Conclusion

Altruism was the most important motivation for patients to participate in the cohorts. Some misconceptions exist regarding components of informed consent. However, these misconceptions do not seem to be more prevalent in cmRCT than in standard RCTs.

Acknowledgements

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A7

Ethical Issues in a TwiCs study in early PsA

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Study Design

This study will recruit newly diagnosed psoriatic arthritis (PsA) patients. The cohort will receive best practice therapy following European Recommendations: a "treat to target" approach where treatment is escalated aiming for an objective target. Treatment will be escalated from one standard disease-modifying agent (DMARD), combination DMARDs and finally to biologics.

Two initial studies are planned. A randomised feasibility study will assess whether patients with mild PsA could be treated conservatively without DMARDs. A powered trial in moderate/severe PsA with two interventional arms will test more intensive drug therapies within the treat to target approach. One arm will receive combination DMARDs from the time of diagnosis, the other arm will receive an initial 6 month course of biologics tapering to DMARDs after this.

Ethical issues raised by the TwiCs design

The TwiCs design was chosen to allow analysis of real life outcomes in the cohort and treatment comparisons in the trials, producing generalizable results with the aim of changing routine practice.

Positive ethical issues

It will not be practical to "blind" therapy in these studies. This raises the issue of disappointment bias in patients who receive the "treatment as usual" comparator if they are aware that they have not been given the more intensive treatment. The use of the TwiCs design will avoid any disappointment bias allowing accurate comparisons of treatment.

Ethical issues of concern

The two stage consent for the cohort and then potentially for an interventional study must occur prior to starting treatment in newly diagnosed patients. Appropriate assessment at baseline in the cohort will have to rapidly allow randomisation to interventions and the consent forms and information given will have to be easily understandable to the patients to avoid overwhelming them.

In a usual RCT design, only patients consenting to the interventional study would be included in an intention to treat analysis. Whilst we plan to use complex statistical methods to adjust for the patients offered the intervention but declining (based on CACE analysis), a low consent rate for the offered interventions may affect our later analysis.

The studies planned within the TwiCs are both controlled trials of investigational medicinal products. As patients within the cohort will be acting as a "control" group for the interventions, additional detailed information relating to adverse events will have to be collected in the cohort beyond that which would normally be collected in a cohort placing an additional burden on these patients.

A8

The importance of oversight in Trials within Cohorts (TwiCs): experiences from the Community Ageing Research 75+ (CARE 75+) study

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The Community Ageing Research 75+ (CARE 75+) study is using a Trials within Cohorts (TwiCs) design to build ageing research capacity. TwiCs is also considered a useful method for recruiting potentially hard to reach groups such as people with frailty1. As part of the NIHR Collaboration for Leadership in Applied Health Research and Care Yorkshire & Humber (NIHR CLAHRC Y&H), CARE 75+ is recruiting community-dwelling older people (≥75 years) from across the UK (n =280) . The primary objective is a prospective epidemiological analysis of frailty, disability and quality of life trajectories with health, social and economic data captured at baseline, 6, 12, 24 and 48 months.

There are recognised challenges of using a multiple studies platform which have relevance for other researchers studying frailty, disability and cognitive impairment. We have observed that the initial cohort consent procedure is more complex and time-consuming than usual as researchers explain about requests for future study participation and that their data may be used as control data. We have also observed confusion between involvement the CARE 75+ observational study and involvement in sub-studies with participants sometimes not recognising the discrete nature of different studies.

To meet these challenges we have worked alongside our theme-wide patient and public group, the Frailty Oversight Group (FOG)2. Firstly, the FOG have scrutinised all sub-studies at the outset to ensure there is no unnecessary burden for participants, such as replication of outcome measures. Secondly, the FOG have observed researchers undertaking consent and assessments to improve the process from the participants' perspective. Thirdly, we inform all participants of new up-and-coming studies by newsletters but stagger invitations to ensure equal access whilst not overburdening them with information. We will continue to work with the FOG to assist with improving branding of information sheets and consent forms to ensure clarity and discrimination between CARE 75+ and sub-studies. To date, 83% of CARE 75+ participants agreed to contact about future studies (e.g. qualitative research and pilot work for future randomised controlled trials).

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Ethical challenges for trials within cohorts (TwiCs) in low and middle income countries

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Background

Poor populations face the greatest burden from disease and disability [1] but medical research priorities are driven largely by the global market for treatments [2]. Consequently, the healthcare needs of people in low and middle income countries (LMICs) are often neglected. There is an urgent need for more pragmatic research in LMICs but clinical trials in LMICs are highly sensitive to what the European Commission describes as 'ethics dumping'. Due to the progressive globalisation of