Call for research in Global Maternal and Neonatal Health – Invited Research Grant Applicant Guidance

PLEASE NOTE THE DEADLINE FOR SUBMITTING AN INVITED RESEARCH GRANT APPLICATION IS 15 OCTOBER 2019 16:00 BST

If you have any questions regarding your application, please contact:

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This guidance is relevant to applicants submitting an invited research grant proposal to the Global Maternal and Neonatal Health funding call 2019. Separate guidance is available for applicants submitting seed-funding applications.

Contents

1. Important application information

Your application should be submitted through the **Joint electronic-Submission (Je-S) system.**

Most of the requirements are the same as for a standard MRC application. The MRC Guidance for Applicants can be found on the MRC website: **http://www.mrc.ac.uk/funding/guidance-for-applicants/**

This document provides additional information specific to the call for invited research grant applications in global maternal and neonatal health. Where guidance in the present document differs from that in the MRC Guidance for Applicants, you should follow the guidance in this document.

Updated guidance for research involving human participants in low and middle-income countries (LMICs)

MRC recently updated its ethical guidance for research involving human participants in LMICs; please refer to **Section 5.2.2** of MRC's Guidance for Applicants for further information.

1.1 MRC guidelines for management of global health trials

Applications proposing the use of clinical trials are required to adhere to the UK Clinical Trials Regulations 2004 and any relevant amendments. MRC policy on UK clinical trials regulations can be found on the MRC **website**. In addition to this, MRC has recently put together specific guidelines for the management of global health trials which can be **downloaded here**. It is essential that applicants proposing the use of clinical trials consult these resources as they put together their application.

1.2 Responding to peer review

All invited research grant applications will be peer reviewed by independent scientific experts. Information can be found in **section 2.5** of the guidance for applicants and also on **MRC's peer review webpages**. All invited research grant applicants will be given an opportunity to respond to peer review comments as per MRC standard policy in **November 2019 (approximately).**

2. Creating your full application on Je-S

Please note that for all queries relating to the Je-S system please contact the **Je-S Helpdesk:**

Email: JeSHelp@je-s.ukri.org
Phone: +44 (0) 1793 44 4164

The **Je-S handbook** is also a useful resource that will answer many questions about Je-S: **https://je-s.rcuk.ac.uk/Handbook/Index.htm.**

2.1 Je-S registration for co-investigators

All Co-investigators (Co-Is), including Researcher Co-Investigators (RCoIs), should be registered on the Je-S system and added to the online application. It is important that you do this so that reviewers can immediately see who is providing the scientific leadership for the proposed research.

Investigators based in LMICs should ensure their Research Organisation has been added to the Je-S database, preferably before they start their proposal. Applicants have the option to self-register their overseas organisation which allows the direct submission of proposals by LMIC applicants, when their organisation has not been through the IRO Je-S Registration process. This applies to the Research Organisation of the Lead Applicant and any Research Organisations (including NGOs) of individuals listed as Co-Applicants, but not Project Partners or sub-contractors.

Please ensure your Je-S registrations are completed at least 10 working days in advance of the submission deadline as the accounts have to be manually processed before investigators can be included in the proposal. Registration is not an instant process and if you leave registration until the last week before the deadline it may not be possible for your Co-Is to be registered in time.

2.2 Creating your Je-S application

In order to submit your proposal to the correct scheme please ensure you select the following categories when you create your application:

- Select Council: **MRC**
- Select Document Type: **Standard Proposal**
- Select Scheme: **Research Grant**
- Select Call/Type/Mode: **INVITE ONLY - Global Maternal and Neonatal Health 2019**
- Select **'Create Document'** option

2.3 Application submission:

The deadline for submission is the date by when your research organisation needs to submit your proposal to the MRC. You may need to submit your proposal to colleagues within your research organisation several days before the deadline so that they have time to approve the proposal for submission to the MRC.

Please ensure you comply with your research organisation's rules with regards to application submission.

Once you have completed the Project Details section of the Je-S form you are able to find out the submission arrangements for your organisation. **Select the Document Actions Button** and then **Select Show Submission Path**.

If the screen shows **With Owner** and **With Council,** then the proposal will be submitted directly by you.

If the screen shows **With Owner** and **Submitter Pool** (there should be names listed against this section) and **With Council,** then the proposal has to be approved and submitted by one of your research organisation's named submitters. You should allow at least 48 hours for them to do this, your research organisation may require longer, and we would strongly advise you check this.

Please check that at least one of your organisation's named submitters will be available on the day you plan to submit it. Please note that they will need to do this no later than 16.00 UK time on the date the call closes.

3. Online Je-S proposal form

The Je-S form will cover the administrative and financial aspects of your application. It includes: Objectives; Summary; Technical Summary; Academic Beneficiaries; Communication Plan; Impact Summary. You will need to provide details of all researchers and staff on the award.

Please access the Je-S system well in advance of the deadline so that you have time to complete these sections. You do not have to use the whole word limit for each section, especially if you feel you have provided sufficient detail for some items already in your case for support.

Highlighted below is guidance on completing the Budget and the Project Partners sections of the Je-S proposal form. These are two areas where we feel that specific guidance may be helpful.

Further information on the Je-S proposal form can be found in the **MRC Guidance for Applicants** and in the **Je-S Handbook**.

3.1 Completing the Budget section on Je-S:

Applicants are required to provide detailed financial information as part of their full application. **Section 3** of the MRC Guidance for Applicants describes the MRC's rules for requesting resources. It is important that all of this information is entered correctly as the total amount requested is determined by the information provided here.

The majority of queries received by the office concern the financial section of the Je-S form. Please note the following common issues:

- All UK costs entered should be in line with the standard **MRC resources guidance**. Please note, **for this scheme all costs claimed by UK investigators should be claimed at 80% of the full economic cost (FEC) (the MRC standard).**
- **All overseas costs need to be entered as Exceptions and claimed at 100% full economic cost (FEC).** For example, all salary costs incurred by overseas investigators should be entered as Exceptions and claimed at 100%.
- A contribution towards Indirect and Estates costs at the overseas organisations is permissible where the research is being undertaken in a low or middle income country (LMIC). This should be calculated using the overseas institution's standard overhead calculations but cannot exceed 20% of the total costs claimed by the overseas organisation. **Please note that these costs need to be entered on the Je-S form as "Other Directly Incurred Costs" and entered as Exceptions funded at 100%.**
- Indirect and Estates costs cannot be claimed by research organisations based in a high income country outside of the UK.
- Please note that **only single pieces of equipment over the value of £10,000** should be categorised under the "**Equipment**" heading on the Je-S system. All equipment under the value of £10,000 should be categorised as "**Other Directly Incurred Costs**". For example 20

laptops with a total cost of £20,000 should NOT be entered under the Equipment heading, as in this scenario a single laptop would cost less than £10,000.

- Staff costs cannot be included for **staff based at MRC Units** whose salary costs are already met through core support (i.e. as part of Unit funding rather than other awarded grants).

Grants will be managed per UKRI and MRC standard terms and conditions and any additional MRC-NIHR specific terms and conditions. Funding is not available for PhD or Masters studentships, or for capital equipment.

All costs associated with overseas Co-Is, whether salary, fieldwork, equipment or travel and subsistence should be entered as 'Other Directly Incurred Costs' and should be marked as an 'Exception' using the tick box. To enable MRC to meet transparency and external reporting requirements all overseas costs must be entered into this section using the format 'Organisation: Country: Cost Category: Cost Description'. For example:

- University of Nairobi: Kenya: Staff: 1 x PDRA
- University of Nairobi: Kenya: Travel and Subsistence: 4 x flights
- University of Nairobi: Kenya: Other Directly Incurred Costs: 5 x Workshops including catering and accommodation

Costs for work undertaken at an overseas organisation should be calculated in GBP based on prevailing exchange rates at the time of application (see MRC Guidance for Applicants **Section 3.3**). Applications led by a UK Research Organisation must consider how the finances will be managed and deployed between partners, and the financial controls and risk mitigations that will be put in place for the transfer of funding to overseas organisations. The time taken for these assurances to be put in place should be factored in to the proposal.

3.2 Completing the Project Partners section on Je-S:

PLEASE NOTE: Institutions where the PI and Co-Is are based are not classed as Project Partners and should not be listed in this section.

Applicants are strongly encouraged to engage with local stakeholders, including local government, policy makers, and local communities. A project partner provides a substantial intellectual contribution to the project, and their organisation may also provide resources either in-kind or financially. Project partners are not expected to request MRC funding to participate. The contribution and involvement of project partners should be acknowledged in the project partner section of the application form and described in detail in the Case for Support.

Projects may also involve collaboration with industry. If the project partner is from industry, applicants must follow the guidance relating to the MRC Industry Collaboration Agreement (MICA). Please see the MRC **MICA webpages** and **Section 1.3.4** of the MRC Guidance for Applicants for more information.

Please note that all listed project partners must provide a letter of support. Please also note that you should include a nominal sum of £1 when adding project partners who are not contributing financially to the project.

Please note that it is expected that any resulting intellectual property from the research will be vested in the UK and/or LMIC research organisation(s). Where this arises as a result of joint UK and LMIC activity we expect that arrangements are made to ensure equitable and fair distribution of intellectual property rights.

4. Required application documentation (attachments)

You are required to submit several attachments with your Je-S submission. Please carefully read the following information regarding each attachment.

Section 2.2 of the MRC Guidance for Applicants provides guidance on the required attachments. **Where this document differs from the MRC Guidance for Applicants please follow the guidance provided in this document.**

The following table summarises the required documents along with the maximum accepted page lengths for each document:

Required Documents	Notes
Online Je-S Proposal Form	Word limit specified in Je-S
Case for Support	Maximum 8 sides A4 (12 for clinical trial proposal) including references, plus: • Capacity Building annex (additional 1 side A4; mandatory) • Statistical Design and Reproducibility annex (additional 1 side A4; recommended)
ODA Compliance Statement (Please use Je-S attachment option: **Non-UK Components)**	Maximum 1 side A4
Pathway to Impact	Maximum 2 sides A4
Justification of Resources	Maximum 2 sides A4
Data Management Plan	Maximum 3 sides A4
Letter(s) of Support	Maximum 2 sides A4 each
Covering Letter	Maximum 2 sides A4
CV's	Maximum 2 sides A4 each
Publications	Maximum 1 side A4 each

4.1 Case for Support

The Case for Support should be a self-contained description of the proposed work with relevant background information and should not depend on additional information.

Please remember that your invited research grant application, including the Case for Support, will be circulated for external peer review and reviewed by a panel of experts. Previous panel feedback has highlighted that the Case for Support should be clear, succinct and accessible. Section 6 of this guidance outlines the criteria against which proposals, including the Case for Support, will be assessed.

If you plan to include unpublished data, it must be included in the Case for Support. Manuscripts in press or submitted to journals should not be included.

Applications should follow the standard Case for Support format as outlined in the MRC Guidance for Applicants **Section 2.2.3.3**. The page limit is eight pages for a standard research project or 12 pages for a clinical trial, including a maximum one page for references, with an additional one page each for the Capacity Building annex (mandatory), ODA Compliance Statement (mandatory) and Statistical Design and Reproducibility annex (recommended).

The Case for Support should use the following headings:

- Importance
- Scientific potential
- Ethics and research governance
- Exploitation and dissemination
- Project Partners

Full information of what information should be provided under each of these headings can be found in the MRC Guidance for Applicants **section 2.2.3.3**.

There is no distinct Case for Support document for applicants proposing clinical trials. However, it is the applicant's responsibility to ensure that the case for support includes all necessary information to judge the proposed trial. For this reason, a 12-page Case for Support is permitted for trial applications. Where a trial is proposed applicants may choose to use the following headings:

- Trial summary information
- The proposed trial
- Rationale for the trial
- Trial management
- Trial partners
- Proposal history

Suggested content to include within these headings is provided in **Annex 1** of this document, although applicants should use their judgement as to which of these headings are relevant/necessary. Where a clinical trial is proposed it is strongly recommended that applicants use the additional one-page Statistical Design and Reproducibility annex to provide further detail.

Where the research proposed includes the development or evaluation of an intervention information on potential for replicability, acceptability, scalability, and affordability should be included. Projects which assess the effectiveness of a particular intervention without situating that assessment within a broader research and policy context will not be funded. It is up to applicants to consider how the cost of any intervention is supported. Researchers are advised to refer to the MRC framework on the development and evaluation of complex interventions for further guidance on interventions, where appropriate to their proposed plans.

4.1.1 Capacity Building annex (mandatory)

Applicants are required to include an annex with their Case for Support to provide important additional information on capacity building. This annex should be included as part of the Case for Support submission at the end of the document. It should be clearly titled and can be a maximum of 1 side A4.

All funders are committed to supporting capacity building in research. Capacity-building elements should be set out in relation to the core intellectual agenda of the research proposal and not treated separately; the focus should be on the quality and impact of the research, and how increasing research capacity contributes to this.

Examples of capacity building include:

- increasing capability of staff to work across disciplines and in partnerships
- support and mentoring for more junior team members
- building leadership skills amongst early career researchers
- mentorship opportunities
- co-design, analysis and dissemination of research
- opportunities for those with relevant skills to orient their research towards global issues
- formation of LMIC research networks.

UK investigators should demonstrate an understanding of the national and local context and work harmoniously and effectively with local stakeholders to ensure the research programme does not undermine local research capacity. These factors will be taken into account by the panel of experts.

4.1.2 Reproducibility and statistical design annex (recommended)

Applicants are encouraged to include an annex with their Case for Support to provide important additional information on reproducibility and statistical design. This annex should be included as part of the Case for Support submission at the end of the document. It should be clearly titled and can be a maximum of **1 side A4**.

Please refer to **Section 2.2.3.4** of the MRC Guidance for Applicants for more information as to the correct usage of this annex.

4.2 ODA Compliance Statement

Research funded through this call will form part of the UK's Official Development Assistance (ODA), as defined by the Development Assistance Committee (DAC) of the Organisation for Economic Co-operation and Development (OECD). The ODA compliance statement should explain how your proposed research is compliant by answering the following questions:

1. **Which country/countries on the DAC list of ODA eligible countries will directly benefit from this proposal?**
2. **How is your proposal directly and primarily relevant to the development challenges of this country/these countries?**
3. **How do you expect that the outcome of your proposed activities will promote the economic development and/or welfare of this country/these countries?**

Please note: this document should make clear the ODA relevance of the proposed research without reference to other documents in the proposal (i.e. Case for Support, Pathways to Impact). It should also include meaningful project specific detail. Proposals that do not articulate clearly the ODA relevance of the research throughout their application will be rejected prior to peer review.

4.3 Pathway to Impact

The Pathway to Impact document should be used to clearly demonstrate the potential economic and societal benefits of the proposed work. Applications should have clear potential to have an impact on Global Maternal and Neonatal Health. This document should be no longer than 2 sides A4.

Please see **Section 2.2.5** of the MRC Guidance for Applicants for full details on the requirements of the Pathway to Impact.

4.4 Justification of Resources

It is important that all resources requested in your application are fully justified. The Justification of Resources should be used to justify the resources required to undertake the research project and is mandatory. It should be no longer than **2 sides of A4**.

Please see **Section 2.2.4** of the MRC Guidance for Applicants for full details on the requirements of the Justification of Resources.

Full details of costings should be detailed on the Je-S online form. **It is important that the figures quoted in the Justification of Resources clearly match up with those entered in the Je-S online form.**

As part of your justification of resources for this scheme, please include the following table:

Financial breakdown per participating research organisation

Participant organisation name	Total amount	Total amount requested from this scheme*
Participant Organisation 1 (please enter name)		
Participant Organisation 2 (please enter name)		
etc.		
TOTAL		

*Costs claimed by UK institutions should be calculated at 80% of the full economic cost (fEC). **Costs claimed by institutions in low and middle income countries must be claimed at 100% fEC.**

4.5 Data Management Plan

The Data Management Plan should demonstrate how the Principle Investigator (PI) will meet, or already meets, their responsibilities for research data quality, sharing and security. Please see **Section 2.2.8** of the MRC Guidance for Applicants for full details on the requirements for the Data Management Plan. This document should be no longer than **3 sides A4**.

4.6 Letter(s) of Support

It is very important that you obtain the necessary letters of support from stakeholders engaged in the project. Stakeholders may include the lead research organisation, collaborating research organisations in the UK and overseas, local or national government authorities, and project partners (e.g., industrial partners, NGOs). Each letter of support should be no longer than **2 sides A4**.

Please see **Section 2.2.7** of the MRC Guidance for Applicants for the full details on the requirements for Letters of Support for Project Partners.

4.7 Covering Letter

You may wish to provide a Covering Letter with your full stage application, maximum **2 sides A4**. Please see **Section 2.7** of the MRC Guidance for Applicants for full details on the requirements for the Covering Letter.

4.8 CVs and Publications

A CV should be provided for each investigator and each named researcher. Each CV should not exceed **2 sides A4**.

A list of publications should be provided for each investigator and each named researcher. Each list of publications should not exceed one side of A4.

Please upload all CVs and publications as one attachment with the publication document following on from the CV of each researcher.

Please see **Section 2.3.1** of the MRC Guidance for Applicants for more information about CVs and see **Section 2.3.2** for more information about Publications. Please disregard the requirement to upload these documents separately.

5. Applicant eligibility

PIs should be based at an eligible LMIC or UK Research Organisation.

UK PIs or Co-Is must be based at a UK higher education institution or at an eligible independent research institution.

LMIC PIs or Co-Is must be based at a higher education institution, non-profit research institution, or non-governmental organisation. Applicants should check with their Research Office whether previous applications have been submitted to MRC. If they have not, applicants should contact international@headoffice.mrc.ac.uk to determine eligibility prior to submitting their application.

Researchers based at MRC University Units and the Francis Crick Institute are eligible to apply for funding, as either a PI or Co-I. However, they should address in their cover letter how the proposed research is distinct from that already supported through existing 'core' support.

Researchers from overseas research organisations not based in LMICs may be Co-Is if they provide expertise not available in the UK or an LMIC. Inclusion of these Co-Is and any costs associated with their activities must be discussed and agreed with the relevant MRC programme manager in advance

of application (please email any queries to international@headoffice.mrc.ac.uk). Costs for overseas non-LMIC organisations must not exceed 30% of the total budget requested in the application.

Industrial collaborators are welcomed, but it should be noted that they cannot be PIs/Co-Is or recipients of funding (i.e. Project Partners or Sub-contractors only). The role of industrial partners must be clearly explained, with special emphasis on the benefit to LMICs. When an industrial collaborator is involved, a MICA form must be submitted within the proposal. Please see MRC **MICA webpages** and **Section 1.3.4** of the MRC Guidance for Applicants for more information.

6. Assessment process

All applications will be checked internally for fit to remit, page lengths, mandatory attachments, ODA eligibility etc., before being sent for external peer review. Invited research grant applicants will have the opportunity to respond to reviewer comments in approximately November 2019. The full proposal, peer reviewer comments, and PI response to comments will be shared with an external panel of experts who will convene in February 2020. Applicants will be contacted via email shortly after the panel to inform them of the panel's decision (award or decline). Panel decisions are final and are not subject to appeal.

The panel will assess your application based on the following criteria:

Importance of the question/likely impact of the study

- Does the study address an important research question relevant to the burden of maternal and/or neonatal mortality and/or morbidity in LMICs?
- Does the study justify the importance of the research question with reference to i) the burden of maternal and/or neonatal mortality and/or morbidity; ii) the existing evidence base?
- Does it propose a high-quality research approach to answer that question?
- Is the study relevant and novel in the proposed location(s)?
- How important an advance would this be?
- What is the likelihood that the findings will have academic and/or economic and societal impact?
- Is it likely to lead to significant improvements in maternal and/or neonatal mortality and/or morbidity in LMICs?
- Are the findings likely to be of relevance to LMIC locations outside of those named in the application where similar maternal and neonatal health challenges are faced?

Study design and feasibility

- Is the design of the study appropriate to answer the question?
- Does the methodology allow a rigorous, valid, and reliable investigation?
- Is the timeline realistic and achievable?
- Is the sample size sufficient and based on a reproducible power calculation? Is there a feasible recruitment strategy? Has attrition been realistically accounted for?
- Are there any ethical concerns?
- Have major scientific, technical or organisational challenges been identified, and are plans in place to address them?

Research Team

- Do the named investigators have experience of conducting studies to a high standard?

- Does the research team have the necessary interdisciplinary expertise to undertake the study?
- Have LMIC researchers had intellectual input into the setting of the research agenda and its ongoing strategic direction? Is the partnership equitable?
- Have relevant stakeholders been identified and engaged from outside of the academic community? If they have not yet been engaged are there clear plans to do so?
- Do the named investigators have experience of achieving academic and/or economic and societal impact?
- How suitable is the host organisation(s) (i.e. commitment to providing appropriate levels of support to the research team)?

Capacity building

- Have appropriate capacity building activities been embedded within the research proposal?
- Are opportunities for the development of LMIC/early career researchers provided?
- Where relevant, are early career researchers provided with sufficient support and mentorship to enable them to lead/participate in the project?

Justification of resources and appropriate financial management/risk assurance

- Does the study and its proposed size and scale represent value for money?
- Is the distribution of funding across UK and LMIC partners appropriate for the intended contribution of partners within the research proposal?
- Are there any financial dependencies, e.g. co-funding arrangements?
- Have risks to the work been identified and appropriate plans for mitigation outlined?
- Has appropriate time been allocated for risk assurance and establishing financial management arrangements with partners?

Clear and effective pathways to impact

- Have the potential beneficiaries of the research been identified?
- Where appropriate, has consideration been given to how scale up of the research findings into policy and practice would occur? What is the likelihood of uptake of the research findings e.g. has a cost effectiveness evaluation, where relevant, been included as part of the proposed research?
- Where relevant, are the capacity building activities proposed likely to yield tangible benefit in the near future?
- Is there sufficient engagement with relevant stakeholders within the country/countries of focus?

Compliance with ODA eligibility requirements

- Will the research directly benefit a country or countries on the OECD DAC list of ODA eligible countries?
- Is the proposal directly and primarily relevant to the development challenges of this country/these countries?
- Could the proposal's outcomes promote the economic development and/or welfare of a country or countries from the OECD DAC list of ODA eligible countries?

7. Further guidance documents

For further guidance about your proposal please refer to:

Je-S Helpdesk pages
https://je-s.rcuk.ac.uk/Handbook/Index.htm
Please note for any submission issues please email the Je-S Helpdesk directly: **JeSHelp@je-s.ukri.org**

MRC Guidance for Applicants
http://www.mrc.ac.uk/funding/guidance-for-applicants/

MRC Terms and Conditions
http://www.mrc.ac.uk/funding/guidance-for-mrc-award-holders/

MRC Research Policy and Ethics (including MRC data sharing policy)
http://www.mrc.ac.uk/research/research-policy-ethics/

United Kingdom Research and Innovation guidance on pathways to impact
https://www.ukri.org/innovation/excellence-with-impact/pathways-to-impact/

Department for International Development guidance on research uptake
https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/514977/Research_uptake_guidance.pdf

Annex 1 – Clinical trial Case for Support suggested content

1 Trial Summary Information

1.1 Full title of trial (no more than 150 characters)
1.2 Acronym (if applicable - this is not a requirement)
1.3 In which country(ies) will the trial take place?
1.4 Duration in months
1.5 What is/are the principal research question(s) to be addressed?

2 The Proposed Trial

When completing this section please ensure you give adequate attention to the below issues:

- Please include relevant pilot data and ensure it is clearly described.
- Please provide as much information as possible about the feasibility of the proposed intervention.
- Please clarify why you believe that it is specifically a trial, using your proposed methodology, which is needed to address the research question.
- Be specific about the nature of the intervention so that it is clear to the panel exactly what will take place in the experimental and control arms (if applicable) and how this compares to usual practice and standard of care in the trial locations.
- Ensure that all statistical aspects of the trial and the assumptions on which these are based (such as power calculations, sample sizes and effect sizes) are clearly explained and well-justified. Please ensure that you allocate sufficient space to this aspect of the proposal so that it can be clearly understood by reviewers. In previous years, incomplete or poorly explained trial statistics has been a common reason for reviewers to have concerns about proposals.
- Justify clearly the outcome measures to be used. Having the right primary and secondary outcome measures, and a robust methodology to collect data for those outcome measures, is a major issue considered by the panel at peer review
- It is important that all studies funded by this scheme have outcomes that might offer a realistic and cost-effective opportunity to improve health. Please consider and explain whether your proposal needs a health economic analysis and provide information and justification on how that analysis will be conducted, and who by.

2.1 The proposed study
Give a summary of the proposed trial (<100 words)
2.2 What is the proposed trial design?
(e.g. open, double or single blinded, number of arms, etc)
2.3 What are the proposed outcome measures?
Please provide justification for primary and secondary outcomes and their measures and clarify how they are aligned to the scientific hypothesis.
2.4 Has any pilot work been carried out?
Please provide a clear description of relevant feasibility or pilot data.
2.5 Which centres will be involved?
Please give numbers and brief details of participating centres, including a rationale for their selection.
2.6 What are the planned trial interventions?
Give clear details of both experimental and control – if control is 'usual care' please describe. Please describe the interventions clearly and explain clearly why those interventions have been chosen.
2.7 What are the proposed practical arrangements for allocating participants to trial groups?
(e.g. randomisation method. If stratification or minimisation is to be used, give reasons and factors to be included.) Applications involving the use of sealed envelopes are asked to consider other options and explicitly outline the reasons for their choice.

2.8 Please detail any risks to the safety of the patients in the trial

2.9 What are the proposed methods for protecting against sources of bias?

(e.g. blinding or masking. If blinding is not possible please explain why and give details of alternative methods proposed, or implications for interpretation of the trial's results.)

2.10 What are the planned inclusion/exclusion criteria?

2.11 What is the proposed sample size and what is the justification for the assumptions underlying the power calculations?

Include both control and intervention groups, a description of the power calculations detailing the outcome measures on which these have been based, and give event rates, means and medians etc. as appropriate.

NB It is important to give the justification for the size of the difference that the trial is powered to detect. Does the sample size calculation take into account the anticipated rates of non-compliance and loss to follow-up?

2.12 What is the proposed duration of treatment period?

2.13 What is the proposed frequency and duration of follow-up?

2.14 What is the planned recruitment rate?

How will the recruitment be organised? Over what time period will recruitment take place? What evidence is there that the planned recruitment rate is achievable? Has the study sample been defined adequately in relation to the target population so that the results will have meaning?

2.15 Are there likely to be any problems with compliance?

On what evidence are the compliance figures based?

2.16 What is the likely rate of loss to follow-up?

On what evidence is the loss to follow-up rate based?

2.17 Are there any planned subgroup analyses?

2.18 What is the proposed type of analyses?

2.19 What is the proposed frequency of analyses?

2.20 What are the potential hazards inherent in the trial which might cause problems in its implementation? Give details of the risk assessment.

2.21 How will health economics issues be addressed?

Please justify inclusion/exclusion of any health economics analysis. If a health economics study is planned please include details of the perspective adopted (e.g. health service vs societal), analytical approach (e.g. cost-effectiveness, cost-minimisation, cost-utility analysis etc.), choice of any outcome measures (e.g. DALYs or QALYs) and whether the study will include any modelling analysis. Where relevant, please outline whether the study will also consider issues around the overall affordability and sustainability of the intervention. Please state whether an economist is already in place to design the economics study in advance of the start of the main trial.

2.22 Will there be local health service cost implications for this trial?

2.23 What involvement from local patient and/or community groups has there been in developing the trial design?

2.24 What on-going involvement would patient and/or community groups have in the trial?

2.25 Please provide a brief timeline for the trial.

3 Rationale for the Trial

3.1 Why is a trial needed now, and why is it needed in the proposed location?

(evidence from the medical literature, professional and consumer consensus and pilot studies should be cited if available; include any ongoing or planned studies elsewhere).

In responding to this point, please consider issues such as burden of disease and priority for the relevant local, regional and national health services etc.

3.2 Give references to any relevant systematic review(s) and discuss the need for your trial in light of these review(s)

(if you believe that no relevant previous trials have been done, give details of your search strategy for existing trials)

3.3 Describe how the proposed trial will differ from or complement any relevant planned, ongoing or recently completed trials internationally.

3.4 Further to your Impact Summary and Pathways to Impact document, please summarise briefly how the results of the trial will be generalisable beyond the immediate research setting of the trial in a way that will maximise the impact of the results?

4 Trial Management

4.1 What are the arrangements for day to day management?

(*e.g. randomisation, data handling, and who will be responsible for co-ordination)*

4.2 What will be the responsibilities of the applicants?

Please give details of the roles of the named applicants. Please indicate which investigators have experience in successfully running large multi-centre trials. Please highlight if you will be working with a clinical trials unit/office. Please also particularly highlight how social sciences, health services/economics/operations research expertise will be incorporated into the study to ensure that the results are implementable in local settings.

4.3 To what extent are institutions in the countries where the trial will take place involved in scientific leadership of the trial?

4.4 What will be the responsibilities of the staff employed on the grant?

Please give details of the roles of the staff requested on the grant.

4.5 What will be the roles of the named collaborators?

Please give details of the roles of the named collaborators.

4.6 Who is providing statistical support?

4.7 Who will be the Sponsor(s) for the trial?

The sponsor is the individual, or organisation (or group of individuals or organisations) that takes responsibility for confirming there are proper arrangements to initiate, manage, monitor, and finance a study. We would usually expect the sponsor to be the Principal Investigator's Host Institution. If the sponsor will be a different organisation, please provide a rationale for this decision in your proposal.

The funders will not act as sponsor to funded trials, unless the PI's Host Institution is an MRC Unit or Institute, in which case MRC would normally be the sponsor.

A letter of agreement from the sponsor should be uploaded to the Je-S application.

4.8 Please describe the ethical review and research governance arrangements that would apply to the work done.

4.9 Trial Steering Committee

Please give names and affiliations of the proposed trial steering committee to include - independent Chairman, independent members, principal investigators.

4.10 Intellectual Property/Commercial exploitation – please address the following points:

- Does the proposed research use technology, materials or other invention that, as far as you are aware, is subject to any patents or other form of intellectual property protection? If yes, give brief details.
- Is the proposed research, in whole or in part, subject to any agreements with commercial, academic or other organisations? If yes, give brief details.
- Is proposed research likely to lead to patentable or commercially exploitable results? If yes, please give brief details.
- If any potentially commercially exploitable results may be based upon tissues or samples derived from human participants, please confirm that there has been appropriate informed consent for such use.

4.11 Risks of research misuse: it is the responsibility of institutions in receipt of funding from this scheme to ensure that any risks that research could be misused for harmful purposes are managed in the appropriate manner. Please confirm that you have considered whether your proposed research could generate outcomes that could be misused for harmful purposes.

- Have you identified any tangible risks of this type?
- If yes, please briefly describe these risks and the steps that you and your institution will take to manage them.

5 Trial Partners

5.1 Indicate any commercial or other organisation involved

If a company or other organisation is being approached for the supply of the intervention (experimental and control), what arrangements have been made?

5.2 Please give details of any other major funding partners

Include anticipated contribution and the status of discussions.

5.3 Please give details of links which are likely to improve the likelihood of successful implementation of results of the trial.

(e.g. health service providers, community/patient groups)

5.4 Please give details of other key partners

Whose participation is necessary to the success of this – what agreements have been made.

6 Proposal history

6.1 Has the proposal been submitted to other funders?

If so, please indicate the status of your submission to other funders.