Collaboration invitation

Dear Trial Investigator [personalise]

Exercise Training for Chronic Heart Failure (ExTraMATCH II): individual patient data meta-analysis

In 2004, the ExTraMATCH collaboration (led by Dr Massimo Piepoli) published the first individual patient data meta-analysis of randomised controlled trials of exercise training in chronic heart failure (copy of PDF attached). In the last decade a number of important trials of exercise training in heart failure have been published. The ExTraMATCH II international collaborative has been formed to bring together this new trial data to produce an updated individual patient data meta-analysis. We are contacting all the lead investigators of trials of exercise training in heart failure to seek their participation.

As a contributor of data [reference] to the previous ExTraMATCH collaboration we are hoping that you will again agree to make available your trial individual patient dataset for the purpose of this new project.
OR
Your trial [reference] was identified in our recently updated 2014 Cochrane review of exercise-based interventions for heart failure (in press). We would like to invite you to join ExTraMATCH II as a collaborator and make available the individual patient dataset from your trial for the purpose of this project.

We request that you read the attached frequently asked question document and reply back to us as indicated.

We very much look forward to hearing from you, and hope you will wish to be involved in this important international collaboration in the field of exercise-based rehabilitation for heart failure.

Yours sincerely

Professor Rod Taylor, University of Exeter Medical School, Exeter, United Kingdom
And on behalf of the ExTraMATCH II International Steering Group
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ExTraMATCH II – Invitation letter to trial investigator

Frequently asked questions

How does an individual patient data meta-analysis differ from a standard meta-analysis?

Traditional meta-analysis methods involve combining and analysing trial level (or 'aggregate') results typically obtained from publications from that trial. An alternative and increasingly popular approach is meta-analysis of individual patient data (IPD), in which the raw individual level data for each study are obtained and used for analysis.

IPD meta-analyses offer a number of advantages over traditional meta-analyses, including:

- statistical analysis can be standardised across studies (for example, the analysis method, how continuous variables are analysed, the time points assessed etc.) and more advanced methods (e.g. time to event) can be applied where necessary;
- superior power to assess the treatment effects in specific subgroups of participants (e.g. NYHA I and II patients vs NYHA III and IV patient), and differential treatment effects (e.g. centre-based training vs. home-based programmes); and
- missing data can be observed and accounted for at the individual level.

What data am I being asked to share?

The initial phase of the ExTraMATCH II project is seeking individual patient data for the following outcomes from your trial:

- patient baseline data (socio-demographic characteristics, clinical characteristics e.g. heart failure aetiology, ejection fraction)
- mortality (all-cause death, death due to heart failure, and sudden cardiac death): rates and time-to-event;
- hospital admission/re-admission (all-cause, heart failure specific): rates and time-to-event;
- disease specific health-related quality of life assessed by the Minnesota Living With Heart Failure questionnaire and other validated quality of life outcomes: outcome at baseline and at 6, 12, 24 and >24 months' follow-up;
- exercise capacity (irrespective of assessment method): outcome at baseline and at 6, 12, 24 and >24 months' follow up.

Do I need ethics (IRB) permission to make my data available?

No. Participants have consented to participate in their original trial. Given that the analyses proposed by the ExTraMATCH II project are simply an extension of the core analysis of the constituent trials, we do not anticipate that additional ethical permission will be required.

Will my data be securely held?

Yes. We will ensure that datasets shared as part of the project include no patient-identifiable information (such as names and addresses), and that all data storage complies with the regulations governing research at University of Exeter Medical School.

All data will be received and stored in a secure database at the Clinical Trials Support Network, University of Exeter Medical School, Exeter, United Kingdom. A copy of the dataset will be held by both the coordinating centre at University of Exeter Medical School, and Duke Clinical Research Institute (DCRI) in the USA (coordinating centre for HF ACTION trial).

How should I organise the transfer of my data?

We will work with you and each individual trial site to determine the best way to transfer your patient level data.

What will be done with the data?

Individual trial datasets will be combined into one overall dataset with standardised variables, working with individual trial authors to ensure standardisation of variables and to check that our initial analyses of individual datasets are consistent with the published results from the trial. Once the combined dataset has been developed, the first phase of ExTraMATCH II data analysis will be to address the following three primary objectives:

- to obtain reliable and precise estimates of the impact of exercise-based interventions in HF on the following outcomes: time to death and admission to hospital (overall and heart failure specific), exercise capacity and disease-specific health-related quality of life;
- to compare the effects of exercise-based interventions in HFpEF and HFrEF subgroups and other patient clinical and demographic characteristics (e.g. disease severity, gender and age), and to compare intervention effects according to whether it is delivered in a centre- or home-based setting
- to assess whether the change in exercise capacity mediates the effect of the intervention on disease-specific health-related quality of life and clinical outcomes and the extent to which exercise capacity acts as an acceptable surrogate outcome for mortality and hospitalisation.

Who owns the data?

Data from individual datasets will remain the property of the ExTraMATCH collaborators who have provided IPD. You remain the custodian for your own data and retain the right to withdraw your data from the ExTraMATCH II collaboration at any time.

How will I be acknowledged on presentations and publications based on the ExTraMATCH II data?

All publications from the combined data will include the ExTraMATCH II research team and all collaborators. Where collaborators involve multiple individual authors, nominations for authorship will be made to the management committee. Requirements for authorship are those of the International Committee of Medical Journal Editors (http://www.icmje.org). Before publication of any ExTraMATCH II manuscripts, drafts will be circulated for comment, revision and approval. Publications using these data will be authored on behalf of the ExTraMATCH II Collaboration, either with specific named authors, or on behalf of the Collaboration as a whole; names of other participating Collaborators will be listed in the Acknowledgements.