Workshop on modelling tools for vaccination

Monday October 24th, 2025

International Conference Centre of Sorbonne University, Paris, France. 4 place Jussieu, Paris 5e. Building 44-45, 1st floor (access through building 44). Conference room 108.

Program

09:30-10:00: Registration and welcome

10:00-10:15: Introductory talks by Hervé Raoul (deputy director of ANRS-MIE), Rodolphe Thiébaut (Bordeaux U.) and Eric Quéméneur (director of the France Vaccins programme) - France Vaccins, collaborative R&D as a catalyst for vaccine development.

10:15-10:45: Yves Lévy (Vaccine Research Institute, Henri Mondor de Créteil Hospital) - Do modelling tools add value to systems vaccinology? Why, How, When?

10:45-11:40: Pre-clinical vaccine development

Véronique Godot (Paris-Est Créteil University) - Broad and durable antibody responses following CD40.Pan.CoV vaccination: Biological insights leading to modelling approaches

Roger Le Grand (CEA) - TBA

Mélanie Prague (INRIA Bordeaux) - Mathematical modeling of humoral response and mechanistic correlates of protection against SARS-CoV-2 variants in pre-clinical studies

Short break

11:50-12:30: Clinical vaccine development

Laura Richert (Bordeaux University) - Optimizing early-phase clinical development of vaccines

Liem Binh Luong Nguyen (AP-HP, Paris Cité University) - Measuring vaccine efficacy: how models can help

12:30-13:10: Viral evolution and impacts on vaccines

Jean-Sébastien Casalegno (UCBL, Hospices Civils de Lyon) - Escalating immune pressure against RSV fusion protein: Are vaccines and monoclonals on the razor's edge?

Noémie Lefrancq (ETH Zürich) - Monitoring the impact of vaccine implementation on population-level pathogen fitness dynamics

Lunch break [reception hall 102]

14:15-15:10: Decision support for vaccine strategies

Andrea Lasserre (Haute Autorité de Santé) - How vaccines are evaluated by the French National Authority for Health and role of models in this evaluation

Paolo Bosetti (Institut Pasteur) - Modeling the impact of meningococcal vaccination in France over the next 40 years

David Smith (University of Oxford) - Modelling to guide vaccine rollout in low- and middle-income countries: the example of Lassa fever

15:10-16:05: Session on efficacy assessment in populations

Mahmoud Zureik (EPI-PHARE, UVSQ, AP-HP) - Epidemiological surveillance of Covid-19 vaccines: Efficacy/Safety

Naïm Ouldali (AP-HP, Paris Cité University) - Assessing effectiveness of new vaccines through population-based cohorts

Lulla Opatowski (UVSQ, INSERM, Pasteur Institute) - Challenges in modelling vaccine impact for multi-strain pathogens

Coffee break [reception hall 102]

16:30-17:25: Vaccine hesitancy and social issues around vaccines

Alessia Melegaro (Bocconi University) - Integrating human behaviour into epidemiological models: Insights from vaccination decision research

Patrick Peretti-Watel (INSERM, Aix-Marseille University) - Using various data and models to study vaccination behaviors. Some examples from a work in progress

Jocelyn Raude (EHESP) - What modelers should know about vaccine acceptance: instrumental and axiological factors in vaccination decision-making

17:25-17:30: Conclusion

Titles and abstracts

Yves Lévy: Do modelling tools add value to systems vaccinology? Why, How, When?

Understanding how the human immune system reacts to vaccines is incredibly difficult. We need new technologies and a comprehensive approach to overcome the challenges of complex immune responses, identifying markers of protection, and predicting vaccine effectiveness. Systems vaccinology, which uses advanced "omics" technologies that measures various parameters of responses to vaccines leverage from multidisciplinary, computational, and modelling approaches. I will discuss why, how, and when these modeling tools may add significant values in the understanding of the human immune system in responses to vaccines and identification of disease biomarkers.

Véronique Godot: Broad and durable antibody responses following CD40.Pan.CoV vaccination: Biological insights leading to modelling approaches

Our research examines the immunological mechanisms contributing to enhanced and long-lasting antibody responses against SARS-CoV-2 variants. Through immunological analyses, we have identified significant biological differences between a subunit vaccine targeting conserved SARS.CoV-2 antigens to antigen-presenting cells through the CD40 receptor, the CD40.Pan.CoV vaccine, and the Pfizer mRNA vaccines. These findings raised important questions regarding the longevity of antibody responses, which our experimental methods alone could not completely address. This biological complexity prompted us to investigate mathematical modelling approaches to understand better how antibody responses are maintained over time.

Roger Le Grand: TBA

Mélanie Prague: Mathematical Modeling of Humoral Response and Mechanistic Correlates of Protection Against SARS-CoV-2 Variants in pre-clinical studies

SARS-CoV-2 continuously evolves to evade immune responses, reducing the neutralizing capacity of antibodies elicited by vaccination. Consequently, assessing protection requires not only quantifying antibody levels but also evaluating their neutralization capacity. We developed a mathematical model to analyze the humoral response in mice vaccinated with various vaccine strategies. Additionally, non-human primate models can be used to evaluate vaccine efficacy under challenge conditions. We propose a model-based approach integrating viral dynamics modeling with immunological marker analysis. We found that neutralization is a good mechanistic correlate of protection against infection. Integrating these analyses into a joint mechanistic model of immune and viral responses, while bridging parameter values between species from mice to non-human primates, will enhance the translational relevance of preclinical findings. This approach can improve predictions of vaccine efficacy across species and accelerate the development of next-generation vaccines.

Laura Richert: Optimizing early-phase clinical development of vaccines

As with therapeutic drugs or other biomedical interventions, clinical vaccine research typically follows a structured development plan, progressing through clinical trials from Phase I and II to Phase III. Phase I and II trials are early- to mid-stage studies designed to assess safety and explore immunogenicity in a limited number of participants. However, with the advent of modern vaccine platform technologies, the potential number of candidate vaccine strategies against a given pathogen that must be narrowed down during early clinical development has grown considerably. Indee, many vaccine characteristics—such as the vector, antigen inserts, dosages, adjuvant formulations, and injection intervals—are now modifiable, leading to an enormous theoretical number of strategies that is untestable within the current clinical development framework. Therefore, it becomes crucial to prioritize the most promising candidates and make informed “no-go” decisions at early stages. In this context, the use of modelling can enhance the development process by: a) improving our understanding of the effects of vaccine interventions (e.g., dose, timing of injections, adjuvant effects, and prime-boost combinations); b) enabling the in silico down-selection of promising vaccine strategies from a wide range of theoretical options; and c) guiding adaptive trial designs for early-phase trial to further refine and narrow down candidate strategies in humans. Adaptive clinical trial designs, starting with a large number of vaccine strategies, should be developed to ensure efficient, unbiased down-selection throughout the trial, ultimately accelerating the identification of the best vaccine candidates during early-stage development.

Liem Binh Luong Nguyen: Measuring vaccine efficacy: how models can help

Vaccines are pharmaceutical drugs with specific properties, namely their use for prevention at both the individual and population level, in addition to their prolonged effects. Consequently, each stage of the clinical development must account for these distinctive. The issue of safety is constantly scrutinised, while the definition and measurement of efficacy is complex to define and hard to measure. Post-market studies are of particular importance in re-evaluating the risk-benefit ratio, as real-life vaccine effectiveness may deviate from that observed in pivotal studies, the under-detection of rare side effects during Phase 3, and the occurrence of epidemiological changes. Finally, the challenge posed by emerging infectious diseases underscores the critical importance of modelling to inform vaccine policies

Jean-Sébastien Casalegno: Escalating immune pressure against RSV fusion protein: Are vaccines and monoclonals on the razor's edge?

Viral evolution is a fundamental pillar of the evolutionary ecology of infectious disease systems. There is a constant interplay between the variation in the viral dynamics in our population (i.e., epidemiology) and the variation in the virus population genetics (i.e., evolutionary genetics). Vaccines, through immune pressures, alter the inter-host and intra-host genetic diversity of the virus. To what extent can the infectious disease systems-induced changes counteract the benefit of the vaccine implementations? This is a main concern for the respiratory syncytial viruses (RSV), a common cause of

respiratory tract infections in children and adults. RSV has a negative-sense, single-stranded, non-segmented genome with 15,200 nucleotides that encodes for eleven proteins, including the attachment (G) and fusion (F) glycoproteins, which are the main target for the host's humoral and mucosal antibody responses. In just a few years, the RSV surface F protein is becoming the target of long-lasting monoclonals (Nirvesimab, Clesrovimab), recombinant F-protein vaccines (Abrysvo®,Arexvy®) and RNAm vaccine (mRESVIA®) administered in the different at-risk groups (premature, newborn, infant, pregnant mother, immunocompromised adults, elderly). What is the risk of selecting escape variants harboring resistant mutations in the RSV fusion protein antigenic sites? May the variants fitness allow them to spread to other at-risk groups or even the general population? How will RSV diversity (type, clade) evolve under this increasing immune pressure? We will review the current evidence obtained from *in vitro*, clinical, and genotypic surveillance studies. These cumulative pharmaceutical interventions may further drive selection in the viral population with global public health implications. Interdisciplinary approaches combining ecology, epidemiology, and genetics are urgently required to explore further this issue.

Noémie Lefrancq: Monitoring the impact of vaccine implementation on population-level pathogen fitness dynamics

Vaccines, through shifts in immune pressures, have the potential to alter strain diversity in the population. However, this has been challenging to measure as doing so requires long-term genetic data and adequate analytical tools to identify strains with differential levels of fitness. Here, I will present a novel modelling framework, phylowave, that summarises changes in the population composition in phylogenetic trees, enabling the automatic detection of lineages based on shared fitness and evolutionary relationships. Using Bordetella pertussis as a case study, the bacterium causing whooping cough, I will highlight how this method enables us to track pathogen evolution in a timely manner, identify mutations associated with increased fitness and explore the role of vaccination. This approach, when integrated with data on pathogen characteristics (e.g., antigenicity) and patient metadata (e.g., age, vaccination), provides an opportunity to monitor in near real-time the drivers of strain fitness in the population. I will discuss its potential and limitations to detect the impact of vaccines and treatments on strain fitness and to help predict how the strain landscape may evolve in future years.

Andrea Lasserre: How vaccines are evaluated by the French National Authority for Health and the role of models in this evaluation

Paolo Bosetti: Modeling the impact of meningococcal vaccination in France over the next 40 years

Invasive meningococcal disease (IMD) represents a significant global health burden, with high fatality rate and substantial risk of lifelong sequelae. Most cases worldwide are caused by six serogroups (A, B, C, W, X, and Y). Effective vaccines are available to prevent disease caused by serogroups A, B, C, W, and Y. In France, approximately 500 IMD cases occur each year. Since the introduction of mandatory vaccination

against serogroup C, the majority of IMD now involve serogroups B, W, and Y. Given these changes in the epidemiology of IMD, French National Authority for Health decided to reconsider its recommendations for meningococcal vaccines. Here, by using an age structured compartmental model describing meningococcal carriage and IMD cases dynamics of serogroups B, W, and Y, we estimated the expected impact of introducing vaccination against serogroup ACWY or serogroup B on IMD cases in France over the next 40 years. Several scenarios were tested to determine the benefits of vaccination at different ages for both ACWY and serogroup B vaccination, in terms of burden reduction and number of vaccinations needed. For ACWY vaccination the optimal strategy is to target infants and adolescents, supplemented by a catch-up campaign up to the age of 25, which could reduce IMD-W cases by 93% after 20 years. After 5-10 years, focusing only on adolescents may achieve similar outcomes, balancing public health benefits while minimizing costs. For serogroup B vaccination, results showed a limited impact, with the overall reduction of IMD-B cases remaining below 20% in all studied scenarios, even in the long term. This evaluation informed the discussions of the Technical Vaccination Committee regarding the vaccination strategy for meningococcus and was included in the recommendations of the French National Authority for Health, endorsed by the Ministry of Health.

David Smith: Modelling to guide vaccine rollout in low- and middle-income countries: the example of Lassa fever

Global health funders are met with the difficult task of deciding which vaccines to prioritize given budget constraints, data limitations and fundamental uncertainty about future epidemic risk. Mathematical modelling can help to guide funding allocation decisions by providing estimates of the health and economic impacts of different vaccine rollout strategies. In this talk, I will present recent work evaluating the returns-on-investment of various strategies for administering vaccines targeting Lassa fever, a cryptic zoonotic disease endemic to several countries in West Africa. I will also explore the potential benefits of Lassa fever vaccine investment in the context of a hypothetical Lassa-related virus emerging in the near future and causing the next pandemic.

Mahmoud Zureik: Epidemiological surveillance of Covid-19 vaccines: Efficacy/Safety

Naïm Ouldali: Assessing effectiveness of new vaccines through population-based cohorts

Lulla Opatowski: Challenges in modelling vaccine impact for multi-strain pathogens

Alessia Melegaro: Integrating Human Behaviour into Epidemiological Models: Insights from Vaccination Decision Research

Mathematical modelling is a cornerstone for analyzing the dynamics of endemic and emerging pathogens, assessing population-level risks, and evaluating intervention strategies. However, vaccination programs and other preventive health behaviors are frequently treated as static, exogenous factors in these models—unresponsive to the infection process, evolving individual attitudes, or shifts in risk perception. This project aims to bridge this gap by incorporating the complex determinants of human behavior, particularly vaccination decisions, into epidemiological models to enable more realistic and effective policy evaluation. To achieve this, we conducted surveys with nationally representative samples in six countries (Italy, France, Germany, Hungary, Spain, and the United Kingdom), extending the Capability, Opportunity, and Motivation Behaviour (COM-B) framework. Our approach incorporates critical elements relevant to disease modelling, including: i) Social contact and discussion matrices to map infection and opinion dynamics, respectively; ii) Vaccine-related opinions across participants' social networks, and iii) The temporal evolution of individual risk perceptions related to both disease and vaccination. Our findings offer a detailed, context-specific understanding of the multidimensional factors influencing vaccination behavior throughout different phases of an epidemic. These insights are instrumental in evaluating compliance with vaccination campaigns and their impact under diverse epidemiological and social conditions. Moreover, the data facilitate the identification of specific behavioral targets and prerequisites for driving behavior change among vaccine-hesitant populations, thereby enhancing the effectiveness of future public health interventions.

Patrick Peretti-Watel: Using various data and models to study vaccination behaviors. Some examples from work in progress

Different kinds of data (qualitative interviews, samples survey date, vaccination coverage data…) and models (with or without equations and statistics) can be used to study vaccination behavior, and in this case specifically anti-Covid-19 vaccination in France in 2020-2021. We first compared models derived either from the rational choice theory or from the sociology of deviance, and then we considered two potential motives for vaccination: the ‘health pass’ and the influence of significant others.

Jocelyn Raude: What modelers should know about vaccine acceptance: instrumental and axiological factors in vaccination decision-making