Editorial Two:

Avoidable research waste in dermatology: what are the solutions?

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In the last editorial, I provided examples of research waste in dermatology and suggested that it was due to a system failure rather than just a few "bad apples". Here, I focus on possible solutions, mainly in relation to clinical trials, building on examples from work at the Centre of Evidence-Based Dermatology (CEBD) and other research groups.

Prioritisation and outcomes: Taking stock of existing research before rushing into undertaking new research is a good starting point. High quality systematic reviews or guidelines are a useful source for identifying research gaps, supplemented by updated searches of bibliographic databases and trial registers. Other evidence mapping exercises for specific diseases such as atopic eczema are available in the resources section of the CEBD website.

Checklists are available to help authors decide whether to replicate a systematic review[1]. Techniques such as trial sequential analysis can indicate whether updating an existing review, such as the Cochrane review that found no benefit of probiotics for the treatment of eczema[2], is likely to change review conclusions. A trial sequential analysis conducted as part of that review indicated that the necessary sample sizes of new studies needed to demonstrate even a small benefit with adequate power had already been exceeded, suggesting that further trials with similar probiotic strains are likely to be futile.

Simply identifying a possible clinical research question is not enough – the results need to be *useful* to a range of stakeholders including patients and healthcare providers. Methods on how to work effectively with a range of stakeholders to identify *and prioritise* research questions have developed over the last 17 years through organisations such as the James Lind Alliance (JLA). The JLA produce a guidebook and provide help in how to set up a priority setting partnership (PSP), gathering and verifying uncertainties, and how to prioritise the final "top ten" topics. Seven dermatological JLA PSPs have been facilitated at the CEBD including eczema, vitiligo, psoriasis, cellulitis, lichen sclerosis, hyperhidrosis and pemphigus/pemphigoid.

Funders can also play a more active role in prioritising research rather than working in solely in response mode. The National Institute of Health Research Health Technology Assessment Programme (NIHR HTA) for example actively identifies and prioritises clinical research questions that need answering. It then invites teams to apply in open competition to deliver such commissioning briefs. Such an approach of "pulling research that is needed" has been a feature of the HTA Programme since its inception 1993. Other funders could adopt similar commissioned approaches for funding priority topics.

Outcomes in clinical trials need to measure something important to patients, and need to be reliable, valid, sensitive to change and clinically interpretable. Core sets of valid/reliable outcomes that should be used in all clinical trials on a particular skin disease are needed so that studies can be compared and combined. The pioneering work of the HOME (Harmonising Outcome Measures for Eczema) group has been instrumental in this regard. Working to the HOME roadmap for developing core outcome sets[3], a complete a set of core outcomes and recommended instruments for eczema trials is now complete. Over 20 other groups are working on developing core outcome sets in diverse dermatological conditions such as skin cancer or incontinence-associated dermatitis, using up-to-date methods supported by the Cochrane Skin Core Outcomes Set Initiative (CS-COUSIN).

Appropriate methods: Working with methodologists such as those found in a clinical trials unit (statisticians, data managers and health economists) is key to minimise bias at the design stage. Understanding basic methods and knowing how to critically appraise a clinical trial that could benefit patients is a core competency for clinical dermatologists. Better training is needed. Numerous online resources such as critical appraisal checklists and catalogues of bias in healthcare research are available from groups such as the Centre for Evidence-Based Medicine in Oxford. The CEBD runs an annual course in better evaluation of evidence and statistics (BEES) that focusses exclusively on dermatology.

Overcoming publication biases: This is perhaps the easiest stage of research waste to address by adhering to the simple principle of "place your bet and show us your hand"[4]. In other words registering a clinical trial study plan and primary outcome in a publically available trials register before recruitment starts and then publishing the full study results as planned. It sounds simple, but despite 20 years of calls for such action to become standard practice, including campaigns such as AllTrials (all trials registered, all trials reported), publication bias (failing to publish study results) and selecting which outcomes to report is still widespread. Leading dermatology journals such as the *British Journal of Dermatology* now mandate trial registration and full publication using CONSORT reporting guidelines. The same principles of publishing a plan and then publishing the full results applies to all dermatological research studies in order to minimise potentially misleading data-driven results. It is good practice to register the plan for a systematic review in the international prospective register of systematic reviews (PROSPERO) and to make sure that all the key items listed in the PRISMA statement are included in the reports. The EQUATOR (Enhancing the QUAlity and Transparency Of health Research) network website is a useful resource of reporting guidelines for a range of study types.

The problem is that with so many journals available (over 300 in dermatology alone), poor quality or misleading research is easy to publish. Funders have a key role to play here by not giving out "grants" but, like the NIHR HTA Programme, making it a contracting requirement for the study to be registered and keeping back say 10% of the award until full publication in complete. Perhaps the greatest potential to reduce bias rests with journal readers to call out research waste when they see it eg through critically appraised topics[5], letters to the editor[6] or just rapid responses.

The 5th column and the joy of joined-up research: The Chalmers/Glasziou framework on avoidable research waste was pivotal, but it did not emphasise the importance of dissemination and implementation of research findings sufficiently. Implementation science and knowledge mobilisation is still an evolving area[7], but mature enough for the NIHR to add a fifth column of "findings are appropriately and effectively disseminated" to its adding value framework.

It is also worth re-evaluating the current model of clinical research by moving away from the fragmented approach of producing a systematic review that quickly becomes out of date and that may or may not be picked up in a subsequent guideline some years later, to a more dynamic living research ecosystem (Figure)[8]. Such a system of living systematic reviews coupled with rapid living guidelines offers a timely and joined up approach for patient benefit. Such a notion has already become a reality with initiatives such as the MAGIC Evidence Ecosystem Foundation during the COVID-19 pandemic.

Conclusion: These two editorials have raised awareness that research waste exists in dermatology and that there are simple ways of reducing the problem. The key point is that reducing research waste is everyone's business. "More research" is not needed – less research is needed, but better research that is prioritised, conducted well and reported fully. Patients deserve nothing less.

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Figure: Evidence ecosystem that facilitates a culture of continuous improvement for a given disease[8] (reproduced with kind permission from the publishers)