Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections

D9.1

Publication of research priorities identified as gaps

WP9 | Prioritizing and implementing research and innovation for public health needs

Leader acronym | INSERM, FHI

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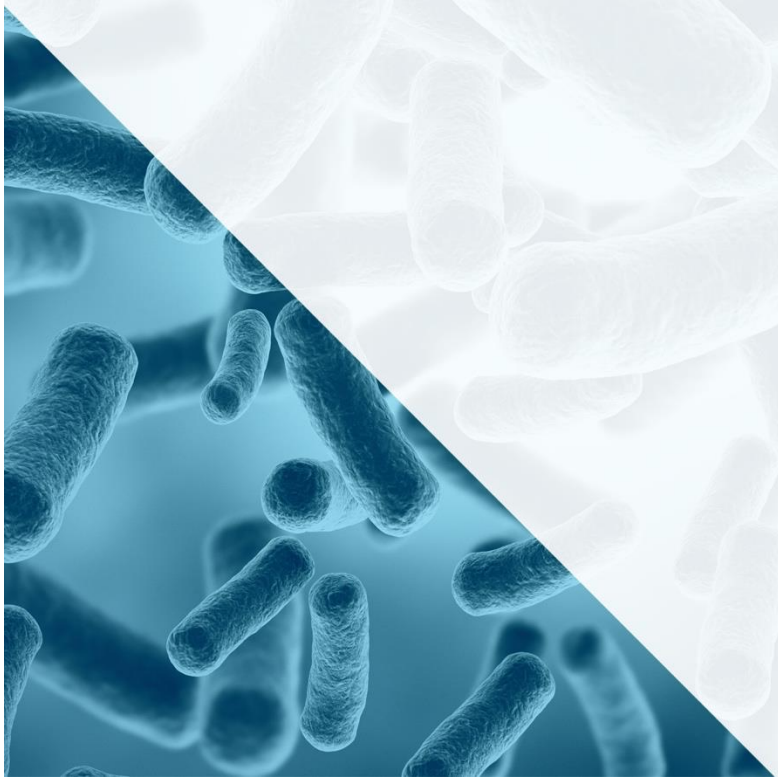

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List of abbreviations

AMR: AntiMicrobial Resistance

ECDC: European Centre for Disease Prevention

EJP: European Joint Programme

ESCMID: European Society for Clinical Microbiology and Infectious Diseases

EUCIC: EUropean Committee on Infection Control

EU-JAMRAI: EUropean Joint action on AntiMicrobial Resistance and healthcare Associated Infection

HCAI: HealthCare Associated Infection

IMI: Innovative Medicines Initiative

JPIAMR: Joint Programming Initiative on AntiMicrobial Resistance

MS: Member State

SRIA: Strategic Research and Innovation Agenda

UK: United Kingdom

WHO: World Health Organisation

WP: Work Package

Summary

Work package (WP) “Research and Innovation” aim is to contribute to a coordinated European response against antimicrobial resistance (AMR) by assisting Member States (MS) in devising policies to (i) prioritize, (ii) stimulate and (iii) utilize research and innovation related to AMR and healthcare associated infections (HCAI).

To ensure that One Health knowledge gaps are included as research priorities in the development of European Strategic Research Agendas and align with existing international AMR recommendations, the WP “Research and Innovation” has:

1. Identified research gaps in current European AMR research programmes with the help of seven voluntary countries through a mapping exercise.
   Identified gaps are:
   - Research on AMR within the environmental field
   - Research on AMR within the food chain context
   - Research on how to improve clinical trial efficiency
   - Applied research on IPC to support effective implementation
2. Compared identified gaps with existing multi-country research agenda to identify opportunities for complementary research priorities
3. Formulated and validated 16 infection prevention and control (IPC) research priorities.

We are confident that these 16 research priorities can favourably complement existing research agendas and provides important research opportunities to help European health systems to better prevent and control outbreaks, both in the community and healthcare setting, and limit the impact of future pandemics.

The EU-JAMRAI is now urging researchers, funding agencies, policymakers and relevant stakeholders to prioritise, fund, and research these identified gaps.

Introduction and objectives

WP “Research and Innovation” objectives

The main objective of the work package “Research and Innovation” is to contribute to a coordinated European response against antimicrobial resistance by assisting MS in devising policies to (i) prioritize, (ii) stimulate and (iii) utilize research and innovation related to AMR and HCAI.

This deliverable focuses on the first specific objective of the WP “Research and Innovation” whose overreaching goal is to ensure that One Health knowledge gaps are included as research priorities in the development of European Strategic Research Agendas and align with existing international AMR recommendations.

Publication of research priorities identified as gaps

To reach that objective, the WP “Research and Innovation” has worked extensively on the identification of gaps in existing European AMR related research programmes and the formulation of specific research priorities to (i) address the identified gaps and (ii) complement existing European Strategic Research Agendas. Results of this work should contribute to a strengthened process for European wide and international agreement on research and innovation priorities to meet the public health goals related to AMR and HCAI.

This document relates the process and results of this work.

Methodology

This work was carried out in 3 steps, allowing to:

- **Identify gaps** in AMR research programmes through a mapping exercise
- **Identify opportunities** for additional research priorities by comparing the mapping results with existing research agendas
- **Formulate and validate research priorities** complementing existing research agendas

Mapping of the European AMR research priorities to identify gaps

Gathering of national research priorities

Partners from the WP "Research and Innovation were asked to extract research priorities from their national action plan and translate them into English.

Requests were sent to partners from nine different countries: France, Greece, Italy, Netherlands, Norway, Slovenia, Spain, Sweden and the United Kingdom (UK).

Mapping exercise

All reports from responding countries were analysed using a systematic approach to cluster retrieved research priorities into various broader research areas. Using this clustering, a mapping of the European research priorities was ultimately implemented using a yes/no indicator (is country X reporting this research area as a research priority?)

This mapping exercise allowed to highlight the strengths and weaknesses of Europe in term of AMR related research.

Comparison of mapping results with existing research agendas to identify opportunities

Results of the mapping exercise were compared with the existing multi-country strategic research agendas to identify opportunities for additional complementary priorities addressing the identified gaps. For this comparison, we considered 3 multi-country strategic research agendas:

1- The Joint Programming Initiative on Antimicrobial Resistance (JPIAMR) Strategic Research and Innovation Agenda (SRIA) [1]
2- The Innovative Medicines Innovative (IMI) strategic research agenda (The right prevention and treatment for the right patient at the right time. Strategic Research Agenda for Innovative Medicines Initiative.) [2]
3- The One Health European Joint Programme (One Health EJP) strategic research agenda [3]

Formulation and validation of research priorities to complement existing research agendas

Formulation of IPC research priorities through a narrative literature review

To formulate research priorities, we performed a narrative literature review following a 4 steps framework including:

1- A grey literature analysis to narrow down our research
2- Targeted Pubmed research to formulate preliminary research priorities
3- An enrichment process to refine preliminary research priorities
4- The formulation of draft research priorities to be validated by experts from the field

We specifically excluded literature on vaccines since research priorities have already been documented in the Wellcome Trust and BCG "Vaccines to tackle drug resistant infections" [4] and literature on viral/parasitic diseases since our focus here is bacterial resistance.

This literature review aimed at identifying all research gaps in the field. Overlap with existing agenda was therefore possible.

More detail on the methodology used for this narrative literature review, including keywords used, are available in **Figure 2.A** (see page 14).

Validation by IPC experts through a survey analysis

Validation of the draft research priorities was performed through a survey analysis (Annex 2). The same survey was sent to two different groups of IPC experts to assess the level of emergency of each of the identified research priority and rank

them. Experts could also make comments on the research priorities we formulated and propose additional ones.

We choose to target two different groups of experts to assess inter-agreement on the most urging needs using statistical tools:

- the linearly weighted Cohen's kappa coefficient measuring the degree agreement between both groups on their sorting of research gaps (either no, low, medium, high or critical priority)
- the Kendall rank correlation coefficient measuring the degree agreement between both groups on their ranking of research gaps

The first group was composed of 18 European IPC experts chosen on the basis of their publication record or involvement in specific organisation making sure to have enough geographic diversity. This group included one "One Health" expert with expertise on both animal health and AMR in the environment. The second group targeted IPC experts from the European Committee on Infection Control group (EUCIC) from the European Society for Clinical Microbiology and Infectious Diseases (ESCMID). This group was only composed of human health experts.

Results

Mapping of the European AMR research priorities to identify gaps

Gathering of national research priorities

Seven out of the nine countries contacted sent back documents highlighting their national research priorities related to AMR (response rate 78%).

Mapping exercise

Analysis of the documents received from partners allowed to extract 38 research priorities which were ultimately clustered into 14 research areas. Using this clustering, we mapped back the research priorities of the seven responding countries.

Comprehensive analysis of the mapping exercise is presented in **Figure 1**. Extensive results of the mapping are available in Annex 1.

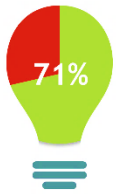
Figure 1: Results of the EU-JAMRAI European mapping of AMR related research priorities.

A. European current priorities.

All participating countries consider **fundamental research** on AMR as a priority (bacterial mechanisms involved, causes and consequences of the appearance and spread of resistance,…)

All participating countries consider **strengthening surveillance** as a priority

participating countries consider assessment of **best practices and strategies for antibiotic stewardship** as a priority



participating countries consider development of **antibiotics, alternatives to antibiotics or diagnostics** as a priority

B. Europe steadiness to structure and improve AMR research networks.

European steadiness to **structure and improve AMR research networks**

71% of the participating countries see **International/European research collaborations** as a priority

58% of the participating countries have developped a "**national steering committee**" to structure and coordinate research regarding AMR

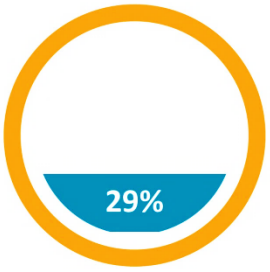
C. Europe could do better.

participating countries consider research on the **interaction of AMR with the veterinary sector** (transfer of resistances between animals and humans, dissemination of resistances, ...) as a priority

participating countries consider **involvement of socio-economic science** to improve knowledge of the critical aspects that lead to inappropriate use of antibiotics as a priority

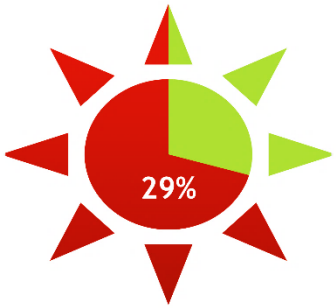
participating countries consider research on **new economic incentives** to foster innovation as a priority

D. Europe critical gaps.



Participating countries with research on cleansing measures or how to implement IPC programmes in the environment

Environmental field
------- STILL -------
left **BEHIND**



Participating countries with research on the drivers of resistance (disinfectants, biocides, manure, heavy metals...) in the environment

Only **1** out of **7**
--- countries ---
reports research on
CLINICAL TRIALS
--- efficiency ---

Laconic research
-- on the SPREAD --
of **resistance genes**
-- through FOOD --
or **IPC measures** in
-- the FOOD CHAIN --

E. The specific case of IPC.

All participating countries consider **implementation of IPC programmes** as a priority

Yet, both the ECDC and WHO have warned on the **dearth of evidence** on several IPC measures

participating countries considering the **investigation of IPC programmes effectiveness/cost-effectiveness** as a research priority

While providing interesting results, this mapping exercise also has some limitations. Only a handful of countries were engaged in the mapping activity and relevant gaps on AMR research priorities might have been missed due to low country participation. Furthermore Italy did not respond to our survey and Germany was excluded from the analysis (not a WP partner) meaning that only 3 of EU5 countries were considered in this mapping.

Highlights of the mapping exercise:

Three critical research gaps were identified:

- Research on AMR within the environmental field
- Research on AMR within the food chain context
- Research on how to improve clinical trial efficiency

While not being as alarming as the three mentioned before, the EU-JAMRAI is also concerned about the lack of research on the cost effectiveness and best way to implement IPC measures. As a result, sub-optimal IPC programmes, without the full capacity to prevent and handle pandemics, are implemented all around Europe. This has been further emphasised by the current Covid_19 pandemic.

Comparison of mapping results with existing research agendas to identify opportunities

Our analysis of the JPIAMR, IMI and One Health EJP research agendas revealed that the critical research gaps highlighted by our mapping exercise were fairly covered in multi-country strategic research agendas:

- Research on AMR in the environmental field is one of the pillars of the JPIAMR SRIA
- Research on AMR in the food chain context is covered by the One Health EJP research agenda which provides research opportunities to prevent foodborne zoonoses and prevent the transmission of AMR within the food chain
- Research on how to improve clinical trial efficiency is covered by the IMI research agenda which has launched several initiatives like the COMBACTE project to meet the challenges of clinical development of antimicrobials.

Regarding IPC, the JPIAMR SRIA outlines six research priorities of which three address IPC on a general level. Given the importance of IPC in health systems and the dearth of evidence in the field, we can clearly see an opportunity here for the development of specific IPC research priorities. It would advantageously complement the existing multi-country strategic agendas while providing evidence for health systems to better prevent and handle pandemics both in the community and healthcare setting.

Highlights of the comparison exercise:

The three critical research gaps, identified in the mapping exercise, are well covered in the existing multi-country research agendas meaning that clear research directions and opportunities are available to address these gaps in the future years.

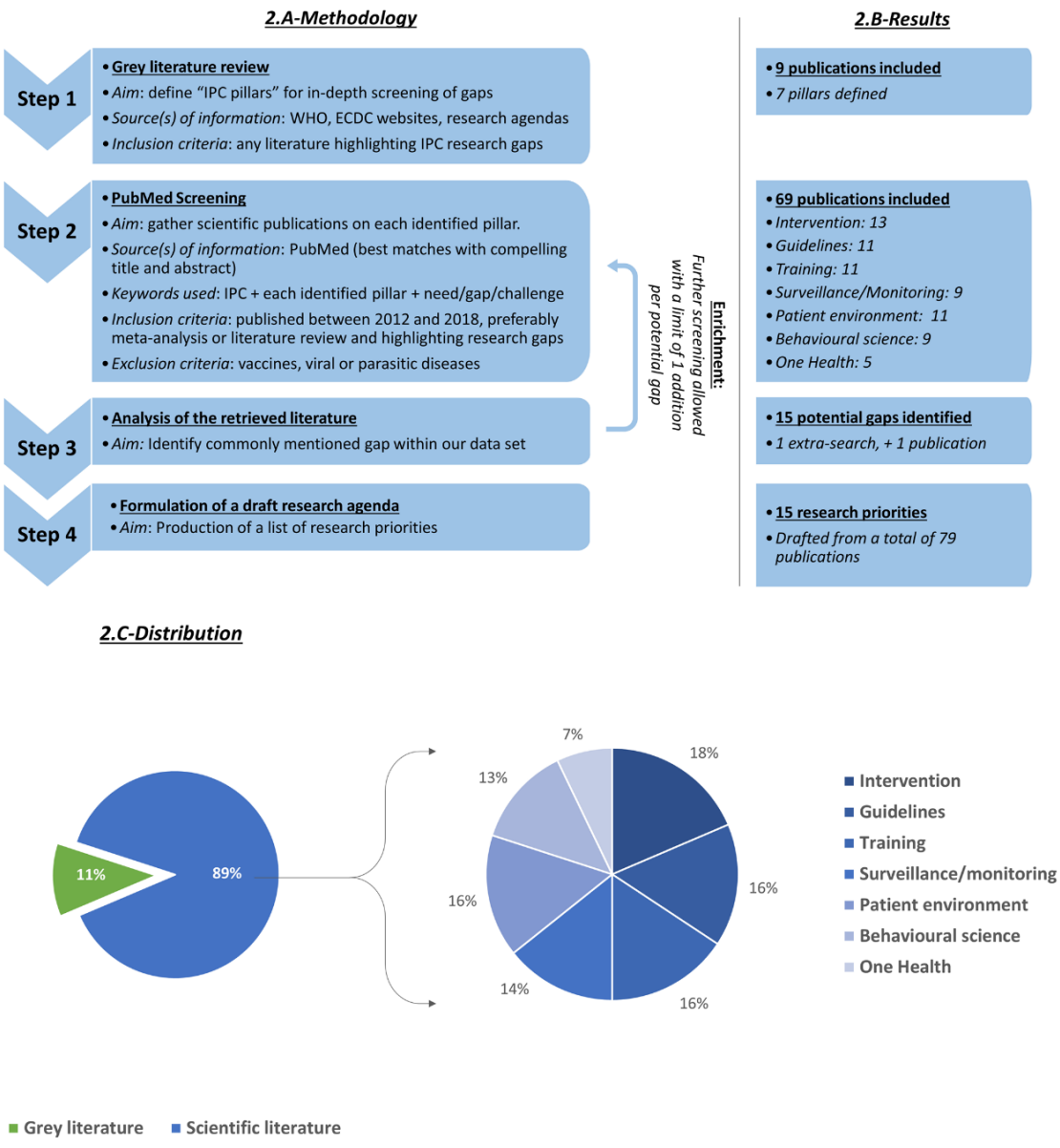
On the other hand, additional IPC-related research priorities would be a valuable addition to the existing research agendas and would help countries to better prevent and handle outbreaks.

Formulation and validation of IPC research priorities to complement existing research agendas

Formulation of IPC research priorities through a narrative literature review

The literature review was performed in December 2018. 79 publications were used to identify research gaps and formulate 15 IPC research priorities. They were clustered in 7 sub-topics (**Figure 2.B and 2.C**).

Figure 2: Overview of the 4-step narrative review framework used to build the draft IPC research priorities.



2.A-Methodology. A 4-step framework was used to perform the literature review and build the draft research priorities.

2.B-Results. 79 publications were retrieved from the literature review.

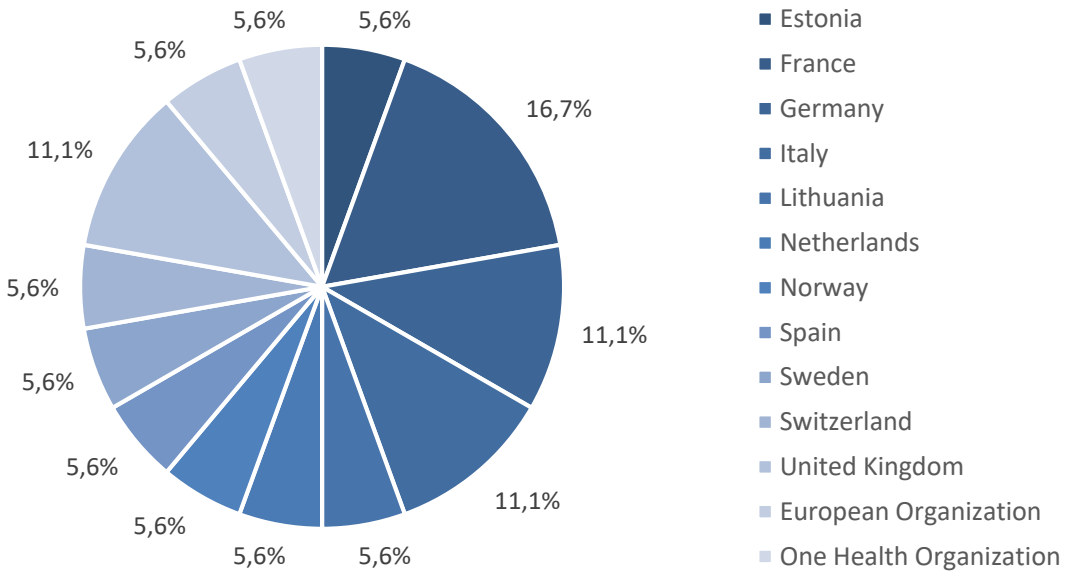
2.C-Distribution. Overall, publications were fairly distributed between pillars. We also make sure to include One Health literature in our analysis.

The 15 IPC research priorities extracted from this literature review are presented in **Table 1** (see page 17).

Validation by IPC experts through a survey analysis

44 experts were consulted through our survey. They were clustered in two groups. The first group was composed of 18 IPC experts from 11 European countries who were surveyed from February to March 2019. Diversity of this panel is presented in **Figure 3**.

Figure 3: Diversity within the first IPC expert target group.



This group contains 18 IPC experts from 11 European countries and 2 relevant organizations, one European organization working on infectious diseases control and one organization working on the animal and environmental field (referred as One Health organisation in the chart pie).

The second group targeted human health experts from the EUCIC group. The survey was distributed in September 2019 upon agreement with the EUCIC Executive Board. For the first group, we got a response rate of 61% (11/18 respondents). For the second group, 33 IPC experts responded to our survey through an open link posted on the EUCIC website.

Survey results tended to validate our attempt at building a list of truly important IPC research needs with (i) no research gap below the medium priority category on average, (ii) mostly supportive and informative comments on research gaps, (iii) only few requests for additions to the list. Feedback from experts also allowed to identify an additional research gap on the interaction between the human and hospital microbiomes (mentioned by 9% of experts) leading to the final formulation of 16 IPC research priorities presented in **Table 1** below.

Table 1: EU-JAMRAI research priorities on IPC:

Research priorities	*Priority ranking*
Composition and impact of IPC programmes	
1. There is a lack of high-quality studies addressing the effectiveness of IPC programmes, including their impact, cost-effectiveness, and ideal composition	4
IPC guidelines evaluation and implementation	
2. Many best practice IPC recommendations are based upon weak evidence. For example, the World Health Organization identified, in its Global Guidelines for the Prevention of Surgical Site Infection, 20 recommendations with a "low" quality of evidence. The evidence base supporting IPC guidelines needs to be strengthened.	6
3. Situational analyses in different settings (high, medium or low-income countries) but also different healthcare settings (ICU, short or long stay, medico-social facilities) are needed to better adapt IPC guidelines.	7
4. A better understanding of the different patient screening strategies is needed for risk management. This includes who should be screened, when (start/stop of screening), and how movement between healthcare institutions should trigger screening. Research should include both clinical impact and cost-effectiveness.	9
Training	
5. Additional tools are needed to evaluate IPC training programmes and implement them.	14
6. New innovative ways of training should be evaluated (e-learning, simulation, self-directed training modules or mentorship). There is a lack of study on the impact of these innovative training tools on the practice change and HAI rate in healthcare facilities.	8
7. Minimal standard requirements for the recruitment and training of IPC professional should be investigated and refined.	13
Surveillance and monitoring	
8. Research is needed to assess and validate the reliability of surveillance based on available patient clinical information (syndromic-based surveillance) rather than microbiological data or prescription databases.	11
9. There is a lack of published standards to monitor IPC practices beyond hand hygiene. Evidence-based standardized audit protocols need to be created addressing, for example, catheter related bloodstream/urinary tract infections or ventilator associated pneumonia as well as surgical site infections.	5

10. There are several innovative, new methods to monitor compliance to IPC practices, including electronic and infrared approaches for example. These need to be tested in multiple settings to assess their value for IPC programmes.	15
Impact of patient environment on HCAI and AMR reduction	
11. Insufficient data are available on the impact of infrastructural changes at the facility level on the reduction of HCAI and AMR (accessibility to specific equipment, density of hand washing points, single room, facilitation of care circuits, and more).	3
12. Research is needed to explore the impact of patient-to-bed ratio on the spread of HCAI and AMR, including instances of overcrowding. This should include analyses of staff workload, available staffing (including presence of infection control professionals), bed occupancy, and visitor frequency.	2
13. Research is needed to study the interaction between human and hospital microbiome.*	n/a
Behavioural science	
14. Studies are needed to assess the demographic, organizational, economic, sociological, and behavioural barriers/facilitators for the implementation of effective IPC programmes.	1
15. Patients and their family are key elements in the chain of transmission in healthcare facilities. Studies addressing the impact of patient and family-oriented education and communication campaign (involving patients associations) on the rate of HCAI are needed.	10
One Health	
16. Research is needed to assess the impact of IPC measures in different operational contexts including small/industrial farms, feedlots, slaughterhouses, fish farms… Tested measures may include the density of the animal populations as well as the infection control measures taken by workers (vaccination, hand hygiene, antibiotic use…).	12

*Through our literature review, we extracted a list of 15 IPC research priorities. They are presented in the first column of this table. Each of them was surveyed by two groups of IPC experts. Experts were asked how urgent each of the identified gaps was. Based on survey results we ranked the priorities from the most (ranked 1) to the less urgent one (ranked 15). The survey also allowed to identify an additional research priority. It is highlighted by a * mark in the table. For this additional priority, no ranking could be provided since added after survey consultation.*

Overall agreement between both expert groups was average (Cohen's κ = 0.21 and Kendall's τ = 0.43) but with strong alignment on the highest priorities:

- Priority #14 on the **assessment of organizational, socio-economic, and behavioural barriers/facilitators for the implementation of IPC programmes** (ranked first by both groups),
- Priority #12 on the **impact of overcrowding on the spread of infections** (ranked second by both groups),
- Priority #11 on the **impact of infrastructural changes, at the facility level, on the reduction of infection** (ranked 5th and 3rd by each group).

Also, overall inter-agreement between experts might have been underestimated in our analysis since Cohen's κ have been shown to be naturally lower when computing more than three categories (five in our survey).

Interestingly, some of the research gaps we highlighted in this study are mentioned in the JPIAMR SRIA. Priority #14, the top priority in the field, is notably covered in the SRIA meaning that JPIAMR funds might be available for researchers to address this gap. Other two top priorities are however absent from existing agendas.

Some limitations of our survey analysis include the small number of respondents (44) and the under-representation of animal and environmental IPC experts in our panel. Under-representation of animal and environmental IPC experts in the survey might have further undervalued the priority of this research aspect.

Despite limitations, we are confident that the 16 research priorities presented in **Table 1** can favourably complement existing research agendas and provides important research opportunities to help European health systems to better prevent and control outbreaks and limit the impact of future pandemics. The EU-JAMRAI is now urging researchers, funding agencies, policymakers and relevant stakeholders to prioritise, fund, and research these identified gaps.

Highlights:

IPC can be one of the most cost-effective interventions to guard against AMR [5]. It is also essential to improve overall health outcomes at healthcare institutions. Therefore, it is remarkable that the research needs of IPC have been to date undervalued in existing research agendas.

To address this issue, the EU-JAMRAI has developed a list of sixteen IPC research priorities, supported by experts which includes three urgent needs (**Table 1**). We now encourage researchers, funding agencies, policymakers and relevant stakeholders to prioritise, fund, and research these identified gaps.

Conclusions

To ensure that One Health knowledge gaps are included as research priorities in the development of European Strategic Research Agendas and align with existing international AMR recommendations, the WP "Research and Innovation" has:

1. Identified research gaps in current European AMR research programmes, namely:
    - Research on AMR within the environmental field
    - Research on AMR within the food chain context
    - Research on how to improve clinical trial efficiency
    - Applied research on IPC to support effective implementation
2. Compared identified gaps with existing multi-country research agenda to identify opportunities for additional complementary research priorities
3. Formulated and validated 16 IPC research priorities presented in Table 1.

We are confident that these 16 research priorities can favourably complement existing research agendas (JPIAMR, IMI and One Health-EJP ones as well as the Wellcome Trust and BCG "Vaccines to tackle drug resistant infections") and provides important research opportunities to help European health systems to better prevent and control outbreaks and limit the impact of future pandemics.

To ensure visibility to these important results, the WP "Research and Innovation" has written both a scientific article (under revision, will be uploaded later) and a policy brief (Annex 3) to respectively target researchers and policymakers.

The EU-JAMRAI is now urging researchers, funding agencies, policymakers and relevant stakeholders to prioritise, fund, and research these identified gaps.

This work also provided the opportunity for the EU-JAMRAI to work hand in hand with the JPIAMR and the EUCIC group, allowing to strengthen European collaboration on AMR related research questions.

Acknowledgements

The WP “Research and Innovation” deeply thanks all its partners for their input, feedback and commitment along the project. We are also grateful to people from the JPIAMR, especially Patriq Fagerstedt and Laura Marin, as well as people from the EUCIC group, notably Evelina Tacconelli and Nico Mutters. Finally, we would like to thank all IPC experts who accepted to answer our survey.

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Annexes

Annex 1: Mapping the AMR-related research priorities of 7 European countries.

WP9 partners were asked to extract research priorities from their national action plan and translate them into English. Requests were sent to partners from nine different countries: France, Greece, Italy, Netherlands, Norway, Slovenia, Spain, Sweden and United Kingdom

Seven out of the nine countries sent back documents highlighting their national research priorities. All reports from responding countries were analyzed by INSERM. This analysis led to the extraction of 38 research priorities clustered into 14 sub-topics.

Using this clustering, a mapping of the research priorities of the seven responding countries has ultimately been implemented. It is presented in the table below.

How to read this table:

38 research priorities have been extracted from the documents sent by our partners.

Research priorities have then been clustered into 14 sub-topics (each associated with a different color).

A green cell means that a specific country (column) has identified a specific topic (row) as one of its national priorities.

Text in boxes is meant to give information on each country interest or top priority.

Disclaimers:

This chart only represents the priorities explicitly addressed in the documents sent by our partners. A white box doesn't mean a country is not doing any research on a specific subject, but that this subject is not a priority in that country.

		Country						
		France	**Greece**	**Netherlands**	**Norway**	**Slovenia**	**Spain**	**UK**
Incentives	*Work on new economic incentives or funding to foster research and innovation*	Others incentives		More funding	More funding		Other incentives	Other incentives
Interaction	*Work to encourage International/European research collaborations*							
	Work to encourage private/public research collaborations							
	Work to encourage interdisciplinary research collaborations							
Structuring	*Development of a "national steering committee" to structure and coordinate actions regarding AMR*							
Development of new tools	*Development of new antibiotic molecules*							
	Development of new alternatives to antibiotics (vaccine, phages, antibodies, peptides …)							
	Development of new diagnostic tools							
Fundamental research	*Research on the bacterial mechanisms involved in resistance*							
	Research on the causes and consequences of the appearance and dissemination of AMR							
	Other specific research unrelated to animals nor environment	*Clostridium difficile*		membrane biogenesis, microbial ecology	continued carriage, microbial ecology			microbiome
	Investigating new technologies to help developing antimicrobial molecules or diagnostic tools.	artificial intelligence		synthetic biology				genomic technologies
IPC in healthcare	*Implementation, testing and evaluation of diverse IPC measures in the human health sector*	**Research**	Intervention	**Research**	**Research**	Intervention	**Research**	Intervention
Antibiotic stewardship	*Implementation, testing and evaluation of new measures for practitioner to improve their use of antibiotics*							
	Research of new treatment strategies or ways of using known antibiotics (combination therapy, optimal dosing regimens, …)							
Surveillance	*Strengthen surveillance and monitoring of AMR (human, animal or environmental surveillance)*							
	Develop new tools to facilitate the communication of surveillance data							
Training	*Strengthen the training and education of practitioners (human/animal medicine) or patient*							
Clinical trials	*Research on how to create a high-quality clinical and laboratory trial network in Europe to optimize clinical trials*							
	Development of cutting edge predictive technologies to assess how well a molecule might behave as a drug			Organ on chip, zebrafish				

		France	Greece	Netherlands	Norway	Slovenia	Spain	UK
Socio-economic science	*Improve knowledge of the critical aspects that lead to inappropriate use of antibiotics*							
	Evaluate the socioeconomic consequences of antibiotic resistance							
	Evaluate the socioeconomic consequences of inappropriate antibiotic prescriptions (too much or too little antibiotics)							
	Improve knowledge of the quality of therapeutic care in primary and hospital care							
	Evaluate the impact of behavioural changes or interventional measures within and beyond the health care setting on AMR							
Animal sector	*Research on the interaction of AMR with the veterinary sector (transfer of resistances between animals and humans, dissemination of resistances, …)*							
	Research of new antibiotics for use in veterinary medicine							
	Improve understanding of the critical factors that lead to a high consumption of antibiotics in farms							
	Evaluate the impact of food additives used in animal feeds (copper, zinc, coccidiostats, …) on the AMR							
	Implementation, testing and evaluation of diverse IPC measures in the veterinary sector							
Environmental sector	*Research on the interaction of AMR with the environment (transfer of resistances between the environmental bacteria and human pathogens, dissemination of resistances, …)*							
	Explore the effect of different drivers of resistance (disinfectants, biocides and heavy metals, …) in nature							
	Explore the impact of fertilizers, especially manure, on the spread of AMR							
	Investigate the cost-effectiveness of cleansing environment measures							
	Implementation, testing and evaluation of diverse IPC measures in the environmental sector							
Food chain sector	*Improve knowledge about the spread of resistance genes through food*							
	Assess the need of new infection control measures in the overall food chain							
	Assess the need of new recommendation concerning kitchen hygiene and risk communication on food handling							

Annex 2: EU-JAMRAI survey on IPC research priorities.

EU-JAMRAI - Research priorities for Infection Prevention and Control (IPC)

The EU Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI) is undertaking a survey to identify the research priorities of Infection Prevention and Control (IPC). The aim of this survey is to develop an IPC research agenda that can inform research funders of the pressing research needs of IPC.

As member of the ESCMID/EUCIC group, we would greatly appreciate if you could take few minutes to complete this survey. We estimate that it will take approximately 10-15 minutes. Your responses will be treated confidentially.

If you have any questions, please feel free to contact Dr. Yohann Lacotte (yohann.lacotte@inserm.fr) or Dr. Christine Årdal (chaa@fhi.no).

Thank you!

* 1. **In your opinion, what priority level are the following research gaps?**

	Not a priority	Low priority	Medium priority	High priority	Critical priority	I don't know
1. There is a lack of high quality studies addressing the effectiveness of hospital-based IPC programmes, including the impact, cost-effectiveness, and ideal composition of IPC programmes.	○	○	○	○	○	○
2. Many best practice IPC recommendations are based upon weak evidence. For example, the World Health Organization identified, in its Global Guidelines for the Prevention of Surgical Site Infection, 20 recommendations with a "low" quality of evidence such as, for example, for the optimal timing for preoperative surgical antibiotic prophylaxis. The evidence base supporting IPC guidelines needs to be strengthened.	○	○	○	○	○	○
3. Situational analyses in different settings (high, medium or low-incomes countries) but also different healthcare settings (ICU, short or long stay, medico-social facilities) are needed to better understand potential adaptations of IPC guidelines.	○	○	○	○	○	○
4. A better understanding of the different patient screening strategies is needed for risk management. This includes who should be screened, when (including start and stop of screening), and how movement between healthcare institutions should trigger screening. Research should include both clinical impact and cost-effectiveness.	○	○	○	○	○	○
5. Additional tools are needed to evaluate ICP training programmes and implement them.	○	○	○	○	○	○
6. New innovative ways of training should be evaluated such as e-learning, simulation, self-directed training modules or mentorship for ICP education. There is a lack of study on the impact of these innovative training tools on the practice change and HAI rate in healthcare facilities.	○	○	○	○	○	○
7. Minimal standard requirements for the recruitment and training of ICP professional should also be investigated.	○	○	○	○	○	○

8. Research is needed to assess and validate the reliability of surveillance based on available patient clinical information (syndromic-based surveillance) rather than microbiological data or prescription databases, i.e., data gathered for other primary purposes.

9. There is a lack of published standards to monitor IPC practices beyond hand hygiene. Evidence-based standardized audit protocols need to be created addressing, for example, catheter related bloodstream/urinary tract infections or ventilator associated pneumonia.

10. There are a number of innovative, new methods to monitor compliance to IPC practices, including electronic and infrared approaches for example. These need to be tested in multiple settings to assess their value for IPC programmes.

11. Insufficient data are available on the impact of infrastructural changes at the facility level on the reduction of HCAI and AMR (accessibility to specific equipment, density of hand washing points, single room, facilitation of care circuits, and more).

12. Research is needed to explore the impact of patient-to-bed ratio on the spread of HCAI and AMR, including instances of overcrowding. This should include analyses of staff workload, available staffing (including presence of infection control professionals), bed occupancy, and visitor frequency. Ideally, studies would be performed in high, medium, and low-resource settings but also in different healthcare settings (ICU, short or long stay, medico-social facilities).

13. Studies are needed to assess the demographic, organizational, economic, sociological, and behavioral factors facilitating success but also the barriers and challenges to implement effective IPC programmes.

14. Patients and their family are key elements in the chain of transmission in the healthcare facilities. Studies addressing the impact of patient and family-oriented education and communication campaign (involving patients associations) on the rate of HCAI are lacking.

15. Research is needed to assess the impact of IPC measures in different operational contexts including small farms, industrial farms, feedlots, slaughterhouses, fish farms, and more. IPC measures may include the density of the animal populations as well as the infection control measures of the workers (vaccination, hand hygiene, antibiotic use and more).

2. **If you have a suggestion for another formulation or comments on the listed research priority, please write it below.**

1. There is *a* lack of high quality studies addressing the effectiveness of hospital-based IPC programmes, including the impact, cost-effectiveness, and ideal composition of IPC programmes.

2. Many best practice IPC recommendations are based upon weak evidence. For example, the World Health Organization identified, in its Global Guidelines for the Prevention of Surgical Site Infection, 20 recommendations with a "low" quality of evidence such as, for example, for the optimal timing for preoperative surgical antibiotic prophylaxis. The evidence base supporting IPC guidelines needs to be strengthened.

3. Situational analyses in different settings (high, medium or low-incomes countries) but also different healthcare settings (ICU, short or long stay, medico-social facilities) are needed to better understand potential adaptations of IPC guidelines.

4. A better understanding of the different patient screening strategies is needed for risk management. This includes who should be screened, when (including start and stop of screening), and how movement between healthcare institutions should trigger screening. Research should include both clinical impact and cost-effectiveness.

5. Additional tools are needed to evaluate ICP training programmes and implement them.

6. New innovative ways of training should be evaluated such as e-learning, simulation, self-directed training modules or mentorship for ICP education. There is a lack of study on the impact of these innovative training tools on the practice change and HAI rate in healthcare facilities.

7. Minimal standard requirements for the recruitment and training of ICP professional should also be investigated.

8. Research is needed to assess and validate the reliability of surveillance based on available patient clinical information (syndromic-based surveillance) rather than microbiological data or prescription databases, i.e., data gathered for other primary purposes.

9. There is a lack of published standards to monitor IPC practices beyond hand hygiene. Evidence-based standardized audit protocols need to be created addressing, for example, catheter related bloodstream/urinary tract infections or ventilator associated pneumonia.

10. There are a number of innovative, new methods to monitor compliance to IPC practices, including electronic and infrared approaches for example. These need to be tested in multiple settings to assess their value for IPC programmes.

11. Insufficient data are available on the impact of infrastructural changes at the facility level on the reduction of HCAI and AMR (accessibility to specific equipment, density of hand washing points, single room, facilitation of care circuits, and more).

12. Research is needed to explore the impact of patient-to-bed ratio on the spread of HCAI and AMR, including instances of overcrowding. This should include analyses of staff workload, available staffing (including presence of infection control professionals), bed occupancy, and visitor frequency. Ideally, studies would be performed in high, medium, and low-resource settings but also in different healthcare settings (ICU, short or long stay, medico-social facilities).

13. Studies are needed to assess the demographic, organizational, economic, sociological, and behavioral factors facilitating success but also the barriers and challenges to implement effective IPC programmes.

14. Patients and their family are key elements in the chain of transmission in the healthcare facilities. Studies addressing the impact of patient and family-oriented education and communication campaign (involving patients associations) on the rate of HCAI are lacking.

15. Research is needed to assess the impact of IPC measures in different operational contexts including small farms, industrial farms, feedlots, slaughterhouses, fish farms, and more. IPC measures may include the density of the animal populations as well as the infection control measures of the workers (vaccination, hand hygiene, antibiotic use and more).

3. **Are there additional IPC research priorities that should be included?**

Send responses

Annex 3: EU-JAMRAI policy brief on IPC research priorities.

Policy brief:

The urgent need to foster research on infection prevention and control to improve health security

The problem

Effective Infection Prevention and Control (IPC) measures are necessary to control the spread of infections, like Covid-19, as well as reduce the incidence of healthcare-associated and community-acquired infections. Fewer infections result in lower consumption of antibiotics, thereby reducing antibiotic resistance. Yet, despite the critical importance of IPC measures, its research needs are often neglected.

As Covid-19 has demonstrated to the world, the only steps that can be taken to control the spread of a novel virus with pandemic potential are effective Infection Prevention and Control (IPC) measures, like handwashing, social distancing, and even isolation. In non-pandemic times IPC measures are also critical to reduce the incidence of infections and limit the spread of infections. Every year more than 2.5 million healthcare-associated infections occur in the European Union and European Economic Area, causing millions of extra days of hospital stays.[1] Fewer infections result in lower consumption of antibiotics, thereby reducing antibiotic resistance.

Effective IPC measures go well beyond handwashing. Ideally IPC should be designed into any new healthcare facility. For instance, purchases of sinks, showers, or bathtubs in healthcare institutions should include an analysis of the evidence of how easily they can be disinfected. Placement and design of hand sanitisers should be based upon evidence of where healthcare personnel are most likely to use them. Avoidance of ventilator-associated infections should be based on evidence for sterilising both the equipment and insertion site. IPC evidence is crucial, but scarce. When IPC research projects compete for funding against other thematic areas, like breakthrough technologies to combat climate change, big data against social inequities, or potential new cancer treatments, they are often perceived as dull, receiving low innovation marks.

This neglect is apparent in the evidence available. Many IPC guidelines are based upon weak scientific evidence.[2,3] The research priorities of IPC are often neglected in important international research agendas. Many countries do not identify IPC research as important in hindering the spread of antibiotic resistance.[4] In this regards, many countries implement a bundle of IPC interventions without knowing which ones are the most cost-effective for their particular context.

The recommendation

With European IPC experts the EU-JAMRAI has developed a list of IPC research priorities. Financing these research priorities is critical to strengthening infection prevention and control.

The lack of IPC research may be due to a global lack of awareness of the most urgent IPC needs and knowledge gaps. To address this issue, the European Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections (EU-JAMRAI) has developed a list of IPC research priorities (overleaf), based upon existing scientific literature and validated by European IPC experts including few One Health ones.[5] The most urgent priorities are in bold text. We urge policymakers, research funders, academics, and industry to adopt and prioritise these research needs. **Investment will have wide-ranging benefits, including lowering the number of hospitalised patients, hindering antibiotic resistance, and strengthening global health preparedness for the next pandemic.**

Interventions

1. There is a need of high-quality studies addressing the effectiveness of hospital-based IPC programmes, including their impact, cost-effectiveness, and ideal composition.

Guidelines

2. Many best practice IPC recommendations are based upon weak evidence. For example, the World Health Organization identified, in its Global Guidelines for the Prevention of Surgical Site Infection, 20 recommendations with a “low” quality of evidence. The evidence base supporting IPC guidelines needs to be strengthened.
3. Situational analyses in different settings (high, medium or low-incomes countries) but also different healthcare settings (intensive care units, short or long stay, medico-social facilities) are needed to better understand potential adaptations of IPC guidelines.
4. A better understanding of the different patient screening strategies is needed for risk management. This includes who should be screened, when (including start and stop of screening), and how movement between healthcare institutions should trigger screening. Research should include both clinical impact and cost-effectiveness.

Training

5. Additional tools are needed to evaluate IPC training programmes and implement them.
6. New innovative ways of training should be evaluated such as e-learning, simulation, self-directed training modules or mentorship for IPC education. There is a lack of study on the impact of these innovative training tools on the practice change and infection rate in healthcare facilities.
7. Minimal standard requirements for the recruitment and training of IPC professionals should be investigated.

Surveillance and monitoring

8. Research is needed to assess and validate the reliability of surveillance based on available patient clinical information (syndromic-based surveillance) rather than microbiological data or prescription databases, i.e., data gathered for other primary purposes.
9. There is a lack of published standards to monitor IPC practices beyond hand hygiene. Evidence-based standardised audit protocols need to be created addressing, for example, catheter-related bloodstream/urinary tract infections and ventilator-associated pneumonia.

10. There are a number of innovative, new methods to monitor compliance to IPC practices, including electronic and infrared approaches. These need to be tested in multiple settings to assess their value for IPC programmes.

Patient environment (facilities and staffing)

11. **Insufficient data are available on the impact of infrastructural changes at the facility level on the reduction of infections and resistance. This includes the accessibility to specific equipment, density of hand washing points, availability of single occupancy rooms, and more.**
12. **Research is needed to explore the impact of patient-to-bed ratio on the spread of infections and resistance, including instances of overcrowding. This should include analyses of staff workload, available staffing (including presence of IPC professionals), bed occupancy, and visitor frequency.**
13. Research is needed to study the interaction between the human and hospital microbiome.

Behavioural science

14. **Studies are needed to assess the demographic, organizational, economic, sociological, and behavioural factors facilitating success but also the barriers and challenges to implement effective IPC programmes.**
15. Patients and their families are key elements in the chain of transmission in healthcare facilities. Studies addressing the impact of patient and family-oriented education and communication campaigns (involving patients associations) on the rate of hospital-acquired infections are needed.

One Health

16. Research is needed to assess the impact of IPC measures in different operational contexts including small farms, industrial farms, feedlots, slaughterhouses, fish farms, and more. Tested measures may include the density of the animal populations, vaccinations and antibiotic use in animals, as well as the infection control measures taken by workers.

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Joint Action on Antimicrobial Resistance and Healthcare-Associated Infections

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