CHIEF SCIENTIST OFFICE

CODE: HIPS/18/30

RESEARCH PROJECT BRIEFING

Multimorbidity and clinical guidelines

AIMS

The aim of the study was to work with national clinical guideline developers to examine how people eligible for clinical trials differed from people excluded from clinical trials. It also aimed to design and pilot a data analysis tool to make data about the clinical population accessible to guideline developers, to inform consideration of evidence applicability.

KEY FINDINGS

- Using qualitative interviews and working with the National Institute for Health and Care Excellence (NICE), we identified key information of interest to the guideline development group for the NICE gout guideline.
- Eligibility for 26 trials used in the gout guideline was examined for 33,483 people with gout using data from the Clinical Practice Research Datalink.
    - The 26 trials excluded between 26% and 80% of people with gout
    - People with gout excluded from trials were older, more likely to be women, much more likely to be frail or have chronic kidney disease, and much more likely to be prescribed drugs that potentially interacted with the treatments evaluated in trials
    - People excluded from trials had much higher rates of subsequent adverse outcomes associated with treatment including cardiovascular disease, gastrointestinal bleeding and acute kidney injury
- We co-designed and successfully piloted an online data analysis tool for guideline developers to use, and have obtained additional funding to develop this further.

WHAT DID THE STUDY INVOLVE?

The study used mixed methods including interviews with guideline developers and other stakeholders to understand perceptions of applicability of evidence, quantitative analysis of a routine healthcare dataset from the Clinical Practice Research Datalink that included 33,483 people with gout and co-design work with guideline developers (NICE and SIGN) to create and pilot a data analysis/visualisation tool allowing exploration of the characteristics of clinical populations. The study advisory group included public contributors as well as stakeholders from guideline developers, with contribution to study design and interpretation.

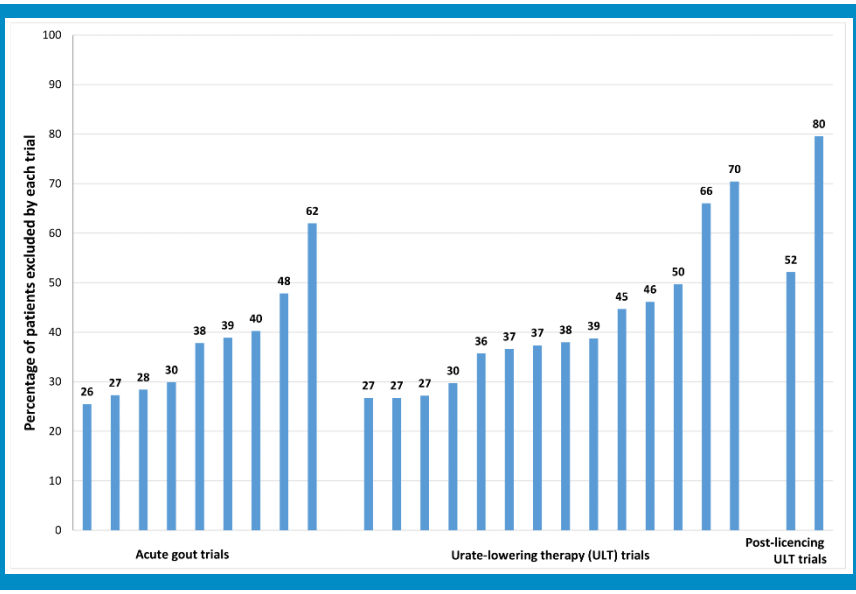
WHAT WERE THE RESULTS AND WHAT DO THEY MEAN?

Initial qualitative work with guideline developers identified that the applicability of trial evidence was of considerable concern, but variably dealt with during guideline development, in part because of a lack of high-quality data about the clinical population.

We examined exclusion for 26 trials considered in the NICE gout guideline, where median 38% (range 26% to 80%) of people with gout were excluded (see figure). People with gout excluded from trials were older, more likely to be women, and had more multimorbidity than those eligible for trials. For example, for the nine acute gout flare trials, the median age of ineligible patients was 72 years vs 63 years for eligible patients; 51% vs 16% had moderate/severe frailty; and 38% vs 16% had chronic kidney disease.

People excluded from trials had much higher rates of subsequent adverse outcomes associated with treatment. For example, for acute gout flare trials, people excluded from trials were three times more likely to be admitted to hospital with a gastrointestinal bleed in the next three years (median hazard ratio [HR] 3.1, range 1.9 to 3.3) and four times more likely for acute kidney injury (median HR 4.3, range 2.6 to 7.8). This means that the most commonly evaluated treatment in acute gout flare trials (non-steroidal anti-inflammatory painkillers) are much riskier in the excluded than the trial-eligible.

Percentage of people with gout excluded by 26 trials of treatments for acute gout and for long-term prevention of gout.



WHAT IMPACT COULD THE FINDINGS HAVE?

Key implications:

- For patients and practitioners: When discussing treatment options, consider asking 'am I different to the people in trials in ways that matter?' such as terms of life expectancy, and side effect risks due to age, the presence of other conditions, and other drugs prescribed.
- For guideline developers: The applicability of evidence should be more explicitly considered, ideally based on data examining the characteristics of the clinical population.
- For trial designers: The implications of different inclusion/exclusion criteria should be explicitly considered during the design of trials, ideally using data examining the characteristics of the clinical population.

HOW WILL THE OUTCOMES BE DISSEMINATED?

Academic dissemination will include papers published in peer-reviewed journals. Dissemination to guideline developers including involving both the National Institute for Health and Care Excellence and the Scottish Guidelines Interdisciplinary Network in the design and conduct of the study, and we will present the findings to the National Institute of Health and Care Excellence Technical Forum. Building on the co-designed pilot data visualisation tool we developed, we have obtained additional funding to develop an online data analysis tool for guideline developers. Further research is needed to examine the implications of trial (in)applicability for other conditions and treatments.

CONCLUSION

Existing clinical trial evidence is usually internally valid (true in its own right) but will often be of limited applicability to at least some subgroups of the clinical population. Bringing epidemiological data examining the characteristics of the clinical population into guideline development has the potential to make consideration of applicability more explicit and more structured, but will require creation and adoption of new data visualisation and analysis tools.

RESEARCH TEAM & CONTACT

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Additional Information

The study ran from1st September 2019 to 31/3/2022 (with a delay due to COVID-19), with funding of £233,161