## Annual Cochrane Skin Group Meeting 2016

**Location**: British Association of Dermatologists, Willan House, 4 Fitzroy Square, London W1T 5HQ

**Attendees**: Hywel Williams, Finola Delamere, Liz Doney, Helen Scott, Laura Prescott, Maxine Whitton, Ching-Chi Chi, Karen Thomas, Monica Paoloa Novoa, Esther van Zuuren, Sally Wilkes

Jan Kottner, Matthew Grainge, Jo Leonardi-Bee, Amanda Roberts, Laurence Le Cleach, Olivier Chosidow, Kim Thomas, Arash Valipour, Lesley Exton, Firouz Mustapa.

### Monday 22nd February, 2016 (Day 1, 12 pm – 5 pm)

**Hywel Williams explained what we planned to discuss in the meeting, inviting comment throughout the session.**

Progress in the Cochrane Skin Group

Finola gave a brief update of what the Skin Group had been up to as well as an overview of Cochrane (what it is, how it came about, and its structure).

Targeted update on haemangioma

Monica gave an introduction to her hospital and dermatology department. She explained that 10% of the paediatric dermatology cases that she sees in her clinic have vascular disease, which is why she and her colleagues, in collaboration with the Cochrane unit within their hospital, wanted to update the Cochrane Review ‘Interventions for infantile haemangiomas (strawberry birthmarks) of the skin’. Monica explained the objective of the Targeted Update (TU) project. Her TU took approximately 10 months to complete:

* Phase 1: Approval and first meeting (March 2015).
* Phase 2: Development of project.
* Phase 3: Editing of documents and peer review process (January 2016).

She described the included studies and talked about how beta-blockers work.

Hywel assured the room that quality wasn’t compromised in TUs, stating that we’re not advertising them as a substitution for review updates, but as another opportunity for authors to produce a timely and clinically useful focused update. Laurence asked how we chose the topics. Hywel replied that the TUs work best with new interventions, those with a “buzz” around them, or for assessing a rapidly changing field where there were arguments around treatment use. He re-iterated that TUs are not formalised yet. Finola asked Monica if the TUs had changed her clinical practice. Monica said that the treatments were used before, but the last publication did not include trials for beta-blockers. She said that the new trials showed what dose to use. Hywel asked if there were ongoing studies, and Monica said there were. Jan asked if there were many cases where oral propranolol doesn’t work, and Monica replied that there were not. Amanda asked if patients were involved in the TU, and Monica replied that they weren’t. Hywel wondered if patient involvement slows down progress and Kim T asked if eligibility criteria were dictated by studies. Amanda asked where she’d find the TUs, and Hywel explained that there were lots of uncertainties around their publication, but they should appear in the *Cochrane Library*.

Summary of Findings ‘SoF’ – let’s do it right (talk and practical training session)

Esther started with an explanation of GRADE (**Grading of Recommendations, Assessment, Development and Evaluations)**, stating that the quality of evidence rating incorporates methodological flaws, consistency of results, generalisability, and magnitude of effect. [www.ebgrade.mcmaster.ca](http://www.ebgrade.mcmaster.ca) was highlighted as a resource for tutorials and information. Esther explained that the GRADE approach looked at the PICO (Population/patient, Intervention/indicator, Comparator/control, Outcome): studies, outcomes, effect estimates for each outcome, rating of the quality of evidence for each outcome. She said that all randomised controlled trials (RCTs) started as high quality, but could be downgraded. Observational studies start at low quality and can be upgraded.

Quality of the evidence reflects the extent of our confidence that estimates of effect are correct. Factors that lower quality of evidence are as follows:

1. Study limitations: limitations in design and execution (risk of bias).
2. Inconsistency of results: unexplained heterogeneity of results across studies.
3. Indirectness of results: evidence comes from different research questions.
4. Imprecision: when are results precise enough? Consider sample size, number of events (rule of thumb = rate down if less than 300 events), and wide confidence intervals.
5. Publication bias: systematic over or under estimate of the effect due to selective publication of studies.

Esther reminded us that for each comparison of alternative management strategies, all outcomes should be presented in 1 ‘SoF’. After delegates completed some data extraction, Esther guided us through using GradePro. She told us not to assess imprecision until we see the total number of events. Finola asked what the rule of thumb for wide confidence intervals was, and Esther said it depends on the context of the outcome. The quality considerations aren’t the same for each outcome. Jan asked about what would happen if there were lots of excellent RCTs, but 1 poor trial – would you downgrade all fields for one study? Hywel said you would have to come to a judgment across all trials. GRADE tries to pool risk of bias. Esther reminded us to look at the particular outcome you’re assessing. Matthew suggested you’d conduct a sensitivity analysis. Hywel re-iterated that the point is to be sure of why you’re downgrading and being explicit about it. Make footnotes informative. The articles published by the GRADE Working Group were highlighted for guidance.

Interface between Cochrane Skin Group reviews and guidelines

Hywel asked us to think about the relationship between the CSG and guideline producers. Laurence talked about her experience of guidelines, mentioning the new French Centre of Evidence-Based Dermatology. She said that in collaboration with the HAS (The French National Authority for Health, which is equivalent to the National Institute for Health and Care Excellence (NICE) in the UK), they are producing their first guideline, which is on acne. Collaborating to avoid duplication of effort was raised as an issue as well as whether guideline topics should be based around available Cochrane reviews or upcoming reviews. Hywel stated that it was difficult for us to predict when reviews would be completed, and he mentioned the dilemma of when to “release” draft reviews for inclusion in guidelines if needed prior to the review’s publication.

Finola talked about guidelines in the context of the CSG. She mentioned the long lead-in time of reviews used in guidelines, which the UK Cochrane Centre captured, and that part of prioritisation by CSG editors is them thinking of whether a title will impact a guideline. She talked of the relationship that has developed between the British Association of Dermatologists (BAD) and CSG in terms of their guideline pipeline and our review production pipeline and talked about the Co-ordinating Editor approaching decision-makers and informing guideline makers of CSG reviews, e.g., #126. Finola said that pro-active authors help facilitate Cochrane review inclusion in guidelines and mentioned that one author is actively involved in writing a guideline and suggested a CSG review that would specifically fit within that guideline. Finola finished by mentioning that the CSG is sometimes approached by the World Health Organisation (WHO) specifically for pre-publication information.

Esther said that she still doesn’t think that Cochrane is well known and noted that often Cochrane doesn’t cover everything that a dermatologist is interested in, with minor treatments not used often but still used. Hywel asked Firouz and Lesley from the BAD if the arrangement with the CSG was working for them. Firouz mentioned the Cochrane review ‘Interventions for hidradenitis suppurativa’ as an example of the relationship working well. Firouz said that the protocol for the review was useful as a base for the structure of their guideline. He said they look at the number of protocols and refer to what’s been done to gage the topic area’s relevance. Hywel thought it was interesting that protocols rather than reviews were looked at. Bob asked if the guidelines had consumer representatives. Firouz said that the BAD ask for at least one, and Esther said it’s the same in the Netherlands. Consumers are also involved in Columbia but not in Taiwan. Olivier commented that guidelines more than systematic reviews need to mix results of systematic reviews with treatments that have no evidence base but are used every day, and implement a hierarchy. He suggested that systematic reviews are used as evidence for administering treatment in clinical situations. He also thought that a country’s politics and healthcare system could affect their guideline content.

Hywel mentioned the need to look at external (world) and internal (country) validity. Firouz said that the BAD don’t look for worldwide guidelines, just those of relevance to UK practice. Laurence said that there were existing guidelines for acne, but there was a problem of GRADE abuse and conflicts of interest. Olivier talked about a concept of having an initial group without conflicts write the guidelines then inviting experts who may have conflicts to look at them, clearly stating their conflicts – to tap into expertise and diminish conflicts. Hywel asked Amanda and Karen what they thought of the discussion. Karen said she is chased by companies to use her client base. Hywel asked how the BAD dealt with conflicts. Firouz said they need a minimum of 51% (of contributors) without conflicts. Amanda said she struggled with the issue of conflicts as we all have them – where do you draw the line? She felt that guidelines do a different job to Cochrane. She isn’t happy for a guideline to comment on evidence and tell her what to do. Guidelines are for what to do in a particular situation. Hywel asked for Jan’s perception of guidelines and Cochrane. Jan agreed that they are separate entities. He noted that we hadn’t defined a guideline as different in every country. He said he’d reviewed a guideline for pressure ulcers, in which Cochrane reviews scored highest for methodological soundness. Esther said that guidelines should cover all advice, e.g. self-care, and RCT inclusion is limiting. Kim mentioned the usefulness of priority-setting partnerships in asking the right questions. Jan talked about the misuse of Cochrane reviews when no evidence meets the inclusion criteria, asking how they advance clinical healthcare if too narrow or broad. Bob said that the key question was how to ensure that Cochrane reviews are included and used by the guideline groups. The BAD do a number of checks, which are built into their process.

Hywel concluded the day by stating that it was an important debate as our reviews were more likely to benefit patient care if they are included in guidelines. He re-outlined what we’d talked about and said it was important to keep in mind the trajectory of Cochrane reviews.

### Tuesday 23rd February, 2016 (Day 2, 9 am – 12.30 pm)

**Hywel recapped Monday’s meeting.**

Mapping the network of treatments for atopic eczema – have some trial comparisons been deliberately avoided?

Sally gave an example of where there was a lack of active comparisons of topical corticosteroids ‘pimecrolimus’ and ‘tacrolimus’ and talked about work in which she developed a network of comparisons from identified RCTs. Bob commented that comparisons in trials are those where pharmaceutical company products will fare better. Sally’s findings of a high rate of inactive controls seemed to support this. Olivier wondered if it was not so deliberate, but based on products available to dermatologists.

The CSG-COUSIN initiative to develop core outcome sets across the whole of dermatology

Jan introduced COUSIN: what it is; its aims; its history; its structure, i.e., management team, methods groups, project groups. He said its aim is to develop and implement core outcome sets throughout dermatology; they are planning to conduct a meta-epidemiologic study and produce a quick guide for core outcome set (COS) developers. He stated that there was currently no COS standard, so it was another thing open to abuse. Hywel suggested contacting those at COMET (Core Outcome Measures in Effectiveness Trials). There are some dermatology entries in the COMET database that are currently not affiliated with CSG-COUSIN (e.g., scars, melasma, actinic keratosis, alopecia…); it was felt that they should be contacted and at least informed about the initiative. Even if there are many open questions, CSG-COUSIN has at least something to offer (roadmap and checklist).

There was common agreement that COS in dermatology and this initiative is very important and the message needs to be spread widely, because there is not sufficient awareness at the moment. In discussion, it was felt that the following ideas should be implemented:

* develop some key statements at the CSG annual meeting 2017 and promote them widely; and
* engage with industry and policy makers, because the development of valid COS is so important for everyone and is probably supported by industry.

It was also felt that the U.S. Food and Drug Administration and European Medicines Agency should be involved.

Evidence-based dermatology in Taiwan

Ching-Chi talked about the EBM (Evidence-based Medicine) club that his hospital runs and that they enter into a competition run by the Healthcare Quality Improvement Campaign (HQIC) and Taiwan Joint Commission on Hospital Accreditation (TJCHA), which rates applications on their PICO, search, appraisal, and presentation skills. He shared that his centre had won quite a few awards. He talked about Cochrane Taiwan and said that from 2016, Taipei Medical University will run a Masters in EBM. Laurence asked if only a small group of people were interested in EBM, and Ching-Chi replied that very few are interested in it in Taiwan, but dermatologists are aware of its importance, which is a good starting point. Maxine liked the idea of certificates as incentives, and Hywel liked the idea of competitions.

Introduction to trial sequential analysis and whether we should be using it

Jo and Matthew stated that this research question came from a conversation with Christian Gluud of Copenhagen Trial Unit about cumulative meta-analysis. It is a method of display rather than analysis and allows us to see when sufficient evidence has been accumulated. They used the CSG review ‘Probiotics for treating eczema’ as an example. Bob said it was most useful for the ‘Implications for research’ section. He also said it would have useful implications for authors as a tool to see if they need to update, as well as CRGs using it to prioritise updates.

Where is Cochrane consumer involvement going?

The discussion began by Amanda discussing the Cochrane consumer report and sources of support open to consumers, concluding that Cochrane needed to improve in this respect. She talked about the difference between engagement and meaningful engagement and involvement as a consumer author, which can often feel like a “free ride”. Amanda posed a number of questions: why do we involve consumers? How do we involve them in a meaningful way? Karen said that some referee comments forms weren’t in lay terms and could feel like a token. Esther felt it was the responsibility of the lead author to make sure that their review got enough consumer input. Amanda highlighted the panel system as a good system and felt that a “buddy” system is also worth looking into. Finola said we had tried a buddy system in the past but had not enough consumer referees to support this; however, the CSG might try to overcome this by asking a group of willing consumers to act as referees and discuss and comment on protocols and reviews together, which would be a way of people learning from each other. This may be a way consumer referees would gain confidence from each other.

**Hywel closed the meeting.**

Actions

* Consider opening up TSA to more review teams.
* Consider asking a group of willing consumers to act as referees and discuss and comment on protocols and reviews together.