Study Guide 5: How to Prepare a Grant Application

Dr David Chinn,
Research & Development Office,
Queen Margaret Hospital, Dunfermline, Fife.
davidchinn@nhs.net 01383 623623 (ext 20943)
Alternative contact: Dr Amanda Wood amanda.wood3@nhs.net
01383 623623 (ext 20941)

Contents

(1) Overview and learning outcomes

This guide is designed for novice researchers who are seeking funding for a research project. It is a guide only and you should seek additional advice from the literature on securing grant funding and from websites that will contain up to date information. After reading this guide you should have an understanding of:

- The main types of health research funding bodies
- The main types of grants
- The detailed steps in the process of applying for a research grant
- An example of a successful grant application

Associated NHS Fife study guides:

1 How to devise a research question and choose a study design
2 How to write a protocol
3 How to critically appraise the literature
4 How to apply for a 'favourable opinion' from an ethics committee and for R&D management approval
9 An introduction to qualitative research
10 An introduction to medical statistics
11 How to calculate sample size and statistical power
17 How to write an abstract

(2) Introduction

Research can be rewarding for improving the delivery of health care and for career development. On occasions research carried out in health care settings does not need separate funding. However, research questions can emerge from routine and other work that does require additional resources not normally available to a Chief Investigator, or CI (and you, as the lead researcher are likely to be the CI). The search for these resources will require development of a research grant.

(3) The main types of funders and awards for health research

(3.1) Funders

Examples of the main types of funders to support health care research in the UK are listed in Table 1. This list is not comprehensive and there are many more sources identifiable from the internet.

In addition to UK sources of funding other sources can be investigated from, for example, the European Commission:
http://ec.europa.eu/research/health/medical-research/index_en.html

and the USA National Institutes of Health (NIH):
https://www.nih.gov/grants-funding

Table 1 Examples of the main types of funders of health care research (UK)

Government:	Chief Scientist Office (CSO)	http://www.cso.scot.nhs.uk/funding-2/response-mode-funding-schemes/
	Department of Health (DoH) *	https://www.gov.uk/government/organisations/department-of-health
	Health Technology Assessment (HTA)	http://www.nets.nihr.ac.uk/programmes/hta
	National Institute for Health Research (NIHR) *	http://www.nihr.ac.uk/funding/
	UK Govt Centre for Defence Enterprise	https://www.gov.uk/government/organisations/centre-for-defence-enterprise
Research Councils:	Medical Research Council (MRC)	http://www.mrc.ac.uk/funding/
	Wellcome Trust	http://www.wellcome.ac.uk/funding/Biomedical-science/index.htm
	Economic & Social Research Council (ESRC)	http://www.esrc.ac.uk/funding/funding-opportunities/research-grants/
Professional bodies:	Royal College of Nursing	https://www.rcn.org.uk/
	Royal College of Physicians (Edinburgh),	https://www.rcpe.ac.uk/
	Royal College of Surgeons (Edinburgh)	http://www.rcsed.ac.uk/
	Chartered Society of Physiotherapy	http://www.csp.org.uk/tagged/research-funding-8
	College of Occupational Therapists	https://www.cot.co.uk/uk-ot-research-foundation-ukotrf/uk-occupational-therapy-research-foundation-research-grants
Charities:	Association of Medical Research Charities	http://www.amrc.org.uk
	Diabetes UK	https://www.diabetes.org.uk/Research/For-researchers/Apply-for-a-grant/Project-grants/
	Parkinson's UK	http://www.parkinsons.org.uk/content/research-grants
	British Lung Foundation	https://www.blf.org.uk/Page/Available-grants
	British Heart Foundation	https://www.bhf.org.uk/
	Cancer Research UK	http://www.cancerresearchuk.org/funding-for-researchers
Industry:	Pharmacology companies	....various, search online
	Medical device manufacturers	.... various, search online
Institutions:	Universities / Hospitals	.... various, search online for personal bequests etc

* Scottish Institutions are sometimes ineligible for accessing some sources of DoH and NIHR monies. If uncertain about eligibility, send an initial enquiry to the funder's administrator for clarification on eligibility.

(3.2) Awards

Grants are available for multiple purposes including proof of concept studies, pilot studies, training fellowships, travel awards, equipment grants and research projects (small, large and programme). The latter includes funding for secondary analyses, observational and experimental studies, both short- and long-term (for example, 5 years for a programme grant).

Some funders invite applications for commissioned bids (e.g. HTA and NIHR). These usually involve a two-stage process involving a preliminary outline bid followed by an invitation (or not) from the funder to submit a full application.

Training fellowships are a convenient way to develop your career as a researcher. However, they are what they claim to be, namely specifically directed at training. They are not a convenient source of monies to pursue a pet project. When completing an application the trainee is strongly advised to focus on initially identifying their training needs, then to describe the project in which they will develop their new skills.

(4) Initial steps before preparing the grant application

It is assumed you have already devised your research question, selected a study design, completed your initial literature search and written the study protocol.

The research question is critically important as it provides the focus for the study, determines the study design and sets the aims and objectives. Funding bodies will expect to see a focused research question on a topic that is important, that fits with their strategy, and is researchable. Details of how to devise a good research question and choose a study design are available in the NHS Fife Study Guide number 1 (*see list of Associated Study Guides on page 2)*.

A research funder will expect you to have a good understanding of the research evidence available on the topic, including any guidelines to inform current practice. In general, if your question is such a good one then it is likely that someone has already thought of it, researched it and published their findings. Hence, the next step is to conduct a focused literature research around the components of the research question which can usually be represented under 4 headings, collectively referred to as PICO:

Patient / Population / Problem
Intervention
Comparison
Outcome

The databases of medical literature include MEDLINE, PubMed, CINAHL, PsycInfo etc. Be wary if you fail to find any relevant literature as you may be looking in the wrong database or using the wrong search terms. As an example of the latter, when researching industrial injuries such as repetitive strain injury (RSI) in the UK these are referred to as Work Related Upper Limb Disorders (WRULD) whereas in the USA these are referred to as Cumulative Trauma Disorders (CTD). A search on the common term ‘RSI’ may yield very few hits.

Advice on conducting a literature review is usually available from the Health Board's library service. In NHS Fife the contact number is 01592 643355, extension 28790 (email: fifelibraries@nhs.net).

The papers identified should be critically appraised with poor papers discarded and better papers retained. Details of how to critically appraise a paper are given in the NHS Fife Study Guide number 3. Following this process it may be that sufficient evidence already exists to answer your research question. However, this should not stop you considering another study on the same subject as what works in one health care setting may not work in another setting. Hence, previous studies can be replicated with potentially useful findings to improve clinical practice in your setting and research funders may consider such projects favourably.

It can be very helpful to look for one or more recent reviews on the topic you intend to research as the authors will already have searched the literature exhaustively. In addition, they may have identified current areas of unanswered research questions. These reviews can then be cited in your grant application as important drivers in establishing the originality and relevance of your proposed project.

Tip: interrogating MEDLINE and other databases enables you to look back in time. To enable you to look forward, consider using the Web of Science (available via the NHS Knowledge Network) which is a database of citations to the published literature. You can enter a published paper (or review) in the database and identify all the papers published since which have cited that particular paper.

When reviewing the literature make a note of the strengths and, in particular, any limitations identified in these studies. Your own study design can be improved by addressing the limitations of previous studies on the same topic and these may be referred to in the grant application to emphasise the robustness of your chosen methodology.

Finally, consider checking the acknowledgement sections of important published papers to identify their source of funding to help you choose (or avoid) a potential funder.

Every research study requires a protocol containing the detailed methods you intend to use. The protocol is the 'recipe' for the study. It is important to have a comprehensive protocol as this will help when preparing both the ethics form and grant applications. Details of how to prepare a good protocol are in the NHS Fife Study Guide number 2.

(5) Steps in preparing the grant application

The next steps in developing a grant application are outlined in Table 2.

Table 2. Steps in developing a grant application

Step	
1	Check research registers for current research projects
2	Select a potential funder
3	Choose a study team
4	Devise the timetable for preparing the application
5	Write the proposal
6	Proof read it and arrange a peer review amongst colleagues
7	Submit it for management approval at your institution
8	Submit the approved application to the funder
9	Await outcomes

(5.1) Step 1: Check research registers for current research projects

Having completed your literature review it is good practice to also check current research registers to identify any ongoing projects relevant to your proposed research. Researchers are encouraged to register their projects on databases. These include:

National Patient Safety Agency: www.nres.npsa.nhs.uk/researchsummaries

The International Standard Randomised Controlled Trial Number:

http://www.isrctn.com/

The UKCRN Research Portfolio Database: http://public.ukcrn.org.uk/search/

Europe: https://www.clinicaltrialsregister.eu/

USA: https://clinicaltrials.gov/

Charities, for example, the British Heart Foundation:
https://www.bhf.org.uk/research/information-for-researchers/previous-awards

In addition, ethics committees in the UK will register projects for which they have provided a favourable opinion on: http://www.hra.nhs.uk/news/research-summaries/

However, do not be disheartened if there are multiple projects funded in the area you want to research because we seldom rely on only one source of evidence for recommending a change in practice. Reviewing details of other projects may also help you design your own study in particular in relation to relevant outcome measures.

(5.2) Step 2: Select a potential funder

Tip: The Research and Development offices in Health Boards in Scotland are funded by the Chief Scientist Office (CSO). Research activity contributes to a Health Board's annual target as set by the CSO and projects that are funded by certain sources are given greater weight. These sources are on a list of 'eligible funders' available from:
http://www.cso.scot.nhs.uk/wp-content/uploads/2013/05/NRS-Funding-Guidance-Annex-2-Eligible-funders-v4.pdf
Accordingly, when identifying potential sources of grant funding in NHS Fife you are encouraged to submit your application to a funder on this list.

The choice of a potential funder is critical. Check their website and familiarise yourself with their strategy, their guidance documents and note the projects they are currently funding. Some funders apply rigid criteria on what they will, and will not cover in a research grant. Hence, some funders will not support animal studies, others will not pay for computers, conference fees or University overheads (mostly the charities). Some funders invite early outline proposals which are less detailed than a full application. The funder will consider these and either reject the outline or invite the researcher to submit a full application to a given deadline. However, this is not a guarantee that the application will be successful. The deadlines for a full application can be short so it can be prudent to begin putting together the full application anyway. The time is not wasted because if your proposal is declined you have at least made progress in preparing an application for an alternative funder.

(5.3) Step 3: Choose a study team

In general a grant application with just one applicant is unlikely to be accepted. Multiple applicants are advisable to ensure the study will be completed if a member of the team withdraws for whatever reason. Hence, identify co-investigators who can help you and may have expertise to complement your own. Co-investigators may assist with, for example, preparing the grant application by providing specialist knowledge on study design, outcome measures, statistical analyses, health economic considerations etc. Most funders will expect you to have one or more lay members on the project team. Lay members include service users. They should be involved at the earliest stage in development of the project as they can make a significant contribution to the study objectives and provide advice on recruitment and in preparation of patient information sheets.

(5.4) Step 4: Devise the timetable for preparing the application

A strict timetable is needed to prepare the grant application. Deadlines can be tight and it is easy to miss them. However, missing a deadline need not be the end of an application as funders will have a schedule of funding rounds (annual or more frequent) so you can submit the completed application later.

Assign each section of the application to a co-investigator to complete according to the timetable. It is good practice to appoint a co-ordinator (not necessarily the Chief Investigator) to oversee completion of each section.

(5.5) Step 5: Write the proposal

Some funders provide helpful advice on completing their forms to ensure your application meets a high standard. For example, the NIHR provides tips at:

http://www.nihr.ac.uk/funding/pgfar-tips-directors-messages.htm

In addition, some major funders run courses and webinars on applying for their funding. It is sensible to first check out a funder's website to see if they provide training and/or advice on what constitutes a good (and bad) application.

When completing your own application it is important not to underestimate the time required to prepare it. Many drafts and rewrites will be required.

Ensure you have the funder's up to date forms. Read the instructions carefully and prepare your application to the instructions given, including word counts, font sizes, number of pages, details required in the investigator's CV etc. Funders are often swamped with applications and it is convenient for reviewers to discard those easily which do not meet the specified instructions.

If your application is turned down do not be tempted to submit it to another funder without first considering any feedback from the reviewers. Also, check the guidance from the second funder and format your application to the desired instructions. Reviewers are alert to recycled applications so do not infringe the rules of engagement!

The proposal can be based on the protocol but will require additional information such as the budget and the investigator's CVs. Much of what you prepare for the grant application will be relevant for an ethics committee review as well so prepare the text carefully with this in mind. The ethics committee forms can be completed at the same time. Advice on how to do this is available in the NHS Fife Study Guide number 4.

The proposal will require a title, a summary and details under sub-headings:

Title

The title is clearly important and should describe the study including its methodology.

Example: Title

The effects of a nurse run clinic on the quality of life of children with atopic eczema and the impact of the disease on their families: a randomised controlled trial.

Summary or abstract

Reviewers are looking for a clear focussed research question and a summary or abstract (usually about 200 words) that stands alone and fully encapsulates the research design.

Example: Summary

The principle aim of the project is to evaluate the effect of a primary care nurse-led clinic (the intervention) on the quality of life (QoL) of children aged up to 16 years with atopic eczema. A secondary objective is to assess the impact of the intervention on the QoL of the family of these children. Patients will be recruited opportunistically into the trial and randomly allocated to a control group or an intervention group which will be invited to attend the clinic for advice, education and demonstration of treatments (as advised in the recently published British Association of Dermatologists' guidelines). The control group will constitute 'usual care'. Change in QoL will be compared in control and intervention groups from that at baseline with that at 4 weeks and 12 weeks post intervention to assess both short and longer-term effects. The results will contribute to the evidence base on the organisation of care of children with eczema in general practice, methods of improving patient compliance

with medication, appropriate prescribing and use of therapy and the implementation of clinical guidelines.

The required sub-headings for the detailed proposal can vary, but are likely to be similar to the following:

a. Title
b. Background to the project
c. Plan of investigation including the proposed research methodology
d. Project milestones
e. Justification of the support required
f. Methods for dissemination and implementing research results
g Benefits the proposed investigation will bring to the NHS
h. References

Background to the project

The background should adequately summarise the present state of knowledge and put your study in context by describing what is known, what is unknown and how your proposal seeks to fill a gap in that knowledge. The references cited will be checked to see if they are current. They may be limited in number (or available space) so you must be circumspect and very selective. If possible find any relevant guidelines and cite an up to date review. This is particularly helpful if it identifies areas for future research activity so that your proposal is seen in context with current knowledge.

The background may refer to any pilot work you have done. Pilot data can be invaluable in establishing that your methods are robust and the project is deliverable. Similarly, you may be able to cite any published work by your team using identical methods.

Example: Background to the project

Atopic eczema is a common skin disorder affecting between 5% and 15% of school aged children (1-3) and, as with other atopic diseases, the prevalence appears to be increasing (4,5). The disease causes sleep disturbance and misery to sufferers with reduced quality of life (6), psychosocial problems (7,8) and disruption to family life (9). Much of the burden of atopic eczema is managed in primary care where treatment is directed at providing symptomatic relief (10). Referrals to secondary care are often inappropriate (11) and evidence is needed on improving the delivery of dermatology services in primary care (12). The British Association of Dermatologists' guidelines on the management of eczema stress the importance of providing adequate time for education of the patient and explanation and discussion of aspects of treatment (10). Such time is not always available during a single GP consultation and this study will evaluate the additional effects of an intervention from a trained dermatology nurse in a clinic setting in primary care.

Plan of investigation including the proposed research methodology

You should concentrate on describing features of the study that will convince the reviewers that the proposal is viable. Reviewers are also successful researchers and will be fully aware of the pitfalls of conducting research. Features of a good study include:

- Multidisciplinary team
- Descriptive Title
- Clear aim
- Clear achievable objectives
- Realistic milestones
- Robust methodology, appropriate study design for the question being asked
- Subjects clearly defined and representative of the target population
- Selection criteria specified – inclusion/exclusion
- Clear diagnostic criteria
- Recruitment issues identified
- Source of controls appropriate
- Availability of participants noted – numbers needed and likely to consent
- Power calculation – Sample size needed to demonstrate a difference between groups if one truly exists, or a defined level of precision (confidence interval) to estimate a single proportion, prevalence, incidence etc
- Appropriate randomisation, if relevant
- Outcomes specified, measurable, relevant, with quality control processes in place where relevant
- Potential for bias identified
- Realistic timetable, including dissemination plan
- Resources needed identified and available

It is good practice in quantitative studies to include a power calculation to determine a desired sample size. Details of how to undertake a power calculation are in the NHS Fife Study Guide number 11. Alternatively, you can search the internet for advice or, better still, ask a statistician to write the section on the power calculation and analysis plan. It is important to describe the data analysis plan and is not sufficient to state simply ‘the data will be analysed using appropriate statistical techniques’.

Be realistic regarding recruitment and the likely participation rate. Do not overestimate the recruitment rate as your patients may not share your enthusiasm for the study. Recruitment targets can be hard to achieve in practice and the reviewers will be alert to any unsubstantiated and unrealistic estimates.

When devising the timetable be realistic and leave yourself plenty of time for quieter periods (e.g. holidays) when you can make up lost ground. If possible provide a GANTT chart (http://www.gantt.com/) or a visual chart showing in outline the timetable for the study, the study visits and what interventions and measurements are made in each one.

In estimating the budget make sure you cost in all the resources needed with fully justified estimates. For any instruments being purchased include costs for VAT, consumables, delivery, training, maintenance and service costs. Use of some questionnaires may attract a copyright fee. Similarly, you may require software licences for data management and analysis packages. Include costs for inter-library

loans required as part of your literature search (particularly important for systematic reviews), and for printing and postage as it is unreasonable to expect your institution to pick up these additional costs. Similarly, include any travel costs for staff and study participants. Travel costs, conference registration fees and journal publication fees may be incurred in disseminating your study findings. Consult the local Research and Development office for guidance on costings including salaries, overheads and recovery of service costs associated with the work etc. Be aware that some grant bodies will not purchase certain items e.g. computers, expecting the organisation to provide these. Your costs will need to be signed off by your institution's finance department so it is prudent to include them in early discussions. This is particularly important if you are intending to employ new staff as the institution may have restrictive rules on employing temporary staff.

Universities require payment for overheads. These include the costs incurred in employing support staff and providing them with services (electricity, heating, IT services etc). In the 1980s major changes were made to Government funding of academic institutions and costs for overheads were shifted to research councils to which the Government increased its allocation. Charging for overheads can be a source of complaint by NHS staff when collaborating with University staff but this is a legitimate cost that must be recognised.

The methods of dissemination must be clearly identified and feasible within the timetable. The funding body will want a final report and may not pay out the last instalment of the grant until the work is completed and the report received. The grant represents a contract with all the legal responsibilities that this incurs. In addition, the ethics committee also will require a copy of this final report.

The application should include a section on potential benefits for the NHS as this demonstrates to the funder what they are getting for the money. Though not essential, it can be of particular benefit if the application can offer some comment on any health economic aspects of the study.

Example: Plan of investigation including the proposed research methodology

Design: Randomised controlled trial over a nine month period with recruitment of incident cases and those patients requesting a repeat prescription. Control group gets the intervention after the trial but no further follow-up.

Setting: One general practice (10 partners) with a list size of 23,600 of which about 5250 are children younger than 16.

Patients: In the XX general practice 470 children aged between 6 months and 16 years received medication for atopic eczema in the period October 2013-March 2014. On average, about 50-70 children each month consult and receive medication or request repeat prescriptions for atopic eczema and these children will be invited to join the trial (after obtaining parental consent).

Inclusion criteria:

- age 6 months up to 16th birthday,
- diagnosis of atopic eczema made using British Association of Dermatology guidelines (ref),

- new cases and patients requesting repeat prescription for medication issued for a diagnosis of atopic eczema.

Exclusion criteria:
- Poorly controlled asthma defined as patient receiving oral steroids or having a change in dose of medication in the 4 weeks prior to recruitment (children with stable asthma will be included).
- Children from the same family of a child who has already participated in the trial (to eliminate the risk of contamination of intervention and control groups).

Recruitment: Each week a review will be undertaken of the previous week's prescriptions issued for treatment of atopic eczema. Cases will be identified from the list of inclusion and exclusion criteria and eligible patients will be sent a covering letter inviting parents of children to take part in the trial and copies of the Family impact questionnaire (FIQ) and the Children's Dermatology Life Quality Index Questionnaire (CDLQI) (ref) for those children aged 3-16. The parents/ guardians will be asked to complete the questionnaires, with their child, at home and return it to the practice if they wish to take part in the trial.

If they wish to participate in the trial parents/guardians will be requested to complete the questionnaires, with their child, at home and return it to the practice.

The CDLQI and FIQ are validated instruments enquiring into symptoms and disturbances over the previous week. Each questionnaire includes 10 questions about symptoms and effects of the disease on family life. Each question has 4 responses (scored 0-3) and the overall questionnaire score is between 0 and 30, with a high score indicating poor quality of life of the patient or large impact on the family from the child's disease. The FIQ has been validated in children aged 6 months-12 years (ref) and the CDLQI has been validated in children aged 3-16 years (ref).

The returned envelopes (containing the questionnaires) will be passed, unopened, onto a third party not connected with the practice (Dr XXX, University of XXX). The patient will then be randomised by reference to a list of random numbers into the intervention (odd numbers) or control group (even numbers). The practice nurse will be informed of those requiring the intervention and an appointment will be issued to attend within two weeks. Postal questionnaires will be sent out by Dr XXX 4 weeks and 12 weeks after the intervention to assess short-term and longer-term effects, respectively. The control patients will be sent out questionnaires at approximately 6 and 14 weeks post baseline to coincide with the review in the intervention group. These questionnaires will be returned to the practice but addressed to Dr XXX for opening and analysis. Follow-up of non-responders will be made by telephone, where possible, or by post.

Intervention: Demonstration of techniques for applying medication together with advice and education delivered in a single session of 20 minutes by a trained dermatology nurse.

Outcomes: Change in the Family Impact Questionnaire (FIQ) and Children's Dermatology Life Quality Index (CDLQI) recorded at baseline and at 4 weeks and 12 weeks post-intervention.

Statistics: Change in QoL scores between baseline and 4 weeks and between baseline and 12 weeks will be analysed using a two-sample t-test (SPSS).

Four null hypotheses are to be tested:

- There is no effect on change in QoL at 4 weeks (or 12 weeks) from a short intervention by a trained nurse in children aged 3-16 who present with atopic eczema.

- There is no effect on change in the family impact at 4 weeks (or 12 weeks) from a short intervention by a trained nurse in children aged 6 months-12 years who present with atopic eczema.

Timetable:

Recruitment of patients and delivery of intervention	(9 months)
Completion of follow-up	(3 months)
Data preparation and analysis	(1 month)
Preparation of final report	(2 months)

Power studies:

The short-term test-retest standard deviations of the CDLQI score was 2.5 (ref). The FIQ is a new instrument and its repeatability has not yet been established. However, it is scored in an identical manner to the CDLQI and, for this instrument, the number required in each group to identify a change in QoL score of 1 unit with 90% power at 5% significance = 130. Assuming 25% dropout, number required in each group = 170. Assuming the number of new children consulting or requesting repeat prescriptions each month = 50, and the number recruited into trial each month = 40 then the period to reach target numbers = 8.5 months

Project milestones:

01/09/14	Appointment and training of dermatology nurse - completed.
01/01/15-30/09/15	Recruitment into study (40 patients per month, 9 months)
31/12/15	Completion of follow-up of those recruited in September 2015
01/01/16-31/01/16	Delivery of intervention to last group of control patients
31/01/16	Final data preparation and analysis
31/03/16	Submit final report and complete papers ready for publication

Justification of the support required

Staff: A nurse holding the ENB 393 certificate in Dermatology is required to work three days per week for thirteen months (0.6 WTE). In the XX Medical Centre this nurse-run clinic represents an additional service not currently available. The anticipated research activity is to see 10 patients a week rising to 20 patients a week as controls are invited to attend for the intervention after the 12 week trial.

Support costs required are:-

- secretarial duties (1 hour per week for 1 year)
- data preparation,

- project management, academic and statistical support. This is a University post which attracts 40% overheads.

Nurse: 13 months (0.6 WTE Band 6) = £27,520 (includes on-costs)
Secretary: 12 months (0.02 WTE Band 3) = £ 470
Data preparation: = £ 400
Project management, academic and statistical support (University):
= £12,000
Resources:
Stationery - printing costs = £ 500
Postage, to include reminders (2600 mailings) = £ 1,500

Overheads:
40% University salary costs = £4,800

Methods for dissemination and implementing research results

The results will be disseminated at professional meetings and in peer-reviewed journals. The findings may be used to inform the commissioning of the most appropriate model of care in general practice for children with eczema.

Benefits the proposed investigation will bring to the NHS

The results will contribute evidence on the organisation of primary care services for children with atopic eczema and on the implementation of guidelines. The model may lead to improved patient care with better use of resources through more appropriate prescribing and usage of therapy. In addition, an improvement in knowledge about the disease and its impact should promote empowerment of patients and their families thereby influencing quality of life. Finally, if successful, the model of the nurse-led dermatology clinic may be appropriate for other childhood (and possibly adulthood) diseases leading to a reduction in inappropriate referrals to secondary care.

References

(5.6) Step 6: Proof read it and arrange a peer review amongst colleagues

The application must be proof-read as a sloppy product will reflect badly on the research team. Reviewers will take a dim view of an application with multiple typos. After all, if you cannot put together a correct document what confidence can the reviewers have that you will produce a quality research project?

Seek advice from colleagues on the clarity of the application and include a colleague who is not an expert in your field as their views can be very perceptive in identifying flaws in the application.

(5.7) Step 7: Submit it for management approval at your institution

In NHS Fife the application will need to be signed off by both the Finance and Research and Development offices so allow additional time to secure these approvals. For finance you should allow at least one working week. Other groups may also need to approve the proposed study including laboratory services,

pathology services, imaging services etc. You will need letters of support from the service managers of each additional group confirming they are aware of the implications of the study on the service. In turn, these letters may be appended to the grant application as appendices.

(5.8) Step 8: Submit the approved application to the funder

The application must be submitted within the deadline. Late applications will simply be returned. Some funders encourage an early submission so you need not wait until the day of the deadline.

The application will be subjected to the funder's review process. This will include review by a panel made up of a moderate number of reviewers who will screen each application and score it against a predefined set of criteria. The proposals are then ranked and discussed in committee. The reviewers may not necessarily be experts in the field who share your knowledge and experience for the subject. Even if there is a reviewer who knows something about the topic their voice will be one amongst many voices. You have to sell the project to the point where the question is not 'shall I recommend this project for funding' but 'can I afford not to recommend this project'.

As a preliminary, any application that does not conform to the instructions for completing the application is likely to be eliminated early in the process.

The reviewers will first look at the title of the project, then at who will be doing the research, and what support will be available to the researchers to ensure the work is done on time and to standard. A grant with a single author almost always is likely to be turned down. The investigators should comprise a multidisciplinary team, including, if possible, a statistician or epidemiologist if it is a quantitative study irrespective of whether or not it includes a hypothesis. Inclusion of a health economist is another useful member to have onboard though this is not critical as you can often state the outcomes of the study may inform the design for a subsequent study of health economics.

The reviewers will attach importance to the affiliation and reputation, if any, of the Chief Investigator. It helps if, amongst your co-investigators you have a proven track record in successful delivery of a previous research project through to publication but it is not impossible for a novice researcher to get funding. Indeed, some funders are specifically looking to support novice researchers in the early part of their careers.

The reviewers will seek assurance that the work is independent and the approach of the researchers is with an open mind. Do not state in the summary ….'in this study we are going to show that…'. Also, do not state under benefits to NHS ….. 'once we have shown that this treatment is superior to … the NHS will save many millions of pounds…'

Although not part of the review process it is likely that the reviewers will seek to identify any ethical constraints in the proposal. They may also look for any conflicts of interest.

You may be asked to nominate up to six reviewers and, in some circumstances, to nominate named reviewers you would not wish the funder to use. However, you should not have to justify a 'negative' reviewer, or even nominate one if asked to do

so. Any names you quote as 'positive' or 'negative' reviewers should be treated in confidence by the funder although it may be best to assume the names will be disclosed during the review process. The funder may elect to send the application to one or two of your nominees in addition to their own selected reviewers.

(5.9) Step 9: Await outcomes

The outcome of the review process can be acceptance, rejection or an invite to revise and resubmit. Acceptance rates can be very low, perhaps as little as 10% for some major funders. If you are successful the next stage will involve signing contracts, familiarising yourself with the funder's conditions of award, arranging the budget, purchasing equipment and software, advertising for new staff, completing ethics forms if not already started, training staff etc. This is not the time for you to go on holiday, so expect to be busy! Remember to share your good news with all those who have helped you prepare the application.

Pay particular attention to the funder's timetable for interim reports, budget estimates etc. Add these commitments to your study timetable and stick to the schedule.

If your application is rejected do not be disheartened as you are in the majority! A rejection is not necessarily a reflection of a badly designed study. It may be that the funder has accepted an alternative proposal on the same topic or simply not have sufficient funds to support all the highly rated studies in that round. You should pay attention to the feedback from the funder and the reviewers, discuss it with your co-investigators, modify your proposal accordingly and submit it elsewhere. However, in considering the feedback, do not accept the recommendations uncritically because the reviewers may simply not have fully appreciated the detailed rationale behind your proposal. Reviewers can, and do sometimes get it wrong! It is possible to challenge the views of a reviewer if you believe he or she has misunderstood some aspect of your application, perhaps from your inability to present your case coherently. However, you must consider the effort required and the potential negative impact that may occur to your reputation with that particular funder.

If you believe a reviewer has unfairly criticised your proposal due to a misunderstanding then this is an indication that the section needs revising to improve its clarity before submitting the proposal elsewhere.

Unless you receive extremely negative feedback such as:
'this study is fundamentally flawed', 'hopelessly optimistic', 'irrelevant to modern practice', 'destined to failure', 'the wrong design for the wrong question', ' a waste of time and money' then you should consider revising the application and submitting it to an alternative funder.

Do not be tempted to give up at this stage!

If you are invited to resubmit your application, with or without changes, you should consider this favourably as it may be the funder wishes to support the work (as part of its overall strategy) but has insufficient funds from that round. Consider the suggested changes recommended by the reviewers though decide first if the changes are feasible, or even needed. It may be that the changes suggested are so radical that you consider the study, as originally envisaged, is no longer viable. In these circumstances you may be advised to withdraw your application and submit it elsewhere. If the suggestions are feasible and the reviewers have recommended changes to, for example, your chosen outcome measures then consider their alternatives positively and evaluate them in relation to the time required to implement the changes, any training needed, the impact on study participants and costs associated with their adoption (e.g. copyright fees for alternative questionnaires).

The deadline for a resubmission may be short so ensure your study team is available to respond to all the criticisms and to prepare the revised application, including the budget, which will need signing off again by the institution's finance officer, and any other approvals needed.

(6) Common failings in research grant applications

Common reasons why research grant applications are rejected include:

- poorly constructed or unimportant research question
- poor science
- incorrect methodology
- insufficient detail
- over-ambitious or otherwise unrealistic expectations
- insufficient expertise
- lacklustre application
- poorly prepared application with
    - multiple typos,
    - rambling text,
    - too much clinical detail

(7) Where to get help in NHS Fife?

Your Health Board's or Trust's Research and Development office should always be your first port of call. In NHS Fife the principal officers are:

R&D Manager: Dr Amanda Wood, 01383 623623 (ext 20941)
amanda.wood3@nhs.net
Senior Research Advisor: Dr Fay Crawford, 01383 623623 (ext 20943)
Contact via roy.halliday@nhs.net
Research Approvals Coordinator: Aileen Yell, 01383 623623 (ext 20940)
aileenyell@nhs.net
R&D Commercial Manager: Dr Allyson Bailey, 01383 623623 (ext 24047)
Allyson.bailey@nhs.net

(8) Summary

- You need conviction and to be a good 'sales person'.
- Always prepare the application according to the instructions.
- Submit the application in time. Most funders accept electronic copies though some still require hard copies of the signed application. If asked to send multiple copies by post allow plenty of time for the post office to deliver them. Make sure you have evidence of posting and of receipt, so send it by recorded delivery. Also, watch out for the consequences of any industrial action!
- Be prepared for disappointment.
- Think well ahead if you are looking to secure funding for continuity of work and employment of research staff on short-term contracts.
- The review process can be lengthy, so expect delays.
- Apply for a 'favourable opinion' from an ethics committee before the submission of the grant (if possible). It helps if you can state that ethical approval has already been obtained, or just submitted.

(9) Further reading

Writing a plain English Summary:
http://www.invo.org.uk/makeitclear/
http://www.invo.org.uk/makeitclear/how-to-write-a-summary/

INVOLVE jargon buster:
http://www.invo.org.uk/resource-centre/useful-information/jargon-buster/

National Institutes for Health advice on preparing a grant application:
http://grants.nih.gov/grants/writing_application.htm

Appendix: Example of a successful grant application (with consent from the Chief Investigator).

Project Title
The Utility of Whole Body Vibration Exercise in Haemodialysis Patients: a pilot study

Investigators		
	Investigator 1	***Investigator 2***
Name		
Job Title		
Location		
Practice/Dept		
Address		
Address 1		
Post Code		
Telephone		
Email		

Background (citing key references)

Patients with end stage renal disease (ESRD) face specific musculoskeletal problems including rapid functional and physical decline after initiation of haemodialysis [1]. Reduced physical capacity results from decline in strength, aerobic capacity [2], muscle wasting [3], along with enforced immobility during treatment. In addition, ESRD causes mineral bone disease (MBD) with abnormal Calcium and Phosphorus metabolism with Vitamin D and Parathyroid disease, along with exaggerated osteoporosis [4]. As a result, ESRD patients rapidly become frail and increasingly dependent.

A recent mini-review identified the evidence that a physical exercise program can improve general health, including a reduction in weight, improved muscle strength, lowered cholesterol and blood fats, increased cardiac output and greater physical exercise capacity in ESRD patients [5]. Many of these benefits will also reduce the risk of heart disease, a risk which is greater for people with kidney disease than among the general population [6]. Furthermore, routine exercise enhances feelings of self-esteem, maintains independence and improves depression and anxiety [7]. Failure of exercise programs results from basic logistics of arranging sessions and equipment around long dialysis sessions and transport times [8]. Despite all this evidence the majority of ESRD patients fail to achieve physical exercise, either aerobic or weight bearing [9].

Previous studies and exercise programs in ESRD have used exercise bicycles during haemodialysis (HD) or gentle exercises during HD (designed to build muscle). Factors contributing to sustainable exercise programs included: dedicated exercise professionals; encouragement to exercise intradialytically; dialysis and medical staff commitment; adequate physical requirements of equipment and space; interesting and stimulating; cost implications. However, compliance with the exercise protocols can be poor [5]. We have been unable to find any previous studies in the dialysis populations that have reported the use of vibration plates.

Vibration exercise is a novel exercise protocol with origins in the Russian Space program, designed to prevent the loss of muscle strength and bone mineralization during the immobility and weightlessness of space flight [10], a situation surprisingly similar to

haemodialysis. Vibration exercise uses high frequency vibration of muscle groups causing positive feedback of the spinal reflex arc resulting in high levels of muscle contraction to levels of motor unit recruitment otherwise only achievable by severe weight lifting. Furthermore, this can be achieved with several minutes passively standing on the equipment three times per week. There can be multiple physiological benefits from vibration exercise including cardiovascular effects, bone health and muscle strength [11-16]. Vibration exercise might be an ideal exercise intervention incorporated into the routine haemodialysis units with the potential to dramatically improve strength, bone health, function, and quality of life. However, the evidence of its effectiveness and tolerability in this clinical population remains to be established.

Results of any Pilot Studies

This would be the pilot study.

Aims

To provide pilot data on the suitability of the methods, tolerability of the intervention and assessment of the effect of Whole Body Vibration Exercise in ESRD patients to inform the planning of a definitive, multi-centred randomised controlled trial.

Research Questions

(1) What is the tolerability of WBVE in patients with end stage renal disease on dialysis?
(2) What are the practical issues in enabling patients to exercise 3 times a week for a 3-minute duration using WBVE?
(3) Which outcome measures are most appropriate to determine the effect of WBVE on functionality, muscle strength, indirect exercise capacity, nutritional status, bone health, and quality of life of patients on dialysis?
(4) What is the magnitude of effect, if any, on each of these measures?
(5) How many patients would be needed (power calculation) to test a hypothesis in an RCT?

Methods (including statistical power if appropriate)

We wish to test the following methodology:

Patient recruitment

Recruitment will take place at 3 hospitals where patients receive dialysis. We will test our recruitment strategy to determine the likely uptake of the invitation to take part, and the dropout rate. We hope to recruit about 40 patients with a mix of ages, dialysis vintage and genders, and at least 30 completing the study in the time available.

Inclusion Criteria

All ESRD patients currently receiving dialysis (approx 150) and deemed fit to participate by their physician (estimated approx 100).

Exclusion Criteria

Consistently hyper/hypotension`
Recent cardiac event (in past 6 weeks)
Known aortic aneurysm (of any size)
Unstable angina or significant vascular disease
Current infective illness
Poorly controlled diabetes
Active liver disease
Patients who are breathless at rest with visible signs of peripheral oedema
Bilateral amputees or other physical disability
Patients with pacemakers
Known osteoporosis or history of low trauma, fragility fractures
Persistent hyperkalaemia before dialysis

Procedures

Following recruitment patients will have a training session with the measurement techniques then a baseline assessment (**result 1**) which will be repeated in 2 weeks (**result 2**). Thereafter they will receive WBVE 3 times a week, prior to receiving dialysis, for 8 weeks after which the assessments will be repeated (**result 3**). A further assessment will be made 4 weeks after stopping the exercise to estimate any residual effects (**result 4**). This design ensures each patient acts as their own control by comparing:

(1) results 1+2 to assess repeatability, needed for estimating statistical power in the RCT
(2) mean of results 1+2 with result 3 (paired t-test) to determine the effect of the intervention, and,
(3) results 3 and 4 (paired t-test) to determine magnitude of any residual effects.

Specifically we will measure:

- Sit to stand tests,
- Standing equilibrium,
- Hand grip strength (dynamometer),
- Duke Activity Status Index (DASI) (which correlates with peak oxygen uptake) [17]
- Nutrition assessments (skinfold callipers to estimate lean body mass),
- Bone health (ALP, Ca X Pho, PTH, from routinely collected blood measures),
- Protein Catabolic Rate (from routinely collected blood measures),
- QoL Assessment (using the KDQOL-SF) [18]

The WBVE exercise will comprise 3 sessions of 3 minutes/week, with a graded introduction to achieve 3 min maximum isometric exercise. The 'dose' of exercise is a pragmatic choice and the pilot data will provide evidence of effectiveness to support the revised grant application. The vibration plate will be set at a frequency of 50 Hz and a displacement of 10 mm in line with published levels of effectiveness in other populations. The intervention will be delivered by the dialysis nursing staff trained in the technique. Compliance and tolerability of the exercise will be recorded for each patient with a daily diary.

Blood pressure before and after the exercise will be monitored for safety. In addition, bloods are monitored monthly for calcium, phosphate, parathyroid hormone (PTH), alkaline phosphatase (ALP), full blood count (FBC) and protein catabolic rate (PCR) to monitor dialysis adequacy.

At the end of the study, or when patients drop out from it we will, with consent, interview

them to ascertain their views on and experiences of using this type of exercise.

The principal outcome measures relate to physical functioning:

1) the sit-to-stand-to-sit test (the time in seconds to complete 10 full stands from a sitting position (the STS-10) and the number of repeated manoeuvres that can be achieved in 60 seconds (the STS-60)),
2) the handgrip strength, and
3) the DASI

Indicative figures for repeatability and minimal detectable change have been published for the sit-to-stand-sit tests and hand grip strength in dialysis patients [19] but not for the DASI. The results from the present study will be used alongside the available estimates to determine the number of patients required in a randomised controlled trial having 90% power (type II error of 0.1) with a type I error of 0.05 (5% significance).

Data will be analysed with SPSS using parametric tests (e.g. paired t-test) and non-parametric tests according to the distribution of the data. Paired t-tests will be used to compare observed differences with a hypothesised mean difference of zero. If the data justifies it we will run a separate analysis of covariance to adjust for initial levels of function and explore differences due to potential confounders such as age, gender, comorbidity (e.g. diabetes), length of time dependent on dialysis and additional leisure time physical activity undertaken.

Detailed justification for support requested:

Equipment:

(1) 1 WBVE device – cost (including VAT) = £2,400. These devices are programmable and have safety grips for patients to use. The company has agreed to loan us a second device for 6 months if we purchase one device (which they have offered us at half the normal retail price of £4,000). The price includes delivery, installation and a training session. *We are currently applying to the Friends of the XX Hospital to purchase a third device – if this application is unsuccessful we will drop YY hospital as a study cite as the number of patients receiving dialysis there is less than that at the other sites.*
(2) Skin fold callipers – cost (including VAT) = £273
(3) Dynamometer – cost (including VAT) = £40

Salaries:

(1) for a technical instructor (physiotherapist) to undertake the assessments (two days/week, band 4, for 12 months – named member of NHS Staff)
(2) for backfill for a co-applicant and research nurse who will organise the study and collate data (one day/week band 5, for a year)

Travel:

This has been estimated as 40 return journeys of 26 miles and 25 return journeys of 44 miles between base hospital (XXX) and other hospital sites (total mileage = 2060 miles @24p/mile = £514).

Consumables:

Printing costs £50

Team expertise (please list)

Dr XXX (Chief Investigator): study design, ethics application, recruitment, taking consent, report writing.
Research nurse XXX: day-to-day management, recruitment, taking consent, overseeing assessments, data collation, report writing.
Dr XXX: recruitment, taking consent, report writing.
Lead physiotherapist, XXX: professional oversight and advice on measurements.
Technical instructor, XXX: making assessments (XXX has a degree in Sports Science. She has worked with vibration plates before and currently works part-time assessing patients in a rehabilitation service).

Timetable of Work

Timescale and milestones

Week 1 – week 6: Obtain instruments, prepare study documentation and familiarise study staff with procedures
Week 1 – week 8: Obtain 'favourable opinion' from ethics committee (already in process) and management approval from R&D office.
Week 6 – week 8: train dialysis staff in safe use of the WBVE devices
Week 8 – week 30: recruit patients (2 per week) (14 weeks in study, so last patient completed week 44)
Week 8 – week 44: data gathering and preparation of database (SPSS)
Week 45 – week 52: analysis of data and preparation of final bursary report and new grant application.

Proposed Start Date:	1st April 2014	***Proposed Completion Date:***	31st March 2015

Research outcomes relating to NHS implementation potential

WBVE has the convenience of being applied in short bursts while patients attend hospitals for haemodialysis sessions. We acknowledge that there may be practical issues in patients using the devices but if it can be shown that WBVE has utility in improving physical functioning then the exercise modality could be incorporated into routine practice. The results could add to the wider evidence of the potential benefits of exercise for patients in end-stage renal disease and may promote change in services for the rest of the NHS, and possibly international audiences, providing services for renal patients attending hospitals for haemodialysis.

The study's findings will provide evidence on the suitability of its methodology for planning a robust RCT comparing WBVE with other modalities of exercise (e.g. self managed rather than supervised exercise). Other studies might be devised to identify the usefulness of WBVE for maintaining physical function in new patients for whom the evidence suggests will deteriorate markedly in the months following initiation of dialysis.

Finally, WBVE may have utility in other chronic disease patients who require rehabilitation but find it difficult to initiate or maintain an exercise programme. Hence, if our study is associated with positive findings there may be opportunities to investigate other patient cohorts through further grant-funded studies.

Key References

1 Tamura MK et al. Functional Status of Elderly Adults before and after Initiation of

Dialysis. *N Engl J Med* 2009; **361**: 1539-1547.
2 Painter P et al. Exercise capacity in hemodialysis, CAPD, and renal transplant patients. *Nephron* 1986; **42**: 47–51.
3 Carrero JJ et al. Muscle atrophy, inflammation and clinical outcome in incident and prevalent dialysis patients. *Clin Nutr* 2008; **27**: 557-564.
4 Morrow B, Qunibi W. Specific Bone and Mineral Disorders in Patients with Chronic Kidney Disease. *Clin Rev Bone Min Meta* 2012; **10**: 184-208
5 Kosmadakis GC et al. Physical exercise in patients with severe kidney disease. *Nephron Clin Pract* 2010; **115**: c7-c16.
6 Ocak G et al. Mortality due to pulmonary embolism, myocardial infarction, and stroke among patients starting dialysis. *J Thrombosis & Haemostasis*. 2012; 10: 2484-93.
7 Kouidi E et al. Depression, heart rate variability, and exercise training in dialysis patients. *Eur J Prev Cardiol* 2010: **17**: 2160-2167.
8 Bennett PN. Sustaining a Hemodialysis Exercise Program: A Review. *Seminars in Dialysis* 2010; **23**: 62-73.
9 Tentori F et al. Physical exercise among participants in the Dialysis Outcomes and Practice Patterns Study (DOPPS): correlates and associated outcomes. *Nephrol. Dial. Transplant* 2010; **25**: 3050-3062.
10 Rittweger J. Vibration as an exercise modality: how it may work, and what its potential might be. *Eur J Appl Physiol* 2010; **108**: 877-904.
11 Cardinale M et al. Gastrocnemius medialis and vastus lateralis oxygenation during whole-body vibration exercise. *Med Sci Sports Exerc* 2007; **39**:694–700
12 Hazell TJ, Lemon PWR. Synchronous whole-body vibration increases VO2 during and following acute exercise *Eur J Appl Physiol* 2012; **112**: 413-420.
13 Bautmans I et al. The feasibility of Whole Body Vibration in institutionalised elderly persons and its influence on muscle performance, balance and mobility: a randomised controlled trial. [ISRCTN62535013]. *BMC Geriatri* 2005; **5**:17
14 Blottner D et al. Human skeletal muscle structure and function preserved by vibration muscle exercise following 55 days of bed rest. *Eur J Appl Physiol* 2006; **97**:261–271
15 Armbrecht G et al. Resistive vibration exercise attenuates bone and muscle atrophy in 56-days of bed-rest: whole body DXA and biochemical markers of bone metabolism. *Osteoporos Int* 2010; **21**: 597-607. 597-607.
16 Dolny DG, Reyes FC. Whole body vibration exercise: training and benefits. *Curr Sports Med Reports* 2008; **7**: 152-157.
17 Hlatky et al A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 1989; **64**: 651-654.
18 Hays RD, Kallich JD, Mapes DL, Coons SJ, Amin N, Carter WB. Kidney disease quality of life short form (KDQOL-SF^{TM}), version 1.3: a manual for use and scoring. 1995 Santa Monica, CA: RAND, P-7994.
19 Segura-Ortí E, Martínez-Olmos FJ. Test-retest reliability and minimal detectable change scores for sit-to-stand-to-sit tests, the six-minute walk test, the one-leg heel-rise test, and handgrip strength in people undergoing hemodialysis. *Phys Ther.* 2011; **91**: 1244-52.

Ethical Approval is:	~~***Attached***~~		***Being Sought***	***X***	~~***Not required***~~	

Financial Support Requested and Justification

Staff (Including Release from Clinical duties)** (1) Technical Instructor (Physiotherapy) to undertake the assessments (two days/week, band 4, for 12 months) (2) Backfill for co-applicant and research nurse who will organise the study and collate data (one day/week band 5, for a year)	£ 9,272 £ 6,808
Travel & Subsistence	£ 514
Consumables	£ 50
Equipment <u>Equipment:</u> (1) 1 WBVE device – cost (including VAT) = £2,400 (2) Skin fold callipers – cost (including VAT) = = £273 (3) Dynamometer – cost (including VAT) = £40	£ 2,713
Overall Total Requested	£ 19,357