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Top research priorities in healthcare-associated infection in the UK

P. Wilson [a,*], K.S. Gurusamy [b], R. Morley [c], C. Whiting [d], B. Maeso [d], G. FitzGerald [a], S. Bennett [e], J. Bostock [e], D. Brealey [f], M. Cann [e,g], M. Kiernan [h], D. Leaper [i], M. Moore [j], B. Oppenheim [k], P. Thompson [e], A. Tingle [e]

[a] *Clinical Microbiology and Virology, University College London Hospital NHS Trust, London, UK*
[b] *Division of Surgery and Interventional Science, University College London, London, UK*
[c] *James Lind Alliance, Southampton, UK*
[d] *James Lind Alliance, National Institute for Health Research Evaluation, Trials and Studies Coordinating Centre, Southampton, UK*
[e] *Healthcare-Associated Infection (HCAI) Service Users Research Forum (SURF), London, UK*
[f] *University College London Hospital NHS Trust, and NIHR University College London Hospitals Biomedical Research Centre, London, UK*
[g] *MRSA Action UK, Kirkham, UK*
[h] *Richard Wells Research Centre, University of West London, London, UK*
[i] *University of Huddersfield, Huddersfield, UK*
[j] *University of Southampton, Southampton, UK*
[k] *Queen Elizabeth Hospital Birmingham, Birmingham, UK*

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SUMMARY

Background: There is a mismatch between research questions which are considered to be important by patients, carers and healthcare professionals and the research performed in many fields of medicine. No relevant studies which have assessed research priorities in healthcare-associated infection (HCAI) that have involved patients' and carers' opinions were identified in the literature.

Aim: The Healthcare-Associated Infections Priority Setting Partnership was established to identify the top research priorities in the prevention, diagnosis and treatment of HCAI in the UK, considering the opinions of all these groups.

Methods: The methods broadly followed the principles of the James Lind Alliance (JLA) priority setting activity.

Findings: In total, 259 unique valid research questions were identified from 221 valid responses to a consultation of patients, carers and healthcare professionals after seeking their opinions for research priorities. The steering committee of the priority setting partnership rationalized these to 50 unique questions. A literature review established that for these questions there were no recent high-quality systematic reviews, high-quality systematic reviews which concluded that further studies were necessary, or the steering committee considered that further research was required despite the conclusions of recent systematic reviews. An interim survey ranked the 50 questions, and the 10 main

* Corresponding author. Address: Clinical Microbiology and Virology, UCLH NHS Foundation Trust, 5th Floor Central, 250 Euston Road, London NW1 2PG, UK. Tel.: +44 (0) 203 447 9516.
E-mail address: peter.wilson9@nhs.net (P. Wilson).

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research priorities were identified from the top 32 questions by consensus at a final priority setting workshop of patients, carers and healthcare professionals using group discussions.

Conclusions: A priority setting process using JLA methods and principles involving patients, carers and healthcare professionals was used to identify the top 10 priority areas for research related to HCAI. Basic, translational, clinical and public health research would be required to address these uncertainties.

Introduction

Healthcare-associated infections (HCAIs) can develop either as a direct result of healthcare interventions such as medical or surgical treatment (in secondary care), or from being in contact with a primary healthcare setting [1]. The estimated prevalence of HCAI in Europe is approximately 6% [2]. Overall, an estimated 2.6 million new HCAIs occur every year in Europe [3] and can affect many parts of the body [2]. More than 500 disability-adjusted life years are lost for every 100,000 population annually in Europe due to HCAI [3]. In the USA, the total cost of five major HCAIs was approximately $US 10 billion per year [4].

Failure to address treatment uncertainties through research and implementation can lead to significant suffering and deaths [5]. It is important that research in any field of medicine considers the shared interests of patients, carers and healthcare professionals [6]. However, there is a mismatch between research questions which are considered important by patients, carers and healthcare professionals and the research performed in many fields of medicine [7,8]. The James Lind Alliance (JLA) exists to help address this mismatch [6]. This is achieved by forming 'Priority Setting Partnerships' between patients, carers and healthcare professionals [6]. Formal prioritization of research topics jointly by patients and healthcare professionals has led to increased research on the topic [9,10].

Global Infection Prevention and Control Priorities 2018—22 provides details of the priorities in infection prevention and control (IPC) [11], but not the research priorities. In the only published study on research priorities in the prevention and control of HCAIs, only infection prevention experts were involved [12]. Furthermore, this study identified the broad categories of research priorities rather than specific research questions which could be considered to be research priorities. To the authors' knowledge, there has been no formal research prioritization process involving patients, carers and healthcare professionals in the field of HCAI.

The aims and objectives of the Healthcare-associated Infections Priority Setting Partnership were to work with patients, their carers and healthcare professionals tasking them (termed 'stakeholders') to identify evidence uncertainties about the diagnostic tests and effects of prevention and treatments for HCAI; to agree, by consensus, a prioritized list of those evidence uncertainties or questions for research; to publicize the results and process; and to take the results to research commissioning bodies to be considered for funding, and researchers to encourage them to submit grant applications addressing these uncertainties.

Methods

The methods used for this priority setting activity broadly followed the principles and methods set out in the JLA guidebook [13]. The broad steps involved the following and are summarized in Figure 1.

- Formation of the partnership: the final prioritization to identify the top 10 priorities for HCAI was agreed at a priority setting workshop that included 30 stakeholders with an approximately equal mix of patients, carers and clinicians representing organizations and people affected by HCAI, their carers and healthcare professionals treating people who have had an HCAI. A partnership was formed between PW representing University College London Hospitals NHS Foundation Trust, MC representing MRSA Action UK, and the Healthcare-Associated Infection Service Users Research Forum (SURF), UK. A steering committee was formed. The members of the steering committee who participated in the complete process were PW, KG, RM, SB, JB, DB, MC, MK, DL, CM, MM, BO, PT and AT.
- Establishment of the scope: members of the steering committee discussed the scope and decided that it should include all aspects of HCAI including prevention, diagnosis and treatment. The protocol was published on the JLA website.
- The process to identify evidence uncertainties or unanswered questions from patients, carers and healthcare professionals was undertaken using online surveys (Google forms and Survey Monkey) and face-to-face surveys. This process gathered deliberately open-ended responses to the consultation, was accessible to a wide range of stakeholders, and respondents were able to say what mattered to them.
- The next step in the process was to refine and categorize the broad open-ended responses from narrative into more thematic unique questions for research. This process produced a long list of thematic questions.
- Interim prioritization: in order to reduce the long list of questions to a shorter list for discussion at a face-to-face final prioritization workshop, members of the steering committee were each asked to select 20 questions which they thought required further research. In order to ensure that patient, carer and clinician points of view were considered, only questions identified as an important research priority by at least one healthcare professional and a patient representative of the steering committee were included in the interim set of 50 questions. If less than 50 questions were identified as important by at least one healthcare professional and one patient representative,

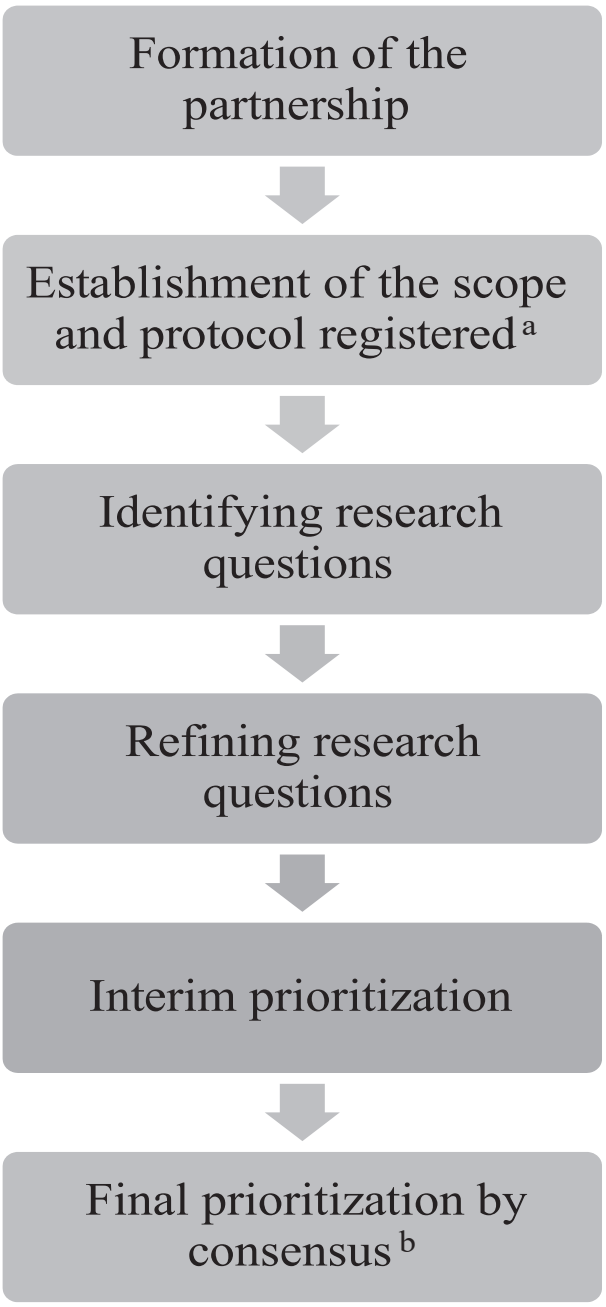

Figure 1. Research prioritization steps. [a]The protocol was agreed and published on the James Lind Alliance website.[b]The final prioritization to identify the top 10 priorities for healthcare-associated infections was agreed at a priority setting workshop that included 30 patients, carers and clinicians.

further questions which obtained the highest total ranks from the steering committee members (which were converted to scores: rank 1, 20; rank 2, 19; rank 3, 18 etc.) were identified to constitute the top 50 research questions.

- In order to ensure that only 'unanswered' questions were included in the prioritization process (i.e. excluding those that had already been answered by research), the existing evidence was checked. Questions were considered 'answered' when recent (within the last 3 years) high-quality systematic reviews (based on low risk of bias studies) concluded that further research was not required. Questions were considered unanswered when there were no recent high-quality systematic reviews, when high-quality systematic reviews concluded that further studies were necessary, or when the steering committee considered that further research was required despite the conclusions of recent systematic reviews. These unanswered research questions were classified as 'uncertainties'.
- To reduce this list of 50 uncertainties to 32 for discussion in the final workshop, an online survey (Google form) and a face-to-face survey were conducted. The participants were asked to identify the top 10 priorities based on their experience. The questions were selected on the basis of the number of times they were identified as top 10 uncertainties by the respondents.
- Final prioritization by consensus
  - The top 10 questions were identified by small group and large group discussions in the final workshop involving 30 participants (15 healthcare professionals and 15 patients, carers and public representatives). The healthcare professionals included microbiologists, infection nurse specialists, intensive care unit specialists, surgeons and clinical researchers in the field of HCAI.
  - The participants in the final workshop were divided into three small groups with approximately equal representation of healthcare professionals and patients, carers and public representatives.
  - Each small group was facilitated by a neutral, trained JLA facilitator. Each participant in each discussion group was asked to identify their top three and bottom three research questions (of the 32 research questions discussed in the final workshop) and provide the reasons for their choice. The questions were then compiled into the following five groups: top research questions that did not feature in the bottom three questions for any participant; bottom research questions that did not feature in the top three questions for any participant; featuring more in the top than bottom; featuring more in the bottom than top; and not featuring in the top or bottom. The main discussion was around where the last three groups fitted: towards the top group or bottom group. During a 2-h discussion, participants were allowed to view the rank of the question based on the number of times a question featured in the top 10 in the interim survey of 50 questions. Consensus was reached by discussion. Following the first set of small group discussions, the questions were ranked in order based on the aggregate results of the first set of small group discussions.
  - This was followed by a short large group session in which the aggregate results from all the first group sessions were presented, clearly indicating the similarities and differences in the ranking between the different small groups.
  - This was followed by a second set of small group discussions (after mixing the groups, ensuring equal representation of healthcare professionals and patients, carers and public representatives) lasting about 45 min. As in the case of the first set of small group discussions, each small group discussion was led by a JLA facilitator. The second set of small group discussions involved

discussing any questions that the group felt were not ranked correctly and revising the ranks by consensus.
- o Following the second set of small group discussions, the aggregate ranking from the second set of small group discussions was summarized. Subsequently, large group discussions were carried out to arrive at a consensus on the top 10 priorities. In the large group discussions, decisions were also made about combining the questions and rewording the questions to improve clarity following discussion and consensus.

Ethical approval was not deemed necessary for online surveys because no personal identifiable information was collected, and the questions being asked of healthcare professionals, patients and their carers were not considered sensitive. In addition, the authors had the full support of patient organizations with involvement of patient representatives throughout the whole process rather than patients visiting the hospitals. For face-to-face surveys conducted at University College London Hospitals NHS Trust, ethical approval was obtained from NHS Research Ethics Committee (South West - Frenchay Research Ethics Committee (REC); REC No. 16/SW/0208).

Patient and public involvement

Patients and the public were involved in all aspects of this project. In line with the principles of JLA, the views of patients and carers (i.e. those with lived experience) were given equal weighting to healthcare professionals. For example, patients and carers were part of the steering committee and were involved in the definition of the scope, methodology used for the prioritization process, identification of further patient and public representatives, participated in the interim prioritization and final workshop, and reviewed the draft report. They will be involved in the dissemination of the findings through patient websites, patient forums and to research funders.

Results

Identification and refining of research uncertainties

In total, 134 patients, carers and those at risk of developing HCAI, and 87 healthcare professionals provided valid research questions which fell under the scope of this prioritization process in the first survey that was conducted between April 2015 and June 2017. This survey resulted in 259 unique valid research questions. The complete list of 259 unique valid research questions in no particular order is available in Appendix 1 (see online supplementary material). This has been converted to the population, intervention, control and outcomes (PICO) format whenever possible.

Interim priorities

To identify an interim shortlist of questions (from the list of 259 questions) that were to be considered for the next step, 43 research questions were identified on the basis of being selected by at least one patient or carer and healthcare professional of the steering committee, and an additional seven questions were identified on the basis of obtaining the highest ranks among the members of the steering committee. This process was conducted between June 2017 and August 2017. The list of 50 questions identified as interim priorities is available in Appendix 2 (see online supplementary material). The interim ranking of the 50 questions to 32 questions was carried out between January 2018 and September 2018. Forty-four valid responses were obtained during this period. The list of 32 questions that were discussed in the final workshop, the conclusions from any recent systematic reviews (published in the previous 3 years), the number of times it was identified in the top 10 priorities, and comments on interpretation by systematic review authors are available in Appendix 3 (see online supplementary material).

Final workshop

The final workshop took place in February 2019. The rankings of the questions in the different small groups facilitated by the three JLA advisers are listed in Appendices 4 and 5, respectively (see online supplementary material). The final ranking of the 32 questions following the small group discussions is listed in Appendix 6 (see online supplementary material). Two pairs of questions were combined and two questions were revised to improve clarity. The final list of top 10 priorities in the order of ranking is listed in Table I.

Discussion

To the authors' knowledge, this is the first priority setting partnership on HCAI involving patients and carers. This included a wide range of HCAIs, and 259 unique research questions were identified that met the scope of this priority setting partnership. By both small and large group discussions, consensus was reached on the top 10 research priorities.

In general, the research priorities were broad: most of the top 10 priorities could include different patient populations, interventions and controls. The research questions for primary research may have to be decided by existing or new systematic reviews and/or group discussions among researchers, clinicians and patients to identify the patient groups and interventions which are most likely to result in clinical benefit.

There are several potential limitations to the priority setting process. The first limitation is selection of the steering committee. This study selected a steering committee with representation from different types and specialities of healthcare professionals, as well as patients and carers. Except for the interim prioritization which required shortlisting from 259 questions to 50 questions, non-steering committee members were involved in the remaining processes. This might have decreased any bias due to the research interests of the steering committee members. The second limitation is the use of open discussions to achieve consensus. There can be perceived or real power imbalances in such open discussions, particularly when a group of stakeholders consider another group of stakeholders as being more knowledgeable. However, the involvement of neutral JLA facilitators in the final priority setting workshop meant that the principles of JLA were upheld. They aimed to ensure that the viewpoints of those with lived experience were equal to those of people with professional backgrounds. Their role in the workshop was to ensure that all voices around the table were given equal opportunity to input

Table I
Top 10 research priorities in healthcare-associated infection (HCAI)

1	How can infections be identified early?
2	How can we change the behaviour of healthcare professionals to follow best practices in preventing and controlling HCAI?
3	Can rapid point-of-care testing (bedside testing) for infections decrease antibiotic use, decrease community antibiotic resistance, and improve patient outcomes in primary and secondary care?
4	What is the most effective cleaning agent, technique and system to prevent multi-drug-resistant organisms?
5	Can antibiotic stewardship policies (including decreased antimicrobial use by health professionals) decrease antibiotic resistance, and do they cause any harm to the patients?
6	How can we educate patients to look for clinical signs of HCAI?
7	What is the role of change of bacteria in patients or the environment in the development of infection in hospital?
8	In people with antibiotic-resistant bacteria, what is the impact of single-room isolation compared with open-ward care on the overall care and mental health of the person with antibiotic resistance and in preventing transmission of infections to others?
9	Does infection prevention and control training of patients and carers help in the prevention of infection in patients at high risk of infection being cared for in their own homes?
10	How can the development and severity of urinary tract infections in elderly people be decreased?

Priority 3: Rapid point-of-care testing has the potential to identify people with infection and initiate the appropriate antibiotic where deemed necessary. This will avoid giving ineffective antibiotics to people with infection, and also avoid giving unnecessary antibiotics to those who do not have infection. This has the potential to decrease antibiotic resistance. Primary care indicates early diagnosis of infection by a general practitioner; secondary care indicates early diagnosis of infection in a hospital.
Priority 4: 'Prevention' refers to the acquisition of multi-drug-resistant organisms.
Priority 7: 'Change of bacteria' refers to the microbiomes in the environment and in the patient.

and provide their perspectives. Therefore, the impact of perceived knowledge imbalance is likely to be small. The third potential limitation is the subjectivity of the process. There were some major differences in the first round of small group discussions; however, by the second round of small group discussions, the differences had decreased, and in the third round, consensus was reached. This might have been because of shifting views of people based on discussions, but could also be due to fear of opposing general views because of lack of anonymity. However, these are all recognized limitations in this form of priority setting partnership process. These potential limitations were minimized in this priority setting partnership.

The steering committee was constituted of representatives from England alone. Most of the participants in the small and large group discussions were from England. However, the findings are likely to be applicable in countries with a similar spectrum of HCAI and similar treatment options available.

In conclusion, there are significant uncertainties in the prevention, diagnosis and treatment of HCAI. Further high-quality research is necessary to address these uncertainties, which may require programmes of basic, translational, clinical and public health research. For issues with diverse and unproven treatment options, randomized controlled trials may be the only mechanism for identifying the most effective treatment and the treatments that represent good value for money for the National Health Service.

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Conflict of interest statement
PW: Roche Drug Safety Monitoring Group, MSD paid lectures. DL: Chair NICE Guideline Development Group on Surgical Site Infection, paid consultant advisor for Johnson & Johnson. SB: Guideline development group EPIC3. BO: Consultant Microbiologist now working for Cepheid. MK: Now working for GAMA Healthcare, UK. All other authors declare no conflicts of interest.

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Appendix A. Supplementary data

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