

THE JAMES LIND ALLIANCE APPROACH TO PRIORITY SETTING FOR PROSTATE CANCER RESEARCH: AN INTEGRATIVE METHODOLOGY BASED ON PATIENT AND CLINICIAN PARTICIPATION Artitaya Lophatananon¹, Sandy Tyndale-Biscoe², Emma Malcolm³, Helen J. Rippon⁴, Kate Holmes⁴, Lester A. Firkins⁵, Mark Fenton⁶, Sally Crowe⁷, Sarah Stewart-Brown¹, Vincent J. Gnanapragasam^{8,9} and Kenneth Ross Muir^{1,9} – ¹Health

Sciences Research Institute, Warwick Medical School, University of Warwick, Coventry, ²The Prostate Cancer Support Federation, Stockport, ³Prostate Action, London, ⁴The Prostate Cancer Charity, London, ⁵James Lind Alliance Strategy and Development Group, James Lind Alliance, Summertown Pavilion, Oxford, ⁶Database of Uncertainties about the Effects of Treatments, Summertown Pavilion, Oxford, UK, ⁷James Lind Alliance Monitoring and Implementation Group, James Lind Alliance, Summertown Pavilion, Oxford, ⁸Department of Uro-oncology and Surgery, University of Cambridge and ⁹Addenbrooke's Hospital, Cambridge, UK

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V.J.G. and K.R.M. are joint senior authors.

INTRODUCTION

Research in many fields of medical investigation is principally researcher and response led. The medical industry is advancing in both treatments and technologies, but the ideas and views of both patients and clinicians are often forgotten, even though these groups clearly have a

shared interest in research. Patients themselves are becoming increasingly familiar with research, particularly through the internet, and with their direct experience of disease they should be an important voice when identifying research priorities [1].

There are a range of both quantitative and qualitative methodologies, from focus

groups to cross-sectional surveys, for gathering and consolidating the views of relevant patient and clinician groups. Each of these methods has different strengths and weaknesses [2].

The James Lind Alliance (JLA) is an independent organization funded by the National Institute of Health Research and Medical Research Council, UK. The organization's role is to provide a platform for an independent and integrative approach to determining both patients' and clinicians' views on setting the research agenda. This is known as 'priority setting'. The JLA has established a methodology (Fig. 1) that aims to incorporate aspects of both quantitative and qualitative approaches to the inclusive participation of a range of different parties' views [3–5].

The purpose of the present paper is to describe the methodology exemplified by a recent JLA partnership investigation into the uncertainties that surround the treatment of prostate cancer, the major male cancer which kills over 10 000 men in the UK every year.

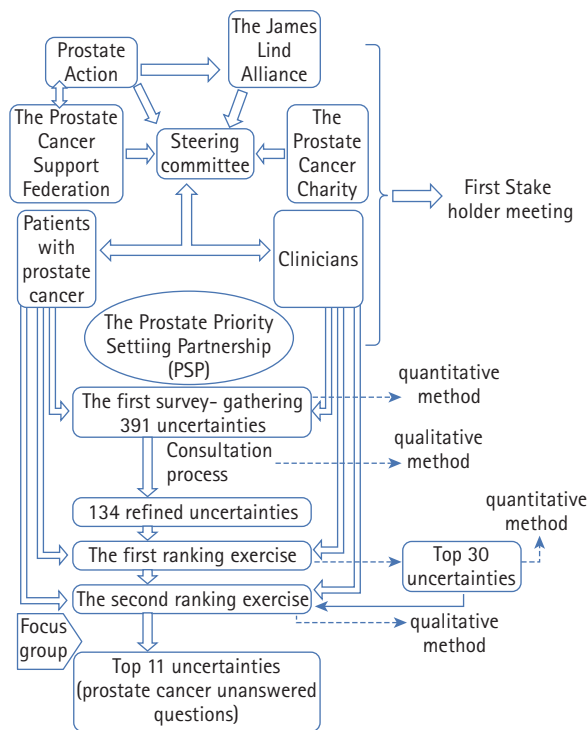
METHODOLOGY AND PRIORITIZATION OUTCOME

Forming the prostate priority setting partnership

The JLA process starts with a disease-focused public or professional group approaching the JLA. In the present example, Prostate Action and the Prostate Cancer Support Federation (PCSF) approached the JLA to carry out a prostate cancer priority setting exercise.

An initial group was formed to coordinate the prostate Priority Setting Partnership (PSP) and to organize its activities. The steering group consisted of members of the JLA, Prostate Action, the PCSF and the Prostate Cancer Charity (PCC). The steering group worked together to approach patients with prostate cancer and clinicians to become 'affiliates' and to form a PSP. The aim of the PSP was to identify patient/carer and clinicians' shared priorities for research into the treatment of specific health problems, in this case prostate cancer. Members of the partnership were identified through patient and clinician networks and organizations.

FIG. 1.
The prostate cancer priority setting process.



A first stakeholder awareness meeting of potential partners was held to explain the process involved, to gauge interest in the process and to complete a declaration of interests, including disclosing relationships with the pharmaceutical industry. There were over 40 attendees.

THE JLA METHOD STAGE 1: GATHERING THE UNCERTAINTIES – QUANTITATIVE METHOD

The first survey using a 'harvesting form'

After the partnership setting meeting, the steering group agreed on the design of a 'harvesting form'. The form consisted of two parts, the first requesting general information about the respondent and the second requesting details of their unanswered questions about prostate cancer, so called 'treatment uncertainties', which are questions about the effects of diagnosis, treatment and prognosis that cannot be answered through a relevant and reliable systematic review. A cumulative list was compiled by sending the harvesting form out widely to interested partner organizations and individuals. Treatment uncertainties were defined as any factors that respondents felt could potentially influence disease outcome but that had not yet been fully addressed by existing

research. For each uncertainty submitted, the respondent was also asked to provide details of the uncertainty and optional information including why they thought it important, suggestions about ways to answer their uncertainty and any evidence they had asked to support the true question. In parallel, the PCC, who shared the idea of setting the research agenda through patient and clinician need, had launched their own web-based survey. In their structured questionnaire, there were two free text questions that asked respondents to give their top prostate cancer research priorities and the reasoning behind them. The results of this work were subsequently merged with the data from the main PSP survey. A survey of current research recommendations from National Institute for Health and Clinical Excellence (NICE) Guidelines and Cochrane Systematic Reviews was also undertaken, with the results also merged with those from the PSP survey.

The process of gathering uncertainties aimed to gather representative views of the participating organizations and individuals. Different stakeholder organizations used different methods, such as membership meetings, direct mail or email consultation, mail or web-based questionnaires, internet message boards and focus group work [5].

This harvesting exercise aimed to gather as many non-overlapping uncertainties as possible. In total, completed harvesting forms were received from six representatives of clinicians, 32 representatives of patients and two researchers. There were 282 uncertainties submitted through PCC invitations. The total number of uncertainties submitted was 391.

THE JLA METHOD STAGE 2: CONSULTATION PROCESS TO REFINE UNCERTAINTIES

A discussion process within the steering group was undertaken to produce and refine the list of 'raw' questions on prostate cancer. The 391 raw questions were assembled, categorized and refined into 'collated indicative questions' which were clear, addressable by research and understandable to all. For example, 'Replace PSA with a proper genetic marker for prostate cancer' was rephrased to 'Is there a genetic marker for CaP that would be both more sensitive and more specific than PSA serum level?'. Any similar or duplicate questions were combined where appropriate, e.g. 'Are there dietary measures that can prevent prostate cancer or slow down its progression?' and 'The effect of diet on vulnerability to prostate cancer'. Uncertainties that could already be answered, or that could not be addressed by research, were removed, e.g. 'Will my sex life change because of having prostate cancer, or having treatment for prostate cancer?'. Questions that had already been addressed or were being addressed by major studies were also removed at this stage. This process brought the number of uncertainties down to 134.

THE JLA METHOD STAGE 3: VERIFICATION OF TRUE UNCERTAINTIES

The 134 uncertainties were further reviewed against existing literature to ensure that these refined questions had not been reliably addressed by previous research. The Cochrane Database of Systematic Reviews and the Database of Abstracts of Reviews of Effects (DARE) were searched, any research on the topic reviewed, and the full reference recorded together with the conclusions. The result of the search suggested that all 134 questions were indeed unanswered questions: either the uncertainty had not been directly/clearly addressed by previous research or the research had limitations that

TABLE 1 The top 11 prostate cancer research priorities

Prostate cancer uncertainty	Rank
How can overtreatment for prostate cancer be prevented by identifying and excluding the treatment of harmless tumours? (Tigers & Pussycats)	1
Is there a genetic marker for prostate cancer that would be both more sensitive and more specific than PSA serum level?	2
This item includes the following:	
<ul style="list-style-type: none"> Can genetic testing for prostate cancer reduce my risk of being wrongly diagnosed, and over- or under-treated? 	
What can be done to delay or prevent the onset of hormone-independent prostate cancer?	3
This item includes the following:	
<ul style="list-style-type: none"> Which hormone therapy, continuous or intermittent, is more effective in treating prostate cancer? What is the best way to treat hormone independent prostate cancer? Why do some men with prostate cancer last longer before developing hormone-independent disease? 	
Are there any dietary measures that can prevent prostate cancer or slow its progression?	4
This item includes the following:	
<ul style="list-style-type: none"> What is the evidence that dietary changes reduce the likelihood of recurrence of prostate cancer after radical treatment? Would dietary control of animal fats, and particularly dairy products, help reduce my risk of, or provide a protective effect against my prostate cancer getting worse? 	
Does serial PSA measurement in patients with prostate cancer accurately monitor disease progression?	5
This item includes the following:	
<ul style="list-style-type: none"> Is there a monitoring regime that will give earlier indication of the requirement/need for follow up further treatment for prostate cancer? 	
Would prostate cancer screening targeted at high risk groups, i.e. those with positive family history, and ethnic minorities with higher rates, improve the outcomes of treatment in these groups?	6
Does active surveillance work for treatment of prostate cancer?	7
This item includes the following:	
<ul style="list-style-type: none"> If opting for active surveillance or watchful waiting of my prostate cancer, what are the outcomes? 	
Do variations in GP awareness of prostate cancer affect outcomes?	8=
What is the effectiveness of new treatments for prostate cancer such as high intensity focused ultrasound and cryotherapy?	8=
Is there a vaccine that can prevent prostate cancer?	8=
Are there any non-intrusive diagnostic tests that will identify patients with aggressive prostate cancer whilst not identifying harmless cancers? (Tigers and Pussycats)	8=

made it impossible to draw a definitive conclusion.

THE JLA METHOD STAGE 4: THE FIRST RANKING EXERCISE – QUANTITATIVE METHOD

The list of 134 unanswered questions under 32 broad headings was sent to affiliated partners. The partners were asked to look at all 134 submitted uncertainties, select their top ten, and rank those ten according to importance. These ranking scores were subsequently used to produce a sum score for each uncertainty. For example a score of 10 was assigned to the first ranked uncertainty, giving an uncertainty 10 points each time it was ranked as a top priority. Conversely, a score of 1 was assigned to the tenth ranking uncertainty on the list. Each item was then sorted according to its total score from all submitted scores from all partners. Examination of the resulting list showed unevenness in the grouping of topics which was skewing the results. To

correct this, the weighted scores for some uncertainties were adjusted by adding those of very similar uncertainties. The uncertainties with the top 30 scores were listed for the further prioritization process in the form of a priority setting workshop.

THE JLA METHOD STAGE 5: PRIORITY SETTING WORKSHOP – QUALITATIVE METHOD

The prostate cancer PSP workshop

A workshop was held in which we used an adapted Delphi method exercise, involving extensive discussion within groups and an iterative prioritization process [6]. The workshop aimed to identify the shared top 10 prostate cancer uncertainties. All partners had been invited to attend the workshop as the final stage of the priority setting exercise.

All participants were randomly allocated to one of two groups, adjusted to ensure a

balanced distribution of clinicians in each group (the number of clinicians attending was lower than patients). Each member voted on each of the unanswered questions and was encouraged to provide comments/suggestions on their vote, and the census method was used to prioritize the top ten uncertainties. In the second round of focus group discussions, all members were again randomly allocated to one of the two new groups and the same exercise repeated, but instead of re-starting the prioritization process, the group used the results from the first session as their starting point. This process was about reiterating all information by different members of the same group to the other new members of the group to ensure widest possible discussions across the two groups (because group A and B had different participants for each session). Extensive discussion between members was encouraged on the results of the previous voting. At the end of the process, the 'top 10' prostate cancer uncertainties were obtained from each

group. There was a very remarkable agreement between the two groups, each group having an identical first seven items in their list. This meant that the final step, bringing the results from two groups of the second session for a further final discussion with all members present, was a simple and rapid process. And so the final ranking was done and the top 11 prostate cancer uncertainties obtained (there were four research questions that shared the eighth ranking, resulting in the top eleven of the final list). Table 1 shows the final list of priorities produced.

DISCUSSION

The JLA initiative provides a platform for setting medical research priorities that are driven entirely by patient and clinician need within a particular health problem. The JLA method has enabled a set of priorities for prostate cancer research to be produced that is both inclusive and objectively based. The fact that patients and clinicians not usually involved in setting research directions have had full opportunity to join this exercise should help to focus research more directly on clinically relevant work and identify gaps in the current research effort.

The JLA method integrated quantitative and qualitative approaches. Each component part had inherent strengths and weaknesses but in combination, these two approaches complemented one another. The quantitative process encompassed a structured questionnaire and produced numerical data as the basis for the subsequent ranking. The limitation was the extrapolation of the data as the survey was collected from a limited study population (a network of participating individual/organizations/

groups), although these represented stakeholders with a direct and vested interest in helping to improve prostate cancer research [2].

The subsequent qualitative process was designed to provide a further perspective through direct interaction between the people involved. The workshop process provides an in-depth view on each uncertainty through interactive debate, leading to a greater understanding of the context of the participants' decision making [7]. The limitation here again lies with the limited numbers present in the group discussion stage, which reflected both lack of availability and perhaps some apathy on behalf of some clinicians [8]. Furthermore, the uneven number of patients and clinicians could have produced biased results. Future initiatives could be improved by achieving a greater number and better balance of numbers between the two parties.

These limitations aside, the JLA prostate cancer priority setting exercise has yielded a list of top 11 uncertainties, as set out by patients and clinicians dealing directly with the disease. Prostate cancer research has gained a great deal of attention during recent years. It is hoped that this list of uncertainties – obtained specifically to highlight the most pressing clinical needs as perceived by patients and clinicians working in the field – will help funding organizations and researchers themselves to set their research priorities. By integrating quantitative and qualitative methods, the exercise has enabled us not only to gather many validated uncertainties but also to understand the rationale behind them. We believe the JLA process offers a tested and inclusive approach to setting priorities in research.

CONFLICT OF INTEREST

None declared.

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Correspondence: Emma Malcolm, Prostate Action, 6 Crescent Stables, 139 Upper Richmond Road London, SW15 2TN, UK. e-mail: emalcolm@prostateaction.org.uk

Abbreviations: JLA, James Lind Alliance; PCSF, Prostate Cancer Support Federation; PSP, Priority Setting Partnership; PCC, Prostate Cancer Charity.