow-up session at 6 weeks post-course, which is standard for DAFNE course attendees. There was no chance to how insulin was accessed for the trial – participants collected insulin from their pharmacist as normal.  The reliance on course attendance for 5 consecutive days use has the potential to limit participation for a significant group of people. People that work full time, people that have caring responsibilities (children, elderly relatives etc), people with chronic illness or other conditions that are fluctuating in their impact for whom 5 consecutive days of education is not possible, and people experiencing socioeconomic disadvantage. | |
| 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.]**  Individuals were eligible for the trial if they were aged 18 or over, had type 1 diabetes for at least 12 months at the time of the DAFNE course, were fluent in speaking, reading, and understanding English, were willing to undertake intensive insulin therapy with self-monitoring of blood glucose, carbohydrate counting and insulin self-adjustment, had no preference for either pump of multiple daily injections, and were happy to be randomised, were currently using, or willing to switch to, insulin detemir, and had a need for structured education to optimise diabetes control. Individuals were excluded from the trial if they had already completed a diabetes education course, had a pump in the previous 3 years, were unable to give informed consent, along with various other exclusion criteria.  The main issue with the criteria above is the exclusion of people that have previously attended at a diabetes education course means participants are excluded. There are various types of education courses on offer in the UK, including DAFNE. These are recommended by NICE and listed on diabetes.co.uk, a global diabetes community website, on the Diabetes UK website, and provided by various NHS Trusts across the UK. It is not clear how well these courses are taken up, and whether people from specific ethnicities are more likely to attend than others.  The need to speak, read, and understand English, as well as being able to provide consent, is an issue too. These criteria will disproportionately impact people for whom English may not be a first language (particularly older members of ethnic minority communities who may be more comfortable with spoken English rather than written).  A variety of methods were used to make potential participants aware of the trial, all require some level of prior engagement with healthcare services which may limit the participation of people with lower levels of health literacy and those that don’t trust or feel comfortable with healthcare professionals. Ethnic minority individuals are known to engage poorly with healthcare, with many of these barriers a result of issues with language, communication, and culture.  The trial’s primary outcome was the change in HbA1c in participants whose baseline was > 7.5% (58 mmol/mol) at 24 months, and the key secondary outcome was the proportion of participants reaching the NICE target of a HbA1c level of < 7.5% (58 mmol/mol) at 24 months. High density lipoprotein cholesterol, total cholesterol, and albumin-to-creatinine ratio were measured with blood and urine tests. Blood glucose diaries were used, and participants asked to complete them for a period of 4 weeks prior to 6, 12, and 24 months follow ups.  The main issues are likely to be around the data collected to support outcomes, rather than the outcomes themselves. As mentioned earlier, 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) then translation of written and oral material into some languages other than English is likely to be essential (see above). These linguistic issues are likely to be more relevant among older generations. |

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 disease being studied is type 1 diabetes. In type 1 diabetes glucose levels in the blood are too high because the body cannot make the insulin hormone. [Type 1 is less common](https://www.diabetes.org.uk/professionals/position-statements-reports/statistics) than type 2 diabetes; approximately 90% of people with diabetes have type 2, approximately 8% of diabetics have type 1, and around 2% of people with diabetes have rarer types of diabetes such as monogenic diabetes, cystic fibrosis-related diabetes, and other diabetes caused by rare syndromes. The UK has one of the [highest rates](https://jdrf.org.uk/information-support/about-type-1-diabetes/facts-and-figures/) of type 1 diabetes in the world, for reasons which are currently unknown. The incidence of type 1 diabetes is [highest in the temperate regions](https://pmj.bmj.com/content/81/958/486) and declines progressively towards the equator.  There is no conclusive evidence to suggest that prevalence of the disease varies between ethnic groups, though there is [some research based](https://pubmed.ncbi.nlm.nih.gov/28464767/) in the US that suggests that non-Hispanic white populations have consistently higher type 1 diabetes incidence and prevalence rates than Hispanics. |
| How might the severity of the disease vary between each ethnic group? | **Response:** Type 1 diabetes can cause long-term complications such as heart disease, stroke, retinopathy, kidney disease, and neuropathy which can cause leg, foot, or toe amputations. A [UK based-study](https://pmj.bmj.com/content/81/958/486) found no ethnic differences in diabetes related amputation in women, in men, the amputation risk in African-Caribbeans was one-third that of Europeans.  South Asians experience significant morbidity and mortality from complications of diabetes – including [diabetic retinopathy](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2646018/), [coronary artery disease, cerebrovascular disease](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4026332/), and [chronic kidney disease](https://care.diabetesjournals.org/content/29/6/1383). Kidney disease is also known to [progress faster](https://care.diabetesjournals.org/content/29/6/1383) in people of South Asian descent in comparison to people of European descent.  There is also evidence that African-Caribbean people with diabetes have poorer outcomes than the general population. The [prevalence](https://pubmed.ncbi.nlm.nih.gov/8762376/) of stroke and chronic kidney disease is higher in African-Caribbean people than in the general population of the UK.  In [about 5-15% of cases](https://pubmed.ncbi.nlm.nih.gov/16085737/), type 1 diabetes is associated with other autoimmune conditions such as hypothyroidism, hypoadrenalism, pernicious anaemia, autoimmune hepatitis, and rheumatoid arthritis. Ethnic differences between the incidences of these autoimmune conditions among people with type 1 diabetes have not been reported. |
| How might the disease present in people from each ethnic group (this may include symptoms, type or pattern or rate of disease progression)? | **Response:** The [peak age](https://www.cdc.gov/diabetes/basics/diabetes-type-1-diagnosis.html) for being diagnosed with type 1 diabetes is around 13 or 14 years old, but people can be diagnosed when they’re much younger (including babies), and older. The disease does not appear to present differently in people from various ethnic groups. | |
| How close is the match between each ethnic group living with the disease and the ethnic groups living in the areas where the trial is to be run? | **Response:** The prevalence of the disease does not show variation within ethnicities, but the potential complications from the disease do have the potential to disproportionately impact people with South Asian heritage, and people with African-Caribbean heritage. For that reason, it is important to include these groups in the trial.  The REPOSE trial includes 8 recruiting sites across England and Scotland: Sheffield, Glasgow, London, Cambridge, Harrogate, Dumfries and Galloway, Lothian, and Nottingham. The ethnic diversity at the surrounding populations is good, and there is no reason to suggest that the trial could not recruit a representative population at these sites. | |
| 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:** [Research based](https://diabetesjournals.org/clinical/article/35/1/27/35423/Stigma-in-People-With-Type-1-or-Type-2-Diabetes) in the US has shown the people living with type 1 diabetes do experience stigma associated with the condition. In an [online survey](https://diabetesjournals.org/clinical/article/35/1/27/35423/Stigma-in-People-With-Type-1-or-Type-2-Diabetes) sent to 12,000 people with diabetes, perceptions of stigma were significantly higher among respondents with type 1 diabetes than those with type 2 diabetes. The highest rates of stigma were reported by parents of children with type 1 diabetes, with reports of ‘looks of contempt’ when injecting insulin in public, workplace discrimination, and limitations in traveling, maintaining friendships, and adopting children.  The [experience of stigma](https://diabetesjournals.org/clinical/article/35/1/27/35423/Stigma-in-People-With-Type-1-or-Type-2-Diabetes) disproportionately affects those with a higher BMI, higher A1C, and poorer self-reported blood glucose control, suggesting that those who need the most help are also the most negatively impacted by social stigma. None of this research linked stigma with specific ethnic groups, but it is feasible that these experiences with stigma are more widespread in communities that are known to mistrust and/or distrust medical and healthcare professionals.  It is important that the trial team provide clear, transparent information about the trial – why it is being done, what any potential participant may be asked to do, and clarity around potential benefits and harms. | |
| How might ways of describing the disease be different for each ethnic group? | **Response:** Diabetes is sometimes called ‘high sugar’, (e.g., some South Asians) – this seems to be the case for both type 2 and type 1 diabetes. Other terms may be used 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:** Generally, several ethnic minority groups essential for the trial have a [deep mistrust of medical research](https://www.demanddiversity.co/resources). In other regards it is unclear to what extent beliefs and traditions might affect acceptability of the interventions in the trial.  Many [South Asian people are unwilling to participate](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2571097/) in trials because they accept their illness as an unalterable punishment from God, or have a fear of what research entails. This point of view is likely to be found more in older individuals, and people that are more religious.  The fact that the REPOSE trial includes people with type 1 diabetes may alleviate fears around research that are usually due to the need to ingest medicines, because type 1 diabetes will have been ingesting insulin (via insulin pens or a pump) before the trial. REPOSE is simply looking at different ways of delivering insulin – continuous subcutaneous insulin infusion (CSII) or multiple daily injections (MDI). | |
| How or when might people in each ethnic group access healthcare for this disease differently? | **Response:** In general terms, [health literacy is low among some ethnic groups, and this is a known barrier to seeking healthcare support](https://www.england.nhs.uk/wp-content/uploads/2017/07/inequalities-resource-sep-2018.pdf). This means that individuals from ethnic minority communities may present later than their white counterparts, which is likely to lead to increased complications and poorer health outcomes.  A [2014 systematic review](https://diversityhealthcare.imedpub.com/cultural-barriers-impeding-ethnic-minority-groups-from-accessing-effective-diabetes-care-services-a-systematic-review-of-observational-studies.php?aid=1595) assessed cultural barriers that impede ethnic minority groups from accessing effective diabetes care services. Eight key cultural issues emerged, namely participants’ strong adherence to cultural norms, religious beliefs, linguistic diversity, low health literacy levels, different beliefs about health and illness, belief in expert and professional support, low accessibility of culturally-appropriate services/information, and low concordance with western professional advice.  [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. As mentioned earlier, [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. [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: | | |

**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 interventions are different methods of delivering insulin; pump or multiple daily injections. [Some evidence](https://www.diabetesincontrol.com/race-ethnicity-linked-differences-seen-in-type-1-diabetes-management/) suggests that use of insulin pumps over multiple daily injections is higher among white people versus Black people, but these findings were in the US and are thought to be a result of barriers to healthcare and insurance coverage. |
| How, and in what way, were people from each ethnic group involved in selecting or designing the trial intervention/comparator? | **Response:** As part of recent work funded by an NIHR programme grant, 15 DAFNE graduates were recruited to act as the trials ‘user group’ and contribute to different aspects of the work, two of these graduates were invited to join both the steering group and other investigator meetings. In addition, one of the project team is a pump user. These individuals provided input to the trial design, implementation, and dissemination, including all participant materials. The work included qualitative studies in which barriers to self-management of type 1 diabetes were explored. This work led to the development of a pilot study within the programme grant work, in which a modified dose adjustment for normal eating (DAFNE) course incorporating a pump curriculum was developed and piloted in three centres. It is not clear what ethnicities were represented within this group. |
| 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:** Participants in the multiple daily injection arm attended a standard DAFNE (dose adjustment for normal eating) structured education course. Courses are conducted over 5 consecutive days, providing an average of 38 hours of structured education, delivered to groups of 5-8 adults, aged 18 years or older, in an outpatient setting. Courses are delivered by diabetes specialist nurses and dietitians who attend an educator training course, the DAFNE education programme, a seven-part programme consisting of 105 hours of structured training.  Participants on the insulin pump arm attended a modified DAFNE course. The 5-day structure was maintained while incorporating the additional skills and learning outcomes that were considered necessary to use pumps successfully. The need to introduce ‘pump skills’ required the addition of a pre-course group session, delivered 1-3 weeks before the DAFNE course.  After course attendance, participants received the trial treatment for 2 years from the secondary care service. All participants in both groups were invited to an additional DAFNE follow-up session at 6 weeks post-course, which is standard for DAFNE course attendees. There was no chance to how insulin was accessed for the trial – participants collected insulin from their pharmacist as normal.  The potential impact here will be from the people delivering the course – specialist diabetes nurses and dietitians. It is unclear whether these people will have an impact on engagement with the trial. Clear, culturally sensitive communication between the educators, and the patient and family will, be helpful for the trial, and if staff members represent a diverse range of ethnicities that will undoubtedly ensure participants feel at ease. |
| 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:** As above, the DAFNE courses are delivered face-to-face. The reliance on course attendance for 5 consecutive days use has the potential to limit participation for a significant group of people. People that work full time, people that have caring responsibilities (children, elderly relatives etc), people with chronic illness or other conditions that are fluctuating in their impact for whom 5 consecutive days of education is not possible, and people experiencing socioeconomic disadvantage.  With the face-to-face delivery the main issue is likely to be getting to the sites (e.g., use of public transport) and the time needed to complete the measures. Again, these issues may disadvantage people experiencing socioeconomic disadvantage. People from ethnic minority communities are at higher risk of socioeconomic disadvantage, and participation could therefore be limited. |
| 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:** As above, 38 hours (assuming during working hours) of structured education over 5 consecutive days requires a significant time commitment from participants. This will undoubtedly limit participation from people that work full time, people that have caring responsibilities (children, elderly relatives etc), people with chronic illness or other conditions with fluctuating symptoms. |
| Other factors to consider: | |

\*These factors are taken from TIDieR ([http://www.equator-network.org/reporting-guidelines/tidier/](about:blank)).

**Worksheet 3a**

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

**Trial eligibility and participation factors that might affect how some groups engage with the trial**

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| **Eligibility** | How might eligibility criteria exclude members of each ethnic group in the target population for reasons other than their clinical eligibility for the trial (e.g. availability of medical history, must speak English, location, gender, age, discussing pregnancy, internet/mobile telephone access)? | **Response:** Individuals were eligible for the trial if they were aged 18 or over, had type 1 diabetes for at least 12 months at the time of the DAFNE course, were fluent in speaking, reading, and understanding English, were willing to undertake intensive insulin therapy with self-monitoring of blood glucose, carbohydrate counting and insulin self-adjustment, had no preference for either pump of multiple daily injections, and were happy to be randomised, were currently using, or willing to switch to, insulin detemir, and had a need for structured education to optimise diabetes control. Individuals were excluded from the trial if they had already completed a diabetes education course, had a pump in the previous 3 years, were unable to give informed consent, along with various other exclusion criteria.  The main issue with the criteria above is the exclusion of people that have previously attended at a diabetes education course means participants are excluded. There are various types of education courses on offer in the UK, including DAFNE. These are recommended by NICE and listed on diabetes.co.uk, a global diabetes community website, on the Diabetes UK website, and provided by various NHS Trusts across the UK. It is not clear how well these courses are taken up, and whether people from specific ethnicities are more likely to attend than others.  The need to speak, read, and understand English, as well as being able to provide consent, is an issue too. These criteria will disproportionately impact people for whom English may not be a first language (particularly [older members](https://onlinelibrary.wiley.com/doi/epdf/10.1111/dme.13895) of ethnic minority communities who may be more comfortable with spoken English rather than written).  [Some evidence](https://www.diabetesincontrol.com/race-ethnicity-linked-differences-seen-in-type-1-diabetes-management/) suggests that use of insulin pumps over multiple daily injections is higher among white people versus Black people, but these findings were in the US and are thought to be a result of barriers to healthcare and insurance coverage.  A blood test is required at baseline, which may deter people with a needle phobia, but there’s no evidence to suggest that this would disproportionately impact people from any ethnicity. |
| 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:** A variety of methods were used to make potential participants aware of the trial: PIs or educators identified people from DAFNE waiting lists and then contacted them via telephone or letter, individuals attending a clinic appointment with a trial PI or educator were offered the option of a future or immediate consultation regarding the trial, clinicians (GP, dietitian, nurse) provided information to patients and referred them to PIs to be screened and enrolled, details of the trial were advertised through the use of posters and leaflets in clinics (diabetes outpatient, dietetic, GP surgery), reception staff in diabetes clinics were informed about the trial and provided with leaflets to give to patients who expressed an interest, and participant identification centres were used at some research centres to assist in the identification of suitable participants. Those who were either interested in taking part were invited to attend a local information meeting, or were provided with a patient information sheet and consent form and given the opportunity to ask further questions.  These methods all require some level of prior engagement with healthcare services which may limit the participation of people with lower levels of health literacy and those that don’t trust or feel comfortable with healthcare professionals. Ethnic minority individuals are [known to engage](https://raceequalityfoundation.org.uk/health-care/effective-methods-of-engaging-black-and-minority-ethnic-communities-within-health-care-settings/) poorly with healthcare, with many of these barriers a result of issues with language, communication and culture.  These methods do give a good mix of contact methods within the healthcare environment; written, face-to-face, and passive. [Some research](https://trialsjournal.biomedcentral.com/articles/10.1186/1745-6215-12-220) suggests that the response to written invitations via healthcare staff may be 5.2% lower in South Asians than in general populations, with community oriented, in-person approaches being more successful. Social class may also play a part here, as we know that ethnic minority individuals are more likely to experience socioeconomic disadvantage; letters from healthcare professionals can often look ‘official’ – usually in a brown envelope, and may give the impression that they are a bill or other negative form of post, reducing the chance of the letter ever being opened and/or the amount of trust in the letter writer even before the letter is read. |
| How might the information that tells potential participants about the trial (e.g. participant information leaflet) limit the participation of each ethnic group? | **Response:** The trial report does not detail the information contained in the invitation letter or the brochure that accompanied it.  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 that are at higher risk of complications from type 1 diabetes) 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).  The trial report explains that there was some patient and public involvement done, particularly mentioning input to participant materials. It is not clear what ethnicities were represented within this group or how they were specifically involved in development of the participant materials. |
| How might cultural practices, beliefs and traditions change the way each ethnic group perceives the information they are given? | **Response:** As above. |
| 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:** Participants were asked to complete a written consent form in one of three ways; 1) by returning a completed consent form in the post, 2) by completing the form with the PI or educator, or 3) by completing the form at a local information meeting. The consent form was only available in English. [Written consent may limit participation](http://arc-em.nihr.ac.uk/clahrcs-store/increasing-participation-black-asian-and-minority-ethnic-bame-groups-health-and-social) of some groups (e.g., South Asians) who may prefer verbal discussion to written documents. | |
| How might the way people would like to discuss participation with family before providing consent differ for each ethnic group? | **Response:** [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 family. Involvement of family members in the consent process should therefore be considered. | |
| How might the way the research team can check how well consent information is understood differ for each ethnic group? | **Response:** The trial report does not detail whether the research team assessed how well consent information was understood.  The chief challenge for the research team to understand how well consent information has been understood is around language ability and cultural competence (i.e., an awareness of issues that maybe be important to some ethnic groups but not others, or more to some groups than others). If the research team member is white-British it is unlikely that he/she/they will have this for any ethnic group other than white-British unless he/she/they has received training. | |
| Other factors to consider: | | |

**Worksheet 3b**

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

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

|  |  |  |
| --- | --- | --- |
| **What** | How, and in what way, were people from each ethnic group in the target population involved in selecting the trial outcomes? | **Response:** As part of recent work funded by an NIHR programme grant, 15 DAFNE graduates were recruited to act as the trials ‘user group’ and contribute to different aspects of the work, two of these graduates were invited to join both the steering group and other investigator meetings. In addition, one of the project team is a pump user. These individuals provided input to the trial design, implementation, and dissemination, including all participant materials. The work included qualitative studies in which barriers to self-management of type 1 diabetes were explored. This work led to the development of a pilot study within the programme grant work, in which a modified dose adjustment for normal eating (DAFNE) course incorporating a pump curriculum was developed and piloted in three centres. It is not clear what ethnicities were represented within this group or how they were specifically involved in selecting the trial outcomes. |
| 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:** The trial’s primary outcome was the change in HbA1c in participants whose baseline was > 7.5% (58 mmol/mol) at 24 months, and the key secondary outcome was the proportion of participants reaching the NICE target of a HbA1c level of < 7.5% (58 mmol/mol) at 24 months. High density lipoprotein cholesterol, total cholesterol, and albumin-to-creatinine ratio were measured with blood and urine tests. Blood glucose diaries were used, and participants asked to complete them for a period of 4 weeks prior to 6, 12, and 24 months follow ups.  The main issues are likely to be around the data collected to support outcomes, rather than the outcomes themselves. As mentioned earlier, 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) then translation of written and oral material into some languages other than English is likely to be essential (see above). [These linguistic issues are likely to be more relevant among older generations](https://onlinelibrary.wiley.com/doi/epdf/10.1111/dme.13895).  Participation could be limited for those with a needle phobia, but this is not a problem specific to any ethnic group.  It is also important to note that general scepticism of research from ethnic minority individuals is not insignificant. There is a lot of data being collected here, which may be a red flag for some. |
| Other factors to consider: | |
| **Who** | How might the people who collect data limit the participation of each ethnic group in the target population? | **Response:** Study visits took place at the participants’ diabetes centre. A data collection form was completed by the educator with the participant. Blood and urine samples were taken and analysed at local laboratories.  The ethnic profile of healthcare workers in the NHS is [more diverse than the wider population](https://www.ethnicity-facts-figures.service.gov.uk/workforce-and-business/workforce-diversity/nhs-workforce/latest#by-ethnicity), with around 40% coming from ethnic minority backgrounds. Asians represent almost 30% of NHS medical staff. This may help with recruitment of some ethnic groups, although racism and prejudice among some members of the majority population could have the opposite effect.  [Ethnic minority patients report lower satisfaction and less positive experiences](https://bmjopen.bmj.com/content/bmjopen/6/6/e011938.full.pdf) of care overall and ethnic minority patients remained less positive than those in the white British group, after statistical adjustment. Ethnic minority patients also reported lower confidence in, and less understanding of, healthcare professionals, including clinical nurse specialists, doctors, and ward nurses. |
| Other factors to consider: | |
| **How** | How might data collection methods limit the participation of each ethnic group in the target population? | **Response:** Data are collected in two ways; paper diaries completed by participants for a period of 4 weeks prior to 6, 12, and 24 months follow ups, and at face-to-face visits for blood and urine tests. Paper diaries the trial team are relying on participants having the time, energy, and memory needed to complete them. This is likely to be difficult for everyone, particularly those who work full time and have busy lives, particularly people experiencing socioeconomic disadvantage, which is known to intersect with ethnic minority experiences. Blood tests may deter people with a needle phobia, but there’s no evidence to suggest that this would disproportionately impact people from any ethnicity. |
| Other factors to consider: | |
| **Where** | How might where data are collected limit the participation of each ethnic group in the target population? | **Response:** Data collection clinics at diabetes centres in Sheffield, Cambridge, Dumfries and Galloway, Edinburgh, Glasgow, Harrogate, London, and Nottingham. These sites should enable the trial team to engage with people with various ethnicies across the UK.  The main issue is likely to be getting to the sites (e.g., use of public transport) and the time needed to complete the measures (e.g., leaving work or getting away from caring responsibilities to attend appointments). These issues may disadvantage people experiencing socioeconomic disadvantage. People from ethnic minority communities are at higher risk of socioeconomic disadvantage, and participation could therefore be limited. |
| Other factors to consider: | |

**Worksheet 3c**

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

**Factors that might affect the planned analysis of trial results**

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| **Retention** | How might the trial data available for participants differ between each ethnic group in the target population? | **Response:** Some of the data will be collected during research visits at clinic sites – see worksheet 3b for discussion of the potential issues with this. Numerous 4-week paper diaries are also required to monitor glucose levels. See previous comments around the intersection between ethnicity and socioeconomic disadvantage and how this may impact on data collection. |
| Other factors to consider: | |
| **Benefits** | How might the benefits of the trial intervention(s) differ between each ethnic group in the target population? | **Response:** We know that prevalence of type 1 diabetes does not differ between ethnic groups, but there is evidence to suggest that complications resulting from the disease do. This may be due to stigma that leads to poor management of blood glucose levels, so it is feasible to think that one trial intervention (the pump) would benefit those experiencing stigma more than the other (multiple daily injections). |
| 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. We know that prevalence of type 1 diabetes does not differ between ethnic groups, but there is evidence to suggest that complications resulting from the disease do.  The need for this pre-planned subgroup analysis suggests that over-sampling of South Asian and Black participants 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**

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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:** As part of recent work funded by an NIHR programme grant, 15 DAFNE graduates were recruited to act as the trials ‘user group’ and contribute to different aspects of the work, two of these graduates were invited to join both the steering group and other investigator meetings. In addition, one of the project team is a pump user. These individuals provided input to the trial design, implementation, and dissemination, including all participant materials. The work included qualitative studies in which barriers to self-management of type 1 diabetes were explored. This work led to the development of a pilot study within the programme grant work, in which a modified dose adjustment for normal eating (DAFNE) course incorporating a pump curriculum was developed and piloted in three centres. It is not clear what ethnicities were represented within this group. |
| Other factors to consider: | |
| **How** | How might planned reporting and dissemination methods limit engagement with each ethnic group in the target population? | **Response:** Details about the reporting and dissemination methods are not clear from the trial report. We can assume that the trial team will publish scientific manuscripts from this trial, in which case they should be open access. In addition, public-facing engagement methods such as presentations, activities, newsletters, and other methods, should be designed and developed with people from various ethnic groups to ensure that the trial’s results reach all who may be impacted by them. |
| 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:** As above. |
| Other factors to consider: | |

Worksheet for thinking through measures to address factors that might prevent full community involvement

Use this worksheet to list key factors that might affect the involvement of some ethnic groups in the target population of your trial, along with measures to mitigate the effect of those factors and their cost. Add extra rows as needed.

Please remember that there are also differences *within* ethnic groups, especially between generations and between men and women. No ethnic group is homogenous.

|  |  |  |
| --- | --- | --- |
| **Factors that may prevent full community involvement** | **Proposed measures (several options may be needed)\*** | **Cost of measures** |
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\*See https://centreforbmehealth.org.uk/resources/toolkits/ for suggestions for how to address factors that affect community-wide involvement.

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:

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[Centre for Black and Minority Ethnic Health](https://centreforbmehealth.org.uk/)

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

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

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