

# Covid-19, community trials, and inclusion

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The Covid-19 pandemic has changed the research landscape with emergence of 'platform trials'. These are adaptive clinical trials where patients with a single disease are randomly allocated to different treatments based on an algorithm whether any agent has benefit.[1]

In the Lancet, the PRINCIPLE Collaborative Group [2] report no benefit of Azithromycin, compared to usual care, for suspected COVID-19 in older adults in the community. This result is important not only for giving unnecessary treatment but also for antimicrobial stewardship. Further, the result mirrors that for hospitalised patients. [3]

Randomised trials provide robust evidence for clinical management with random treatment allocation that promotes homogeneity in baseline characteristics between treatment groups; maximising internal validity and reducing both bias and confounding. This trial recruited 2,265 participants aged over 65 or over 50 with comorbidity from the community over 6 months which is remarkable in itself. It is also important to remember that during this time national guidance and restrictions were in place restricting movement of people and this is reflected in 70% participants recruited via online/telephone. The PRINCIPLE trial and vaccination roll-out has highlighted the importance of having a good primary care platform to address challenges to health of the population. As a result, *primary care* is now needed more than ever in the UK as well as globally.[4]

The PRINCIPLE trial goes some way to reflect the groups that are vulnerable to more serious complications of Covid-19 infection and is a step in the right direction for external validity. This can be a limitation in clinical trials where strict inclusion and exclusion criteria mean that participants are usually younger and with fewer morbidities than the target population of the intervention. [5]

Only 31.3% of participants with suspected Covid-19 had PCR confirmed SARS-CoV-2 infection due to low availability of community testing though this increased during the trial. The initial composite primary endpoint was hospitalisation and mortality which was amended to

self-reported illness duration due to lower than expected hospitalisation during the changing pandemic.

Although many of the challenges of conducting a trial during the Covid-19 pandemic were successfully navigated, important limitations remain. First, a lack of representation by people of Black and minority ethnic (BAME) backgrounds that is also reflected in other Covid-19 clinical trials.[6] Given the large trial and the disproportionate impact of Covid-19 on minority ethnic communities [7,8], it is surprising that so few participants from these communities were recruited - for example, only 7 from the Black group and 55 South Asians. The inclusion strategy is not detailed in the paper. However, the PRINCIPLE website [[News — PRINCIPLE Trial](#)] states that a BAME expert joined the collaboration 3 months before trial end to facilitate recruitment from these vulnerable communities.

The reasons for exclusion of minority ethnic groups are complex. These maybe related to doctor and/or researcher factors, language barriers and cultural and wider societal factors. [9] In reported trials it may not be clear what the range of contributory factors are, what the main reasons are, and whether the real issue is one of 'planned exclusion', 'inadvertent exclusion', 'non-participation,' or a mixture of these. [10] Indeed studies have highlighted that minority ethnic groups are willing to participate in research if the study has direct relevance to them and their community; and if they are approached with sensitivity and given clear explanations of what participation involves. [11,12] There is need for researchers to state in their protocol how they will ensure inclusion of marginalised groups including minority ethnic communities. Guidance exists with recommendations for research funders applying a checklist to assess whether research proposals have been co-designed with under-served groups, and that proposed recruitment methods are likely to successfully recruit under-served groups in COVID research. [13] Additionally, it is recommended that funders ensure additional funds are available to research teams to support recruitment of under-served groups. Indeed it is

incumbent on funders to ensure that funds are available to enable this to occur. Further, policy makers need to question the validity of results before implementation.

Second limitation is that participant deprivation has not been considered though participants were recruited from across the UK. Deprivation is a major determinant of health outcomes [14] and should be reported in baseline table.

One of the many lessons of the Covid-19 pandemic is the disproportionate effects it has had on vulnerable communities particularly those from minority ethnic and deprived backgrounds, further widening the existing health inequalities. This pandemic provides the opportunity for greater equity in health for all vulnerable populations with their inclusion in trials in the UK as well as globally.

#### *Conflicts of interest*

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