EU-JAV
EUROPEAN JOINT ACTION ON VACCINATION

Vaccine research and development: prioritization and funding at a Europe scale

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Background

- The objective of EU-JAV is to find the ways to **increase vaccine coverage** and therefore defining research questions that aim to reach this goal is a key question

- With the great diversity of possible topics, in a context of ***limited resources***, ***prioritizing*** research questions becomes a necessity.

- The ***research funding*** system in Europe is still **very complex**, involves many actors and is ***fragmented***

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Aims

- Report on guidelines / best practices to establish priorities for vaccine and vaccination research to increase vaccination coverage
  - ✓ In the specific context of vaccination, this selection process must be carried out rigorously, in accordance with best practices.
  - ✓ This process focus on ***public health research*** aiming at improving vaccine coverage, and not on R&D aiming at developing novel vaccines. Many of the subjects to be prioritized will therefore most likely concern epidemiology, human and social sciences as well as implementation research.
  - ✓ The objective was to implement a process leading to ***evidence-based and transparent*** definition of research priorities in Europe in the field of vaccination research

- Potential mechanisms to increase collaboration in vaccine and vaccination research and cooperation for funding these programmes among MS
  - ✓ Need to better understand different organizations priorities and EU MS use of financing mechanism on vaccine and vaccination research
  - ✓ Review of joint and collaborative EU funding mechanism
  - ✓ Understand opinions on mechanisms to fund and collaborate on shared funding for common priorities of research in vaccination

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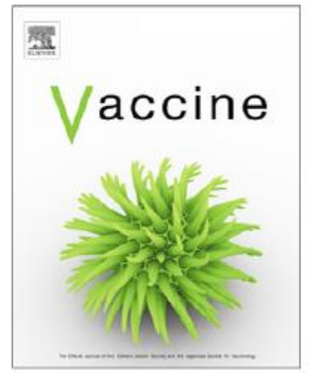
Prioritization framework

- Framework based on a ***multi-criteria decision analysis*** inspired from the Child Health and Nutrition Research Initiative (CHNRI) by Rudan et al (*Child Health and Nutrition Research Initiative; 2006)*
- The general principle of the framework is that each research proposition is assessed through a series of steps

Selecting of the managing team (MT)	• WP7.1 team • Inclusion of an expert in applied informatics
Definition of the scope of the process	• Research to increase vaccination coverage in the EU population
Definition of research questions	• Broad web-based consultation / Direct sollicitation of relevant experts • Consolidation of a final list of research questions to prioritise
Choice of criteria	• First proposition by the MT based on CHNRI criteria • Web-based meeting to reach a consensus on them
Weighting of criteria	• Web-based survey to ask experts to perform pairwise comparison • Web-based meeting to reach a consensus on weighting
Scoring of research propositions	• Web-based survey to gather individual expert's rating of each research question using the various criteria • Virtual meeting to reach consensus

General principles throughout the project

- Participating experts should be the most representative as possible
- Involvement of different experts at each step
- To ensure transparency sollicitation of an independent observer



Francis-Oliveiro F et al « Research priorities to increase vaccination coverage in Europe (EU joint action on vaccination » **Vaccine,** 2021

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First annual list focusing on four pilot vaccines *(Influenza, Measles containing vaccine, HPV and pertussis)*

- Assess and compare strategies for systematic ***measles vaccination catch-up*** in adolescence/adulthood for people who missed vaccination during childhood, in view of increasing immunity against measles in the population;
- Perform a review of evidence and impact of various social media interventions on the perception of ***HPV vaccination*** in adolescents and their close adult parents/guardians
- Explore the acceptability of the systematic use of tetravalent (D-T-Polio + ***Pertussis***) vs trivalent (D-T-Polio) for revaccination during adulthood;
- Investigate the effectiveness of various ***influenza vaccine*** formulations and products (live attenuated, high-dose, adjuvanted, quadri- vs tri-valent, cell-based, recombinant) in key target groups, i.e. (very) young children >65, frail and institutionalised older persons;
- Evaluate the effectiveness of vaccinating children of various ages on ***protecting vulnerable persons*** (in particular elderly family members) against ***influenza***;
- Investigate across Europe whether and to what extent ***authorising pharmacists*** to administer seasonal influenza vaccine to the general population increases influenza vaccination coverage.

	General	Influenza	Pertussis	Measles combination	HPV	Total
Human and Social sciences	24	13	2	4	7	48
Clinical research	0	9	3	0	1	9
Epidemiology	3	6	8	6	1	21
Other	24	5	2	2	1	34
Total	51	33	14	12	10	124

Health Programme under Grant Agreement no. 801493.

Second annual list focusing on COVID19 vaccines

- Study whether – as compared with other new vaccines - the ***centralised purchasing and distribution*** method used in the EU has helped to reduce inequalities or access difficulties among and within countries and should therefore be generalised in case of a new pandemic

- Generate evidence to optimise vaccine strategies for people with ***underlying conditions*** including immunodeficiency (additional dose, double dose, cocooning) – Covid-19

- Study which are the appropriate diagnostic tests to ***track persistence/decline of immunity***, and guide re-immunisation policy in subsequent years? – Covid-19

- Analyse the different vaccination strategies implemented in European countries and ***model these strategies in terms of impact*** (on mortality, hospitalisation, economic indicators)

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- Analyse and detail the determinants of ***Covid-19 vaccine hesitancy*** and to assess whether they are different from those identified for other vaccines

Questions
n= 35

General
n = 8

COVID19
social sciences n = 16
biological sciences n= 11

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Lessons and recommendations regarding the different steps

1. Selecting managers and experts

Methodological recommendations:

Ensure a diversity of expertise in the pool of experts

Associate as far as possible an external observer to ensure transparency

2. Definition of the context/scope of the process

Methodological recommendation:

The scope should be presented and explained as often as necessary in order to avoid submission of out-of-scope research questions and to support an objective and appropriate assessment from experts

3. Identification of proposed health research options/questions

Methodological recommendation:

As much as possible, use live events such as conferences to target relevant stakeholders to ensure good understanding of the scope of the process and increase response rate.

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Lessons and recommendations regarding the different steps

4. Choice of criteria

Methodological recommendation:

As experts will assess each research option/question based of a set number of weighted criteria, it is very important to ensure that these criteria are unambiguous and understandable.

5. Weighting of criteria

Methodological recommendation:

A meeting to get a to final consensus on weights was necessary to highlight potential misunderstanding regarding criteria.

6. Final ranking

Methodological recommendation:

This meeting need to be rigorously led to ensure that: All experts express their opinion when necessary - All research questions will be discussed

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Main findings from the national research organizations on funding

EU funding mechanisms and collaboration in vaccine research and development and vaccination research are very fragmented and complex

Funding of research and development as well as vaccination research is not evenly distributed along the value chain

Key focus areas:

- General research and development of vaccines
- Basic research
- Pre-clinical development

- Some financed research on influenza, pandemic influenzas and HPV - very few or none support research on measles, mumps, rubella or pertussis

- Some wanted to prioritise EU funding on vaccines for emerging infectious diseases/pandemic vaccines/vaccines to be used during epidemic outbreaks

- Others wanted to prioritise funding of specific vaccines in the immunisation schedule for which more data on safety and follow-up is needed, and funding of influenza vaccine research due to low vaccine effectiveness

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Cooperation mechanisms - national research organizations

- Most frequent mechanism are joint calls as well as bilateral and multilateral cooperation with research funding organisations from other countries

Mechanisms to increase cooperation

- Need for clear guidance and options for collaborations to be built into their governance system
- A joint evaluation and selection process must be in place prior to the announcement of the call
- Need for sufficient lead time to approve and agree on topics for calls for proposals
- Alignment of financial rules

Opinions on a potential future joint European mechanism?

- Less than half of the organisations believed a potential future joint European mechanism (i.e., a JPI) would increase collaborative efforts in vaccine R&D and vaccination research
- Voluntary mechanism could be more suitable
- One area they mentioned as a particular need for collaboration with the vaccine field was late-stage clinical trials and phase III/phase IV trials

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Multilateral organizations are very active in financing vaccine R&D

Several multilateral organizations additionally receive funding from the EU member states or are very active in financing vaccine R&D

- Innovative Medicines Initiative, IMI
- Coalition of epidemic preparedness innovation (CEPI)
- UK Vaccine Network
- Global Alliance for Vaccines and Immunization (Gavi)
- The Bill and Melinda Gates Foundation
- Wellcome

Some EU MS use official development assistance (ODA) financing for this purpose
These investments are neither aligned with the EU-JAV strategies nor the health strategies for public health purposes from the EU MS ministries of health

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COVID-19 vaccines as a paradigm for joint funding and new EU instruments?

- R&D funding of COVID-19 vaccines have been at an unprecedented speed on vaccine candidate's development
- Massive public funding of the manufacturing process with involvement from national and multinational organizations
- Direct investment to R&D implementers and to public private partnership organisations
- The EU MSs have primarily invested in pharmaceutical companies and ensured regional manufacturing
- Ensured sufficient supplies for MSs through Advance Purchase Agreements (APAs)

Implementation of Health Emergency Preparedness and Response Authority (HERA)

- Strengthen Europe's ability to prevent, detect, and rapidly respond to cross-border health emergencies
- Ensuring the **development**, manufacturing, procurement, and equitable distribution of **key medical countermeasures**

- **A key task will be to promote research and innovation to develop effective, safe and affordable medical countermeasures, including diagnostics, therapeutics, and vaccines focused on key and emerging pathogens**

- Coordinate EU health security before and during crises, bring the EU MSs, industry and relevant stakeholders together and **enforce development**, production, procurement, stockpiling and equitable distribution of medical countermeasures

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Policy Recommendations

- With the great diversity of possible topics, in a context of limited resources, ***prioritizing research questions becomes a necessity*** - More research on real-world effectiveness of vaccines, implementation of new vaccines in national public health programmes and follow-up on long-term safety and safety signals should be prioritised - Prioritization of vaccine research questions is now on the agenda of many organizations such as the WHO or more recently Vaccelerate

- Establishment and funding of HERA key to ensure better vaccine preparedness in Europe, but should not be at the expense of other important priority initiatives

- WP7 of the EU-JAV has developed an ***effective methodology*** that has been used for two consecutive years to define clear evidence-based and transparent research questions to improve immunization coverage. This methodology effectively classifies research questions but ***does not define them***. Therefore, a key element for the success of such a process is to have ***a significant investment of all partners*** in order to obtain questions initially from all disciplinary fields and all regions of Europe in order to have a wide coverage of the needs.

- The success and impact of such a selection then depends on the possibility ***of funding the research*** questions raised while the research funding system in Europe remains very complex, involves many actors and is fragmented

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