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Establishing and Prioritising Research Questions for the Prevention, Diagnosis and Treatment of Hair Loss (excluding Alopecia Areata): The Hair Loss Priority Setting Partnership

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Summary

Background

Hair and scalp problems are common. Unfortunately, many uncertainties exist around the most effective management and treatments strategies for these disorders.

Objectives

To identify uncertainties in hair loss management, prevention, diagnosis and treatment that are important to both people with hair loss and healthcare professionals.

Methods

A hair loss priority setting partnership was established between patients, their carers and relatives, and healthcare professionals to identify the most important uncertainties in hair loss. The methodology of the James Lind Alliance was followed to ensure a balanced, inclusive and transparent process.

Results

In total 2747 treatment uncertainties were submitted by 912 participants; following exclusions 884 uncertainties relating to hair loss (excluding alopecia areata) were analyzed. Questions were combined into "indicative uncertainties" following a structured format. A series of ranking exercises further reduced this list to a top 25 that was taken to a final prioritization workshop where the top 10 priorities were agreed.

Conclusions

We present the top 10 research priorities for hair loss (excluding alopecia areata) to guide researchers and funding bodies to support studies important to both patients and clinicians.

What's already known about the topic?

- Many uncertainties exist around the management and treatment of hair loss

What does the study add?

- We present the top 10 uncertainties in hair loss management, prevention, diagnosis and treatment that are important to patients, their carers and healthcare professionals
- These prioritized research uncertainties can be used to guide researchers and funding bodies when deciding to invest in hair loss research studies

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Introduction

Hair and scalp problems are common in the general population with an overall prevalence of 8.2% reported in one UK study [1]. Various conditions can result in hair loss and may present as increased hair shedding (telogen effluvium) [2], hair thinning (in a pattern or diffusely) or patchy to complete hair loss (e.g. alopecia areata, primary cicatricial alopecias) [3-5]. In some conditions the hair may regrow, in others the alopecia is permanent. Frequently overlooked is the psychological impact of hair loss on an individual. The visible nature of hair loss and fear of progression may lead to low self-esteem, anxiety and depression [6]. Many uncertainties exist about the most effective ways to manage these different hair loss disorders. Our limited understanding of disease pathogenesis and natural history, with the relative lack of validated

severity scales for each condition is reflected in the poor quality of evidence for treatments and interventions currently available.

The James Lind Alliance (JLA) is a project funded by the National Institute of Health Research (NIHR) with support from the Medical Research Council. The aim of the JLA is to provide infrastructure and support to patients and clinicians working together to identify the most important treatment uncertainties affecting their particular interest, in order to stimulate and prioritize future research in that area. The Priority Setting Partnership (PSP) presented here was proposed by the British Hair and Nail Society (BHNS) to address treatment uncertainties highlighted by systematic reviews, treatment guidelines and clinical experience, for all types of hair loss. Working with the JLA and funded by the hair loss charity Alopecia UK, the Hair Loss PSP presents priorities for UK hair research in a bid to raise the profile of hair loss disorders and to open funding streams to address these important research questions.

The objectives of the Hair Loss PSP were (1) to work with people with hair loss, their partners / parents / carers and healthcare providers to identify uncertainties about hair loss management, prevention, diagnosis and treatment, (2) survey the research literature to identify uncertainties and research recommendations, (3) agree by consensus a prioritized list of those uncertainties, (4) translate these prioritized uncertainties into research questions that can be tested, (5) publicize the results of the PSP and process of obtaining them, and (6) take the results to research commissioning bodies to be considered for funding. All identified uncertainties from this process will be added to the UK Database of Uncertainties about the Effects of Treatments (UK-DUETs) (www.library.nhs.uk/duets).

In contrast to previous dermatology PSPs [7-9], the challenge of this process was how to represent the broad range and incidence of conditions that manifest with hair loss. We initially opened the PSP to address all types of hair loss within the same process. However, analysis of the initial survey revealed that around half of the responses related to alopecia areata (AA; including *alopecia totalis / universalis*). Therefore, the Steering Group (SG) felt it was appropriate to separate the analysis at this point into two separate PSP processes that would run in parallel yet remain under supervision of the same SG membership. The rationale for this change was to prevent one condition dominating the process whilst maximizing identification of important uncertainties across all conditions studied. The alopecia areata PSP outcomes are reported separately [ref to be inserted].

Methods

Following the principles and guidelines set by the JLA, the hair loss PSP adhered to a pre-determined protocol to ensure transparency and inclusivity of all parties within the process (www.jla.nihr.ac.uk/priority-setting-partnerships/hair-loss). The SG was established in March 2014 and comprised four people with hair loss representing various patient support groups, four Dermatologists, a Psychologist, a registered Trichologist and a General Practitioner (GP). A JLA representative provided independent oversight of the PSP and chaired the SG. All potential conflicts of interest were declared prospectively. The five stages of the PSP process are outlined below and summarized in Figure 1.

Stage 1 – Identification and invitation of potential partners

Key stakeholders were identified through a process of consultation and peer knowledge, building on SG members' networks and existing JLA affiliates. Special consideration was given to how all the different types of hair loss would be represented in this process. Thus, a broad range of stakeholder groups were approached and invited to become partners in the PSP process.

In addition to the BHNS, JLA and Alopecia UK, the following partners engaged in the hair loss PSP: The British Association of Dermatologists, UK Dermatology Clinical Trials Network (UK DCTN), The Institute of Trichologists, British Dermatology Nursing Group, Skin Conditions Campaign Scotland, Alopecia Help and Advice (Scotland), Scottish Alopecia Support Group, My New Hair, British Association of Skin Camouflage, Changing Faces, European Hair Research Society, "Look Good, Feel Better", British Association of Hair Restoration Surgery and the Cicatricial Alopecia Research Foundation.

Stage 2 – Invitation to submit uncertainties

Survey 1 took place from 8th September 2014 – 31st October 2014 and was advertised as open to anyone residing in the UK. Geographical analysis of respondents who provided location details showed that 2% (14/630) did not reside in the UK. The initial invitation to submit uncertainties involved an online survey (Survey Monkey™) accessed through the Alopecia UK website (www.alopeciaonline.org.uk). In addition, paper surveys were available on request and were also distributed at key events. Through engagement with the various partner organizations, local advertisement and via social media, a range of people with different hair loss conditions, their carers and relatives, and healthcare professions were targeted.

Uncertainties were invited by asking the following question: "Do you have questions about prevention, diagnosis or treatment of hair loss that need to be answered by research?". Participants were permitted to submit as many or as few questions as they wished, and these could relate to one or more hair loss conditions. The survey questionnaire was designed to link the research question with hair loss type as it was anticipated that questions relating to more than one condition would be generated by an individual, with healthcare professionals in particular anticipated to submit uncertainties relating to different disease types. The survey contained a participant information sheet to provide background to the process and survey text was designed to be easy to understand and provide all the relevant information for self-completion. Submitting the completed survey was considered as consent to participate in the PSP process and publish the (anonymized) uncertainties on UK-DUETs.

Stage 3 - Collation

The aim of this stage was to review all the submitted questions, exclude questions outside the remit of the PSP and generate "indicative uncertainties" (i.e. a collation of similar questions into one clear, understandable question presented in a standard format). Non-questions (e.g. statements or comments) and questions not directly relating to a hair loss disorder were excluded. Questions that could be resolved with reference to existing research evidence (so called "unknown knowns") were identified from existing sources of information, in particular systematic reviews, evidence based guidelines and prospective trial registers. Exclusion of questions or comments outside of the remit of the Hair Loss PSP were made by consensus within the SG. Uncertainties which were not adequately addressed by previous research were collated and entered into a hair loss section within UK DUETs (www.library.nhs.uk/duets).

Stage 4 – Ranking of treatment uncertainties

The aim of this stage was to generate a short-list of indicative uncertainties deemed by both people with hair loss and healthcare professionals to be important. To reduce the large number of indicative uncertainties generated in stage 3 to a reasonable number for ranking, an "interim list" was created using criteria agreed by the SG. These criteria were designed to identify which questions were asked most frequently, with inclusion of questions asked by more than one person and questions asked by both people with hair loss and healthcare professions independently. The SG also identified 5 questions that were asked by only one person that were felt warranted inclusion and also a further 2 questions written by the steering

group to express the concerns illustrated in the free text statements of participant personal experience. This process generated a list of 56 questions to go forward to the second survey.

The second online ranking survey ran from 22nd September 2015 to 4th October 2015 and was completed by previous participants to further refine the interim list into a short-list of 25 uncertainties to take to the final workshop. Participants were invited to choose up to ten uncertainties from the interim list but were not asked to prioritise them. The responses obtained were used to rank the uncertainties by number of votes. The priorities of the different groups of responders were listed separately and compared.

Stage 5- Final workshop

The final workshop took place on 7th November 2015 at Willan House in London. The aim of this stage was to prioritize through consensus the most important uncertainties relating to the management, prevention, diagnosis and treatment of hair loss. This was carried out by eligible members of the SG and the wider partnership that represents people with hair loss and healthcare professional (including Dermatologists, Trichologists, GPs, Hair Transplant Surgeons and a Psychologist). The process was facilitated by the JLA to ensure fairness, transparency and accountability. Using nominal group technique, consensus was achieved through a series of ranking and plenary sessions, eventually generating the top ten research priorities. Those attending the priority setting workshop were asked to complete a declaration of interests, including disclosure of relationships with for-profit organizations.

Results

The initial survey was completed by 912 participants generating 2747 responses, with 83% of submissions being completed by people with hair loss, carers or relatives and 13% by healthcare professionals or hair loss organizations (Figure 2). After removal of non-questions and those deemed "out of scope", 1823 uncertainties remained. After exclusion of uncertainties relating to AA (reported separately), 884 uncertainties related to all other types of hair loss remained.

Eleven of the 884 submitted uncertainties could be answered from available evidence and so were excluded. Indicative uncertainties were generated by combining similar questions and standardized using "PICO" (**P**opulation **I**ntervention **C**omparator **O**utcome) formatting. In addition to specific disease related questions, "generic" uncertainties relevant to all types of

hair loss were also identified. Where appropriate, similar questions submitted for a number of conditions were combined into an indicative question relevant to "all hair loss types". This process generated an interim list of 201 uncertainties that was further reduced by ranking questions based on the number of times submitted, with priority given to those questions submitted by both people with hair loss and healthcare professionals. The top 56 uncertainties were taken forward to the second ranking survey and of these the top 25 uncertainties were then taken to the final workshop.

Of note, the additional 7 questions identified by the steering group at interim ranking phase were not prioritized in the second survey for the final workshop, with the exception of the question "How aware are GPs of the early signs of hair loss and their management?", ranked number 7, which seemed to represent the large number of free text comments related to diagnosis in General Practice in the initial survey.

Participants at the final workshop were divided into three groups, each with an independent facilitator and including similar numbers of people with hair loss, healthcare professionals and representatives of partner organisations. A series of group and plenary sessions used discussion to select the "Top 10" research uncertainties by consensus (Table 1).

Independent facilitators, with prior experience of PSP workshops, provided by the JLA ensured that the discussions were not influenced heavily or steered by any particular individual or group. Participants signed a declaration of interest form prior to participation in the workshop to ensure no personal or commercial interests influenced the final prioritization process.

Discussion

Here we present an overview of this PSP that has demonstrated a number of uncertainties relating to the management, prevention, diagnosis and treatment of hair loss. By adhering to the JLA ethos of inclusivity and transparency, and using a combination of online surveys and face-to-face workshops, we can feel confident that the outcomes generated here accurately reflects the consensus view of both people with hair loss and healthcare professionals in determining future priorities for research.

Feedback from participants in the final workshop revealed that the opportunity to discuss the questions allowed different viewpoints to be aired, identified positions that they had not previously considered and lead to a more balanced appraisal of the priorities. Thus, the final top 10 did not exactly reflect the ranking (performed independently) from the second survey. Discussion on position of ranking was frequently influenced by the other questions presented, with certain questions relegated in priority if they were deemed to be covered by other uncertainties more highly ranked in the process. Although deliverability of the research was considered in appraising each question, it was acknowledged that the questions broadly represented a theme for research that would require refinement before being developed into a completed research question.

The top 10 uncertainties are open and broad but reflect the true wording of submissions from participants. Creation of focused research questions from the themes identified is a later-stage process and these specific research questions will then need to define a population, intervention, comparator and outcome and take into account feasibility of such trials. We can be confident that the broad theme of any subsequent research, and associated funding, will then follow the priorities identified here and not a separate research track with less impact for stakeholders and participants.

Interestingly, a significant proportion of the originally submitted questions did not represent an uncertainty at all, but reflected a lack of information around treatment options and service provision. Recurring themes included availability of services, treatment strategies, wig provision and the low priority given to hair loss in the NHS. Striking was the frequency of comments relating to experiences of patients accessing medical services, particularly seeing GPs, with many describing a perceived lack of knowledge, reluctance to refer and in some cases a lack of compassion when dealing with their distressing problem. Thus, a greater awareness and education of GPs / healthcare professionals around hair loss was suggested to highlight and address the (openly acknowledged) inadequate dermatology training currently received in the UK by many medical students and GP trainees in the field of hair loss. .

Some problems were encountered during the process, mainly around data handling and the large number of uncertainties originally submitted (2747 questions). By necessity a "Data team" was set up to process these results. However, some inconsistency in taxonomy allocation to categorize questions occurred that may have been overcome by just one or two

people only handling the results, although this would have significantly prolonged the process in time and costs. Another area of difficulty was around engagement of key stakeholders. In general smaller and specialized organizations were keen to become partners in the process. However, some larger organizations were reluctant to commit to partnership but agreed to advertise the PSP to their members, whereas other groups refused to engage completely. These decisions appeared to relate to the inability of such large organizations to commit to these types of projects for which they are frequently approached to support. As the number of PSPs in all fields are likely to increase, with many groups anticipated to want engagement with similar stakeholders each time it was felt by the SG that the JLA should consider setting up a higher level agreement with the main stakeholder groups (particularly the Royal Colleges and Specialist Associations) to provide a minimum level of commitment for all future JLA-supported PSP processes.

We present an overview of the hair loss PSP process, including pitfalls encountered along the way. By presenting the top 10 uncertainties in hair loss (excluding AA) identified as important by both patients and clinicians we hope to raise awareness of these disorders and influence research priorities in the future. The outcomes will be put forward to researchers and funding bodies with the ultimate aim of securing meaningful research funds to address these important issues.

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Figure legends

Figure 1- Overview of the Hair Loss Priority Setting Partnership process

Figure 2- Division of participants of initial survey by category (n= 912)

Table 1- Top 10 research uncertainties for hair loss disorders (excluding alopecia areata) prioritized by consensus.

Table 1- Top 10 research uncertainties for hair loss disorders (excluding alopecia areata) prioritized by consensus.

Rank	Uncertainty
1	What is the most effective treatment for Frontal fibrosing alopecia?
2	What are the causes of Frontal fibrosing alopecia? For example- dietary, genetic, autoimmune, skin care products, medications, hormonal, environmental, vaccination, infection.
3	What are the causes of female pattern hair loss? For example- genetic, hormonal and childbirth, autoimmune, dietary, other medical conditions, environmental factors.
4	In all types of hair loss, are psychological therapies effective in improving patient outcomes?
5	In all types of hair loss, what outcome measures should be used to assess severity of hair loss, progression and impact on the individual?
6	Is spironolactone helpful in managing female pattern hair loss?
7	In all types of hair loss, does raising ferritin levels/replacing iron improve hair growth? And what is the optimal level of ferritin?
8	What is the most effective treatment for Lichen planopilaris?
9	In all types of hair loss, do certain diets or nutritional supplements (for example vitamin D) prevent or improve hair loss?
10	In female pattern hair loss, does hormone replacement therapy (HRT) halt progression of the hair loss compared to placebo?

Stage 1: Identification and Invitation of Potential Partners

Stage 2: Invitation to Submit Uncertainties (Initial survey)
912 responders with 2747 responses

Stage 3: Collation
884 uncertainties for hair loss disorders (excluding alopecia areata)

Stage 4: Ranking of Treatment Uncertainties

Stage 5: Final Workshop

Initial Survey : Participants by category (n=912)

4%

13%

83%

- People with hair loss, carers and relatives
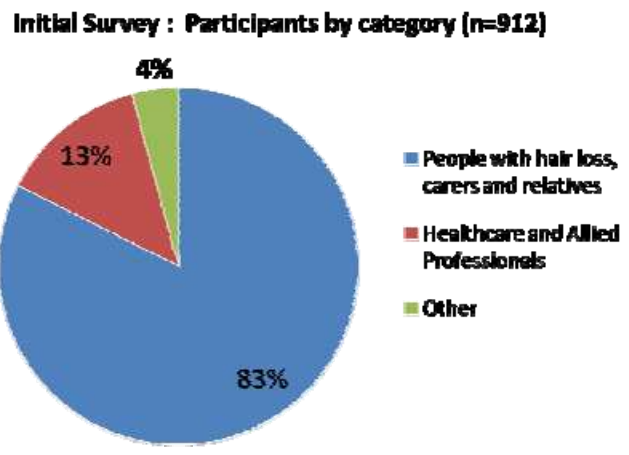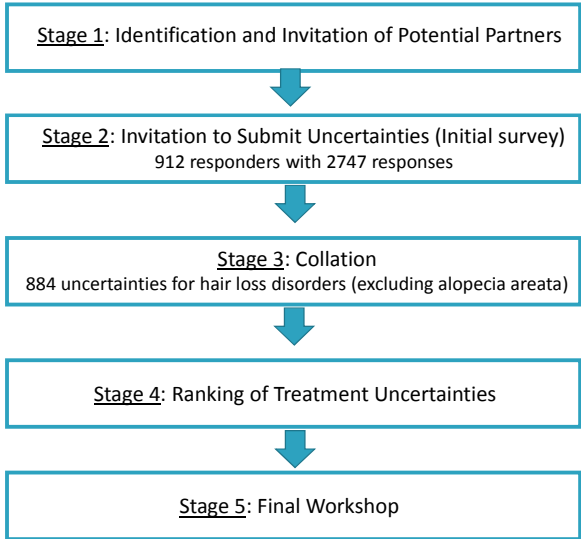- Healthcare and Allied Professionals
- Other

Figure 2- Division of participants in initial survey by category (n= 912)