Improving diversity in research: methods to support inclusion

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" Diversity in research isn't simply a matter of social justice. It's a critical part of learning how to improve the health of every person.

[NEJM 2021]

Importance of diversity in health and care research

- Research is essential to improving health and wellbeing – but not everyone has access to research studies

- Without inclusion of diverse research participants, it is difficult to understand how study findings will translate into the real world

- Many of the barriers relating to inclusion in research are the same as those impacting access to care and wider health inequalities

- Groups considered under-served in clinical research are heterogenous - often considered in terms of protected characteristics e.g ethnicity, disability, or age …..

- … But what constitutes under-served is complex and context-specific—and may be disease or study-specific

More health inequality: Black people are 3 times more likely to experience pulse oximeter errors

World View | Published: 13 January 2021

Women and children last? Shaking up exclusion criteria for vaccine trials

- Ethnic minority groups disproportionately affected by COVID
- Deaths from COVID two to four times greater than those among the White population (England & Wales)
- Black patients were three times more likely than white patients to have low oxygen levels that were missed by pulse oximeters – issue known about since 1980s

- Pregnancy and breastfeeding common exclusion criteria in clinical trials
- Three-quarters of trials for COVID treatments or vaccines explicitly excluded pregnant women
- Pregnant women with COVID are at increased risk for serious adverse outcomes
- Lack of evidence affects vaccination decision-making

Consequences of a lack of inclusivity – example of COVID (2)

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Related video: EU imposes export controls on Covid-19 vaccines

Macron claims Oxford-AstraZeneca Covid vaccine 'quasi-ineffective' on older people

French president criticises UK's rollout strategy amid row over EU delay

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Eight in 10 deaths of people with a learning disability are COVID related as inequality soars

2 February 2021

Eighty percent of the deaths of people with a learning disability in England were COVID-19-related in the week ending 22 January.

- COVID disproportionately affected older people
- Review found <u>half</u> of COVID trials excluded older people
- <u>All</u> COVID vaccine trials in the review excluded older people - led to claims that COVID vaccines don't work for older people

- People with a learning disability at high risk from COVID
- Mortality rate up to <u>6 times</u> higher during the first wave of the pandemic than general population
- People with learning disabilities not initially classified as high priority in the COVID vaccine plan

Under-served groups in research

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Some key characteristics that are common to under-served groups are:

- Lower inclusion in research than would be expected from population estimates

- High healthcare burden that is not matched by the volume of research designed for the group

- Important differences in how a group responds to or engages with healthcare interventions compared to other groups

Why under-served groups must be included in research:

- Results may not be generalisable to those groups (effectiveness, benefits and risks)

- Research that is not inclusive will not command the confidence of patients, healthcare professionals or the public

- Opportunity to contribute to, and benefit from, research should be equitable

Exclusion leads to *evidence-biased* care and widens health inequalities

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HbA1c test may be inaccurate for thousands of South Asian people, research finds

Tens of thousands of people of South Asian heritage with diabetes and pre-diabetes may have underestimated HbA1c levels researchers have said, after they identified a genetic variant that affects the accuracy of the test.

by Emma Bower

Commission on Race and Ethnic Disparities

Research and analysis
Ethnic disparities in the major causes of mortality and their risk factors – a rapid review
Updated 28 April 2021

Contents

Social disparity by ethnic group

Life expectancy, healthy life expectancy, overall mortality and premature mortality

Leading causes of mortality

Behavioural risk factors

Role of genetics and epigenetics in explaining differences between ethnic groups

Healthcare utilisation, disease management and risk factor control

Some conclusions from the data presented

Ethnic disparities in the major causes of mortality and their risk factors in the UK – submission to the Commission on Race and Ethnic Disparities.

Raghib Ali, Avirup Chowdhury, Nita Forouhi, Nick Wareham. MRC Epidemiology Unit, University of Cambridge.

This paper mainly focuses on the 2 leading causes of death in the UK: cancers and cardiovascular diseases which account for 55% of deaths in the UK, and their major risk factors.

In considering disparities, we look at both ethnicity and deprivation as there are strong associations between ethnicity and deprivation, and between deprivation and most health outcomes.

Impact on wider inequalities in care – women

Research reveals striking inequalities in NHS heart care

05 October 2023   Laura Piercy

Category: Research

Stark inequalities in diagnosis and treatment of four of the most common heart conditions in the UK have been revealed in research we've funded published today in The Lancet Regional Health - Europe.

Why is there is a gender difference?

"There's something wrong with the way the guidelines are explained per gender for interpreting the biomarker. It's possible that a woman's hormones are interfering with the results of the test," the Biomedical and Nutritional Sciences Assoc. Prof. Mahdi Garelnabi who published the analysis on why women suffer worse outcomes than men during heart diseases. In a blood test, a high-sensitivity troponin assay biomarker, is used by doctors to detect heart diseases; however, the result of the biomarker should not be analysed the same way it is analysed for men.

THE LANCET

Cardiology's problem women

The Lancet

Published: March 09, 2019 • DOI: https://doi.org/10.1016/S0140-6736(19)30510-0 • Check for updates

Asked to describe a typical heart attack, most people (including most doctors), would describe a man with crushing chest pain, probably with a background history of hypertension. But this traditional teaching, it turns out, is only telling us half the story. Cardiovascular disease is also the leading cause of death in women globally and, in the USA, leads to a similar number of deaths in men and women. The failure to recognise the prevalence of heart disease in women and the different set of symptoms in women (feeling generally unwell or unexplained weakness) during a heart attack contribute to delays in women seeking help and the loss of vital time in a cardiovascular emergency. Even after seeking help, women get consistently worse care. US data, published in *Women's Health Issues* in December, last year, showed that women with heart attack symptoms were less likely to receive aspirin, be resuscitated, or be transported to the hospital in ambulances using lights and sirens than were men. These factors contribute to the disproportionately higher mortality in women with cardiovascular disease than men. A major shift in thinking is required to realise that the traditional medical textbooks and many public and professional assumptions about who gets and dies from heart disease and how it manifests are simply wrong. For both men and women, evidence-based approaches are needed to minimise the time from onset of symptoms to treatment.
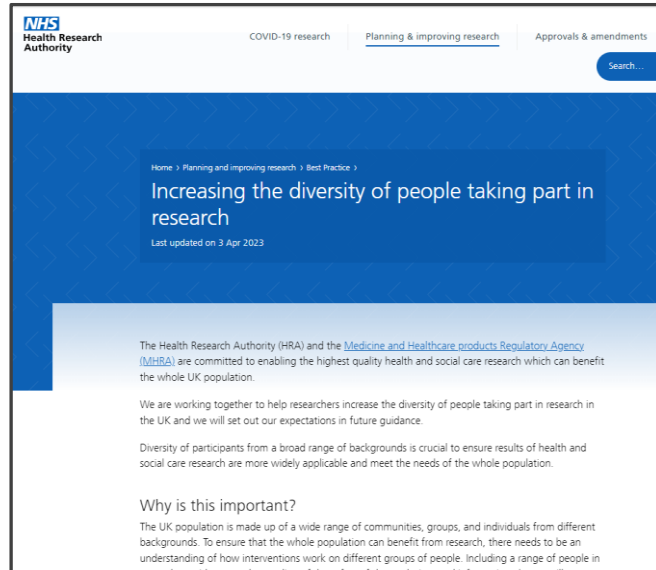
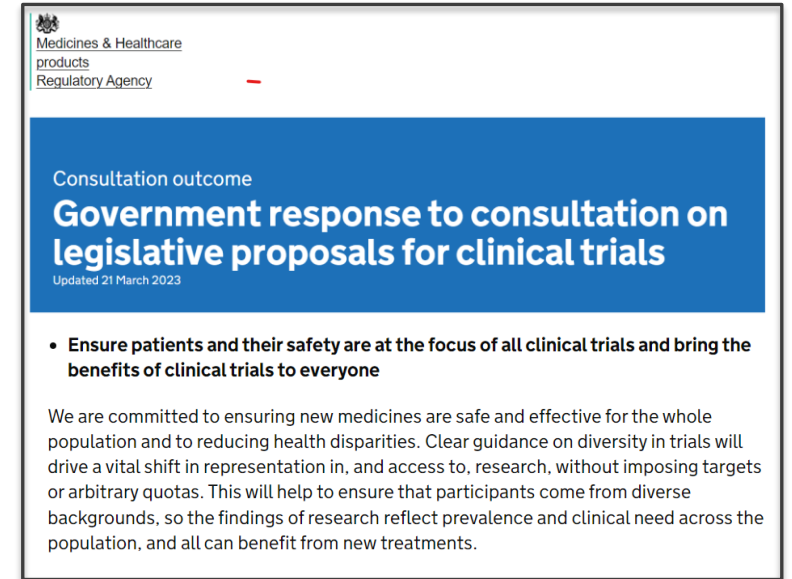# Focus on addressing the lack of inclusivity in research

Funders

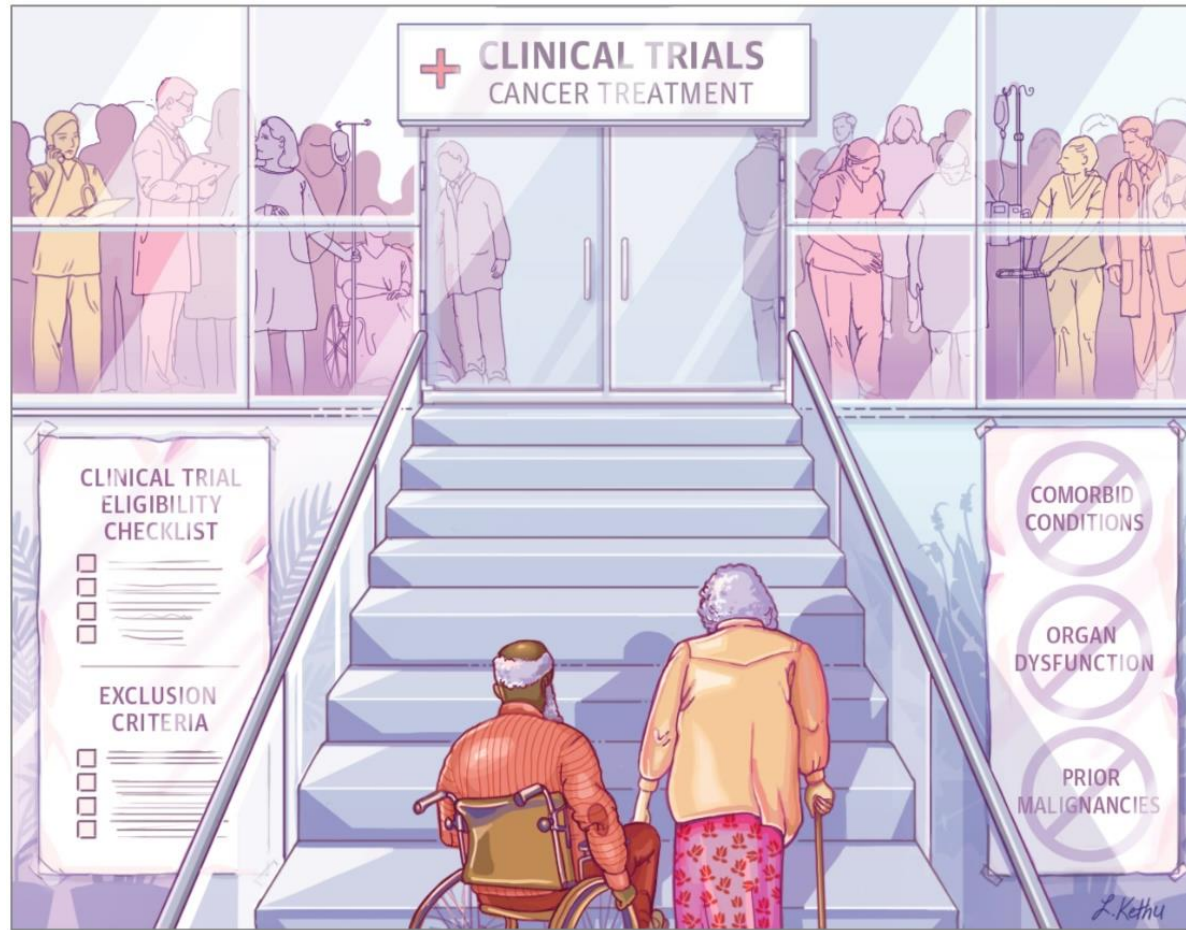**Ethics**
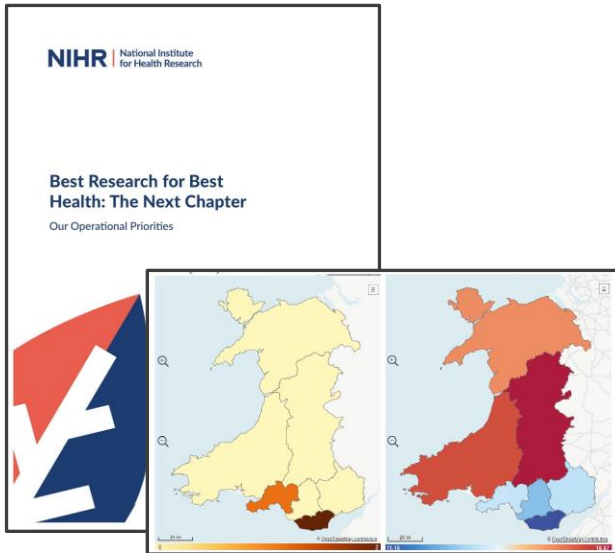
Legislation

Research following need

13.   Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

Barriers to the inclusion of under-served groups in research

Summary of the barriers to inclusion

Barriers are context-specific, but literature* suggests common themes:

- Language and communication e.*g ability to speak/read English, literacy, disability*

- Lack of trust e.*g previous experience of adverse events*

- Access to trials e.*g inability to access healthcare or research centre*

- Eligibility criteria e.*g explicit exclusions, those that indirectly exclude*

- Attitudes and beliefs e.*g privacy concerns, stigma, lack of social approval*

- Lack of knowledge e.*g about clinical trials*

- Logistical and practical issues e.*g transport, costs associated with participating*

- Other barriers e.*g lack of recruiting staff, small populations*

Bodicoat et al 2021 https://doi.org/10.1186/s13063-021-05849-77

Methods to support inclusion
– general

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- Include diverse perspectives in establishing research priorities, funding decisions, approvals processes, research teams, and in design and delivery of research

- Training e.g via NIHR Learn (free to access) and equity-focused tools and resources e.g https://forequity.uk/, Equality Impact Assessment (EqIA) toolkit https://arc-em.nihr.ac.uk/clahrcs-store/equality-impact-assessment-eqia-toolkit

- Use inclusivity-focused methodological approaches e.g participatory research

- Consider PROGRESS-PLUS factors when reviewing evidence and assessing the effects of interventions:

  Place of residence
  Race/ethnicity/culture/language
  Occupation
  Gender/sex
  Religion
  Education
  Socioeconomic status
  Social capital
  Plus personal characteristics associated with discrimination (e.g age, disability), relationships

Good practice guidance for improving inclusion

Good-practice guideline	Description
1. Consider the communities that the research needs to involve	Researchers should work to ensure that there is proportionate representation of ethnic minority (and all under-served groups where possible) groups, and that the research team is provided with the skills and tools to be able to achieve this
2. Undertake effective patient and public involvement (PPIE) in research	Researchers should recognise how important PPIE is to conducting good-quality health research and plan PPIE from the outset of the research, and have a strategy in place for how to achieve this
3. Conduct effective recruitment in ethnic minority communities	There is a need for researchers to have sufficient knowledge of access and engagement strategies (and how they should be tailored to different population groups) to ensure effective recruitment of all populations who need to be involved
4. Ensure cultural competence in the conduct of the research	All researchers who are engaging with patients should ensure that their teams have undergone cultural competency training so that they can engage respectfully and effectively with people of all cultures, ethnic backgrounds, religions, and other diversity factors
5. Provide effective feedback to research participants	Findings of research should be communicated back to all communities involved (and not solely within the academic context), and be tailored to different population groups where required

Routen et al (2022) https://bjgp.org/content/72/722/444

Designing more inclusive research

INCLUDE roadmap to improve inclusivity in clinical studies:

Involved stakeholders: Patients, public, funders, clinicians, researchers, regulators, industry, policymakers

| Research Priority Setting | Funding Bodies Strategic Priority | Research Investigator questions | Initial Study design/funding | Final Study Design | Dynamic Study Delivery | Study Closure Report | Impact Dissemination & Engagement |
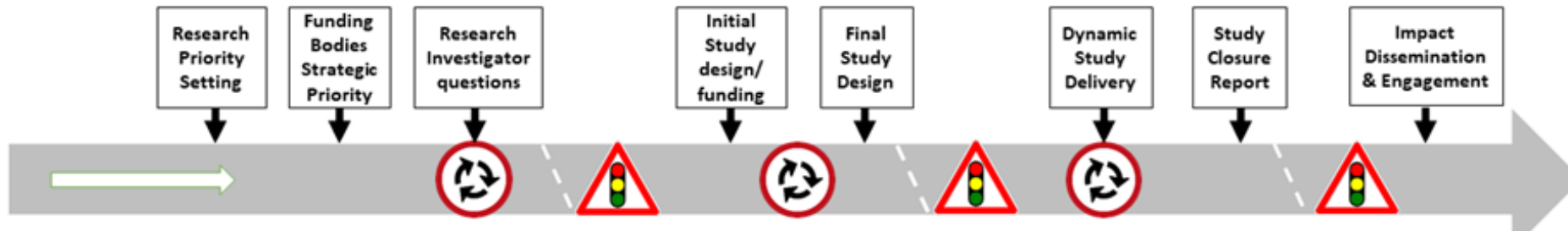
INCLUDE website of resources:

INCLUDE
BETTER HEALTHCARE THROUGH MORE INCLUSIVE RESEARCH

NIHR INCLUDE resources https://bit.ly/3T6vLaZ

Designing more inclusive research

Questions to guide research teams in designing inclusive research:

1. What are the characteristics/demographics of the population which your research looks to serve?

2. How will your inclusion/exclusion criteria enable your study population to match this population(s)?

3. Justify any difference between your projected study population and the population you aim to serve

4. How will your recruitment and retention methods engage with under-served groups?

5. What evidence have you that your intervention is feasible and accessible to those populations?

6. Are your outcomes validated and relevant to the populations that your research seeks to serve?

NIHR | National Institute for Health and Care Research

NIHR INCLUDE resources   https://bit.ly/3T6vLaZ

There is a peculiar paradox that exists in trial execution - we perform clinical trials to generate evidence to improve patient outcomes; however, we conduct clinical trials like anecdotal medicine. (Heart Fail Review 2012; 19: 135-52)

Monica Shah
National Heart Blood and Lung Institute, Bethesda, USA.

TRIAL FORGE

Trial Forge will make trials more efficient by looking for marginal gains across all trial processes, from research question to implementation into routine care. It will encourage everyone connected with trials to be more sceptical of what we do by asking for the evidence behind all of our trial decisions.

TRIAL FORGE resources https://www.trialforge.org/

Using evidence to design more inclusive research

TRIAL FORGE

IMPROVING TRIAL DIVERSITY

HOW TO CONSIDER SEX AND GENDER IN TRIALS

HOW TO DECIDE WHICH ETHNIC GROUPS YOUR TRIAL NEEDS

HOW TO INCLUDE PEOPLE WITH IMPAIRED CAPACITY TO CONSENT IN TRIALS

HOW TO INCLUDE SOCIOECONOMICALLY DISADVANTAGED PEOPLE IN TRIALS

HOW TO INCLUDE OLDER PEOPLE IN HEALTH AND SOCIAL CARE RESEARCH

HOW TO APPLY A TRAUMA AND RESILIENCE-INFORMED APPROACH IN TRIALS

PRO EDI: IMPROVING HOW EQUITY, DIVERSITY AND INCLUSION IS HANDLED IN EVIDENCE SYNTHESIS

TRIAL FORGE resources   https://www.trialforge.org/improving-trial-diversity/

Methods to support inclusion – context-specific tools

Guidance to help researchers to:

- Consider sex and gender in research

- Apply a trauma-informed approach to research

- Include older people in research

- Recruit and retain people from ethnic minority groups

- Collect and use ethnicity data in research

INCLUDE frameworks to help researchers design inclusive trials:

- Ethnicity Framework

- Socioeconomically Disadvantage Framework

- Impaired capacity to consent Framework

TRIAL FORGE

https://www.trialforge.org/improving-trial-diversity/

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METHODOLOGY

Trial Forge Guidance 3: randomised trials and how to recruit and retain individuals from ethnic minority groups—practical guidance to support better practice

1: Ensure your eligibility criteria and recruitment pathway do not limit participation in ways you do not intend
Ensure that eligibility criteria do not disproportionally affect the ability of ethnic minority groups to take part in the trial.

2: Ensure your trial materials are developed with inclusion in mind
Consider language and not just in written form but also verbal and expressed in other ways.

3: Ensure trial staff are culturally competent
Provide support and training to all staff on cultural competency to avoid stereotypes and increase their confidence to engage with different ethnic groups.

4: Build trusting partnerships with community organisations that work with ethnic minority groups
Spend time to build relationships with local community organisations and ensure you allocate time and resources to this when designing the trial.

Fig. 1 Four recommendations for designing and running trials that include the ethnic groups needed by the trial

INCLUDED

(INCLUsivity through improving the practice anD utility of Ethnicity Data collection in trials)

INCLUDED Recommendations

Before the trial
1. Identify the diverse ethnic communities from which participants in the trial need to be drawn.
2. Clearly articulate the reason(s) for ethnicity data collection in the trial.
3. If possible, engage with organisations or networks that connect relevant diverse ethnic communities with the research sector.
4. Engage individual patient/public members in communities identified in recommendation 1.

During the trial
5. To funders: communicate why and how ethnicity data will be collected and disseminated.
6. On data collection forms investigators use a question which allows people to self-describe their ethnicity.
7. Investigators make an explicit decision about whether a list of pre-defined ethnic categories will be used to collect data in the trial in addition to collecting self-described ethnicity.
8. Better communication to participants about why ethnicity data are being collected, what data will be collected, and how they will be used.
9. Investigators source high quality training for the whole trial team focused on better understanding of the culture of, and building trust with, diverse ethnic communities.
10. Trial team talk about inclusion and diversity.
11. Identify an individual or group trained in leading inclusion and diversity work who can support the inclusion and diversity work within the trial.

After the trial
12. When disseminating results, ethnicity is reported as transparently as possible.
13. Investigators include ethnicity data when reporting to participants, to PPIE members especially diverse ethnic community members, and to community connectors involved in designing the ethnicity data collection.

Dawson et al 2022 https://doi.org/10.1186/s13063-022-06553-w

Trial Forge resources https://www.trialforge.org/

INCLUDE Socioeconomic Disadvantage Framework – 3Ps

Pockets *(Income and economic resource availability)*

Benefits (e.g. uptake, adequacy, sanctions)

Unemployment

Low income

Childcare

Food poverty / use of food banks

Limited/no access to technological resources

Feeling powerless/ vulnerable due to financial circumstances

Covert situations within relationships (e.g. financial abuse)

Prospects *(Expectations and life chances)*

Mental health

Household type (e.g. lone parent)

Educational attainment

Literacy

Health literacy

Co-morbidities

Low self-confidence/motivation, which plays into perceived power disparities and mistrust

No/limited access to sources of reliable health/trial information

Acceptance of 'how it is'

Intersectionality with other underserved and/or vulnerable groups

Place *(Housing and the local environment)*

Housing

Being homeless

Being part of a traveller community

Being in prison

Being an immigrant or refugee

No/limited access to transport systems

No/limited access to community services

Local labour market

Local services (e.g. access to childcare)

Healthcare access and engagement

THE NIHR INCLUDE SOCIOECONOMIC DISADVANTAGE FRAMEWORK

https://www.trialforge.org/trial-diversity/socioeconomic-disadvantage-framework/
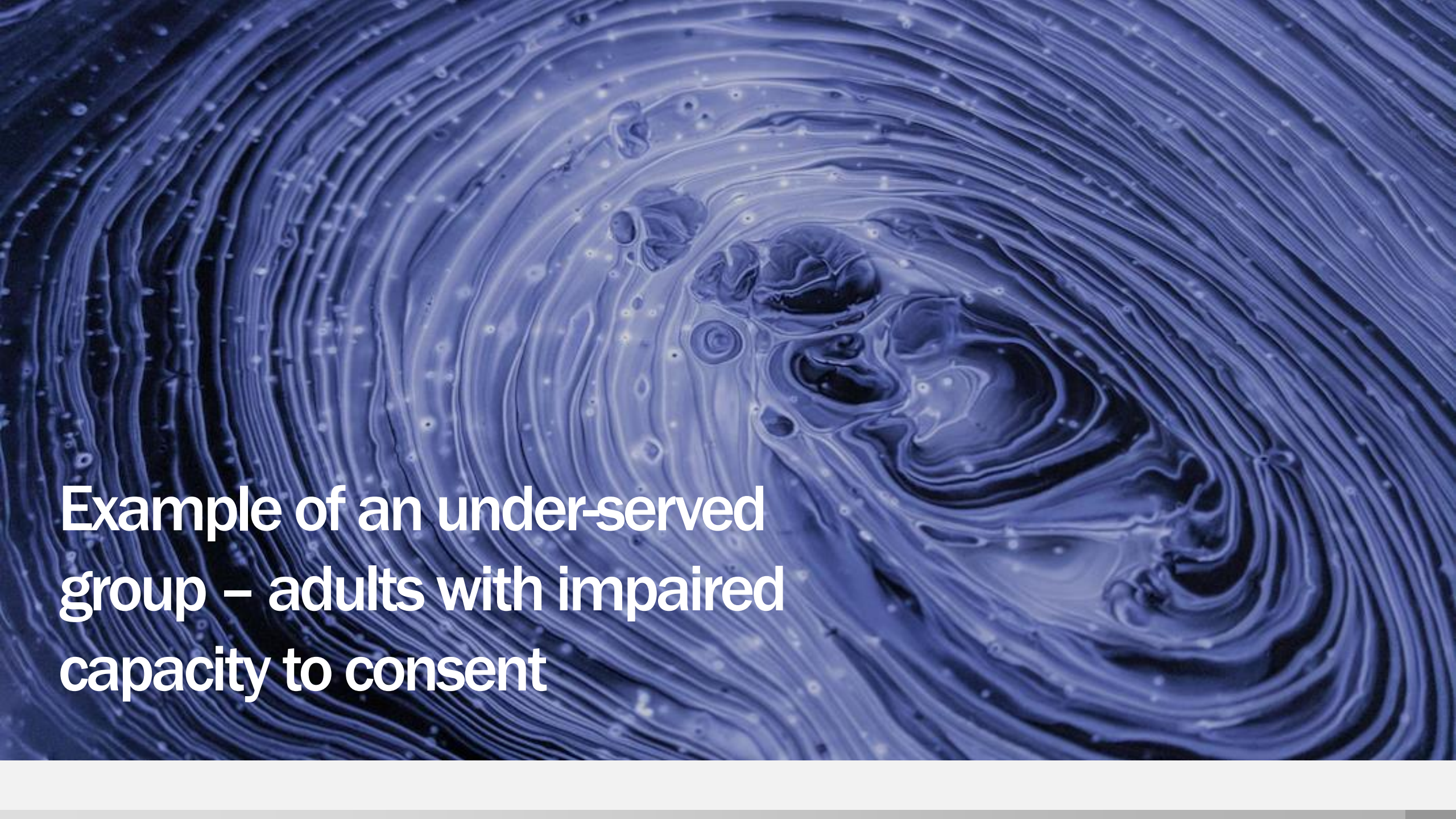
Strategies to support inclusion of older people in research

Summary of best practice recommendations

Individual factors

Studies should not have upper age limits in inclusion criteria

Studies should be designed to be inclusive of those with cognitive impairment

Studies should not have comorbidity exclusions (except where there is an intervention contraindication)

Use of clear explanations of why research is relevant to older people's health and wellbeing

Interpersonal factors

Advocates and peers as well as health and social care professions with expertise in ageing should be involved in designing research that meets the needs of older people

Communication about research should be tailored to the needs of older people

All older people who meet the eligibility criteria should be offered the opportunity to participate in research

Consider the involvement of carers or family members and the impact involvement can have on them and the older person

Organisational factors

Those commissioning, funding and approving research should ensure the inclusion of older people and intersectional factors, such as demographics and health status, have been considered

Those commissioning, funding and approving research should include older people and those with expertise in ageing

Community factors

Researchers should consider different and flexible approaches to promote accessibility of the research e.g. financial support to attend research centres or offering home visits for data collection

Support, or alternatives should be offered to digital data collection and interventions

Example of an under-served group – adults with impaired capacity to consent

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- Exclusion of people with cognitive impairment is widespread - even in conditions/areas where there may be high levels of cognitive impairment in the target population (Shepherd et al 2020)

- 1 in 3 patients with hip fractures have concomitant cognitive impairment but 8 out of 10 hip fracture trials exclude or ignore this population (Mundi et al 2014)

- 1 in 3 studies in older people exclude those with cognitive impairment (Taylor et al 2012)

- >90% of trials designed in ways that automatically exclude people with intellectual disabilities from participating (Feldman et al 2014)

- Impact of consent-based recruitment bias seen in emergency trials such as CONTROL (acute haemorrhagic shock) – unrepresentative population, trial halted for a lack of efficacy (Holcomb et al 2011)

- Often excluded as research involving adults with impaired capacity to consent is particularly challenging to conduct - over past decade little attention has been paid to how this can be improved

Shepherd et al (2020) https://bit.ly/3Gl5jmu

Barriers to research involving adults with impaired capacity
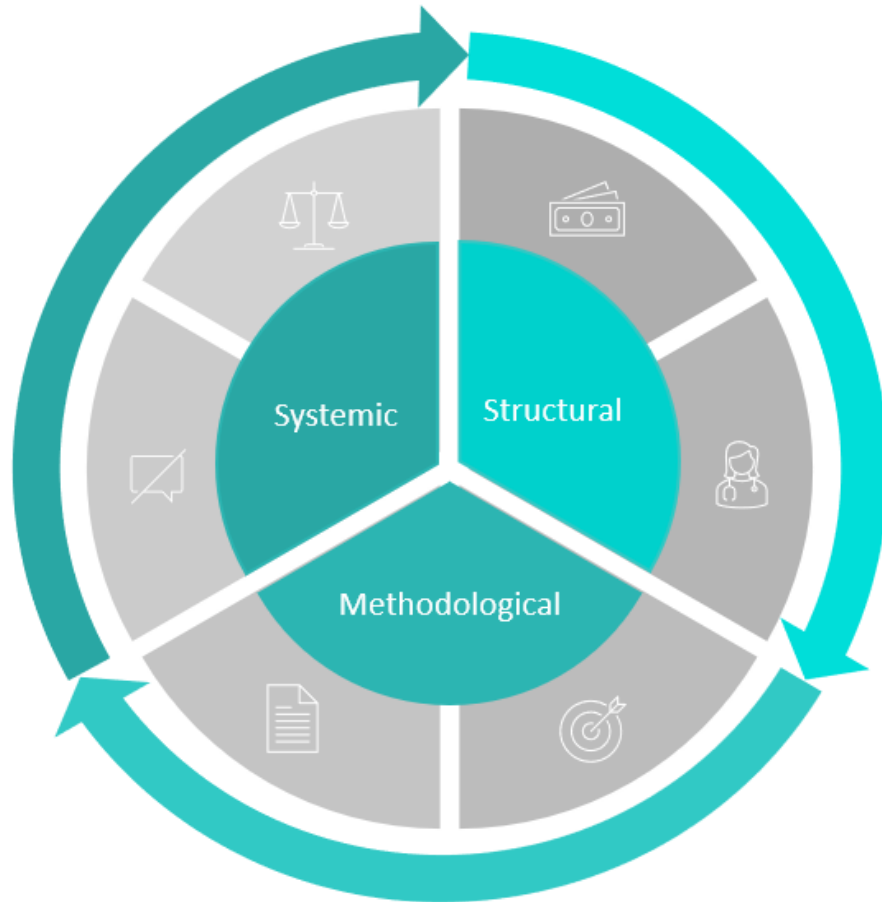
Systemic

- Complex legal frameworks
- Ethical review processes
- Paternalistic protection

Structural

- Resources required
- Research infrastructure
- Lack of support

Methodological

- Restrictive eligibility criteria
- Appropriate interventions and outcome measures
- Alternate consent pathways

Shepherd et al 2020 https://tinyurl.com/yweubw6h

Development of INCLUDE Impaired Capacity To Consent Framework
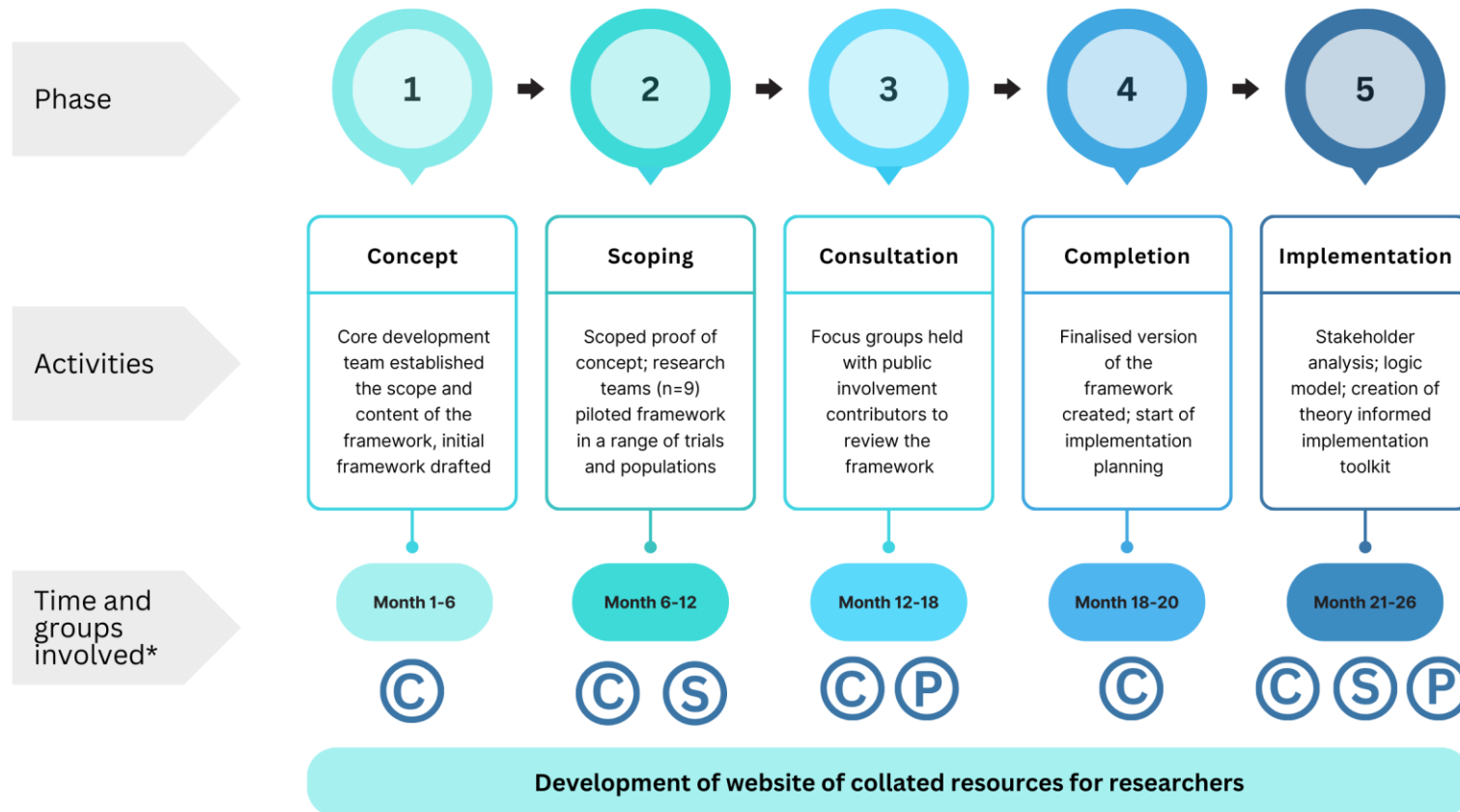
INCLUDE Impaired Capacity To Consent Framework for researchers

Q1 Who should my trial results apply to?
People with particular types or severity of conditions or disabilities

Q2 Are they likely to respond to the intervention in a different way?
Worksheet A - condition/disability related factors, other factors

Q3 Will my intervention make it harder for them to respond?
Worksheet B – intervention/comparator (who, what, how, where, when)

Q4 Will my trial design make it harder for them to take part in or remain in the trial?
Worksheet C – eligibility, recruitment
Worksheet D – data collection
Worksheet E – analysis (subgroup etc)
Worksheet F – reporting, dissemination

Summary of actions and resources needed
Worksheet G – key factors, actions, costs/resources

Key recommendations for using the INCLUDE frameworks

Research teams should use the framework as part of a collaborative process

Most useful at earliest opportunity - and revisit during the design and conduct stages

Public involvement (that is inclusive) is essential throughout

Review the relevant legal frameworks before considering the framework questions

Useful for all populations who experience impaired capacity – for all types of studies

Set aside time to address inclusivity, and include any associated costs in the funding application

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- Decisions about research on behalf of a someone who lacks capacity should be based on their wishes and preferences - wishes often unknown, some families find it challenging and experience an emotional and decisional burden

- Decision aid developed to support families to make decisions that are more informed and preference-based

- Effectiveness being evaluated in CONSULT SWAT embedded in 5 host trials; primary outcome is decision quality measured by CONCORD scale

- 'Advance research planning' could enable people to express their wishes and who should be involved – particularly relevant to people living with capacity-affecting conditions

- CONSULT-ADVANCE exploring acceptability and feasibility of implementing advance research planning in UK

- Aim is to develop an advance research planning intervention

Cardiff University
Making decisions about research for others

A guide to decision making

Part One Why am I being approached?
Part Two What am I being asked to do?
Part Three What would be involved?
Part Four Making a decision
Part Five Thinking it over and next steps

97% Members of the public were interested in taking part in advance research planning

94% Professionals thought it was important for public/patients to undertake advance research planning

CONSULT

- Need for better understanding about how to reach the widest range of participants who are representative of the populations with multiple long-term conditions (MLTC) who will benefit from the findings of the research

- NIHR are encouraging researchers to consider an MLTC perspective in their projects through funding 'Studies within a Project' (or SWAP) which are methodological studies embedded within clinical trials

- Embedding a SWAP with the aim of optimising inclusion in two upcoming trials 1) SCC-AFTER (adjuvant radiotherapy in patients with high-risk primary cutaneous squamous cell carcinoma after surgery) and 2) TIPTOE (MulTI-domain Self-management in Older People wiTh OstEoarthritis and Multi-Morbidities)

- Identify additional recruitment and retention challenges and develop strategies to promote inclusion, including areas such as clinician equipoise around recruiting frail older patients and where trial processes are conducted remotely

NIHR | National Institute for Health and Care Research

Search nihr.ac.uk...

Multiple long-term conditions - Studies within a project (SWAP)

SCC-AFTER

✳️ TIPTOE

Conclusions – diversity requires a whole system approach

- Research does not currently reflect the populations encountered in clinical practice – resulting in an evidence bias and exacerbating health inequalities

- Urgently need to change the way we design and conduct research

- Applying a health equity lens across the whole research system helps to identify and address population-wide and context-specific challenges

- Support is available for researchers through:
  - Free-to-access training and resources
  - Supportive tools such as INCLUDE Frameworks
  - Evidence-based interventions to support inclusion

- Developing methodological evidence – interventions can be used to ensure that research is more inclusive of under-served populations

A diverse mix
of voices
leads to better
discussions,
decisions, and
outcomes for
everyone.

– Sundar Pichai

Science on a Postcard

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🔵 https://www.capacityconsentresearch.com

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