

The James Lind Alliance—Tackling Treatment Uncertainties Together

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Abstract: The James Lind Alliance is a nonprofit making initiative that was established in 2004. It brings patients and clinicians together in priority-setting partnerships to identify and prioritize unanswered questions about the effects of treatments that they agree are most important. This information will help ensure that those who fund health research are aware of what matters to both patients and clinicians. Research suggests involving patients in the prioritization of research questions in this way is rare. To date, the James Lind Alliance has completed prioritization exercises on asthma and urinary incontinence. Partnerships focusing on prostate cancer and vitiligo are in progress. **Key words:** *partnership, patient involvement, research priorities, treatment uncertainties*

WITH the research agenda commonly set by researchers themselves, rather than by patients or the clinicians who treat them, the shared interests of these latter groups may be overlooked. While the pharmaceutical and medical technology industries and academia play essential roles in developing new treatments, their priorities and perspectives may differ from those of patients and clinicians, and research questions that matter to them may thus be neglected.

The James Lind Alliance (JLA) is developing a process for identifying treatment uncertainties that are important to both patients and clinicians, and then working with both groups to prioritize 10 of these treatment uncertainties for research. The JLA convenes and facilitates priority-setting partnerships that bring patient and clinician groups together on an equal footing. A growing body of research sug-

gests that such approaches are rare (Thornton, 2008). The partnerships focus on specific health conditions that to date include asthma, urinary incontinence, vitiligo, and prostate cancer.

This article describes how the JLA works, particularly in terms of involving patients, and what has been learnt and achieved so far.

BACKGROUND TO THE JAMES LIND ALLIANCE

A nonprofit making UK-based initiative, the JLA is part of the James Lind Initiative and is principally funded by the National Institute for Health Research and the Medical Research Council. Established in 2004 by Sir Iain Chalmers (James Lind Library), Sir Nick Partridge (INVOLVE), and Professor John Scadding (Royal Society of Medicine), it takes its name from a pioneer of clinical trials, James Lind (1716-1794) (Figure 1). The JLA is supervised by a steering group that includes representatives from the National Institute for Health Research, the Medical Research Council, and the National Institute for Clinical Excellence (NICE). The day-to-day

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Figure 1. James Lind (1716–1794).

operation is overseen by 3 part-time consultants with administrative support, all primarily laypeople. Organizations and individuals that support the JLA's aims can join as affiliates, via www.lindalliance.org, and will receive a quarterly newsletter. Currently, the JLA has almost 200 affiliates.

The JLA's main activity is supporting priority-setting partnerships, groups whose membership consists of patients, carers, and clinicians and the organizations representing them. They collaborate to identify treatment uncertainties in their condition of interest and then work through a closely managed process to prioritize these. The next crucial step—bringing them to the attention of research funding bodies—is an active process supported by JLA staff and in part through such funders being represented on the JLA steering groups. To date, the JLA has completed priority-setting exercises for asthma and urinary incontinence and is currently supporting groups to identify priorities in prostate cancer, vitiligo, and eczema. Other areas likely to undertake this process shortly include schizophrenia, epilepsy, Tourette syndrome, and type 1 diabetes.

The makeup of a priority-setting partnership can vary but is generally led by a small steering group, representing both patients

and clinicians, with the JLA offering impartial facilitation and infrastructure support. A wider network of partners is identified through a process of peer knowledge and consultation, through the steering group members' networks and through the JLA's register of affiliates. The objective is that every group that feels it could or should have a voice is at least invited.

The JLA process can adapt to address the different needs and the practical implications of working with groups of different sizes. While the Asthma Priority Setting Partnership consisted of 2 partner organizations, Asthma UK and the British Thoracic Society, the Urinary Incontinence Priority Setting Partnership involved more than 20 partner organizations. The recently formed Prostate Cancer Priority Setting Partnership is likely to include around 30 partners.

In mid-2010 the JLA will launch an online Guidebook, providing practical guidance and evidence on its process. This will be at www.JLAGuidebook.org.

PATIENT INVOLVEMENT IN PRIORITY SETTING—THE CONTEXT

The JLA's essential aim is to help create a research environment reflective of the needs of both patients and those who care for them, rather than of the pharmaceutical industry or researchers themselves, who may have little or no firsthand experience of a given condition. In order to gain evidence of how best to prioritize research questions with patients and clinicians collaborating, the JLA documents and reflects on its own processes in detail but has also commissioned research. This has looked into how patients and clinicians are currently involved in setting research priorities, by referring to existing models and projects and establishing the most effective ways of doing this.

Research commissioned by the JLA has found that the majority of research funding bodies (31 out of 52) operate in “responsive” mode, relying on researchers to submit ideas for research and then using a process of peer review to decide which applications to fund. There is considerable variation in the

level of patient and public involvement in the decision-making process, with some involving patients at every stage while others do so only as trustees at the very end. In addition, most commissioning organizations are reluctant to restrict researchers by asking them to address priority topics and few take a systematic approach to addressing identified priorities (Staley & Hanley, 2008).

In a review of published literature, it was found that only 6 studies in 334 compared patients' priorities (or outcomes for assessment) with researchers' priorities, and only 3 compared clinicians' and researchers' priorities (Oliver & Gray, 2006). Further research found that clinicians are more involved than patients in the whole process of research priority setting, with patients far less likely to be consulted as to their priorities. In addition, clinicians and patients are more likely to work separately on identifying research topics, than collaboratively. The JLA priority-setting partnerships are therefore rare (Stewart & Oliver, 2008).

THE JLA METHOD

The aim of a JLA priority-setting partnership is straightforward: To identify the unanswered questions about the treatment of specific conditions from patient and clinician perspectives, and then prioritize by consensus those that both parties agree are the most important, as a "top 10" list of shared patient and clinician treatment uncertainties. Partners are then expected to publicize the results of the exercise and to take them to research commissioning bodies to be considered for funding. Roles, responsibilities, resource commitments, and expectations for the process are agreed by the partnership and set out in a formal protocol document ("The protocol of the JLA Prostate Cancer Priority Setting," n.d.).

There is some flexibility in the method, partly because different groups may be at different stages of the priority-setting journey when they approach the JLA. For example, the Asthma Priority Setting Partnership came to the JLA to begin a new exercise collecting treatment uncertainties for prioritization. Groups representing epilepsy and schizophre-

nia, however, have already carried out exercises to identify uncertainties and are now talking to the JLA about working together simply to prioritize these.

One of the founding principles of the JLA is to undertake methods that are as fair, transparent, and free from bias as they can be. The challenge is that at this stage, JLA methods strive to be methodologically defensible but are also unusual and untested, necessitating a degree of pragmatism when working with the partnerships.

IDENTIFYING TREATMENT UNCERTAINTIES

The JLA definition of a treatment uncertainty is that no up-to-date, reliable systematic reviews exist or up-to-date systematic reviews show that uncertainty exists. Systematic reviews are based on worldwide searches for reliable, relevant evidence, analyzed using methods to reduce biases and the play of chance.

The JLA encourages its priority-setting partnerships to gather their uncertainties from as wide a range of potential sources as possible and to ensure patients are as confident and empowered as clinicians to submit the questions about their treatment to which they have not been able to find answers. In practice, this means ensuring information and forms are clearly written, that participation can take place over e-mail, Internet, or by post and that responses are confidential.

The JLA supports priority-setting partners to approach their members and the individuals they represent to ask them to submit their views. Reaching patients and the public does not need to be costly or time-consuming, as most patient organizations have existing communication mechanisms that can be used.

For example, the Urinary Incontinence Priority Setting Partnership developed a questionnaire that could be completed electronically and e-mailed back or printed out and posted. Incontact (now known as the Bladder & Bowel Foundation) distributed the questionnaire by posting information on its Web site, then adding a link to this from various online message boards and fora on other

urinary incontinence charities' Web sites, and by providing the link and information in various continence magazines and newsletters. The questionnaire was also posted to its 1000 members.

The Vitiligo Priority Setting Partnership developed an online survey that included information about the exercise, written in plain English, and a form for people to submit their uncertainties. This was also available in paper copy and was promoted widely throughout the vitiligo community, reaching a large number of patients and carers.

It is important to be mindful of the potential diversity of patient interests. Patient networks will often be inclusive of multiple perspectives of a condition, so an appeal for treatment uncertainties should seek to involve those different perspectives. The Vitiligo Priority Setting Partnership includes organizations and networks as wide-ranging as those concerned primarily with the psychosocial aspects of disfigurement and those for whom skin camouflage cream is the focus.

As well as uncertainties actually submitted by patients and clinicians, those existing sources of information used by and for them are searched. These include question-answering services, research recommendations in systematic reviews and clinical guidelines, protocols for systematic reviews being prepared, and registers of ongoing research. Among the sources used by the Asthma Priority Setting Partnership were the Cochrane Database of Systematic Reviews, NHS Evidence, BMJ Clinical Evidence, the Database of Abstracts of Reviews of Effects, the National Institute for Health Research Health Technology Assessment Programme, NICE Guidance and the NICE Research Recommendations Database, and relevant Royal Colleges' guidance.

CHECKING THE TREATMENT UNCERTAINTIES

Among the uncertainties it is likely that some can be answered by existing research. Where the answer to a question about treatment exists but is not known, this is a potential indicator of gaps in knowledge or educa-

tion, or a sign that information is not being effectively communicated to those who need it. It is strongly recommended that Partnerships keep a record of these findings and address them separately to the priority setting process. The JLA suggests incorporating this commitment into the Partnership's Protocol.

Uncertainties submitted by patients and clinicians, which are true uncertainties, are identified after checking them against existing systematic reviews. Duplicates can be combined, but their frequency is recorded, as this may influence prioritization. Ineligible submissions are removed, such as those that contain no defined treatment and therefore no clearly defined treatment uncertainty. The remaining uncertainties are rewritten or rephrased where necessary, to ensure consistency in the language used and to clarify the precise research question being submitted. The Patient/Problem, Intervention, Comparison, Outcome format is used, ensuring every question is worded, where possible, to include the patient or problem, the intervention, a comparator, and an outcome.

It is not generally possible to say how many individuals are involved in the process, which relies on snowballing techniques to consult as widely as possible. Partner organizations consult their membership and networks, which, in turn, consult their stakeholders, sometimes simply through word of mouth, and may gather the resulting uncertainties together into one submission before returning them to the JLA. The 2 main partners in the Vitiligo Priority Setting Partnership are the Centre for Evidence Based Dermatology, representing clinicians, and the Vitiligo Society, representing patients and carers. Both groups have access to a range of networks and consumer groups. Evidently a high number of individuals were consulted as a total number of 1341 uncertainties were submitted overall.

Within the urinary incontinence priority-setting process, a total of 519 uncertainties were gathered, of that 102 came from existing sources and 417 were submitted by partner organizations who had gathered them internally and from their members. These were refined to remove duplicates and

nonuncertainties, leaving a total of 226. Of these, 79 came solely from patients and carers, 37 came solely from clinicians, 6 were submitted by patients and clinicians simultaneously, 2 were from patients and research recommendations, and 102 were derived solely from research recommendations.

The checked uncertainties were then entered by an appropriate person identified by the priority-setting partnership, such as an information specialist, into the UK Database of Uncertainties about the Effects of Treatment (UK DUETs— www.library.nhs.uk/duets). UK DUETs, part of NHS Evidence, is a resource to make uncertainties explicit. When each uncertainty is entered into UK DUETs, it might be edited for clarity. However permission is sought from its originator to allow publication of the unedited text within the record, to demonstrate fidelity to the original submission. Submitted uncertainties are tagged according to their originator, whether patient, carer, professionals, or research recommendations. Once the uncertainties are in UK DUETs, the process of prioritization can begin.

PRIORITISING TREATMENT UNCERTAINTIES

Given the large number of uncertainties that can emerge from the process, the most practical approach is to initially shortlist them, in an interim priority-setting exercise, before proceeding to a final priority-setting workshop. In order to participate in this “voting” stage, partners must complete a form declaring their interests. This is to ensure transparency and to identify any potential competing interests. It is also an opportunity to identify expertise, resources, and preferred methods of communication with the different groups.

The interim priority-setting stage may be carried out using e-mail or post, to ensure those without Internet access can participate, whereby organizations consult their membership and ask for their top 10 to 15 most important uncertainties. Members of the steering group will then aggregate and rank those uncertainties according to the importance they

have been given by each respondent and the incidence of submission. This process is closely monitored by the JLA to ensure transparency and minimization of bias.

The Urinary Incontinence Priority Setting Partnership interim priority-setting process, conducted by e-mail, saw 11 partner organizations choosing their top 10 uncertainties from the 226 and ranking them in priority order. A range of techniques was used by the participating organizations to reach their top 10, including consulting members, pooling knowledge, and combining the shortlists of colleagues. These priorities were then scored and a shortlist of 29 uncertainties, which proved to be an appropriate cutoff point, was developed. Finally, organizations planning to attend the last workshop were asked to choose and rank their top 10 from that shortlist as a precursor exercise for the shared priority-setting workshop. Although this worked well, the evaluation suggested that 29 was perhaps too many, and that in future, giving partners a shorter shortlist to consider may be more manageable.

AGREEING A TOP 10

The final stage, to agree 10 prioritized uncertainties, is likely to be conducted in a face-to-face meeting, using small and full group discussions. The methods used for this prioritization process are determined by consultation with the partner organizations and with the advice of the JLA. Methods that have been identified as potentially useful in this process include the following: adapted Delphi techniques, expert panels, nominal group techniques, consensus development conference, electronic nominal group, online voting, interactive research agenda setting, and focus groups. So far the JLA has used an adapted nominal group technique approach.

Nominal group technique involves participants being divided into smaller groups in which ideas are considered and then prioritized independently by each individual. Individuals' priorities are then combined and agreed. Next, participants are brought back into one large group and each of the small groups' priorities are combined and

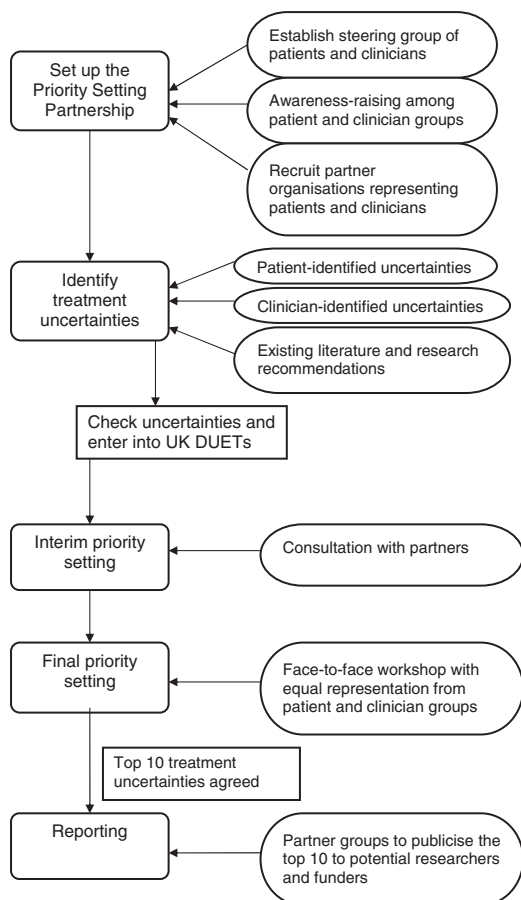


Figure 2. James Lind Alliance-Process diagram.

discussed. One benefit of this technique is that it prevents the domination of discussion by a single person and encourages the participation of less assertive group members. The JLA is conscious of the need to ensure, as far as is possible, that patients and clinicians are equally represented within the discussion groups (Figure 2).

The JLA facilitates this process to ensure transparency, accountability, and fairness. It is important that patients and clinicians can contribute equally. JLA facilitators are conscious of the fact that some patients may be less experienced than professional clinicians at contributing to open debate and are therefore careful to actively include the patients and ensure they have opportunities to share their views and experiences. Information such as participant biographies, glossary of research terms, and a clear structure for discussion and

decision making is sent to participants ahead of the workshop to help with this process.

When the participants in the Urinary Incontinence Priority Setting Partnership were divided into small groups to discuss the short-listed uncertainties, they explained their reasoning for their ranking, to understand each others' perspectives. The dynamic of each group was slightly different, due to different interests, styles, and personalities. The combined contribution of patient representatives and clinicians was particularly powerful, enabling sharing of different perspectives, experiences, and information. Participants challenged each others' assumptions about their interpretation of the questions.

Once the groups had ranked the remaining uncertainties, the scores were combined and entered into a central database. A ranked aggregate list was shared and participants then had an opportunity to debate and contest the uncertainties that they felt should, or should not, be featured in the top 10 (Tables 1 and 2).

MANAGING CHALLENGES

The JLA is open about the fact that while its work is new and groundbreaking, it is not without challenges. One issue that partnerships may need to address is the potential imbalance in the number of patients and clinicians involved during the process and, most important, during the final priority-setting meeting. The JLA partnerships understand the importance of taking active steps to recruit a full and representative group of patient and clinician organizations, and to enable both groups to contribute equally. The JLA is also looking at possible options for addressing overrepresentation of either group at the final priority-setting meeting, perhaps by weighting the responses of the underrepresented group.

Overall, the JLA has developed a very neutral style of facilitation, adopting a nonprescriptive approach to small group prioritization, ensuring groups develop their own way of working and make their decisions without being influenced by the JLA. Interestingly, for both the Urinary Incontinence Priority Setting Partnership and the Asthma Priority

Table 1. Asthma Priority Setting Partnership Top 10 Treatment Uncertainties

Rank	Asthma Treatment Uncertainty
1	(a) What are the adverse effects associated with long-term use of short- and long-acting bronchodilators, inhaled and oral steroids, and combination and additive therapies in adults? (NB: This includes children aged 12 years and older) (b) What are the adverse effects associated with long-term use of short- and long-acting bronchodilators, inhaled and oral steroids, and combination and additive therapies in children?
2	What is the most effective way of managing asthma with other health problems?
3	What are the key components of successful “Self-management” for a person with asthma?
4	What is the most effective strategy to educate people with asthma and health professionals about managing the adverse effects of drug therapies?
5	What is the most effective way of managing asthma triggers?
6	What is the role of complementary therapies in asthma management?
7	What are the benefits of breathing exercises as a form of physical therapy for asthma?
8	What type of patient (children and adults) and health professional education is most effective in gaining asthma control?
9	What is the most effective way to manage consultations and asthma control in adolescence and young people?
10	Psychological interventions for adults with asthma?

Table 2. Urinary Incontinence Priority Setting Partnership Top 10 Treatment Uncertainties

Rank	Urinary Incontinence Treatment Uncertainty
1	What are the optimal pelvic floor muscle training protocols (frequency and duration of therapy) for the treatment of different patterns of urinary incontinence?
2	Can guidance or training for general practitioners on appropriate pathways of care improve the management of patients with urinary incontinence?
3	What is best practice for the treatment of combined stress urinary incontinence and detrusor overactivity?
4	What catheter regimens are most effective in preventing urinary tract infections in patients using intermittent self-catheterization for the management of a neurogenic bladder?
5	Which treatment is most effective for the reduction of urinary frequency and urgency?
6	Is urodynamic testing prior to surgery for urinary incontinence associated with better continence rates and quality of life than surgery indicated without such testing?
7	What is best practice for the management of stress urinary incontinence following failed tension free vaginal tape surgery?
8	What are the most effective treatments of daytime urinary incontinence in children?
9	Are disposable catheters more or less acceptable than reusable catheters in terms of effective bladder management, patient experience, and urinary tract infections?
10	In women with prolapse (symptomatic or asymptomatic) and SUI, should suburethral tapes be inserted at the same time as repairing the prolapse?

Setting Partnership, each small group took strong ownership of its jointly prioritized uncertainties, each expressing a competitive determination to see its priorities carried through to the final top 10.

This has implications for facilitating such meetings and it is essential to be clear about the distinction between patients' individual priorities, based on intensive personal experience, and those that potentially have an impact on a larger group of people may reduce the burden of a disease or represent significant savings in health care. Participants may have to relinquish personal agendas and work with priorities that will deliver benefit overall. It is important to ensure people are treated fairly and with sensitivity and support during this process. Despite the potential challenges this may bring, the approach during those final stages has, in the JLA's experience, been democratic, pragmatic, and unanimous.

WHAT HAPPENS NEXT?

As the JLA process is still relatively new, it has not yet been possible to measure its long-term impact on research. As part of its commitment to learning from its experience and documenting those lessons, partners are asked to complete an anonymous evaluation, online or on paper, indicating whether they represent patients or clinicians. This is an opportunity for all partners to feed back their views on the JLA process, their satisfaction with how they were involved, and the process' strengths and weaknesses. The findings then inform future partnerships. Encourag-

ingly, the majority of participants in the Urinary Incontinence Priority Setting Partnership were positive about their involvement, with a number of clinicians noting that the experience had underlined for them the value of engaging with patients and understanding their views first hand.

In terms of practical achievements, several of the uncertainties identified and prioritized by the Asthma Priority Setting Partnership and the Urinary Incontinence Priority Setting Partnership have been considered by funding bodies and are likely to be funded as research projects in the near future. The National Institute for Health Research's Health Technology Assessment program actively supports the work of the JLA by being represented on the steering group and has indicated its commitment to receiving top 10 lists from JLA partnerships into its own priority-setting processes. For example, the top 10 urinary incontinence priorities were reviewed by the National Institute for Health Research's Health Technology Assessment and 8 were submitted to the program to be considered for prioritization this year.

The JLA's natural assumption is that each priority-setting partnership will take ownership of its top 10 research uncertainties and take them forward to funding bodies to consider. The most positive long-term outcome for any JLA priority-setting partnership will be that research into one or more of the uncertainties it identified is commissioned and that this goes on to have a direct life-changing impact on the treatment available to patients and the way in which clinicians can deliver that.

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