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Prevention and Treatment of Skin Disease:
Setting Priorities and Reducing Uncertainties

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Vitiligo Society

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Introduction

Instead of the usual annual report for our Centre of Evidence Based Dermatology, this year we are presenting a summary of our NIHR Programme Grant for Applied Research. This flagship NIHR award has given us a wonderful opportunity to do really big and useful projects on identifying priorities and reducing uncertainties in the prevention and treatment of skin disease.

Rather than tackling just one skin disease, we have tackled four: eczema, which affects around 20% of UK children; vitiligo - a condition where skin pigment is gradually lost and which can have a profound effect on a person's self-esteem; a rare painful ulcerating condition called pyoderma gangrenosum; and squamous cell carcinoma of the skin - a type of cancer that is becoming more common with our increasingly ageing population who have had a lot of sun exposure.

In each of these areas, we have made important new discoveries, which are described on the following pages. The Programme Grant has also given us a fantastic opportunity to develop new researchers.

As skin disease is so common, there will be something in this report that will be relevant to you, so do flick through it and let us know if you have found something useful for you.

Hywel Williams
Director of the Centre of Evidence Based Dermatology

The National Institute for Health Research (NIHR) Programme Grant for Applied Research has given researchers in Nottingham an unprecedented opportunity to address major questions in the prevention and treatment of skin diseases.

The programme set out to develop new and powerful approaches to identifying research priorities and providing a clear basis for new interventions in skin disease. Beyond its immediate relevance, this work has also provided the basis for a great deal of exciting new research in skin diseases. We have established a generalisable model for the assessment and synthesis of research evidence and the sharing of research knowledge, which we are now applying to other kinds of disease.

The remarkable success of this programme is a tribute to both the vision and commitment of our researchers, and the development of a close and essential partnership with our patients. It fully vindicates the foresight of the NIHR in creating this funding scheme. Nottingham University Hospitals NHS Trust is proud to have hosted such an excellent demonstration of how the NHS and the University can come together to support research for the benefit of our patients.

Brian Thomson
Director of Research and Innovation at Nottingham University Hospital NHS Trust

What was this Research Programme about?

Even though skin diseases are so common, there are large gaps in our knowledge about their causes and treatment. This NIHR Programme Grant for Applied Research set out to prioritise research areas of importance to patients and clinicians, and to reduce uncertainties by conducting high quality research in these areas.

What did we study?

We focussed on four diseases within this award:

- **Childhood eczema** – as this is a big problem for children and parents, has a high cost to the NHS, and is increasing in the UK.
- **Vitiligo -** causes white patches on the skin and has a marked impact on the quality of life of patients; particularly those from black and ethnic minority groups.
- **Squamous cell skin cancer** – a national priority area that is common in white- skinned people and is increasing year on year, especially as our population ages.
- **Pyoderma gangrenosum** – a rare, neglected skin disease that causes painful ulceration of the skin and is difficult to treat.

Why is it important?

Skin disease affects around a third of the UK population and it is one of the top four reasons for visiting a GP. Many people are shocked when they discover how little is known about the prevention and treatment of even common skin diseases such as eczema.

Patients graciously take part in studies across the world and it is our duty as researchers to ensure that this effort is not wasted. Unfortunately, much research can be wasteful. This is because researchers have not asked the right questions, they have not used the right study design to answer the questions, or because they don't report the results fully and honestly - or worse still, they don't report them at all. Instead of suggesting lots more studies, we have concentrated on prioritising the most important questions to patients and health professionals, and we have put a lot of effort into designing the best studies to answer these questions. We have also published our studies in open access journals so that everyone can read and use the information to benefit people with skin disease.

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What did we achieve?

The work conducted over the last five years for this NIHR Programme Grant for Applied Research (RP-PG-0407-10177) comprised a series of interlinked projects that have provided new information in the following ways:

- **Reviewing the evidence** – six systematic reviews have summarised the evidence for skin treatments, as well as exploring methodological issues, such as how treatment success should be measured.
- **Identifying the most important questions** – in collaboration with patients and health professionals to establish the most important areas for future research.
- **Achieving international agreement on how to measure treatment success** – two international initiatives to establish core outcome sets for use in future trials.
- **Making sure that future trials are feasible and able to answer the question posed** – two pilot randomised controlled trials and a case note review have tested out the best ways of recruiting into future trials, and how best to design and conduct the proposed trials.
- **Trial protocols defined for future large-scale national trials** – four trial protocols ready for funding applications, three of which have now been funded.
- **Informing clinical decision-making for the rare skin condition pyoderma gangrenosum** – a full-scale national randomised controlled trial of oral treatments for pyoderma gangrenosum, plus an observational study of treatments applied directly to the skin.

Improving patient care

This research programme has benefitted patients by helping to identify treatments that work and those that do not. This means that clinical guidelines and patient information resources can be updated and written more clearly in the future - taking full account of the research knowledge that we already have. As a broad multi-disciplinary group of researchers, clinicians, health managers and patients, we have been able to ensure that new research evidence is used by the people who need it most.

The following pages of this report highlight some of the success stories and impact that this research has had on the lives of patients and the National Health Service (NHS).

Helping to prioritise the right questions

Ensuring that the right questions are asked in the right way is an important aspect of research prioritisation. To achieve this, we worked with the James Lind Alliance, an initiative involving patients and health care professionals that aims to identify knowledge gaps regarding the effects of treatment. This meant we were able to ensure that future research addresses topics important to both groups.

Why is this important?

Asking the wrong questions, and funding research that answers questions that are important to neither patients nor the clinicians who treat them, is a waste of research funding and valuable resources. By highlighting skin disease as important and clearly identifying significant areas of treatment uncertainty, we hope that future research efforts will be targeted in the right areas.

What did we do?

Two James Lind Alliance Priority Setting Partnerships were conducted to develop a list of priority areas for future research in the fields of vitiligo and eczema. Each partnership included over 500 participants and took approximately twelve months each to complete. The resulting priority topics for research were widely publicised and sent to all main funding bodies in the UK. They were also used to inform our own future research activity, as well as being added to the Database of Uncertainties about the Effectiveness of Treatments (DUETs) (http://www.library.nhs.uk/duets/).

Both of these Priority Setting Partnerships were a great success. As well as giving us the shared priorities and questions, they have helped to develop a vibrant network of patients and clinicians with an interest in skin disease who are willing to engage in and support ongoing research activity.

We now send newsletters and surveys to participants of these partnerships, so that they can see how their input has helped shape our research activity.

As a result of this success, further Priority Setting Partnerships are now under way for other skin diseases, including acne, hair loss and hidradenitis suppurativa (a painful condition that causes abscesses and scarring in the groin and armpits). All of these diseases have a high burden for patients, but have traditionally been under-researched. It is our hope that by demonstrating patient need in these areas, this work will stimulate future programmes of research. Co-ordinated through the UK Dermatology Clinical Trials Network (www.ukdctn.org) these new Priority Setting Partnerships build on the knowledge and expertise gained from the earlier ones conducted as part of this Programme Grant.

Publications

Eleftheriadou VE *et al.* Future research into the treatment of vitiligo: where should our priorities lie? Results of the vitiligo Priority Setting Partnership. *Br J Dermatol* 2011;164(3):530-6.

Ridd M *et al.* Dermatology research in primary care: why, what and how? *Br J Gen Pract* 2011; 61 (583): 89-90.

Batchelor JM *et al.* The Eczema Priority Setting Partnership: a collaboration between patients, carers, clinicians and researchers to identify and prioritize important research questions for the treatment of eczema. *Br J Dermatol* 2013; 168(3): 577-582.

"The process gave a wide variety of people the chance to submit and rate questions. I feel this was an excellent approach to take as it allowed us the chance to submit those burning questions that we would like concrete answers to."

Participant in the Priority Setting Partnership

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Impact on vitiligo

Prior to this programme of work, vitiligo was an under-researched disease area, with very little high-quality research evidence on which to base clinical decisions. The prioritised topics resulting from our work covered a range of interventions including topical therapies, light therapy, psychological support, and new and emerging therapies.

These research suggestions were distributed to relevant funding bodies in the UK. The NIHR Health Technology Assessment funding stream was proactive in picking up these research priorities, and put out a commissioned call designed to address two of the suggested topic areas.

The commissioned trial will be a large-scale, national trial of 440 participants and will start recruiting in ten hospitals across the UK in 2014. The trial has been designed to see if light therapy (used at home) is better than steroid creams, and whether using both treatments at the same time is better than using either treatment individually.

Another important research priority on psychological interventions for the management of vitiligo has been picked up by a group of trainee dermatologists, who are currently working up a project proposal through the UK Dermatology Clinical Trials Network's Trainee Network.

The Priority Setting Partnership has also stimulated industry partners to look at this disease again, and new research programmes have been started looking at the role of afamelanotide (a hormone that is thought to stimulate pigmentation in the skin) for the treatment of vitiligo.

Impact on eczema

The eczema Priority Setting Partnership resulted in 14 priority topics for future research, and many of these topics have already been picked up by funders and researchers for future development.

As a result of this Priority Setting Partnership, the NIHR Efficacy and Mechanisms Evaluation programme launched a commissioned call for research into skin disease in 2013.

The NIHR Health Technology Assessment programme has also been proactive in funding eczema-related research, and has commissioned several projects of relevance to the priority topics. These include:

- A randomised controlled trial of antimicrobial treatments for eczema (CREAM Trial)
- A randomised controlled trial of silk clothing for the management of eczema (CLOTHES Trial)
- A randomised controlled trial of bath emollients for the treatment of eczema (BATHE Trial)
- Systematic review of educational interventions for eczema

In addition, the Cochrane Skin Group **(www.skin.cochrane.org)** has several systematic reviews underway of relevance to the priority topic areas.

New possibilities for the prevention of eczema

What is eczema?

Eczema is a common skin problem that particularly affects young children. It can be very distressing for both the child and their family.

Since there is no known cure for eczema, finding a way to prevent it from developing in the first place is important. Parents with experience of eczema are often anxious to know whether their children will develop eczema and what they can do to reduce the risk.

A number of interventions have been tested to see whether they can prevent childhood eczema from developing but, to date, none have proven to be effective enough to be worth using.

Researchers discovered that children with eczema often have faults in a gene called filaggrin which can lead to problems in developing an effective skin barrier. This has led researchers to consider whether interventions that help to protect a child's skin can help prevent eczema developing.

Could applying moisturisers every day from birth help to prevent eczema?

Why is it important?

For the first time, our work in this area has provided high-quality evidence to suggest that using moisturisers from birth could help to prevent the development of eczema in young children. Although encouraging, this was a small pilot study and so the results should be viewed with caution until a larger definitive trial has been completed. If these results are found to be true, this intervention represents a cheap and simple solution for the prevention of eczema that could be applied worldwide.

What did we do?

We conducted an overview of seven systematic reviews containing 39 trials about the prevention of eczema. This overview of reviews confirmed that none of the interventions tested so far were really very effective in preventing eczema. It also showed that a randomised controlled trial using moisturisers to protect the skin from birth was needed, as this had not been investigated before.

As a result, we carried out a pilot study called the Barrier Enhancement Eczema Prevention Trial (BEEP pilot trial) involving 124 new born babies and their mothers. Half of the mothers were advised to apply moisturisers to their baby's skin every day for six months, and half were asked to follow normal skin care advice. This was a multi-centre, randomised controlled trial that took place at four centres in the UK and one in the USA.

This pilot trial was very successful. It demonstrated that a large scale study was possible and that the methods being used were appropriate. The results suggest that applying moisturisers to a baby's skin from birth may well help to prevent eczema from developing.

As a result of this pilot work, we have now secured further funding from the National Institute for Health Research to conduct a much larger study involving 1,300 families. This larger trial is due to start in 2014. Further details about the trial can be found at www.nottingham.ac.uk/dermatology.

Publications

Foisy M *et al*. Overview of Reviews The prevention of eczema in infants and children: an overview of Cochrane and non-Cochrane reviews. *Evid Based Child Health*. 2011; 6(5):1322-1339.

Simpson E *et al*. How should an incident case of atopic dermatitis be defined? A systematic review of primary prevention studies *J Allergy Clin Immunol* 2012; 130:137-44.

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"I almost avoided having children, so strong was my worry that I couldn't let a child of mine live my life with eczema."

Patient story from National Eczema Society website

Global consensus in measuring treatment response for eczema

When evaluating the success or failure of a treatment, it is important to measure the effects of that treatment in a consistent way. Over the years different researchers have measured treatment success in many different ways for the same condition. This has made it impossible to combine the results of trials and to compare treatments in different studies.

In the field of eczema, over 500 clinical trials have been published, but we still do not know the answer to some of the most basic of questions about its treatment. In part, this is due to limitations in trial design, including a lack of consistency in the use of agreed outcome measures to evaluate the success or failure of treatments.

Through our NIHR Programme Grant, we were able to work towards an international consensus on a core set of outcome measures for eczema research.

Why is it important?

For the first time, researchers, patients and health care practitioners throughout the world are working together to improve the quality of research into the treatment and management of eczema. In so doing, they are improving the quality of all research, answering important clinical questions more effectively, and improving the lives of patients with eczema.

What did we do?

As part of this NIHR Programme Grant, we supported the development of an international initiative to establish a core outcome set for use in future eczema clinical trials. A "Core Outcome Set" is an agreed minimum set of outcomes or outcome measures. It is a recommendation of 'what' should be measured and 'how' it should be measured. Core outcomes do not preclude the use of other outcome measures in addition to the core set.

The Harmonizing Outcome Measures for Eczema (HOME) initiative was first established in 2008 by Professors Jochen Schmitt (Germany) and Hywel Williams (UK). Over the last five years, and with support through our NIHR Programme Grant, this work has progressed in developing international consensus over a core set of outcome measures for use in future eczema research. Further details of the HOME initiative can be found on our website www.homeforeczema.org.

"Not having a defined outcome measure for a particular condition is a bit like watching a football match in which the rules have not been defined. No-one then knows who has won and why."

Lester Firkins,
Chair of the James Lind Alliance

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Through a combination of systematic reviews, e-Delphi consensus studies, and face-to-face international consensus group meetings, the eczema research community have agreed the following:

- Consensus over a core outcome set for eczema research is essential.
- Four key domains should be measured in ALL future eczema trials:
  - eczema signs (clinical signs)
  - eczema symptoms
  - quality of life
  - long-term control of flares
- The Eczema Assessment Severity Index (EASI) should be used to measure eczema signs. This tool is now being recommended for use in all future eczema trials.

Work is ongoing to establish the best way of measuring the remaining three domains (symptoms, quality of life and long term control), and will be the subject of our next international consensus group meeting in 2015.

Core outcomes for other skin diseases

The HOME initiative is now being used as an exemplar of best practice for the development of core outcome sets for other skin diseases. In particular, the Vitiligo European Task Force is currently developing a core outcome set for vitiligo trials (partially supported through this NIHR Programme Grant), and similar work is being developed throughout the world in the fields of acne, psoriasis and vulval skin disease.

Publications

Schmitt J *et al.* on behalf of the HOME Development Group Harmonising Outcome Measures for Eczema (HOME). Report from the First International Consensus Meeting (HOME 1). *Br J Dermatol* 2010; 163: 1166-1168.

Schmitt J *et al* Towards global consensus on outcome measures for atopic eczema research: results of the HOME II Meeting *Allergy* 2012; 67: 1111-1117.

Eleftheriadou VE *et al.* Which outcomes should we measure in vitiligo? Results of a systematic review and a survey amongst patients and clinicians on outcomes in vitiligo trials. *Br J Dermatol* 2012;167(4):804-14.

Schmitt J *et al.* on behalf of the HOME initiative Assessment of clinical signs of atopic dermatitis. A systematic review and recommendation. *J Allergy Clin Immunol.* 2013 Sep 11. pii: S0091-6749(13)01068-3. doi: 10.1016/j.jaci.2013.07.008

Delegates at HOME III meeting in San Diego, USA

Tim's story
Reflections on the HOME III meeting

"I've been suffering from eczema for 27 years, and it affects everything I do and ultimately who I am. I cannot drink alcohol or eat spicy foods, and when I go out in cold weather, my face often becomes quite red so people stare at me. The worst thing for me is probably the itching, especially at night. Often I cannot sleep and have to get up because it's so unbearable.

Because of all this, I was really pleased to be invited to attend the third HOME meeting in San Diego as a patient representative. My role there was to share my views and experience on how it feels to live with eczema and what aspects of it are most difficult to bear. This may vary from patient to patient – for women, how the skin looks often matters most.

The meeting was held over a weekend, and we flew out of Heathrow on a cold and snowy April afternoon, arriving at our San Diego hotel 13 hours later. Although I had done a fair amount of background reading, I was feeling a little nervous about meeting so many eczema experts from all around the world, and worried that I wouldn't be able to follow what they said. But the other delegates soon put me at ease: the researchers asked us patients plenty of questions and very much treated us as equals.

As the meeting progressed, I felt I had enough understanding to be able to make some input. There were several votes on different ways of measuring how well a given treatment is working, with patients and doctors each given one vote. The first day ended with a buffet dinner at the home of one of the American doctors who had kindly invited us round, yes, all 50 something of us!

For me, one particularly interesting aspect of the meeting was to hear delegates from other countries, and what kinds of treatment are favoured there. What I heard was ultimately reassuring – it showed me that the treatment I'm receiving is good. Even in the US, they don't have any eczema treatments which are substantially better than ours.

All in all I found it an amazingly positive experience, and it was hugely encouraging to meet so many specialists with a strong commitment to eczema research and treatment. On a selfish note, I did get some valuable information on eczema treatment from some of the world's leading eczema specialists, now that was a real bonus! I'm now looking forward to doing more work on the project and hope to be able to make some useful contributions along the way."

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Updating the evidence on eczema treatments

Understanding what is already known

Although there is a lot of information available on the treatment of eczema nowadays, it is not always easy to sort out the good evidence from that which is less reliable or biased.

A good place to start is to look at clinical trials that have tested the various eczema treatments to date. Clinical trials are fair tests that typically compare one treatment against another. However, for eczema alone over 500 randomised controlled trials have been published and it is hard to work out what the evidence means for patient care.

This is where the work of our Programme Grant can help, particularly an updated review of clinical trials carried out to date, and the creation of a freely available database known as GREAT (Global Resource of Eczema Trial – **www.greatdatabase.org.uk**).

Why is this important?

Our updated review will be used as the basis for updating clinical guidelines throughout the world.

The review has helped to identify clinical areas for which the answers are already known (and which thus require implementation into practice), and areas that require further research. It has also helped to highlight some of the key methodological limitations of existing research, thereby informing the development of better quality trials in the future.

The GREAT Database provides a simple and easily accessible resource that allows everyone to find relevant evidence quickly and effortlessly. By preventing the international duplication of effort throughout the world, we hope to save money, improve patient care and speed up the generation and implementation of new knowledge.

What did we do?

Back in the year 2000, we identified and summarised all of the clinical trials that had ever been done on the treatment of eczema. Thousands of doctors and patients all over the world found that summary useful as it was written in plain English and was easy to navigate. But the review was out of date and we knew that many more trials had been published since then.

As part of this Programme Grant we have done three important things:

1. Brought the original review up to date – adding over 250 more trials and 50 systematic reviews. The updated review will be freely available as part of the National Institute for Health Research's Journal series.
2. Created the on-line GREAT database including all of the randomised controlled trials and systematic reviews published to date. The database is fully searchable and contains summary information about each of the trials.
3. Produced summary information for patients and clinicians outlining the key new clinical messages.

What did we find?

It is difficult to give a single summary statement for all our findings as so many things have been tried for eczema including creams, oral medicines, ultraviolet light, educational approaches, complementary and alternative treatments, and diets. It is the sort of report that is best browsed when you want to look up something like "antihistamines" or "traditional Chinese herbs". Overall, we found good evidence of benefit to support the use of topical corticosteroids and calcineurin inhibitors – especially when used as weekend therapy to prevent eczema flares; and reasonable evidence to recommend the use of educational interventions. We also felt that there was enough evidence to suggest that some treatments should NOT be recommended. These include the use of creams containing antibiotics when the eczema is not infected, taking evening primrose oil and borage oil, taking probiotics, and installing an ion-exchange water softener in the home if you live in a hard water area.

For many treatments the evidence was not clear enough to reach firm conclusions, but already some big studies are under way to address several of these gaps, such as the role of bath oils, the use of antibiotics for the treatment of infected eczema, and the role of specialized silk clothing for the management of eczema. Further details about these trials can be found on the National Institute for Health Research portfolio database: **www.crncc.nihr.ac.uk/about_us/processes/portfolio**

Who is the GREAT Database designed for?

The GREAT Database is free to access and simple to use. It currently contains over 600 randomised controlled trials and over 50 systematic reviews, but new trials and reviews are added regularly (**www.greatdatabase.org.uk**).

Anyone with an interest in the evidence base for eczema treatments will find this database useful:

- **Guideline writers:** looking for evidence to support their clinical guidelines
- **Systematic reviewers:** saving many hours of searching and filtering search results to identify relevant randomised controlled trials
- **Clinicians:** looking for the evidence to support individual clinical decisions
- **Patients:** looking for the evidence to support their own treatment choices
- **Information specialists:** looking to provide high quality patient information and guidance documents
- **Researchers:** wanting to address methodological questions about the design and conduct of eczema trials

Publications

Nankervis H *et al.* Mapping randomized controlled trials of treatments for eczema – The GREAT database, *BMC Dermatology* 2011 11:10

Nankervis H Prospective Registration and Outcome-Reporting Bias in Randomized Controlled Trials of Eczema Treatments: A Systematic Review. J Invest Dermatol 2012; 132(12): 2727–2734.

Futamura M *et al.* Mapping Systematic Reviews on Atopic Eczema – An Essential Resource for Dermatology Professionals and Researchers. *PLos One* 2013; 8(3): e58484.

Torley D *et al.* What's new in atopic eczema? An analysis of systematic reviews published in 2010-11. Clin Exper Dermatol 2013; 38(5), 449-56

"A user-friendly website for accessing a large amount of focused, filtered information for clinicians and researchers in eczema."

Clinical Researcher

New advances in vitiligo research

What is vitiligo?

Vitiligo is a skin disease that results in white patches on the skin. These patches are not painful, but they can easily burn in sunlight and the patches can affect how people – particularly those with dark skin - feel about themselves and how they interact with others.

At the moment, the only medicine specifically licensed for vitiligo in the UK is cosmetic camouflage (cover-up make-up), although other treatments can be used such as steroid creams, light treatment and psychological support.

During this Programme Grant we have established the groundwork for running a large, national trial of vitiligo treatments.

Why is this important?

We are delighted to say that as a result of our work, major funding has now been secured from the National Institute for Health Research for a full-scale trial involving 440 patients with vitiligo across the UK. This will be by far the largest vitiligo trial ever conducted. It will compare the use of steroid ointments applied to the skin with hand-held NB-UVB light therapy, and the combination of both steroid ointment and NB-UVB light therapy together.

This research is important as the treatments being tested were identified as key areas for future research in our Priority Setting Partnership (see pages 7-8), and the use of light therapy at home to treat small patches of vitiligo when they first appear, has not been tested before.

Until now, light therapy for vitiligo patients has generally been limited to people with severe and widespread disease. As light therapy is usually provided two or three times a week in a hospital setting using full-body units, it is likely to add to the burden on the patient and is not suitable for children. Should home light therapy prove to be an effective treatment for vitiligo patients, this could be an extremely useful addition to the care options available.

Recruitment into the full trial is anticipated to start in 2014 (see **www.nottingham.ac.uk/dermatology** for further details).

What did we do?

We laid the foundations for this large, national trial in the following ways:

- Reviewing the existing evidence for vitiligo treatments and updating the Cochrane systematic review of interventions for vitiligo
- Talking to patients and health professionals to decide what questions needed to be answered most urgently
- Establishing how 'treatment success' has been captured in previous trials, and working with patients to see if the right things are being measured
- Leading an international collaborative effort to achieve consensus over core outcome measures that should be captured in all future vitiligo trials
- Conducting a 'pilot' randomised controlled trial involving 29 patients, to see if a large national trial is feasible and practical
- Developing a standardized training package for people who would like to use narrow band ultraviolet B light therapy (NB-UVB) at home. The package is designed to be used with support from local hospital phototherapy teams. This training video is freely available at **www.nottingham.ac.uk/dermatology**

Publications

Whitton ME Interventions for vitiligo. *Cochrane Database of Systematic Reviews* 2010; Issue 1. Art. No.: CD003263.

Eleftheriadou VE *et al.* Future research into the treatment of vitiligo: where should our priorities lie? Results of the vitiligo Priority Setting Partnership. *Br J Dermatol* 2011;164(3):530-6.

Eleftheriadou VE *et al.* Which outcomes should we measure in vitiligo? Results of a systematic review and a survey amongst patients and clinicians on outcomes in vitiligo trials. *Br J Dermatol* 2012; 167(4):804-14.

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"As a health professional who has extensive vitiligo, it was a privilege to be part of this work, which is leading to serious research into both treatment and support for people with this condition."

Participant of the vitiligo Priority Setting Partnership

Informing guidelines for skin cancer treatment

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What is Squamous Cell Carcinoma?

Squamous cell carcinoma is a type of non-melanoma skin cancer that is common in elderly people. In the UK it is the second most common type of skin cancer, and the majority of lesions develop on sun-exposed areas of skin such as the head and neck. Surgery is the main treatment for most squamous cell skin cancers, although other treatments are sometime used.

Despite being such a common cancer worldwide, squamous cell skin cancer has been relatively neglected in terms of high-quality studies to establish the most appropriate treatments. Thanks to this Programme Grant award, we have been able to conduct the first ever systematic reviews of treatment effectiveness for this cancer.

Why is this important?

Results from these systematic reviews are now being used to inform evidence-based management guidelines for squamous cell skin cancer.

The identification of two clinically relevant research questions and their development into a trial proposal is an important step in preparing what will be the first randomised controlled trial to address the management of the common types of squamous cell skin cancers that are seen in clinics every day.

> “The Scottish Intercollegiate Guidelines Network for SCC (SIGN SCC) are in the process of publishing new guidelines for management of this important cancer and we have been most fortunate in having this excellent systematic review to assist our deliberations.”

Charlotte Proby, Professor of Dermatology, University of Dundee and Chair of the SIGN SCC review panel

What did we do?

The Programme Grant has allowed us to review the evidence base for squamous cell skin cancer treatments thoroughly and to prioritise and develop research ideas for a future randomised controlled trial. This work consisted of:

- Conducting two systematic reviews of the current evidence base for the effectiveness of squamous cell skin cancer treatments
- Talking to health professionals who manage squamous cell skin cancer to establish which clinically important questions need to be addressed most urgently
- Prioritising two important research questions for further development into a proposal for a clinical trial
- Evaluating squamous cell skin cancers submitted for laboratory analysis over a one-year period to establish the numbers and types of skin cancers seen and the clinical outcomes in patients up to five years after treatment
- Conducting questionnaire and focus group feasibility work with people who have experienced squamous cell skin cancer and its treatment in order to assess the acceptability of our proposed trial and to guide development of the trial by identifying potential barriers to recruitment
- Collaborating with the National Cancer Research Institute’s non-melanoma subgroup to develop a protocol for a randomised controlled trial

Publications

Lansbury L *et al.* Interventions for non-metastatic squamous cell carcinoma of the skin. *Cochrane Database of Systematic Reviews* 2010:Art. No. CD007869.

Lansbury L *et al.* Interventions for non-metastatic squamous cell carcinoma of the skin: a systematic review and pooled analysis of observational studies. *BMJ* 2013; 347:f6153

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Providing evidence for rare skin conditions – pyoderma gangrenosum

Why focus on rare skin diseases?

Dermatology is a unique specialty in that it covers over 1000 different skin diseases - many of which are rare and poorly understood.

Pyoderma gangrenosum is a rare condition that causes painful, rapidly spreading ulcers. The condition can be difficult to treat and often recurs. For those affected, it can be extremely debilitating and result in high costs to the NHS.
Whilst the disease is rare, patients with conditions such as pyoderma gangrenosum deserve the same standard of evidence-based health care as those suffering from more common skin conditions. Treatment often involves powerful drugs with serious side-effects, and these are being used without a thorough understanding of their potential risks and benefits for pyoderma gangrenosum patients.

This NIHR Programme Grant provided a unique opportunity to conduct a national randomised trial, the STOP GAP trial, evaluating the two most commonly used medicines for the treatment of pyoderma gangrenosum – ciclosporin and prednisolone.

Why is this important?

For the first time, the STOP GAP trial allows clinicians to make treatment choices about the management of pyoderma gangrenosum based on reliable evidence. Our results suggest that both of the most commonly used treatments are likely to result in similar clinical response, although in both groups only about half of the participants' ulcers had healed after six months of treatment. However, the two drugs have different side effect profiles, and as a result of this trial, clinicians and patients can now make shared treatment decisions based on a combination of clinical suitability and individual patient preference.

At the same time, the trial provided important opportunities for the dermatology clinical community to learn and share expertise. The top recruiting centres have now been identified as specialist centres for the clinical care of pyoderma gangrenosum patients under new NHS commissioning arrangements.

What did we do?

This trial was conducted with the support of members of the UK Dermatology Clinical Trials Network and through support from the Comprehensive Local Research Networks.

Recruitment took place in hospitals throughout the UK. In total, 121 patients were randomised into the main trial, and a further 67 patients were entered into a parallel observational study of topical treatments.

Publications

Craig FF *et al.* on behalf of the UK Dermatology Clinical Trials Network's STOP GAP Trial Team. A multicentre trial of prednisolone versus ciclosporin for pyoderma gangrenosum: protocol for a randomised controlled trial. *Trials* 2012; 13:51.

Ormerod AD *et al.* on behalf of the UK Dermatology Clinical Trials Network's STOP GAP Trial Team. Results of a multi-centre, randomised controlled trial of prednisolone versus ciclosporin for pyoderma gangrenosum: protocol for a randomised controlled trial (in press).

Ormerod AD *et al.* on behalf of the UK Dermatology Clinical Trials Network's STOP GAP Trial Team. Clinical outcomes and response to treatment of patients receiving topical treatments for pyoderma gangrenosum: a prospective cohort observational study (in press).

Prevention and Treatment of Skin Disease:
Setting Priorities and Reducing Uncertainties

"It is very difficult to recruit sufficient patients to studies of rare and serious diseases such as pyoderma gangrenosum. STOP GAP has achieved impressive recruitment to produce evidence, which will guide clinicians in offering patients treatment that is as safe and as effective as possible."

Dr Nick Levell, STOP GAP recruiting clinician

Making the evidence reach the patients who need it

This Programme Grant has summarised, collated and produced research evidence on the treatment and prevention of skin disease. However, unless this information is used, it will not help patients, and it will not help doctors and nurses to treat their patients.

Throughout the period of this grant, we have worked hard to engage with research users to ensure that new information is disseminated as widely as possible, using formats appropriate to different audiences.

Working with guideline developers

We have close links with guideline developers such as the National Institute for Health and Care Excellence (NICE), the Scottish Intercollegiate Guidelines Network (SIGN), NICE Clinical Knowledge Summaries (for general practitioners), the British Association of Dermatologists guideline groups, and international guideline writers. Many of the systematic reviews that we have produced have already been used to inform new clinical guidelines both in the UK and abroad.

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Working with providers of health information

As a result of this Programme Grant, we developed formal links with NHS Choices and NHS Direct to ensure that patient information provided on these sites is based on the most up-to-date research evidence that we have been able to provide. Members of the team also contribute to Map of Medicine care pathways, and Hywel Williams is a clinical advisor for NHS Evidence.

Providing detailed information on trial interventions

Research has shown that all too often published research fails to describe the tested interventions in sufficient detail. This means that findings cannot be replicated, and treatments fail to be incorporated into normal practice. This can be particularly problematic for interventions involving education, or complex treatment packages.

As a result, we have produced training DVDs and manuals for the interventions used in our pilot trials. These materials will now be used in the larger definitive trials, but are also freely available for use in clinical practice. Further details are available at **www.nottingham.ac.uk/dermatology**.

Providing knowledge summaries

In addition to detailed reports, this work has also produced evidence summaries in the form of evidence updates on eczema and skin cancer, maps of systematic review, and "CLAHRC BITEs" – accessible overviews of essential "need to know" information about a piece of research for NHS staff.

Working with patient support groups and charities

One of the very best ways of making sure that research evidence is taken up is to provide it in generally accessible form, and then to encourage patients themselves to become research champions.

Members of our dermatology patient panel now contribute in all aspects of our work and have become staunch advocates in sharing best practice.

We have strong links with the National Eczema Society, the Nottingham Support Group for Carers of Children with Eczema and the Vitiligo Society - all of whom have supported our research by highlighting it on their websites, publishing articles in members' newsletters, helping with the distribution of surveys, and allowing the use of patient forums to conduct focus group discussions.

Investing in people

Whilst this NIHR Programme Grant has delivered significant research outputs that will continue to have an impact on clinical care within the NHS, equally importantly it has also been a catalyst for investment in the next generation of health researchers and patient advocates.

Three students have been trained in research methods, leading to PhD qualifications, and an enthusiastic patient panel has been established to ensure that public engagement is at the very heart of our research activity.

In addition, through support provided to the UK Dermatology Clinical Trials Network, eight Dermatology Specialist Registrars, three SAS clinicians, three dermatology nurses and a GP have been awarded fellowship opportunities to attend training events, visit the Centre of Evidence Based Dermatology, and work alongside senior members of the UK Dermatology Clinical Trials Network in contributing to collaborative projects. Furthermore, a new UK Dermatology Clinical Trials Network Trainee Group has been established, through which new trial projects are being developed.

New Year's Honours

Of course we cannot let this opportunity go by without once more congratulating Lester Firkins (Independent Chair of the Executive Group), Maxine Whitton (Patient lead for the vitiligo work package) and Roger Dainty (member of our patient panel) for their recognition in the New Year's Honours during the period of this award. Lester was awarded an OBE in recognition of his services to medical research, Maxine was awarded an MBE for services to the advancement of knowledge and research into vitiligo and Roger was awarded an MBE for his contribution to scientific research and training.

We are so very proud of them all.

"Thank you very much for providing me with this opportunity to learn about evidence-based medicine with you and your UK DCTN team. This is certainly one of the most important skills I have gained in dermatology training and I am very grateful to you."

Dr Suyin Ong,
UK DCTN SpR Fellow (2010-2012)

"I have recommended the UKDCTN SpR fellowship to pretty much every trainee I know and shall continue to do so in the future, as I have gained a great deal and would like to thank you once again for your time and tuition."

Dr Abby Macbeth,
UK DCTN SpR Fellow (2009-2011)

Establishing a Dermatology Patient Panel

Our Patient Panel was established in 2009 as part of this Programme Grant with the aim of providing support and training to patients and carers involved in our research activities.

Five years on, the panel is well established and has over 20 active members, all of whom are affected by a variety of skin disorders including eczema, psoriasis, skin cancer, vitiligo and rare skin conditions. To date, members have become involved in a wide range of activities including:

- Joining Steering Groups for Priority Setting Partnerships
- Becoming consumer reviewers for the Cochrane Skin Group
- Helping with the design of patient related materials, such as surveys and information leaflets
- Giving feedback on the design of clinical trials
- Being co-applicants on grant applications and becoming members of study teams
- Attending our departmental team working day
- Contributing to national patient involvement initiatives such as the NIHR Dermatology Specialty Group

Patient Panel Meeting May 2012

Viktoria's story
Making an impact in vitiligo research

Why did you want to work on this vitiligo project?
Vitiligo affects millions of people but no cure has yet been found. It is a somewhat neglected disease, often perceived as simply a cosmetic disorder – despite the substantial psychological and social burden associated with it. I have friends who have vitiligo, and know how much it can affect their psychological wellbeing.

Which aspect of this work are you most proud of, and why?
The most rewarding aspect of being involved in research is being able to make a difference long term. It makes me feel great when vitiligo patients tell me: "I know it might take a decade to find the cure, but your research gives me hope to carry on".

What do you see as the most important next steps for vitiligo research?
More research is needed to help us understand what causes vitiligo in the first place. This is crucial in helping us find a cure. In parallel, we also need larger and better quality clinical trials of vitiligo treatments.

Has your work had an international impact?
Yes. I am currently leading an international project with participants from 25 countries to establish outcome measures for future vitiligo trials. So far, there has been no unified scale to measure treatment response in such trials, which makes it impossible to interpret trial results.

Also, our pilot trial on hand-held home phototherapy has generated numerous enquiries from the UK and abroad. The next step is a large-scale clinical trial.

What are you going to be doing next?
Have a baby! And then of course return to clinical practice to carry on my specialty training in combination with research into vitiligo. My career aim is to become an academic dermatologist.

Do you have any advice for other junior researchers thinking of doing a PhD?
The transition from a clinical job to research was one of the most challenging experiences in my life. I had not realised that I would spend so much time writing a protocol, changing and amending it several times before actually getting started.

On the other hand, completing your research and presenting it to your peers and patients is the most rewarding experience ever, and I would certainly do it again!

My opinion is that everyone should experience research. It is an eye opener – it completely changes your mindset and the way you see everything around you. Go for it.

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Amina's story
Getting involved in eczema research

Why did you volunteer to join the dermatology patient panel?
After receiving so much support from dermatologists and nurses over the past 10 years with my children's eczema, I felt passionate about giving something back! Getting involved with the patient panel has really helped me to expand my understanding of research and explore different projects that I can take on alongside my family and work commitments. I was surprised to learn that eczema treatment is often a game of "hit and miss" with a lack of consistent evidence-based research, and that made me even more eager to help.

What projects are you involved in at the moment?
I am involved in two research projects – CLOTHES, which is exploring the effectiveness of silk clothing, and COMET, which is looking at the most effective emollients GPs can prescribe for their primary care patients.

What would your advice be to other patients and carers thinking of getting involved in research?
I know getting involved can be quite nerve-wracking and it takes time to get to grips with all the terminology and understand the process that researchers have to go through, but the patient panel networks do an amazing job supporting new people. You can get a huge sense of satisfaction from joining patient panels, both in terms of extending your own understanding and bringing experts "down to earth" on the realities of dealing with certain conditions and helping them re-think their approach.

Do you think your input has made a difference?
Absolutely! I think patient involvement can really "humanise" research so that patient consideration can be built into the objective, process and outcome of the studies. And at the end, I believe this is the most important part of any research.

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Amina and her son Tahmid giving an interview for BBC local news

Meet the team

The large programme of work has been delivered by a broad range of people from different backgrounds, countries and institutions. We have involved patients, their carers, dermatologists, nurses, general practitioners, pharmacists, psychologists, health service commissioners and managers, as well as methodologists, guideline writers, patient advocates and support groups.

Everyone has contributed in their own way and it is impossible to describe all individual contributions in this summary report. A full list of the people involved in the project is below.

Nevertheless, we would like to take this opportunity to thank some of the key individuals who have been directly involved in the day-to-day delivery of this programme; without them, we would not have been able to carry out this ambitious programme of work.

Lester Firkins – Independent Chair of Executive Group

When I was invited (or did I ask!) to be Chair of the Executive Group, I was hugely excited because I had seen the work that Hywel, Kim and the team had achieved in the past and wanted to be a small part of their future. To be able to read of the REAL discoveries they have made – and indeed how they have now achieved funding to take the opportunities and priorities forward - is wonderful.

It has been one of the easiest roles I have undertaken in the last six years because of their sheer professionalism and deep caring for the individual.

To my mind, they are exemplars in the way they use funders' support to get meaningful and always transparent benefits. The mere publication of this excellent document shows their standards and desire to disseminate their news as widely as possible.

Hywel Williams – Chief Investigator

This Programme Grant has been such an enjoyable, mad and extremely productive experience for me. I am especially pleased that we have delivered on what we set out to deliver, plus about 200% more, thanks to our wonderful team and collaborators. What pleases me most is how relevant all of our research is to patient care and how useful it will be internationally as well as in the UK given our philosophy of making our materials freely available for patient benefit. As chief investigator, I carry a lot of responsibility if things go wrong, but thankfully all has gone very well indeed, and all credit must go to my fantastic colleagues who made this work possible.

Kim Thomas – Programme Manager

As Programme Manager for this work I have been involved in all five work packages, and have seen first-hand the dedication and enthusiasm of everyone involved in this programme of work.

It has been my job to provide a methodological steer across the work packages, to ensure project milestones were delivered to time and target, to maintain budgetary control, and to provide strategic input during the evolution of the award – ensuring that additions and amendments to the planned work were deliverable and represented good value to the NHS and to patients.

Bryony Elliott & Barbara Maston – Programme Administrators

Being involved in the Programme Grant has, for both of us, been our first experience of dermatology research. Our prime task has been to support the Programme Manager but we have also been very fortunate to work closely with all members of the team and become involved in some of the projects and initiatives supported by the Programme Grant. It has been a great opportunity to see dermatology research in action and an experience that we have thoroughly enjoyed.

Joanne Chalmers – Research fellow for the eczema prevention work package

Being involved in the eczema prevention work package of this Programme Grant has been exciting and I have been privileged to be part of a great team both here in the UK, and in the USA and Canada. I am proud to have contributed to the body of knowledge that one day might provide a safe and effective way of preventing children developing eczema. Although this programme is coming to an end, we are just part way through the journey towards eczema prevention, and exciting times lie ahead as we undertake a large trial of emollients that has been funded as a result of the work done here.

Helen Nankervis – Research fellow for the eczema treatments work package

My time working on the eczema treatment work package has given me valuable skills and experience and I am proud to have been part of the international research team. I feel proud to have been involved in research that has such capacity to benefit people with eczema and their families. I have grown as a researcher and I am excited at the prospect of taking on new research opportunities as the programme draws to a close.

Viktoria Eleftheriadou – Research fellow for the vitiligo work package

In working on the vitiligo work package and completing my PhD, I have grown both as a person and as a clinician. I have come to realise that research is medicine and medicine is research. Everything you do in your clinical practice today was conceived by someone and took decades to become "usual clinical practice". Research helped me to become more confident, self-motivated and self-critical. It also made me ask more questions and encouraged me to be more challenging in my everyday life.

Louise Lansbury – Research fellow for the squamous cell skin cancer work package

For a disease which has been so under-researched, it is gratifying to see the impact our work is starting to have on redressing this situation, which I trust will be of benefit to patients in the future. On a personal level, I have been mentally stimulated and intellectually challenged by the work and my associated PhD studies. It has been hard work, but the chance to develop transferable research skills and work with such an interesting group of fellow-researchers, clinicians and patients has made every minute worthwhile.

Anthony Ormerod – Clinical lead for the STOP GAP randomised controlled trial

I have been happy to be the lead clinician for the STOP GAP trial from its inception. Only through development of the UK Dermatology Clinical Trials Network did non-commercial studies of rare conditions like pyoderma gangrenosum become a possibility. STOP GAP activated enthusiastic research involvement right across the country. A 5-year study of a rare disorder across so many centres is challenging in the extreme, and this was the first of its kind in the world.

Eleanor Mitchell – Trial Manager for STOP GAP

I have thoroughly enjoyed the time I spent working as the STOP GAP Trial Manager, and knowing that the trial could help patients with such a painful, debilitating disease as pyoderma gangrenosum has made the job very rewarding. I have built up fantastic relationships with investigators and nurses in the many hospitals that were involved in the trial, which I shall miss. Recruitment of patients for STOP GAP was very difficult due to the rarity of the disease, and so on a personal note I have gained an awful lot of experience in recruitment for clinical trials which I hope to use again in the future.

Maxine Whitton – Patient researcher

I feel very privileged, as a patient, to have been given the opportunity to participate in the research programme as patient lead for the vitiligo work stream. The Priority Setting Partnership was an exciting project which reinforced my conviction that patients can play an important role in deciding research priorities. I believe the programme is a model of good practice, which will have a significant impact on future research in skin disease: the impact on vitiligo research is already evident. It has been a pleasure to work with such a committed team.

Meet the team (contd.)

Programme Grant Executive Group
Professor Hywel Williams
Professor Kim Thomas
Nick Evans
Lester Firkins
Jane Ravenscroft
Andrew Nunn

Programme Grant Steering Group
Fiona Bath-Hextall
Joanne Chalmers
Sally Crowe
Finola Delamere
Viktoria Eleftheriadou
Nicholas Evans
Louise Lansbury
Carron Layfield
Jo Leonardi-Bee
James Mason
Eleanor Mitchell
Helen Nankervis
John Norrie
Andrew Nunn
Anthony Ormerod
Rameshbhai Patel
William Perkins
Kim Thomas
Maxine Whitton
Hywel Williams

Collaborating Institutions
Nottingham University Hospitals NHS Trust
University of Nottingham
University of Aberdeen
University of Durham
Nottingham County Teaching PCT
West Herts Hospitals NHS Trust
Paul Sabatier University and Toulouse University Hospitals, France
Medical Research Council
Clinical Trials Unit
Nottingham Clinical Trials Unit
Birmingham Clinical Trials Unit
James Lind Alliance
Oregon Health and Science University
Imperial College London
University of East Anglia
University of Sheffield
University of Bristol
University of Dundee
Cochrane Skin Group
UK Dermatology Clinical Trials Network
NHS Direct
NHS Choices

Patient Support Groups
National Eczema Society
Nottingham Support Group for Carers of Children with Eczema
The Karen Clifford Skin Cancer Charity
Vitiligo Society

Patient panel members
Amina Ahmed
Tim Burton
Jo Clayton
Anne Collier
Roger Dainty
Adrian Day
Joanne Foster
Marjorie Howard
Carolyn Hughes
Deborah Mason
Kirsteen Murray
Colette O'Sullivan
Jo Parris
Anjna Rani
Jenni Rishworth
Amanda Roberts
Lisa Sharples
Stephen Shippard
Jason Simons
Derek Stewart
Jack Tweed
Maxine Whitton
Jennifer Wildey

Eczema prevention work package
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Ruth Ballington
Gretchen Barron
Sarah Booker
Robert Boyle
Sara Brown
Linda Campbell
Joanne Chalmers
Lisa Charlesworth
Yiyi Chen
Zunqiu Chen
Mike Cork
Andrew Dainty
Simon Danby
Sue Davies-Jones
Kristina Ewing
Adam Ferguson
Matthew French
Jon Hanifin
Lori Kelly
Sandra Lawton
Sian Le-Beau
Matthew Leighton
Jo Llewellyn
Mark Loveland
Troy Lubianski
Irwin McLean
Alan Maplethorpe
Alan Montgomery
Ruth Murphy
Johanna Perdue
Jane Ravenscroft
Alison Raynor
Matt Ridd
Mandy Roper
Tracy Sach
Krisztina Scharrer
Lindsey Severson
Daniel Simpkins
Eric Simpson
Coral Smith
Kim Thomas
Jim Thornton
Susan Tofte
Vanessa Unsworth
Nicola Watson
Hywel Williams
Min Yang

BEEP pilot recruiting sites
Nottingham University Hospitals NHS Trust
The Research Institute at Wheatbridge, Chesterfield
Derby Hospitals NHS Foundation Trust
United Lincolnshire Hospitals NHS Trust
Oregon Health & Science University, Portland, Oregon, USA

Eczema treatment work package
Christian Apfelbacher
Akerke Baibergenora
Sebastien Barbarot
Robert Boyle
Joanne Chalmers
Tessa Clarke
Finola Delamere
Liz Doney
Gordon Dooley
Masutaka Furue
Masaki Futamura
Deanne Hewson
Joseph Jabbar
Sandra Lawton
Alan Mablethorpe
Margaret McPhee
Helen Nankervis
Tom Platts-Mills
Emma Pynn (Smith)
Lesley Rushton
Tracey Sach
Jordan Samuels
Jochen Schmitt
Eric Simpson
Sherie Smith
Phyllis Spuls
Kim Thomas
Hywel Williams

Prevention and Treatment of Skin Disease:
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Vitiligo work package
Anton Alexandroff
Jonathan Batchelor
Joanne Chalmers
Lisa Charlesworth
Sue Davies-Jones
Robert Dawe
Lelia Duley
Viktoria Eleftheriadou
Richard Farley
Joanne Llewellyn
Claire Lushey
Samir Mehta
Alan Montgomery
Johanna Perdue
Jane Ravenscroft
Andy Rogers
Tracey Sach
Miriam Santer
Catherine Shelley
Kim Thomas
Selina Tour
Graham Watson
Diane Whitham
Maxine Whitton
Hywel Williams
Adrian Yong
Susan Yule

HI-LIGHT pilot recruiting sites:
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Leicester Royal Infirmary
NHS Treatment Centre, Nottingham
Nottingham University Hospitals NHS Trust

Squamous cell carcinoma work package
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Joanna Browne
Timothy Goodacre
Louise Lansbury
Paul Leighton
Jo Leonardi-Bee
William Perkins
John Tweed

NCRI Non-melanoma Subgroup of the melanoma CSG:
Catherine Harwood
Charlotte Proby
Pat Lawton
John Lear
Jerry Marsden
Jenny Nobes
Keith Wheatley
Neil Steven
Steve Nicholson
Marc Mancrieff
Carie Corner

Pyoderma gangrenosum work package
STOP GAP Trial Steering Committee – independent members (TSC)
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Calum Lyon
Sarah Meredith
Paul Mussell
Frank Powell (Chair)
Daniel Wallach

STOP GAP Trial Management Group (TMG)
Julie Barnes
Fiona Craig
Kath Foster
Nicola Greenlaw
Ellie Harrison
Alan Maplethorpe
James Mason
Eleanor Mitchell
John Norrie
Tony Ormerod
Aisha Shafayat
Daniel Simpkins
Kim Thomas
Diane Whitham
Hywel Williams

STOP GAP Data Monitoring Committee (DMC)
Angela Crook
Alison McDonald
Julie Schofield (Chair)

STOP GAP Recruiting Centres
Aberdeen Royal Infirmary, NHS Grampian
Aneurin Bevan Health Board
Barts & The London NHS Trust
Basildon & Thurrock University Hospitals NHS Foundation Trust
Betsi Cadwaladr University Health Board
Cardiff & Vale University Health Board
Bradford Teaching Hospitals NHS Foundation Trust
Brighton & Sussex University Hospitals NHS Trust
Cambridge University Hospitals NHS Foundation Trust
Chesterfield Royal Hospital NHS Foundation Trust
City Hospitals Sunderland NHS Foundation Trust
Cork University Hospitals
Countess of Chester Hospital NHS Foundation Trust
County Durham & Darlington NHS Foundation Trust
Craigavon Area Hospital Southern Health & Social Care Trust
Derby Hospitals NHS Foundation Trust
East Kent Hospitals University NHS Foundation Trust
East Sussex Hospitals NHS Trust
Frimley Park Hospital NHS Foundation Trust
Great Western Hospitals NHS Foundation Trust
Guys' & St Thomas' NHS Foundation Trust
Harrogate & District NHS Foundation Trust
Hull & East Yorkshire Hospitals NHS Trust
Hywel Dda Health Board
James Paget University Hospitals NHS Foundation Trust
Newcastle Upon Tyne Hospitals NHS Foundation Trust
NHS Lanarkshire Monklands Hospital
Norfolk & Norwich University Hospitals NHS Foundation Trust
North Cumbria University Hospitals NHS Trust
Northern Devon Healthcare NHS Trust
Nottingham University Hospitals NHS Trust
Oxford University Hospitals NHS Trust
Raigmore Hospital, NHS Highland
Royal Berkshire NHS Foundation Trust
Royal Devon & Exeter NHS Foundation Trust
South London Healthcare NHS Trust
Taunton & Somerset NHS Foundation Trust
Sandwell & West Birmingham Hospitals NHS Trust
Sherwood Forest Hospitals NHS Foundation Trust
South Devon Healthcare NHS Foundation Trust
The Royal Liverpool & Broadgreen University Hospitals NHS Trust
University Hospitals Birmingham NHS Foundation Trust
University Hospitals Bristol NHS Foundation Trust
University Hospitals of Leicester NHS Trust
Weston Area Health NHS Trust
Whipps Cross University Hospital NHS Trust
Yeovil District Hospital NHS Foundation Trust
York Teaching Hospital NHS Foundation Trust

Peer-reviewed publications

Eczema Prevention

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On-line Resources:

Global Resource of Eczema Trials (GREAT Database):
www.greatdatabase.org.uk

Harmonizing Outcome Measures for Eczema:
www.homeforeczema.org

STOP GAP Trial on Facebook
www.facebook.com/STOPGAPTrial

Royal College of Paediatrics and Child Health
Allergy Care Pathways for children with eczema
www.rcpch.ac.uk/allergy

NHS Choice topic on vitiligo: **www.nhs.uk/conditions/vitiligo/pages/introduction.aspx**

Atopic eczema care pathway for Map of Medicine (available through NHS Choices): **www.nhs.uk/Conditions/Eczema-(atopic)/Pages/MapofMedicinepage.aspx**

Eczema module for Clinical Knowledge Summaries (CKS):
www.cks.nice.org.uk/eczema_atopic

Vitiligo module for Clinical Knowledge Summary (CKS):
www.cks.nice.org.uk/vitiligo

Scottish Intercollegiate Guidelines Network:
Management of eczema in Primary Care
www.sign.ac.uk/guidelines/fulltext/125/index.html

CEBD Patient Panel Members contributed to video for NIHR Dermatology Specialty Group speaking about their experiences of being involved in clinical trials and clinical research. **www.crncc.nihr.ac.uk/about_us/ccrn/specialty/dermatology/**

Written interview: Prospective Registration and Outcome-Reporting Bias in Randomized Controlled Trials of Eczema Treatments: A systematic Review. **dermatologistsblog.com/eczema/bias-in-randomized-controlled-trials-of-eczema-treatments**

Viktoria Eleftheriadou and Maxine Whitton, co-authors on "Guidelines for designing and reporting clinical trials in vitiligo" in collaboration with members of the European Task Force for vitiligo. **www.euroderm.org/images/stories/guidelines/Guideline-on-Vitiligo.pdf**

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