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Ensuring that COVID-19 Research is Inclusive - guidance from the NIHR INCLUDE project

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Ensuring that COVID-19 Research is Inclusive - guidance from the NIHR INCLUDE project

*COVID-19 studies need to be designed and delivered in ways that ensure inclusion of at-risk groups
often under-served by clinical research*

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For peer review only

Abstract

Objective: To provide guidance to researchers, funders, regulators and study delivery teams to ensure that research on COVID-19 is inclusive, particularly of groups disproportionately affected by COVID-19 and who may have been historically under-served by research.

Summary of key points: Groups who are disproportionately affected by COVID-19 include (but are not limited to) older people, people with multiple long-term conditions, people from Black, Asian and Ethnic minority groups, people living with obesity, people who are socioeconomically deprived and people living in care homes. All of these groups are under-served by clinical research, and there is an urgent need to rectify this if COVID-19 research is to deliver relevant evidence for these groups who are most in need. We provide a framework and checklists for addressing key issues when designing and delivering inclusive COVID-19 research, based on the NIHR INCLUDE project roadmap. Strong community engagement, co-development and prioritisation of research questions and interventions are essential. Under-served groups should be represented on funding panels and ethics committees, who should insist on removal of barriers to participation. Exclusion criteria should be kept to a minimum; intervention delivery and outcome measurement should be simple, flexible and tailored to the needs of different groups, and local advice on the best way to reach and engage with under-served communities should be taken by study delivery teams. Data on characteristics that allow identification of under-served groups must be collected, analyses should include these data to enable subgroup comparisons, and results should be shared with under-served groups at an early stage.

Conclusion: Inclusive COVID-19 research is a necessity, not a luxury, if research is to benefit all the communities it seeks to serve. It requires close engagement with under-served groups and attention to aspects of study topic, design, delivery, analysis and dissemination across the research lifecycle.

Key words:

COVID-19; recruitment; trial design; inclusivity; guidance

Strengths and Limitations

- We provide detailed guidance across the research lifecycle – a whole-systems approach to improve inclusion in COVID-19 research
- We base the guidance on the robustly-developed INCLUDE roadmap for improving inclusion in research
- The novelty of COVID-19 research precludes our recommendations being based on evidence directly derived from studies with people with COVID-19

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Introduction

COVID-19 is challenging health systems globally and has triggered an unprecedented research response.[1] Across the world, teams are designing and delivering studies encompassing a range of COVID-19 research including epidemiology, disease surveillance, disease consequences, early and late phase clinical trials. Early evidence suggests that some segments of the population are at high risk either of contracting COVID-19 or of more severe consequences of COVID-19 including hospitalisation and death.[2,3] Some of these groups have not been well reached by traditional research design and delivery mechanisms,[4] and there is growing concern that some of the groups most vulnerable to the impact of COVID-19 are under-represented in research studies.[5]

This guidance is designed to facilitate best practice in the design, funding, approval, regulation and delivery of research on COVID-19 and is a product of the ongoing National Institute for Health Research (NIHR) INnovations in CLinical trial design and delivery for the UnDEr-served (INCLUDE) project which seeks to improve research for under-served groups.

What is an under-served group?

There is no single definition of an under-served group in research; the definition is context-dependent and will vary depending on the population, disease and intervention being studied.[6] However, if a group is enrolled in a study at lower rates than one sees in the population affected by the disease, this is evidence that the group is likely to be under-served. Reasons for a group being under-served may include protocol design exclusions, an intervention that is unsuitable for that group, or because research delivery does not enable them to participate in practice.

Who is at risk of contracting COVID-19?

Our knowledge of who is more or less likely to be infected with COVID-19 (as opposed to suffering severe consequences of infection) is limited at present. However, individuals with a high degree of contact with those who are infected, including healthcare workers, retail staff, transport staff and other key workers with face to face roles are likely to be at high risk. Other groups in which risk appears elevated are patients who spend prolonged periods of time in close proximity to other patients (for example patients attending hospital-based haemodialysis [7]) and those in care homes;[8] emerging evidence suggests that once COVID-19 starts to affect a care home it can spread very rapidly through the care home population of both residents and staff.

Who is at risk of severe consequences of COVID-19?

Emerging data suggest that several groups are at higher risk of death or critical care unit admission from COVID-19 infection.[2,3,9] These groups include, but are not limited to, older people (particularly those aged 70 and over); men; people living with obesity; people living with multiple long-term conditions; care home residents and others living with frailty; Black, Asian and minority ethnic (BAME) groups; and people with immunosuppression due to medication, systemic illness or malnutrition.

What groups may be under-served by healthcare and research systems with respect to COVID-19?

This is also likely to be context-specific, but examples include:

- Older people and others who are self-isolating (who may not be able to access healthcare easily) on government advice
- Those who may not be prioritised for hospital admission or critical care unit admission due to perceived limited life expectancy or a low chance of benefitting from such interventions.
- Those who lack digital literacy or access to digital technologies
- People with cognitive problems including dementia, especially those living alone, who may not be able to understand and/or adhere to the symptom reporting and testing needed for diagnosis.
- Socioeconomically deprived groups, who are likely to have less resilience to the economic shocks precipitated by the COVID-19 pandemic response
- People without a car or who live in rural areas (who may find it difficult to access testing facilities that require attendees to come in a car)

In addition, thought needs to be given to the fear that many of the population currently have of leaving their immediate environment, entering a hospital or other healthcare facility. This may disproportionately affect certain segments of the population (for example those with anxiety disorders or who perceive themselves to be especially vulnerable).

How can under-served groups be more successfully included in COVID-19 research?

The INCLUDE project contains a roadmap outlining the potential points of intervention to improve the inclusion of under-served groups (Figure 1) and a structure that may be helpful in guiding teams considering how to focus their efforts. Ensuring that effective training for researchers, funders, delivery teams and regulators is key, as is ensuring that regulation is proportionate, and does not place barriers in the way of including under-served groups. Identifying members of under-served groups

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3 and using their knowledge is critical to successful delivery of research, as is building on existing
4 resources that have been created to facilitate research for specific under-served groups such as older
5 people [10] or people from Black, Asian or minority ethnic (BAME) communities.[11]
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11 **Recommendations from the INCLUDE project for COVID-19 research:**

12 Below, we set out a series of recommendations across the research lifecycle for how under-served
13 groups can be included more successfully in COVID-19 research:
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18 *Research Priority Setting:*

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20 - Representatives from under-served groups should be consulted at the earliest possible time
21 to agree a set of national research priorities for COVID-19 research. A rapid James Lind Alliance
22 project (a priority-setting process co-produced by researchers, patients and a range of other
23 stakeholders) would be one possible way to achieve this, but opportunities also exist to ensure
24 representation on COVID-19 funding committees and prioritisation committees.
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31 *Strategic priorities for funding bodies:*

- 32 - Strategic priorities for research funding bodies (for example government funders and
33 charities) should reflect the views of under-served groups from any national or international
34 research priority exercise, as well as reflecting current scientific paradigms and national health
35 and social care system imperatives.
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39 - Patient and public representation should be in place on all COVID-19-related funding and
40 prioritisation panels, and this patient and public representation should encompass
41 representatives from groups who are at risk of being under-served by COVID-19 research.
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49 *Research investigator questions:*

- 50 - Specific research questions to be answered should be co-developed by research teams,
51 funders, government, and patient and public representatives including people from under-
52 served groups.
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3 *Initial design and funding:*
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- 5 - Inclusion criteria for research studies should be kept to the minimum necessary to ensure
6 patient safety, and that criteria likely to exclude broad sectors of populations should be
7 avoided. In particular, we recommend that studies do not overtly or inadvertently exclude
8 participants on the basis of age, sex, ethnicity, geography, socioeconomic status,
9 multimorbidity, cognitive impairment, body mass index or place of residence, unless studies
10 specifically aim to generate data for groups that have to date been under-served by COVID-
11 19 research.
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18 - Interventions should be designed and selected to be usable by a wide range of participants,
19 including those from under-served groups. If this is not possible, serious consideration should
20 be given to abandoning the intervention on the grounds that it will not be broadly applicable
21 in practice. Exceptions to this are interventions designed to target a specific biological
22 pathway identified by disease severity or other disease characteristics (i.e. stratified or
23 precision medicine approaches), or interventions designed specifically to target under-served
24 groups where current approaches are not sufficiently effective.
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32 - Outcomes should be selected to be relevant to a broad range of participants; outcomes should
33 be simple and should place minimal burden on both participants and research teams.
34 Outcomes should be deliverable under pandemic conditions (e.g. when wearing full personal
35 protective equipment [PPE] in overloaded hospitals). Outcomes that can be collected from
36 routinely collected clinical data, or participant-reported outcomes that have the flexibility to
37 be collected by telephone, by videolink, by remote devices (e.g. accelerometers or other
38 Bluetooth-enabled devices [12]) or by web-based / SMS interfaces should be preferred.
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45 - When outcomes must be collected face to face, these should be able to be collected in a range
46 of different environments including the participant's own home, not just in hospital wards or
47 clinics. Outcomes should where possible be able to be assessed by a range of staff with no or
48 minimal training to ensure that studies are resilient against staff illness or redeployment in
49 future pandemic waves. Research teams should build in the costs of hardware, software and
50 adequate time to support these outcome collection methods into their proposals.
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57 - Researchers should design study protocols to allow recruitment through as wide a range of
58 routes as possible. Without good scientific reason, recruitment should not be limited to
59 hospitals, primary care practices, or care institutions, but should be enabled through all of
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3 these routes and others including through community social hubs and organisations, via
4 adverts, web-based signup, verbally over the telephone, in response to SMS and traditional
5 mail, and other routes appropriate to reach particular under-served groups. The emergence
6 of new community networks to support isolated and vulnerable people during the pandemic
7 provides new opportunities for contacting and engaging under-served groups in research.
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- 13 - Funders can apply the checklist given later in this document to assess whether research
14 proposals have been developed in conjunction with under-served groups, and that proposals
15 are designed and will be delivered in a way likely to be able to recruit under-served groups
16 successfully in COVID-19 research.
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 - 19 - Funders should ensure that additional funds (above and beyond the amount of money
20 traditionally viewed as adequate to support recruitment and retention) are available to
21 research teams to support successful recruitment of under-served groups. This may require
22 funds for home visiting, transportation (in many cases by car or taxi not public transport), PPE,
23 more screening per participant recruited, longer study visits, provision of translators or
24 translated materials.
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33 *Final study design:*

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35 - Research Ethics Committees should pay particular attention to inclusion and exclusion criteria,
36 routes of recruitment, information materials, consent processes (including the needs of those
37 without capacity) and whether under-served groups have been engaged in study design.
38 Where study designs seem likely to fail to include sufficient people from under-served groups,
39 ethics committees should robustly call attention to this, and ask research teams to modify
40 their proposals accordingly even if doing so leads to short delays in approval of projects.
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- 45 - Sponsor organisations should apply similar scrutiny to research proposals at the design stage
46 and insist on changes where the design makes exclusion of under-served groups likely.
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- 50 - Sponsor organisations and Research Ethics Committees should both welcome and encourage
51 novel and efficient methods of approaching, consenting, recruiting and retaining participants
52 in research studies. Many proposals will be very different from those that such organisations
53 are used to seeing, but this should be viewed as an opportunity, not a reason to fall back on
54 traditional (and often ineffective) methods of study conduct.
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5 *Study delivery:*

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7 - Local research delivery teams should seek local advice on how to reach and engage with
8 under-served groups in their areas. In many cases this will entail getting advice from members
9 of specific ethnic communities, or those with lived experience of particular population sectors
10 (e.g. those living in care homes, homeless people).
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15 - Training for research delivery staff (local investigators, research nurses and other research
16 team members) should be delivered to raise awareness of the need to recruit inclusively, to
17 highlight particular under-served groups, and to provide the generic skills required to engage
18 with specific under-served groups.
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23 - Local research teams should configure themselves to be able to recruit in environments other
24 than standard inpatient and outpatient secondary care departments. This should include
25 conducting study procedures in participants' own homes, care homes, conducting study
26 procedures remotely (e.g. via telephone and videolinks). Linking with neighbouring healthcare
27 research organisations will enable cross-cover of research staff in the event of staff sickness
28 or of one organisation becoming overloaded by clinical work in future pandemic waves.
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33 - For trials of medicinal products, dispensing arrangements for oral medications should be put
34 in place to enable delivery of medications direct to participants homes or local pharmacy
35 rather than needing to collect medication from a research facility. This approach will help to
36 build resilience against future restrictions on movement or closure of workplaces.
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43 - Local research support agencies (such as the UK NIHR local Clinical Research Networks and
44 hospital Trusts) should provide local research teams with the equipment and resources that
45 they need to deliver research in non-traditional settings. This may include transportation,
46 contracts and working practice procedures enabling work in participants' homes, provision of
47 COVID-19 testing and PPE in line with national guidance, IT hardware and software to enable
48 videolinks, EConsent and electronic case record form use whilst roaming, translation services
49 and sufficient time to conduct study visits in non-traditional settings.
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56 - Local research support agencies should put in place systems to monitor local recruitment of
57 under-served groups to each study. Combining these local data across studies will enable
58 study teams to adapt their recruitment strategies at an early point, for instance switching
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3 place of recruitment, oversampling particular under-served groups, or changing how study
4 teams approach participants.
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8 *Study closure and analysis:*
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- 10 - Investigators and Sponsors should develop plans for how pauses or discontinuation of study
11 activity due to future pandemic waves will be managed (ideally to at least enable study follow
12 up to continue), and how these plans will be communicated to participants.
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16 - Study reports and analysis plans should report the proportion of relevant under-served groups
17 and compare these proportions to those found in the general population with COVID-19
18 illness.
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23 - Study analysis plans should include prespecified subgroups analyses for key under-served
24 groups, both to explore differences within studies, but also to enable later pooling of results
25 from different under-served groups.
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32 *Impact, dissemination and engagement:*
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- 34 - All studies should devise a comprehensive dissemination and engagement plan, and
35 representatives from under-served groups should be part of the team drawing up these plans.
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38 - Specific engagement plans for different under-served groups should be drawn up to enable
39 appropriate tailoring of messages to different groups, in a way that best encourages feedback,
40 debate and engagement within different groups.
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47 **Conclusion**
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49 At a time when research on COVID-19 is being designed and delivered at an extraordinary speed, it
50 may seem that the urgency of the situation obviates the need to fully engage under-served groups in
51 the design and delivery of COVID-19 research. We argue however that doing so is not a luxury but a
52 necessity and failure to engage represents an enormous wasted opportunity.[13] It will hamper
53 scientific progress and potentially lead to the deployment of ineffective or harmful diagnostics and
54 therapeutics to large sections of the population. This in turn will lead to worse health outcomes for
55 under-served groups, and healthcare resources being wasted. Fully engaging under-served groups and
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3 enabling their inclusion in COVID-19 research is the only way that we will be able to understand the
4 health impacts of COVID-19 in these most vulnerable groups and thus mitigate the impact of COVID-
5 19 on health and society in an equitable way.
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10 **Author contributions**

11 All authors contributed to the generation of the recommendations contained in this guidance. MDW
12 produced the first draft of the text; all authors critically revised the text for intellectual content.
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23 **Competing interests**

24 None declared
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References

1. Ramanan M, Stolz A, Ropplalsingh R, et al. An evaluation of the quality and impact of the global research response to the COVID-19 pandemic. *Med J Aust* 2020; <https://www.mja.com.au/journal/2020/evaluation-quality-and-impact-global-research-response-covid-19-pandemic> [Preprint, 30 June 2020; accessed 11 August 2020].
2. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) consortium. COVID-19 report April 27th 2020. https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_Platform_COVID_19_Report_27APR20.pdf (Accessed 11th August 2020)
3. Williamson EJ, Walker AJ, Bhaskaran K, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. *Nature* 2020;584:430-6.
4. Crome P, Lally F, Cherubini A, et al. Exclusion of older people from clinical trials: professional views from nine European countries participating in the PREDICT study. *Drugs Aging* 2011;28:667-77.
5. Treweek S, Forouhi NG, Narayan KMV, et al. COVID-19 and ethnicity: who will research results apply to? *Lancet* 2020;395:1955-7.
6. Witham MD, Anderson E, Carroll C, et al. Developing a roadmap to improve trial delivery for underserved groups: results from a UK multi-stakeholder process. *Trials* 2020;21:694.
7. Clarke C, Predecki M, Dhutia A, et al. High Prevalence of Asymptomatic COVID-19 Infection in Hemodialysis Patients Detected Using Serologic Screening. *J Am Soc Nephrol* Published online first 30 July 2020. doi: 10.1681/ASN.2020060827.
8. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. *J Infect* 2020;81:411-9.
9. Intensive Care National Audit and Research Centre (ICNARC). ICNARC report on COVID-19 in critical care 31 July 2020. Available from: <https://www.icnarc.org>. (Accessed 24th August 2020).
10. McMurdo ME, Roberts H, Parker S, et al. Improving recruitment of older people to research through good practice. *Age Ageing* 2011;40:659-65.
11. NIHR CLAHRC East Midlands Centre for BME Health. Toolkit for increasing participation of Black, Asian and minority ethnic (BAME) groups in health and social care research. December 2018. <http://learningforinvolvement.org.uk/?opportunity=toolkit-for-increasing-participation-of-black-and-minority-ethnic-bame-groups-in-health-and-social-care-research>. (Accessed 11th August 2020)
12. Morgan C, Rolinski M, McNaney R, et al. Systematic Review Looking at the Use of Technology to Measure Free-Living Symptom and Activity Outcomes in Parkinson's Disease in the Home or a Home-like Environment. *J Parkinsons Dis* 2020;10:429-54.
13. Glasziou PP, Sanders S, Hoffmann T. Waste in COVID-19 research. *BMJ* 2020; 369:m1847.

Box 1. A checklist to guide funders and reviewers in assessing inclusiveness of COVID-19 research

1. Does the topic of the study reflect the priorities elicited by consultation with under-served groups?
2. Have representatives from under-served groups been engaged in the design of the study, and in what way?
3. Does the target population for the study (as defined by the inclusion and exclusion criteria) reflect those who are at risk of contracting COVID-19 or who are at increased risk of the adverse consequences of COVID-19?
4. Have the investigators taken steps to ensure that these potentially under-served groups will be included in the study with appropriate mitigation of any risks?
5. Are there unnecessary or unjustifiable exclusion criteria (e.g. old age, sex, ethnicity, obesity, cognitive impairment, multimorbidity) or research methods that will act as barriers to inclusion of under-served groups at high risk of COVID-19 infection and its adverse consequences?
6. Is the intervention designed and delivered in a way that is acceptable and feasible to a broad range of people most at risk from COVID-19 infection?
7. Are the study outcomes easy to measure, and can they be measured in a range of different environments? Will they still be able to be measured during the peak of a pandemic wave or during population lockdown?
8. Does the study target a specific under-served group? If so, is adequate justification for this given, and is the strategy proposed to target the group likely to succeed?

Box 2. A checklist to guide researchers in designing inclusive COVID-19 research

1. Have I engaged with representatives of under-served groups in designing my study question and protocol?
2. Have I avoided inclusion/exclusion criteria likely to lead to exclusion of under-served groups (e.g. age limits, excluding multimorbidities, BMI limits)
3. Is my study intervention suitable for, and acceptable to, under-served groups (e.g. avoiding gelatine capsules on medication)
4. Are my outcomes validated and relevant to a broad range of patients in the populations that my research seeks to serve? (e.g. cognition assessment tools in translated versions)
5. Have I avoided study burden that is likely to make it more difficult for some groups to participate (e.g. frequent study visits)
6. Have I provided a range of recruitment pathways that give flexibility in how participants are sought and contacted (e.g. not confining recruitment to drive-in testing centres, allowing recruitment from care homes)
7. Have I provided study information in a format that is accessible to under-served groups (e.g. translations of study information, simplified study information, information written with a reading age of 9 or below, written in large font size)
8. Have I enabled consent to be obtained in a way that is flexible and tailored to the needs of different groups (e.g. EConsent for those isolating, assent from relatives for those with cognitive impairment). Have I involved carers and assentees in the design of the assent process for studies where consent cannot be obtained from the participant
9. Will my study still be deliverable in the event of a second pandemic wave, with possible increase in lockdown restrictions and study staff redeployment.

Box 3. A checklist to guide research delivery teams in delivering inclusive COVID-19 research

1. Have we engaged with local representatives from under-served groups to understand how best to approach, recruit and retain participants to this study locally?
2. Are our staff trained to approach and recruit people from under-served groups (e.g. those living in care homes). If not, what training is required and how will we deliver this?
3. Do our staff have the correct equipment to deliver the study to under-served groups (e.g. portable testing and blood taking kit, car transport and PPE to conduct home visits, contracts and lone working policies to support home working, video and phone consulting systems to enable remote follow up)?
4. Do we have staff with particular skills or background who would be well suited to engage with under-served groups (e.g. speak the same language, live in the same area, experience working in a particular healthcare sector)?
5. Do we have processes in place locally to monitor whether we are reaching people from under-served groups – and if not, why not?
6. If recruiting people from under-served groups is taking more time or resources, is the extra time and resource being made available, either from the funder or from local resource?

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Figure 1. The INCLUDE roadmap

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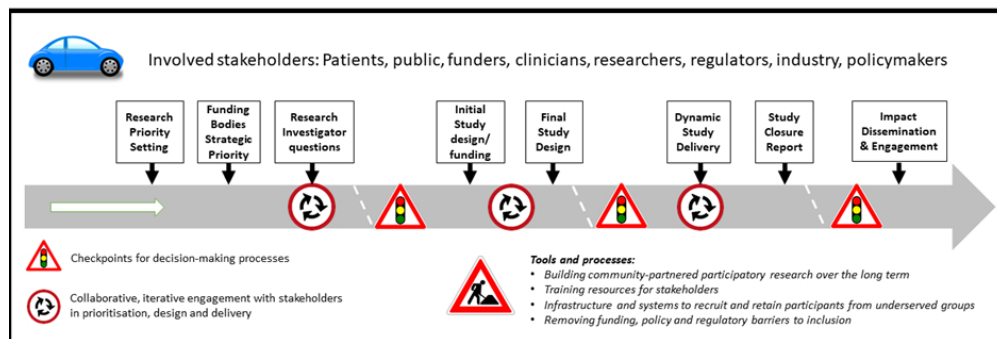


Figure 1. The INCLUDE roadmap

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Ensuring that COVID-19 Research is Inclusive - guidance from the NIHR INCLUDE project

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Ensuring that COVID-19 Research is Inclusive - guidance from the NIHR INCLUDE project

*COVID-19 studies need to be designed and delivered in ways that ensure inclusion of at-risk groups
often under-served by clinical research*

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Abstract

Objective: To provide guidance to researchers, funders, regulators and study delivery teams to ensure that research on COVID-19 is inclusive, particularly of groups disproportionately affected by COVID-19 and who may have been historically under-served by research.

Summary of key points: Groups who are disproportionately affected by COVID-19 include (but are not limited to) older people, people with multiple long-term conditions, people with disabilities, people from Black, Asian and Ethnic minority groups, people living with obesity, people who are socioeconomically deprived and people living in care homes. All these groups are under-served by clinical research, and there is an urgent need to rectify this if COVID-19 research is to deliver relevant evidence for these groups who are most in need. We provide a framework and checklists for addressing key issues when designing and delivering inclusive COVID-19 research, based on the NIHR INCLUDE project roadmap. Strong community engagement, co-development and prioritisation of research questions and interventions are essential. Under-served groups should be represented on funding panels and ethics committees, who should insist on removal of barriers to participation. Exclusion criteria should be kept to a minimum; intervention delivery and outcome measurement should be simple, flexible and tailored to the needs of different groups, and local advice on the best way to reach and engage with under-served communities should be taken by study delivery teams. Data on characteristics that allow identification of under-served groups must be collected, analyses should include these data to enable subgroup comparisons, and results should be shared with under-served groups at an early stage.

Conclusion: Inclusive COVID-19 research is a necessity, not a luxury, if research is to benefit all the communities it seeks to serve. It requires close engagement with under-served groups and attention to aspects of study topic, design, delivery, analysis and dissemination across the research lifecycle.

Key words:

COVID-19; recruitment; trial design; inclusivity; guidance

Strengths and Limitations

- We provide detailed guidance across the research lifecycle – a whole-systems approach to improve inclusion in COVID-19 research
- We base the guidance on the robustly-developed INCLUDE roadmap for improving inclusion in research
- The novelty of COVID-19 research precludes our recommendations being based on evidence directly derived from studies with people with COVID-19

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Introduction

COVID-19 is challenging health systems globally and has triggered an unprecedented research response.[1] Across the world, teams are designing and delivering studies encompassing a range of COVID-19 research including epidemiology, disease surveillance, disease consequences, early and late phase clinical trials. Early evidence suggests that some segments of the population are at high risk either of contracting COVID-19 or of more severe consequences of COVID-19 including hospitalisation and death.[2,3] Some of these groups have not been well reached by traditional research design and delivery mechanisms,[4] and there is growing concern that some of the groups most vulnerable to the impact of COVID-19 are under-represented in research studies.[5]

This guidance is designed to facilitate best practice in the design, funding, approval, regulation and delivery of research on COVID-19 and is a product of the ongoing National Institute for Health Research (NIHR) INnovations in CLinical trial design and delivery for the UnDEr-served (INCLUDE) project which seeks to improve research for under-served groups.

What is an under-served group?

There is no single definition of an under-served group in research; the definition is context-dependent and will vary depending on the population, disease and intervention being studied.[6] However, if a group is enrolled in a study at lower rates than one sees in the population affected by the disease, this is evidence that the group is likely to be under-served. Reasons for a group being under-served may include protocol design exclusions, an intervention that is unsuitable for that group, or because research delivery does not enable them to participate in practice.

Who is at risk of contracting COVID-19?

Our knowledge of who is more or less likely to be infected with COVID-19 (as opposed to suffering severe consequences of infection) is limited at present. However, individuals with a high degree of contact with those who are infected, including healthcare workers, retail staff, transport staff and other key workers with face to face roles are likely to be at high risk. Other groups in which risk appears elevated are patients who spend prolonged periods of time in close proximity to other patients (for example patients attending hospital-based haemodialysis [7]) and those in care homes;[8] emerging evidence suggests that once COVID-19 starts to affect a care home it can spread very rapidly through the care home population of both residents and staff.

Who is at risk of severe consequences of COVID-19?

Emerging data suggest that several groups are at higher risk of death or critical care unit admission from COVID-19 infection.[2,3,9] These groups include, but are not limited to, older people (particularly those aged 70 and over); men; people living with obesity; people with disabilities, people living with multiple long-term conditions; care home residents and others living with frailty; Black, Asian and minority ethnic (BAME) groups; and people with immunosuppression due to medication, systemic illness or malnutrition.

What groups may be under-served by healthcare and research systems with respect to COVID-19?

This is also likely to be context-specific, but examples include:

- Older people and others who are self-isolating (who may not be able to access healthcare easily) on government advice
- Those who may not be prioritised for hospital admission or critical care unit admission due to perceived limited life expectancy or a low chance of benefitting from such interventions.
- Those who lack digital literacy or access to digital technologies
- People with cognitive problems including dementia, especially those living alone, who may not be able to understand and/or adhere to the symptom reporting and testing needed for diagnosis.
- People with disabilities, who may not be able to access information or testing facilities and may struggle to access healthcare and care support during periods of lockdown [10]
- Socioeconomically deprived groups, who are likely to have less resilience to the economic shocks precipitated by the COVID-19 pandemic response
- People without a car or who live in rural areas (who may find it difficult to access testing facilities that require attendees to come in a car)

In addition, thought needs to be given to the fear that many of the population currently have of leaving their immediate environment, entering a hospital or other healthcare facility. This may disproportionately affect certain segments of the population (for example those with anxiety disorders or who perceive themselves to be especially vulnerable).

How can under-served groups be more successfully included in COVID-19 research?

The INCLUDE project contains a roadmap outlining the potential points of intervention to improve the inclusion of under-served groups (Figure 1) and a structure that may be helpful in guiding teams

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3 considering how to focus their efforts. Ensuring that effective training for researchers, funders,
4 delivery teams and regulators is key, as is ensuring that regulation is proportionate, and does not place
5 barriers in the way of including under-served groups. Identifying members of under-served groups
6 and using their knowledge is critical to successful delivery of research, as is building on existing
7 resources that have been created to facilitate research for specific under-served groups such as older
8 people [11] or people from Black, Asian or minority ethnic (BAME) communities.[12]
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17 **Recommendations from the INCLUDE project for COVID-19 research:**

18 Below, we set out a series of recommendations across the research lifecycle for how under-served
19 groups can be included more successfully in COVID-19 research:
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23 *Research Priority Setting:*

- 24 - Representatives from under-served groups should be consulted at the earliest possible time
25 to agree a set of national research priorities for COVID-19 research. A rapid James Lind Alliance
26 project (a priority-setting process co-produced by researchers, patients and a range of other
27 stakeholders) would be one possible way to achieve this, but opportunities also exist to ensure
28 representation on COVID-19 funding committees and prioritisation committees.
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35 *Strategic priorities for funding bodies:*

- 36 - Strategic priorities for research funding bodies (for example government funders and
37 charities) should reflect the views of under-served groups from any national or international
38 research priority exercise, as well as reflecting current scientific paradigms and national health
39 and social care system imperatives.
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- 45 - Patient and public representation should be in place on all COVID-19-related funding and
46 prioritisation panels, and this patient and public representation should encompass
47 representatives from groups who are at risk of being under-served by COVID-19 research.
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54 *Research investigator questions:*

- 55 - Specific research questions to be answered should be co-developed by research teams,
56 funders, government, and patient and public representatives including people from under-
57 served groups.
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Initial design and funding:

- Inclusion criteria for research studies should be kept to the minimum necessary to ensure patient safety, and that criteria likely to exclude broad sectors of populations should be avoided. In particular, we recommend that studies do not overtly or inadvertently exclude participants on the basis of age, sex, ethnicity, geography, socioeconomic status, multimorbidity, disability, cognitive impairment, body mass index or place of residence, unless studies specifically aim to generate data for groups that have to date been under-served by COVID-19 research.
- Interventions should be designed and selected to be usable by a wide range of participants, including those from under-served groups. If this is not possible, serious consideration should be given to abandoning the intervention on the grounds that it will not be broadly applicable in practice. Exceptions to this are interventions designed to target a specific biological pathway identified by disease severity or other disease characteristics (i.e. stratified or precision medicine approaches), or interventions designed specifically to target under-served groups where current approaches are not sufficiently effective.
- Outcomes should be selected to be relevant to a broad range of participants; outcomes should be simple and should place minimal burden on both participants and research teams. Outcomes should be deliverable under pandemic conditions (e.g. when wearing full personal protective equipment [PPE] in overloaded hospitals). Outcomes that can be collected from routinely collected clinical data, or participant-reported outcomes that have the flexibility to be collected by telephone, by videolink, by remote devices (e.g. accelerometers or other Bluetooth-enabled devices [13]) or by web-based / SMS interfaces should be preferred.
- When outcomes must be collected face to face, these should be able to be collected in a range of different environments including the participant's own home, not just in hospital wards or clinics. Outcomes should where possible be able to be assessed by a range of staff with no or minimal training to ensure that studies are resilient against staff illness or redeployment in future pandemic waves. Research teams should build in the costs of hardware, software and adequate time to support these outcome collection methods into their proposals.

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- Researchers should design study protocols to allow recruitment through as wide a range of routes as possible. Without good scientific reason, recruitment should not be limited to hospitals, primary care practices, or care institutions, but should be enabled through all of these routes and others including through community social hubs and organisations, via adverts, web-based signup, verbally over the telephone, in response to SMS and traditional mail, and other routes appropriate to reach particular under-served groups. The emergence of new community networks to support isolated and vulnerable people during the pandemic provides new opportunities for contacting and engaging under-served groups in research. Key issues to consider when designing COVID-19 studies are given in Box 1.
 - Funders can apply the checklist given later in this document (see Box 2) to assess whether research proposals have been developed in conjunction with under-served groups, and that proposals are designed and will be delivered in a way likely to be able to recruit under-served groups successfully in COVID-19 research.
 - Funders should ensure that additional funds (above and beyond the amount of money traditionally viewed as adequate to support recruitment and retention) are available to research teams to support successful recruitment of under-served groups. This may require funds for home visiting, transportation (in many cases by car or taxi not public transport), PPE, more screening per participant recruited, longer study visits, provision of translators or translated materials.

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Final study design:

- Research Ethics Committees should pay particular attention to inclusion and exclusion criteria, routes of recruitment, information materials, consent processes (including the needs of those without capacity) and whether under-served groups have been engaged in study design. Where study designs seem likely to fail to include sufficient people from under-served groups, ethics committees should robustly call attention to this, and ask research teams to modify their proposals accordingly even if doing so leads to short delays in approval of projects. Key issues to consider are listed in Box 2.
- Sponsor organisations should apply similar scrutiny to research proposals at the design stage and insist on changes where the design makes exclusion of under-served groups likely.

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- Sponsor organisations and Research Ethics Committees should both welcome and encourage novel and efficient methods of approaching, consenting, recruiting and retaining participants in research studies. Many proposals will be very different from those that such organisations are used to seeing, but this should be viewed as an opportunity, not a reason to fall back on traditional (and often ineffective) methods of study conduct.

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Study delivery:

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- Local research delivery teams should seek local advice on how to reach and engage with under-served groups in their areas. In many cases this will entail getting advice from members of specific ethnic communities, or those with lived experience of particular population sectors (e.g. those living in care homes, homeless people). Key issues to consider are listed in Box 3.
 - Training for research delivery staff (local investigators, research nurses and other research team members) should be delivered to raise awareness of the need to recruit inclusively, to highlight particular under-served groups, and to provide the generic skills required to engage with specific under-served groups.
 - Local research teams should configure themselves to be able to recruit in environments other than standard inpatient and outpatient secondary care departments. This should include conducting study procedures in participants' own homes, care homes, conducting study procedures remotely (e.g. via telephone and videolinks). Linking with neighbouring healthcare research organisations will enable cross-cover of research staff in the event of staff sickness or of one organisation becoming overloaded by clinical work in future pandemic waves.
 - For trials of medicinal products, dispensing arrangements for oral medications should be put in place to enable delivery of medications direct to participants' homes or local pharmacy rather than needing to collect medication from a research facility. This approach will help to build resilience against future restrictions on movement or closure of workplaces.
 - Local research support agencies (such as the UK NIHR local Clinical Research Networks and hospital Trusts) should provide local research teams with the equipment and resources that they need to deliver research in non-traditional settings. This may include transportation, contracts and working practice procedures enabling work in participants' homes, provision of COVID-19 testing and PPE in line with national guidance, IT hardware and software to enable

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3 videolinks, EConsent and electronic case record form use whilst roaming, translation services
4 and sufficient time to conduct study visits in non-traditional settings.
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- Local research support agencies should put in place systems to monitor local recruitment of under-served groups to each study. Combining these local data across studies will enable study teams to adapt their recruitment strategies at an early point, for instance switching place of recruitment, oversampling particular under-served groups, or changing how study teams approach participants.

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Study closure and analysis:

- Investigators and Sponsors should develop plans for how pauses or discontinuation of study activity due to future pandemic waves will be managed (ideally to at least enable study follow up to continue), and how these plans will be communicated to participants.
- Study reports and analysis plans should report the proportion of relevant under-served groups and compare these proportions to those found in the general population with COVID-19 illness.
- Study analysis plans should include prespecified subgroups analyses for key under-served groups, both to explore differences within studies, but also to enable later pooling of results from different under-served groups.

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Impact, dissemination and engagement:

- All studies should devise a comprehensive dissemination and engagement plan, and representatives from under-served groups should be part of the team drawing up these plans.
- Specific engagement plans for different under-served groups should be drawn up to enable appropriate tailoring of messages to different groups, in a way that best encourages feedback, debate and engagement within different groups.

Conclusion

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3 At a time when research on COVID-19 is being designed and delivered at an extraordinary speed, it
4 may seem that the urgency of the situation obviates the need to fully engage under-served groups in
5 the design and delivery of COVID-19 research. We argue however that doing so is not a luxury but a
6 necessity and failure to engage represents an enormous wasted opportunity.[14] It will hamper
7 scientific progress and potentially lead to the deployment of ineffective or harmful diagnostics and
8 therapeutics to large sections of the population. This in turn will lead to worse health outcomes for
9 under-served groups, and healthcare resources being wasted. Fully engaging under-served groups and
10 enabling their inclusion in COVID-19 research is the only way that we will be able to understand the
11 health impacts of COVID-19 in these most vulnerable groups and thus mitigate the impact of COVID-
12 19 on health and society in an equitable way.
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22 **Author contributions**

23 Miles Witham: Conceptualisation, wrote first draft, critical revision and editing, approval of final
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56 **Competing interests**

57 None declared
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References

1. Ramanan M, Stolz A, Ropplalsingh R, et al. An evaluation of the quality and impact of the global research response to the COVID-19 pandemic. *Med J Aust* 2020; <https://www.mja.com.au/journal/2020/evaluation-quality-and-impact-global-research-response-covid-19-pandemic> [Preprint, 30 June 2020; accessed 11 August 2020].
2. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) consortium. COVID-19 report April 27th 2020. https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_Platform_COVID_19_Report_27APR20.pdf (Accessed 11th August 2020)
3. Williamson EJ, Walker AJ, Bhaskaran K, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. *Nature* 2020;584:430-6.
4. Crome P, Lally F, Cherubini A, et al. Exclusion of older people from clinical trials: professional views from nine European countries participating in the PREDICT study. *Drugs Aging* 2011;28:667-77.
5. Treweek S, Forouhi NG, Narayan KMV, et al. COVID-19 and ethnicity: who will research results apply to? *Lancet* 2020;395:1955-7.
6. Witham MD, Anderson E, Carroll C, et al. Developing a roadmap to improve trial delivery for underserved groups: results from a UK multi-stakeholder process. *Trials* 2020;21:694.
7. Clarke C, Prendecki M, Dhutia A, et al. High Prevalence of Asymptomatic COVID-19 Infection in Hemodialysis Patients Detected Using Serologic Screening. *J Am Soc Nephrol* Published online first 30 July 2020. doi: 10.1681/ASN.2020060827.
8. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. *J Infect* 2020;81:411-9.
9. Intensive Care National Audit and Research Centre (ICNARC). ICNARC report on COVID-19 in critical care 31 July 2020. Available from: <https://www.icnarc.org>. (Accessed 24th August 2020).
10. Kuper H, Banks LM, Bright T, Davey C, Shakespeare T. Disability-inclusive COVID-19 response: What it is, why it is important and what we can learn from the United Kingdom's response. *Wellcome Open Res* 2020;5:79.
11. McMurdo ME, Roberts H, Parker S, et al. Improving recruitment of older people to research through good practice. *Age Ageing* 2011;40:659-65.
12. NIHR CLAHRC East Midlands Centre for BME Health. Toolkit for increasing participation of Black, Asian and minority ethnic (BAME) groups in health and social care research. December 2018. <http://learningforinvolvement.org.uk/?opportunity=toolkit-for-increasing-participation-of-black-and-minority-ethnic-bame-groups-in-health-and-social-care-research>. (Accessed 11th August 2020)

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3 13. Morgan C, Rolinski M, McNaney R, et al. Systematic Review Looking at the Use of Technology to
4 Measure Free-Living Symptom and Activity Outcomes in Parkinson's Disease in the Home or a Home-
5 like Environment. *J Parkinsons Dis* 2020;10:429-54.
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8 14. Glasziou PP, Sanders S, Hoffmann T. Waste in COVID-19 research. *BMJ* 2020; 369:m1847.
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Box 1. A checklist to guide researchers in designing inclusive COVID-19 research

1. Have I engaged with representatives of under-served groups in designing my study question and protocol?
2. Have I avoided inclusion/exclusion criteria likely to lead to exclusion of under-served groups? (e.g. age limits, excluding multimorbidities, BMI limits)
3. Is my study intervention suitable for, and acceptable to, under-served groups? (e.g. avoiding gelatine capsules on medication)
4. Are my outcomes validated and relevant to a broad range of patients in the populations that my research seeks to serve? (e.g. cognition assessment tools in translated versions)
5. Have I avoided study burden that is likely to make it more difficult for some groups to participate? (e.g. frequent study visits)
6. Have I provided a range of recruitment pathways that give flexibility in how participants are sought and contacted? (e.g. not confining recruitment to drive-in testing centres, allowing recruitment from care homes)
7. Have I provided study information in a format that is accessible to under-served groups? (e.g. translations of study information, simplified study information, information written with a reading age of 9 or below, written in large font size)
8. Have I enabled consent to be obtained in a way that is flexible and tailored to the needs of different groups? (e.g. EConsent for those isolating, assent from relatives for those with cognitive impairment). Have I involved carers and assentees in the design of the assent process for studies where consent cannot be obtained from the participant?
9. Will my study still be deliverable in the event of a second pandemic wave, with possible increase in lockdown restrictions and study staff redeployment?

Box 2. A checklist to guide funders and reviewers in assessing inclusiveness of COVID-19 research

1. Does the topic of the study reflect the priorities elicited by consultation with under-served groups?
2. Have representatives from under-served groups been engaged in the design of the study, and in what way?
3. Does the target population for the study (as defined by the inclusion and exclusion criteria) reflect those who are at risk of contracting COVID-19 or who are at increased risk of the adverse consequences of COVID-19?
4. Have the investigators taken steps to ensure that these potentially under-served groups will be included in the study with appropriate mitigation of any risks?
5. Are there unnecessary or unjustifiable exclusion criteria (e.g. old age, sex, ethnicity, obesity, cognitive impairment, multimorbidity) or research methods that will act as barriers to inclusion of under-served groups at high risk of COVID-19 infection and its adverse consequences?
6. Is the intervention designed and delivered in a way that is acceptable and feasible to a broad range of people most at risk from COVID-19 infection?
7. Are the study outcomes easy to measure, and can they be measured in a range of different environments? Will they still be able to be measured during the peak of a pandemic wave or during population lockdown?
8. Does the study target a specific under-served group? If so, is adequate justification for this given, and is the strategy proposed to target the group likely to succeed?

Box 3. A checklist to guide research delivery teams in delivering inclusive COVID-19 research

1. Have we engaged with local representatives from under-served groups to understand how best to approach, recruit and retain participants to this study locally?
2. Are our staff trained to approach and recruit people from under-served groups? (e.g. those living in care homes). If not, what training is required and how will we deliver this?
3. Do our staff have the correct equipment to deliver the study to under-served groups (e.g. portable testing and blood taking kit, car transport and PPE to conduct home visits, contracts and lone working policies to support home working, video and phone consulting systems to enable remote follow up)?
4. Do we have staff with particular skills or background who would be well suited to engage with under-served groups (e.g. speak the same language, live in the same area, experience working in a particular healthcare sector)?
5. Do we have processes in place locally to monitor whether we are reaching people from under-served groups – and if not, why not?
6. If recruiting people from under-served groups is taking more time or resources, is the extra time and resource being made available, either from the funder or from local resource?

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3 **Figure 1. The INCLUDE roadmap**
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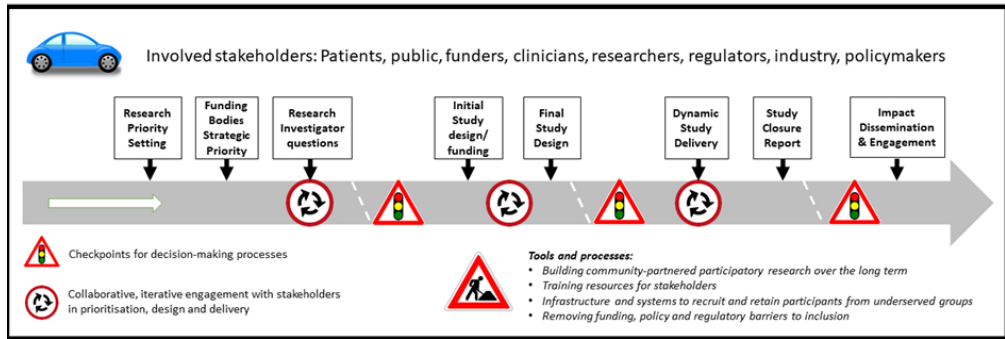


Figure 1. The INCLUDE roadmap

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Ensuring that COVID-19 Research is Inclusive - guidance from the NIHR INCLUDE project

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Ensuring that COVID-19 Research is Inclusive - guidance from the NIHR INCLUDE project

*COVID-19 studies need to be designed and delivered in ways that ensure inclusion of at-risk groups
often under-served by clinical research*

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Abstract

Objective: To provide guidance to researchers, funders, regulators and study delivery teams to ensure that research on COVID-19 is inclusive, particularly of groups disproportionately affected by COVID-19 and who may have been historically under-served by research.

Summary of key points: Groups who are disproportionately affected by COVID-19 include (but are not limited to) older people, people with multiple long-term conditions, people with disabilities, people from Black, Asian and Ethnic minority groups, people living with obesity, people who are socioeconomically deprived and people living in care homes. All these groups are under-served by clinical research, and there is an urgent need to rectify this if COVID-19 research is to deliver relevant evidence for these groups who are most in need. We provide a framework and checklists for addressing key issues when designing and delivering inclusive COVID-19 research, based on the NIHR INCLUDE project roadmap. Strong community engagement, co-development and prioritisation of research questions and interventions are essential. Under-served groups should be represented on funding panels and ethics committees, who should insist on removal of barriers to participation. Exclusion criteria should be kept to a minimum; intervention delivery and outcome measurement should be simple, flexible and tailored to the needs of different groups, and local advice on the best way to reach and engage with under-served communities should be taken by study delivery teams. Data on characteristics that allow identification of under-served groups must be collected, analyses should include these data to enable subgroup comparisons, and results should be shared with under-served groups at an early stage.

Conclusion: Inclusive COVID-19 research is a necessity, not a luxury, if research is to benefit all the communities it seeks to serve. It requires close engagement with under-served groups and attention to aspects of study topic, design, delivery, analysis and dissemination across the research lifecycle.

Key words:

COVID-19; recruitment; trial design; inclusivity; guidance

Strengths and Limitations

- We provide detailed guidance across the research lifecycle – a whole-systems approach to improve inclusion in COVID-19 research
- We base the guidance on the robustly-developed INCLUDE roadmap for improving inclusion in research
- The novelty of COVID-19 research precludes our recommendations being based on evidence directly derived from studies with people with COVID-19

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Introduction

COVID-19 is challenging health systems globally and has triggered an unprecedented research response.[1] Across the world, teams are designing and delivering studies encompassing a range of COVID-19 research including epidemiology, disease surveillance, disease consequences, early and late phase clinical trials. Early evidence suggests that some segments of the population are at high risk either of contracting COVID-19 or of more severe consequences of COVID-19 including hospitalisation and death.[2,3] Some of these groups have not been well reached by traditional research design and delivery mechanisms,[4] and there is growing concern that some of the groups most vulnerable to the impact of COVID-19 are under-represented in research studies.[5]

This guidance is designed to facilitate best practice in the design, funding, approval, regulation and delivery of research on COVID-19 and is a product of the ongoing National Institute for Health Research (NIHR) INnovations in CLinical trial design and delivery for the UnDEr-served (INCLUDE) project which seeks to improve research for under-served groups; the guidance has been made available by the NIHR website. [6]

What is an under-served group?

There is no single definition of an under-served group in research; the definition is context-dependent and will vary depending on the population, disease and intervention being studied.[7] However, if a group is enrolled in a study at lower rates than one sees in the population affected by the disease, this is evidence that the group is likely to be under-served. Reasons for a group being under-served may include protocol design exclusions, an intervention that is unsuitable for that group, or because research delivery does not enable them to participate in practice.

Who is at risk of contracting COVID-19?

Our knowledge of who is more or less likely to be infected with COVID-19 (as opposed to suffering severe consequences of infection) is limited at present. However, individuals with a high degree of contact with those who are infected, including healthcare workers, retail staff, transport staff and other key workers with face to face roles are likely to be at high risk. Other groups in which risk appears elevated are patients who spend prolonged periods of time in close proximity to other patients (for example patients attending hospital-based haemodialysis [8]) and those in care homes;[9] emerging evidence suggests that once COVID-19 starts to affect a care home it can spread very rapidly through the care home population of both residents and staff.

Who is at risk of severe consequences of COVID-19?

Emerging data suggest that several groups are at higher risk of death or critical care unit admission from COVID-19 infection.[2,3,10] These groups include, but are not limited to, older people (particularly those aged 70 and over); men; people living with obesity; people with disabilities, people living with multiple long-term conditions; care home residents and others living with frailty; Black, Asian and minority ethnic (BAME) groups; and people with immunosuppression due to medication, systemic illness or malnutrition.

What groups may be under-served by healthcare and research systems with respect to COVID-19?

This is also likely to be context-specific, but examples include:

- Older people and others who are self-isolating (who may not be able to access healthcare easily) on government advice
- Those who may not be prioritised for hospital admission or critical care unit admission due to perceived limited life expectancy or a low chance of benefitting from such interventions.
- Those who lack digital literacy or access to digital technologies
- People with cognitive problems including dementia, especially those living alone, who may not be able to understand and/or adhere to the symptom reporting and testing needed for diagnosis.
- People with disabilities, who may not be able to access information or testing facilities and may struggle to access healthcare and care support during periods of lockdown [11]
- Socioeconomically deprived groups, who are likely to have less resilience to the economic shocks precipitated by the COVID-19 pandemic response
- People without a car or who live in rural areas (who may find it difficult to access testing facilities that require attendees to come in a car)

In addition, thought needs to be given to the fear that many of the population currently have of leaving their immediate environment, entering a hospital or other healthcare facility. This may disproportionately affect certain segments of the population (for example those with anxiety disorders or who perceive themselves to be especially vulnerable).

How can under-served groups be more successfully included in COVID-19 research?

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3 The INCLUDE project contains a roadmap outlining the potential points of intervention to improve the
4 inclusion of under-served groups (Figure 1) and a structure that may be helpful in guiding teams
5 considering how to focus their efforts. Ensuring that effective training for researchers, funders,
6 delivery teams and regulators is key, as is ensuring that regulation is proportionate, and does not place
7 barriers in the way of including under-served groups. Identifying members of under-served groups
8 and using their knowledge is critical to successful delivery of research, as is building on existing
9 resources that have been created to facilitate research for specific under-served groups such as older
10 people [12] or people from Black, Asian or minority ethnic (BAME) communities.[13]
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20 **Recommendations from the INCLUDE project for COVID-19 research:**

21 Below, we set out a series of recommendations across the research lifecycle for how under-served
22 groups can be included more successfully in COVID-19 research:
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26 *Research Priority Setting:*

- 27 - Representatives from under-served groups should be consulted at the earliest possible time
28 to agree a set of national research priorities for COVID-19 research. A rapid James Lind Alliance
29 project (a priority-setting process co-produced by researchers, patients and a range of other
30 stakeholders) would be one possible way to achieve this, but opportunities also exist to ensure
31 representation on COVID-19 funding committees and prioritisation committees.
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38 *Strategic priorities for funding bodies:*

- 39 - Strategic priorities for research funding bodies (for example government funders and
40 charities) should reflect the views of under-served groups from any national or international
41 research priority exercise, as well as reflecting current scientific paradigms and national health
42 and social care system imperatives.
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48 - Patient and public representation should be in place on all COVID-19-related funding and
49 prioritisation panels, and this patient and public representation should encompass
50 representatives from groups who are at risk of being under-served by COVID-19 research.
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57 *Research investigator questions:*

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3 - Specific research questions to be answered should be co-developed by research teams,
4 funders, government, and patient and public representatives including people from under-
5 served groups.
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11 *Initial design and funding:*

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13 - Inclusion criteria for research studies should be kept to the minimum necessary to ensure
14 patient safety, and that criteria likely to exclude broad sectors of populations should be
15 avoided. In particular, we recommend that studies do not overtly or inadvertently exclude
16 participants on the basis of age, sex, ethnicity, geography, socioeconomic status,
17 multimorbidity, disability, cognitive impairment, body mass index or place of residence, unless
18 studies specifically aim to generate data for groups that have to date been under-served by
19 COVID-19 research.
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26 - Interventions should be designed and selected to be usable by a wide range of participants,
27 including those from under-served groups. If this is not possible, serious consideration should
28 be given to abandoning the intervention on the grounds that it will not be broadly applicable
29 in practice. Exceptions to this are interventions designed to target a specific biological
30 pathway identified by disease severity or other disease characteristics (i.e. stratified or
31 precision medicine approaches), or interventions designed specifically to target under-served
32 groups where current approaches are not sufficiently effective.
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40 - Outcomes should be selected to be relevant to a broad range of participants; outcomes should
41 be simple and should place minimal burden on both participants and research teams.
42 Outcomes should be deliverable under pandemic conditions (e.g. when wearing full personal
43 protective equipment [PPE] in overloaded hospitals). Outcomes that can be collected from
44 routinely collected clinical data, or participant-reported outcomes that have the flexibility to
45 be collected by telephone, by videolink, by remote devices (e.g. accelerometers or other
46 Bluetooth-enabled devices [14]) or by web-based / SMS interfaces should be preferred,
47 ensuring that such platforms can be used by participants with a range of sensory and motor
48 disabilities.
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56 - When outcomes must be collected face to face, these should be able to be collected in a range
57 of different environments including the participant's own home, not just in hospital wards or
58 clinics. Outcomes should where possible be able to be assessed by a range of staff with no or
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3 minimal training to ensure that studies are resilient against staff illness or redeployment in
4 future pandemic waves. Research teams should build in the costs of hardware, software,
5 accommodations for people with disability and adequate time to support these outcome
6 collection methods into their proposals.
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12 - Researchers should design study protocols to allow recruitment through as wide a range of
13 routes as possible. Without good scientific reason, recruitment should not be limited to
14 hospitals, primary care practices, or care institutions, but should be enabled through all of
15 these routes and others including through community social hubs and organisations, via
16 adverts, web-based signup, verbally over the telephone, in response to SMS and traditional
17 mail, and other routes appropriate to reach particular under-served groups. The emergence
18 of new community networks to support isolated and vulnerable people during the pandemic
19 provides new opportunities for contacting and engaging under-served groups in research. Key
20 issues to consider when designing COVID-19 studies are given in Box 1.
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28 - Funders can apply the checklist given later in this document (see Box 2) to assess whether
29 research proposals have been developed in conjunction with under-served groups, and that
30 proposals are designed and will be delivered in a way likely to be able to recruit under-served
31 groups successfully in COVID-19 research.
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37 - Funders should ensure that additional funds (above and beyond the amount of money
38 traditionally viewed as adequate to support recruitment and retention) are available to
39 research teams to support successful recruitment of under-served groups. This may require
40 funds for home visiting, transportation (in many cases by car or taxi not public transport), PPE,
41 more screening per participant recruited, longer study visits, provision of translators or
42 translated materials.
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48 *Final study design:*
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- 50 - Research Ethics Committees should pay particular attention to inclusion and exclusion criteria,
51 routes of recruitment, information materials, consent processes (including the needs of those
52 without capacity) and whether under-served groups have been engaged in study design.
53 Where study designs seem likely to fail to include sufficient people from under-served groups,
54 ethics committees should robustly call attention to this, and ask research teams to modify
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3 their proposals accordingly even if doing so leads to short delays in approval of projects. Key
4 issues to consider are listed in Box 2.
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- Sponsor organisations should apply similar scrutiny to research proposals at the design stage and insist on changes where the design makes exclusion of under-served groups likely.
 - Sponsor organisations and Research Ethics Committees should both welcome and encourage novel and efficient methods of approaching, consenting, recruiting and retaining participants in research studies. Many proposals will be very different from those that such organisations are used to seeing, but this should be viewed as an opportunity, not a reason to fall back on traditional (and often ineffective) methods of study conduct.

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24 *Study delivery:*

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- Local research delivery teams should seek local advice on how to reach and engage with under-served groups in their areas. In many cases this will entail getting advice from members of specific ethnic communities, or those with lived experience of particular population sectors (e.g. those living in care homes, homeless people). In selected cases, this may extend to using members of under-served communities to deliver research. Key issues to consider are listed in Box 3.
 - Training for research delivery staff (local investigators, research nurses and other research team members) should be delivered to raise awareness of the need to recruit inclusively, to highlight particular under-served groups, and to provide the generic skills required to engage with specific under-served groups.
 - Local research teams should configure themselves to be able to recruit in environments other than standard inpatient and outpatient secondary care departments. This should include conducting study procedures in participants' own homes, care homes, conducting study procedures remotely (e.g. via telephone and videolinks), taking care to accommodate the needs of those with a range of disabilities. Linking with neighbouring healthcare research organisations will enable cross-cover of research staff in the event of staff sickness or of one organisation becoming overloaded by clinical work in future pandemic waves.
 - For trials of medicinal products, dispensing arrangements for oral medications should be put in place to enable delivery of medications direct to participants' homes or local pharmacy

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3 rather than needing to collect medication from a research facility. This approach will help to
4 build resilience against future restrictions on movement or closure of workplaces.
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- Local research support agencies (such as the UK NIHR local Clinical Research Networks and hospital Trusts) should provide local research teams with the equipment and resources that they need to deliver research in non-traditional settings. This may include transportation, contracts and working practice procedures enabling work in participants' homes, provision of COVID-19 testing and PPE in line with national guidance, IT hardware and software to enable videolinks, EConsent and electronic case record form use whilst roaming, translation services and sufficient time to conduct study visits in non-traditional settings.
 - Local research support agencies should put in place systems to monitor local recruitment of under-served groups to each study. Combining these local data across studies will enable study teams to adapt their recruitment strategies at an early point, for instance switching place of recruitment, oversampling particular under-served groups, or changing how study teams approach participants.

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32 *Study closure and analysis:*

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- Investigators and Sponsors should develop plans for how pauses or discontinuation of study activity due to future pandemic waves will be managed (ideally to at least enable study follow up to continue), and how these plans will be communicated to participants.
 - Study reports and analysis plans should report the proportion of relevant under-served groups and compare these proportions to those found in the general population with COVID-19 illness.
 - Study analysis plans should include adequately-powered prespecified subgroup analyses for key under-served groups, both to explore differences within studies, but also to enable later pooling of results from different under-served groups.

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56 *Impact, dissemination and engagement:*

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- All studies should devise a comprehensive dissemination and engagement plan, and representatives from under-served groups should be part of the team drawing up these plans.

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5 - Specific engagement plans for different under-served groups should be drawn up to enable
6 appropriate tailoring of messages to different groups, in a way that best encourages feedback,
7 debate and engagement within different groups.
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11 **Conclusion**

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13 At a time when research on COVID-19 is being designed and delivered at an extraordinary speed, it
14 may seem that the urgency of the situation obviates the need to fully engage under-served groups in
15 the design and delivery of COVID-19 research. We argue however that doing so is not a luxury but a
16 necessity and failure to engage represents an enormous wasted opportunity.[15] It will hamper
17 scientific progress and potentially lead to the deployment of ineffective or harmful diagnostics and
18 therapeutics to large sections of the population. This in turn will lead to worse health outcomes for
19 under-served groups, and healthcare resources being wasted. Fully engaging under-served groups and
20 enabling their inclusion in COVID-19 research is the only way that we will be able to understand the
21 health impacts of COVID-19 in these most vulnerable groups and thus mitigate the impact of COVID-
22 19 on health and society in an equitable way.
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31 **Author contributions**

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34 version. Eleanor Anderson: Conceptualisation, critical revision and editing, approval of final version.
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Competing interests

None declared

References

1. Ramanan M, Stolz A, Rooplalingh R, et al. An evaluation of the quality and impact of the global research response to the COVID-19 pandemic. *Med J Aust* 2020; <https://www.mja.com.au/journal/2020/evaluation-quality-and-impact-global-research-response-covid-19-pandemic> [Preprint, 30 June 2020; accessed 11 August 2020].
2. International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) consortium. COVID-19 report April 27th 2020. https://media.tghn.org/medialibrary/2020/05/ISARIC_Data_Platform_COVID_19_Report_27APR20.pdf (Accessed 11th August 2020)
3. Williamson EJ, Walker AJ, Bhaskaran K, et al. OpenSAFELY: factors associated with COVID-19 death in 17 million patients. *Nature* 2020;584:430-6.
4. Crome P, Lally F, Cherubini A, et al. Exclusion of older people from clinical trials: professional views from nine European countries participating in the PREDICT study. *Drugs Aging* 2011;28:667-77.
5. Treweek S, Forouhi NG, Narayan KMV, et al. COVID-19 and ethnicity: who will research results apply to? *Lancet* 2020;395:1955-7.
6. National Institute for Health Research. Ensuring that COVID-19 Research is Inclusive: Guidance from the NIHR CRN INCLUDE project. Available from: <https://www.nihr.ac.uk/documents/ensuring-that-covid-19-research-is-inclusive-guidance-from-the-nihr-crn-include-project/25441>. (Accessed 21st October 2020)
7. Witham MD, Anderson E, Carroll C, et al. Developing a roadmap to improve trial delivery for underserved groups: results from a UK multi-stakeholder process. *Trials* 2020;21:694.
8. Clarke C, Prendecki M, Dhutia A, et al. High Prevalence of Asymptomatic COVID-19 Infection in Hemodialysis Patients Detected Using Serologic Screening. *J Am Soc Nephrol* Published online first 30 July 2020. doi: 10.1681/ASN.2020060827.
9. Graham NSN, Junghans C, Downes R, et al. SARS-CoV-2 infection, clinical features and outcome of COVID-19 in United Kingdom nursing homes. *J Infect* 2020;81:411-9.

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2
3 10. Intensive Care National Audit and Research Centre (ICNARC). ICNARC report on COVID-19 in critical
4 care 31 July 2020. Available from: <https://www.icnarc.org>. (Accessed 24th August 2020).
5
6 11. Kuper H, Banks LM, Bright T, Davey C, Shakespeare T. Disability-inclusive COVID-19 response: What
7 it is, why it is important and what we can learn from the United Kingdom's response. *Wellcome Open*
8 *Res* 2020;5:79.
9
10 12. McMurdo ME, Roberts H, Parker S, et al. Improving recruitment of older people to research
11 through good practice. *Age Ageing* 2011;40:659-65.
12
13 13. NIHR CLAHRC East Midlands Centre for BME Health. Toolkit for increasing participation of Black,
14 Asian and minority ethnic (BAME) groups in health and social care research. December 2018.
15 [http://learningforinvolvement.org.uk/?opportunity=toolkit-for-increasing-participation-of-black-](http://learningforinvolvement.org.uk/?opportunity=toolkit-for-increasing-participation-of-black-and-minority-ethnic-bame-groups-in-health-and-social-care-research)
16 [and-minority-ethnic-bame-groups-in-health-and-social-care-research.](http://learningforinvolvement.org.uk/?opportunity=toolkit-for-increasing-participation-of-black-and-minority-ethnic-bame-groups-in-health-and-social-care-research) (Accessed 11th August 2020)
17
18 14. Morgan C, Rolinski M, McNaney R, et al. Systematic Review Looking at the Use of Technology to
19 Measure Free-Living Symptom and Activity Outcomes in Parkinson's Disease in the Home or a Home-
20 like Environment. *J Parkinsons Dis* 2020;10:429-54.
21
22 15. Glasziou PP, Sanders S, Hoffmann T. Waste in COVID-19 research. *BMJ* 2020; 369:m1847.
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Box 1. A checklist to guide researchers in designing inclusive COVID-19 research

1. Have I engaged with representatives of under-served groups in designing my study question and protocol?
2. Have I avoided inclusion/exclusion criteria likely to lead to exclusion of under-served groups? (e.g. age limits, excluding multimorbidities, BMI limits)
3. Is my study intervention suitable for, and acceptable to, under-served groups? (e.g. avoiding gelatine capsules on medication)
4. Are my outcomes validated and relevant to a broad range of patients in the populations that my research seeks to serve? (e.g. cognition assessment tools in translated versions)
5. Have I avoided study burden that is likely to make it more difficult for some groups to participate? (e.g. frequent study visits)
6. Have I provided a range of recruitment pathways that give flexibility in how participants are sought and contacted? (e.g. not confining recruitment to drive-in testing centres, allowing recruitment from care homes)
7. Have I provided study information in a format that is accessible to under-served groups? (e.g. translations of study information, simplified study information, information written with a reading age of 9 or below, written in large font size, screen reader compatible)
8. Have I enabled consent to be obtained in a way that is flexible and tailored to the needs of different groups? (e.g. EConsent for those isolating, assent or supported decision-making from relatives for those with cognitive impairment). Have I involved carers and assentees in the design of the assent process for studies where consent cannot be obtained from the participant?
9. Will my study still be deliverable in the event of a second pandemic wave, with possible increase in lockdown restrictions and study staff redeployment?

Box 2. A checklist to guide funders and reviewers in assessing inclusiveness of COVID-19 research

1. Does the topic of the study reflect the priorities elicited by consultation with under-served groups?
2. Have representatives from under-served groups been engaged in the design of the study, and in what way?
3. Does the target population for the study (as defined by the inclusion and exclusion criteria) reflect those who are at risk of contracting COVID-19 or who are at increased risk of the adverse consequences of COVID-19?
4. Have the investigators taken steps to ensure that these potentially under-served groups will be included in the study with appropriate mitigation of any risks?
5. Are there unnecessary or unjustifiable exclusion criteria (e.g. old age, sex, ethnicity, obesity, cognitive impairment, multimorbidity) or research methods that will act as barriers to inclusion of under-served groups at high risk of COVID-19 infection and its adverse consequences?
6. Is the intervention designed and delivered in a way that is acceptable and feasible to a broad range of people most at risk from COVID-19 infection?
7. Are the study outcomes easy to measure, and can they be measured in a range of different environments? Will they still be able to be measured during the peak of a pandemic wave or during population lockdown?
8. Does the study target a specific under-served group? If so, is adequate justification for this given, and is the strategy proposed to target the group likely to succeed?

Box 3. A checklist to guide research delivery teams in delivering inclusive COVID-19 research

1. Have we engaged with local representatives from under-served groups to understand how best to approach, recruit and retain participants to this study locally?
2. Are our staff trained to approach and recruit people from under-served groups? (e.g. those living in care homes). If not, what training is required (e.g. age inclusion training, disability inclusion training) and how will we deliver this?
3. Do our staff have the correct equipment to deliver the study to under-served groups (e.g. portable testing and blood taking kit, car transport and PPE to conduct home visits, contracts and lone working policies to support home working, video and phone consulting systems to enable remote follow up, accommodations to support the inclusion of people with disabilities)?
4. Do we have staff with particular skills or background who would be well suited to engage with under-served groups (e.g. speak the same language, live in the same area, experience working in a particular healthcare sector)?
5. Do we have processes in place locally to monitor whether we are reaching people from under-served groups – and if not, why not?
6. If recruiting people from under-served groups is taking more time or resources, is the extra time and resource being made available, either from the funder or from local resource?

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3 **Figure 1. The INCLUDE roadmap**
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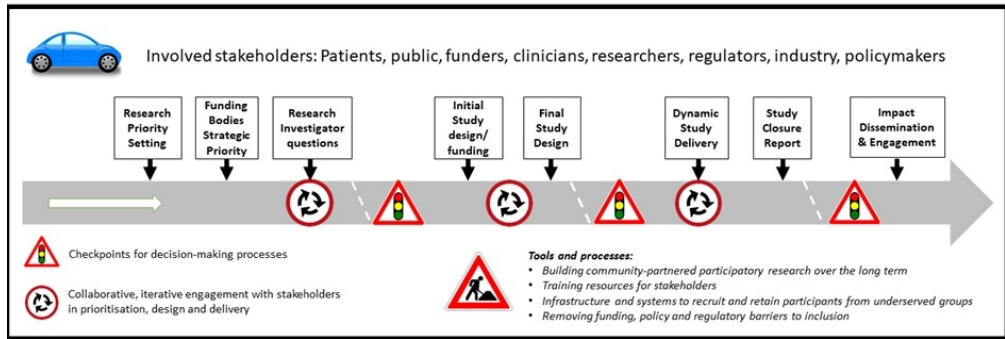


Figure 1. The INCLUDE roadmap

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