The INCLUDE Ethnicity and other Frameworks to improve trial diversity

Shaun Treweek
University of Aberdeen

www.trialforge.org
Design and inequality

• Research design is about making choices.
• Once made, there may be no way back from a bad choice.

• For trials, a common place to make bad choices is around who is involved in the trial. This can bake-in inequality.
Trials and ethnicity: examples

• Largest groups of smokers in UK are those of ‘Mixed’ and ‘Other’ ethnicity. NIHR smoking trial published in 2022 recruited entirely from an English stop smoking service where users are <6% ethnic minorities.

• Work on language criteria (unpublished): for 32 NIHR recent trials (24 depression and 8 diabetes), 18/32 had explicit language restrictions, including trials of talking-based therapies for depression.

• Of the 24 NIHR depression studies, the average proportion of white participants was 92%.
There are plenty of other under-served groups

• People experiencing socioeconomic disadvantage.
• People at age extremes.
• People with impaired capacity to consent.
• See example list at https://www.nihr.ac.uk/documents/improving-inclusion-of-under-served-groups-in-clinical-research-guidance-from-include-project/25435
Researchers have traditionally thought more about how many rather than who needs to be in our trials.
The INCLUDE Ethnicity Framework

London, Feb 4th 2020
The INCLUDE Ethnicity Framework – what is it?

A 2-part tool to help trialists to identify the ethnic groups needed in a trial. The two parts are:

1. Four Key Questions.
2. Worksheets to help you complete the questions.

https://www.trialforge.org/trial-forge-centre/include/
Part 1– Key Questions

1. Who should be in the trial?
2. Will the people identified respond to the treatment differently?
3. Will the intervention itself make it hard for some people to be involved?
4. Will the trial design make it hard for some people to be involved?
Part 2– Worksheets

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.

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

<table>
<thead>
<tr>
<th>Disease</th>
<th>How might the prevalence of the disease vary between each ethnic group in the target population?</th>
<th>Response:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>How might the severity of the disease vary between each ethnic group?</td>
<td>Response:</td>
</tr>
</tbody>
</table>

Worksheet 2

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*

<table>
<thead>
<tr>
<th>What</th>
<th>How might the intervention(s) and comparator limit participation of people from each ethnic group in the target population?</th>
<th>Response:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>How, and in what way, might people from each ethnic group involved in selecting and designing the trial intervention/comparator?</td>
<td>Response:</td>
</tr>
<tr>
<td></td>
<td>Other factors to consider:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Who</th>
<th>How might the person delivering the intervention/comparator limit participation of people from each ethnic group in the target population?</th>
<th>Response:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Other factors to consider:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>How</th>
<th>How might the mode of delivery (e.g., hospital, general practice, local library) limit the participation of people from each ethnic group in the target population?</th>
<th>Response:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Other factors to consider:</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Where</th>
<th>How might the 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?</th>
<th>Response:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Other factors to consider:</td>
<td></td>
</tr>
</tbody>
</table>
PROSPER
(a breast cancer trial)
Questions on the disease itself

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, age at diagnosis is younger in ethnic minority women and the cancer stage at presentation is higher. Uptake of breast screening by ethnic minority women seems unclear with some reports saying uptake is lower, others higher.

Black women have a higher frequency of grade 3 tumours than White and Asian women, and higher proportions of oestrogen negative/progesterone negative/HER2-negative tumours than other ethnic groups.

It is uncertain whether ethnic minority women experience shoulder pain after breast cancer treatment more or less often, or have more or less severe pain etc than ethnic majority women. A 2014 systematic review on post-treatment shoulder pain made no mention of ethnicity or race in its finding.

There are lots of examples at www.trialforge.org
There are other Frameworks

• INCLUDE Socioeconomic Disadvantage Framework
• INCLUDE Impaired Capacity to Consent Framework.
Socioeconomic Disadvantage

1. **Pockets** – Indicators closely linked with income and economic resource availability
2. **Prospects** – Indicators closely linked with wellbeing and life chances
3. **Place** – Indicators closely linked with housing and local environment

Katie Biggs, University of Sheffield
Fran Sherratt, University of Liverpool
Heidi Green, COUCH Health

The 3 Ps from the UK Govt Child Poverty Strategy:
Impaired capacity to consent

Vicky Shepherd, Cardiff

https://www.capacityconsentresearch.com/
Lots of diversity support at www.trialforge.org

A systematic approach to making trials more efficient

The evidence base for how to make the trials process efficient is remarkably thin. Trial Forge aims to change this.
These frameworks don’t fix everything

The first part of a Framework is tricky: who should be in your trial?

In addition, they often highlight problems but not the solutions.
STRIDE – sneak preview of some results

Where the trial team cannot reach a conclusion:

a. The minimum target is that **ethnic groups are included at the same proportion as is found among the population of people with the condition targeted by the trial.**
STRIDE – sneak preview of some results

Where disease data by ethnicity do not exist, or cannot be obtained:

b. The minimum target is that ethnic groups are included at the same proportion as is found in the most recent census data.
Summary and priorities

1. Researchers need to think explicitly about who needs to be in their study. This is more than thinking about the number of participants.

2. Researchers need to involve people who are like the people the trial needs in trial design. Trial teams themselves need to be more diverse.

3. The INCLUDE Frameworks can help (we think) because they ask questions and prompt discussion. Evaluation should be part of their use.

4. Trial teams need more help to do better.