UNIVERSITY OF OXFORD

DEPARTMENT OF PAEDIATRICS

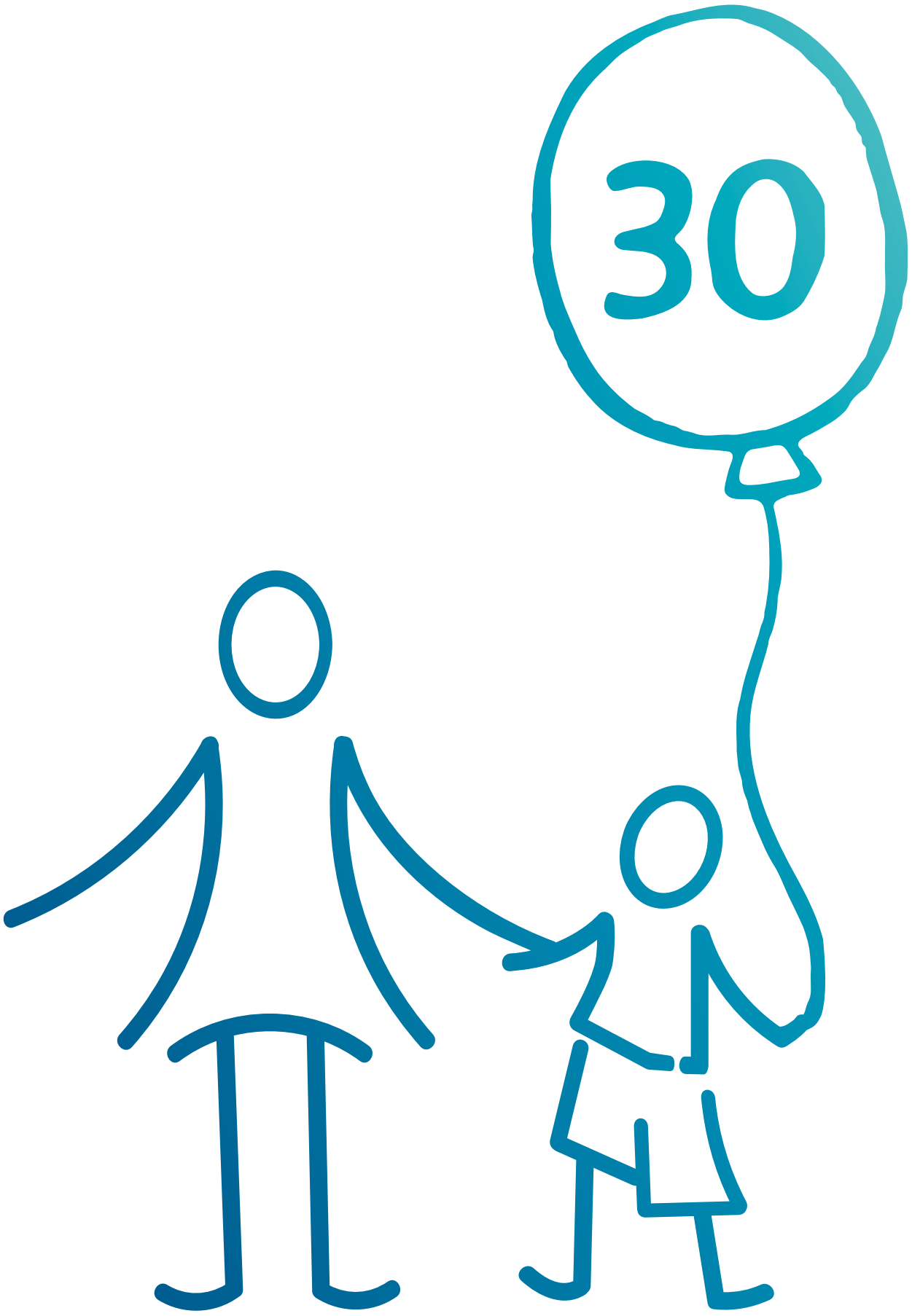
OXFORD VACCINE GROUP

30th ANNIVERSARY SYMPOSIUM

OXFORD VACCINE GROUP

Trinity College

Friday 27th September 2024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Contents










Foreword

Professor Sir Andrew Pollard
Director of the Oxford Vaccine Group

Andrew Pollard with Richard Moxon

This document summarises the content and presentations given at the OVG 30 symposium on 26 September 2024. The event was held in celebration of 30 years of scientific research and development, and it delivered an outstanding showcase of our achievements, by the people who contributed to its success.

Since its inception in 1994, OVG has grown into a vibrant community of around 200 staff and students, dedicated to advancing vaccine science, education, and public engagement. The OVG mission, crafted through collaborative efforts, has guided the group in its pursuit of excellence in vaccine research and development. OVG has focused not only on the scientific aspects but also on the educational and service components that are integral to its work.

Today, we are fortunate to have 15 outstanding Principal Investigators leading various programs within OVG. Their leadership, combined with the efforts of our dedicated staff from diverse research and support areas, enables us to deliver impactful results. Our comprehensive approach, often referred to as the "full stack," allows us to navigate all phases of vaccine development, from discovery to policy and public engagement.

Our achievements are a testament to the collaborative spirit within OVG and our partnerships with institutions worldwide. Despite the challenges, including the financial demands of sustaining a large team, we have thrived thanks to the high-quality research grants secured by our talented team members.

As we reflect on our contributions, such as the significant reduction in under-five mortality rates, we recognise the ongoing challenges and the need for continued efforts. The recent pandemic has underscored the importance of our work and the necessity of being prepared for future public health threats.

The symposium provided a comprehensive insight into the remarkable journey of the Oxford Vaccine Group. Thank you for your support and for joining us to celebrate 30 years of ground-breaking achievements.

The Oxford Vaccine Group Mission

The OVG mission is to improve health through immunisation, using our expertise in scientific discovery, and the development, clinical testing and laboratory evaluation of vaccines; and to share our knowledge.


OXFORD
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OVG 30

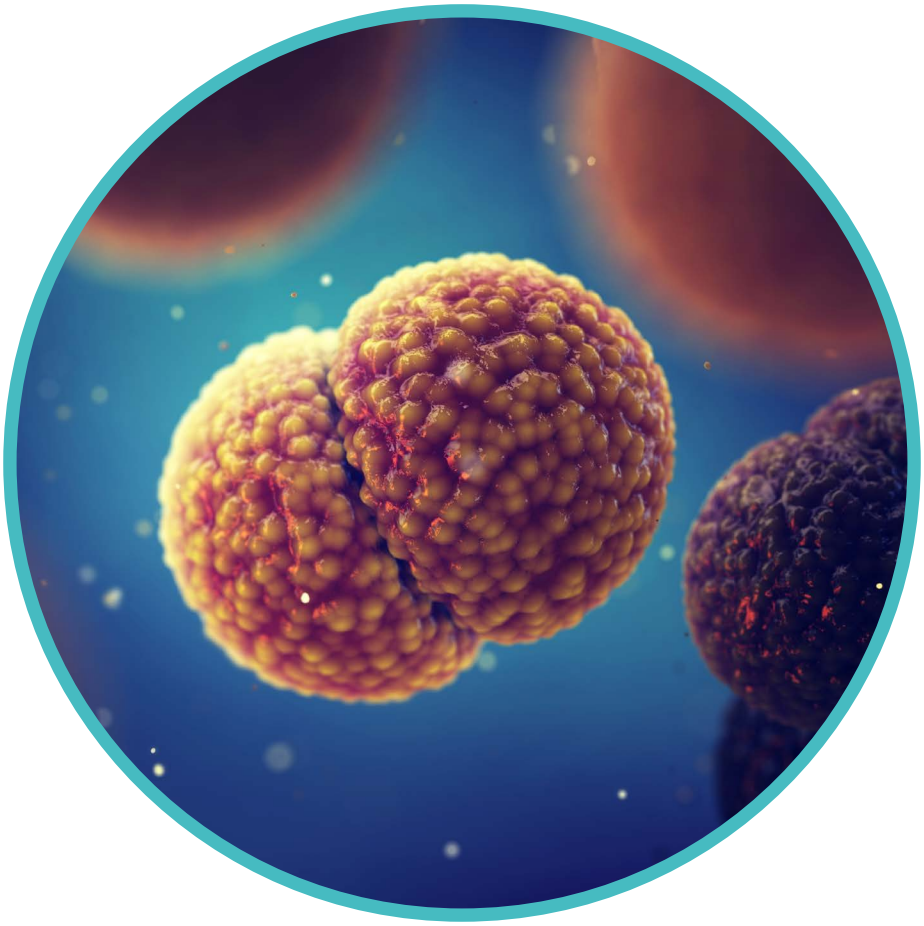

OVG30


Happy 30th Anniversary

Session One

Encapsulated bacteria: Hib, meningococcus

Session Chair: Professor Richard Moxon



Dawn of Conjugate Vaccines

Presenters: *Paul Heath, Gareth Tudor-Williams, Jim Buttery and Robert Booy*

Overview: Paul Heath discussed the development and impact of Hib conjugate vaccines.

Key Points:

- **Early Surveillance:** Initial studies in Oxford identified the burden of Hib disease.
- **Vaccine Trials:** Early vaccine trials demonstrated the immunogenicity, safety and efficacy of Hib conjugate vaccines.
- **Impact:** Introduction of the Hib vaccine led to a significant reduction in Hib disease in the UK.
- **Ongoing Surveillance:** Continued monitoring of vaccine effectiveness, vaccine failures and disease patterns.

Paul Heath

Meningococcal Conjugate Vaccines

Presenters: *Kirsten Perrett, Jenny MacLennan and Maheshi Ramasamy*

Overview: The team discussed the development and impact of meningococcal conjugate vaccines.

Key Points:

- **Disease Burden:** Meningococcal disease causes significant morbidity and mortality.
- **Vaccine Development:** Development of conjugate vaccines for serogroups A, C, W, and Y.
- **Impact:** Introduction of the vaccines led to a significant reduction in meningococcal disease.
- **Ongoing Challenges:** Need for continued surveillance and potential adjustments to vaccination schedules.

Left to Right: Richard Moxon, Jenny MacLennan, Kirsten Perrett, Maheshi Ramasamy

Meningitis in the 21st Century

Presenter: *Manish Sadarangani and Seilesh Kadambari*

Overview: Manish Sadarangani discussed the challenges and advancements in diagnosing and managing meningitis.

Key Points:

- **Impact of Vaccines:** Vaccines have significantly reduced the incidence of bacterial meningitis.
- **Diagnostic Challenges:** Difficulty in diagnosing meningitis due to the low incidence of bacterial cases.
- **Research and Collaboration:** Large-scale studies have been undertaken to improve diagnostics and management of meningitis.
- **Future Directions:** Continued focus on better diagnostics and understanding the etiology of meningitis.

Manish Sadarangani

Insights into B cell kinetics and the B cell receptor

Presenters: *Dominic Kelly, Geraldine Blanchard-Rohner and Johannes Trück*

Overview: The team discussed the importance of B-cell research in understanding vaccine responses.

Key Points:

- **B-Cell Studies:** Early studies on memory B cells and their role in vaccine responses.
- **Techniques and Challenges:** Development of techniques to study B cells and their responses to vaccines.
- **Impact:** Insights into the kinetics of B-cell responses and the development of better vaccines.
- **Future Research:** Ongoing studies to further understand B-cell responses and improve vaccine design.

Dominic Kelly

Geraldine Blanchard-Rohner

Johannes Trück

Development of MenB vaccine

Presenters: *Matthew Snape, Gunnstein Norheim and Christine Rollier*

Overview: The team discussed the development and impact of meningococcal B vaccines.

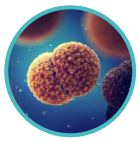
Key Points:

- **Disease Burden:** Meningococcal B disease remains a significant health threat.
- **Vaccine Development:** Development of MenB vaccines using various platforms, including outer membrane vesicles and adenoviral vectors.
- **Clinical Trials:** Extensive clinical trials to demonstrate the safety and efficacy of MenB vaccines.
- **Impact:** Introduction of MenB vaccines has significantly reduced the incidence of meningococcal B disease.
- **Ongoing Research:** Continued studies to understand the long-term impact and optimize vaccination schedules.

Gunnstein Norheim

Christine Rollier

Matthew Snape



Background and need for MenB Vaccine

- **Meningococcal Disease:** Caused by Neisseria meningitidis, it leads to severe infections like meningitis and septicemia. Serogroup B (MenB) is one of the major causes of these infections.
- **Historical Context:** Previous vaccines targeted other serogroups (A, C, W, Y), but MenB posed a challenge due to its genetic diversity and the similarity of its polysaccharide capsule to human neural cell adhesion molecules, making traditional vaccine approaches ineffective.

Early Efforts and Challenges

- **Clonal Vaccines:** Initial vaccines, like those developed in Cuba and Norway, were based on outer membrane vesicles (OMVs) from specific MenB strains. These vaccines were effective in localised outbreaks but had limited broader application due to strain specificity.
- **Reverse Vaccinology:** A breakthrough came with the sequencing of the MenB genome, which allowed for the identification of surface-exposed proteins that could be used as vaccine targets. This approach led to the discovery of several potential antigens.

Development of Bexsero

- **Key Proteins:** The reverse vaccinology approach identified three key proteins: factor H binding protein (fHbp), Neisserial adhesin A (NadA), and Neisserial heparin binding antigen (NHBA). These were combined with OMVs to create a broad-coverage vaccine.
- **Clinical Trials:** Extensive clinical trials were conducted to evaluate the safety and efficacy of the vaccine. The Oxford Vaccine Group (OVG) played a significant role in these trials, contributing to the licensing of Bexsero.
- **Phase 1/2 Trials:** Initial trials assessed the safety and immunogenicity of the vaccine in infants and toddlers.
- **Phase 3 Trials:** Larger trials confirmed the vaccine's efficacy and safety, leading to its approval for use in various age groups.

Post-Licensure Studies and Impact

- **Persistence and Booster Studies:** Studies were conducted to understand the duration of immunity provided by the vaccine and the need for booster doses.
- **Special Populations:** Research included evaluating the vaccine's effectiveness in children with complement deficiencies and other high-risk groups.

- **Carriage Studies:** Large-scale studies, such as the Be on the TEAM study, assessed the impact of the vaccine on MenB carriage in adolescents, which is crucial for herd immunity.

Ongoing Research and Future Directions

- **Understanding Reactogenicity:** Research into the causes of the high rates of fever following vaccination, aiming to improve the vaccine's reactogenicity profile.
- **Global Implementation:** Efforts continue to ensure the vaccine's availability and implementation worldwide, addressing the varying epidemiology of MenB in different regions.

Conclusion

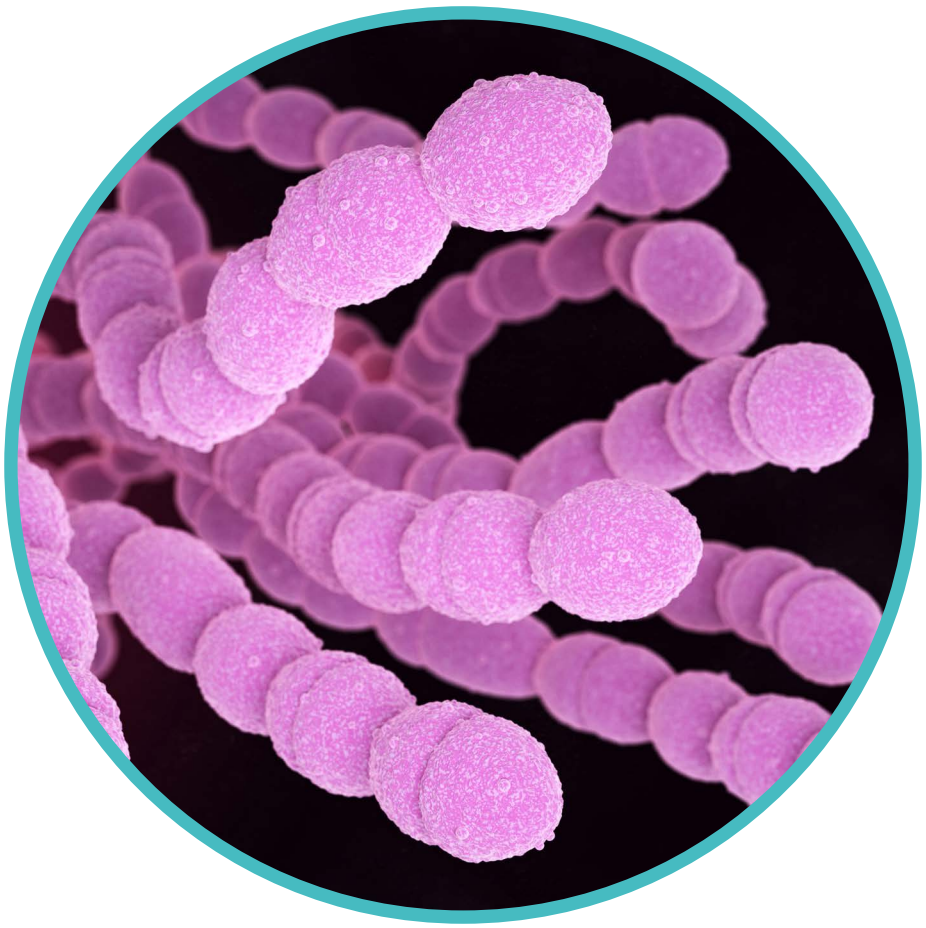
The development of the MenB vaccine, particularly Bexsero, represents a significant achievement in vaccinology. The collaborative efforts of researchers, including those at OVG, have led to a vaccine that provides broad protection against a challenging pathogen. Ongoing research and surveillance are essential to maintain and improve the impact of MenB vaccination programs globally.

Christine Rollier, Richard Moxon, Matthew Snape, Gunnstein Norheim

Session Two

Pneumococcus and Respiratory Viruses

Session Chair: Katrina Pollock



Pneumococcal Vaccines and Carriage

Presenter: *Daniela Ferreira*

Overview: Daniela discussed the pneumococcal challenge model and its applications in understanding pneumococcal disease and vaccine efficacy.

Key Points:

- **Pneumococcal Vaccines:** Various pneumococcal vaccines, including conjugate and polysaccharide vaccines, have been developed and expanded over the years.
- **Human Challenge Model:** Over 2000 participants have been involved in studies where they were deliberately infected with pneumococcus to study colonization and immune responses.
- **Vaccine Efficacy:** Studies showed high efficacy of PCV13 against serotype 6B but not against serotype 3, highlighting the need for ongoing research and development of new vaccines.
- **B-Cell Immunity:** Research on B-cell responses in the nose and lungs has provided insights into the mechanisms of protection against pneumococcal colonization.

Daniela Ferreira

Pneumococcal Epidemiology, Vaccines and Host-Bacterial Interactions

Presenters: *Rama Kandasamy and Mainga Hamaluba*

Overview: Rama presented on the epidemiology of pneumococcal disease and the impact of vaccines in the UK.

Key Points:

- **Disease Burden:** Pneumococcal carriage is common in children, and pneumonia remains a significant health issue.
- **Vaccine Impact:** Introduction of PCV7 and PCV13 vaccines has significantly reduced the incidence of invasive pneumococcal disease (IPD) and carriage of vaccine serotypes.
- **Ongoing Surveillance:** Continued monitoring of pneumococcal disease and carriage is essential to inform vaccine policy and address emerging non-vaccine serotypes.

Rama Kandasamy

The B-Cell and Pneumococcal Vaccines

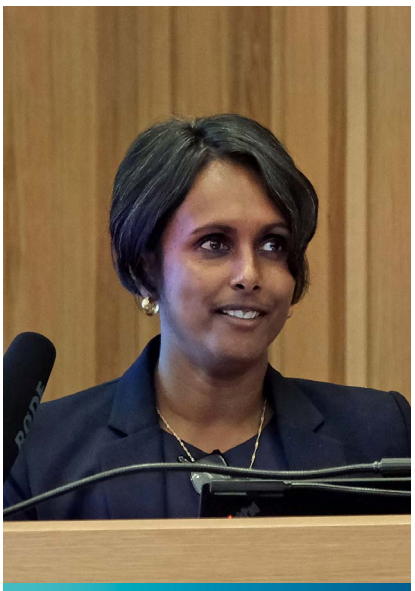
Presenters: *Elizabeth Clutterbuck, Rajeka Lazarus and Britta Urban*

Overview: The team discussed the importance of B-cell responses in evaluating pneumococcal vaccines.

Key Points:

- **Memory B-Cells:** Studies have shown differences in memory B-cell responses to polysaccharide and conjugate vaccines.
- **Vaccine Schedules:** Research on different vaccination schedules has provided insights into optimizing vaccine-induced immunity.
- **Advanced Techniques:** High-dimensional approaches, such as spectral flow cytometry and B-cell repertoire analysis, are being used to further understand B-cell responses and improve vaccine design.

Elizabeth Clutterbuck



Rajeka Lazarus

Britta Urban

Introducing Respiratory Syncytial Virus (RSV)

Presenters: *Simon Drysdale, Christopher Green and Joseph McGinley*

Overview: The presentation focused on the development and impact of RSV vaccines.

Key Points:

- **Disease Burden:** RSV affects individuals from infancy to old age, with significant morbidity and mortality.
- **Vaccine Development:** The first-in-human trials of viral vector RSV vaccines showed promising results in terms of safety and immunogenicity.
- **Epidemiology and Biomarkers:** Large consortia studies have identified biomarkers associated with severe RSV disease and provided insights into the epidemiology of RSV.

Simon Drysdale

Christopher Green

Joseph McGinley

Below is more detail on the RSV vaccine development as discussed in the presentation:

Background and Challenges

- **RSV Burden:** RSV is a significant cause of respiratory infections across all age groups, particularly severe in infants and the elderly. It leads to bronchiolitis and pneumonia, contributing to high hospitalisation rates.
- **Complex Immunology:** Developing an RSV vaccine is challenging due to the complex immune responses required. The immune system's interaction with RSV varies significantly between infants and older adults, complicating vaccine design.

Early Efforts and Setbacks

- **Historical Context:** The first attempts to develop an RSV vaccine in the 1960s using a formalin-inactivated virus led to severe adverse effects, including enhanced respiratory disease upon subsequent RSV infection. This setback delayed further vaccine development for decades.

Recent Advances

- **Viral Vector Vaccines:** The Oxford Vaccine Group conducted pioneering studies using viral vector vaccines expressing RSV antigens. These studies were the first in the world to bring such vaccines into human trials.
  - **RSV001 Study:** This first-in-human trial demonstrated the safety and immunogenicity of the viral vector vaccine, showing it could generate both antibody and T-cell responses. It was also the first-in-world trial for viral vectored vaccines used with RSV antigen in humans.
  - **Older Adults Study:** Subsequent trials in older adults confirmed the vaccine's safety and ability to induce immune responses, crucial for protecting this high-risk group.

Immune Response Studies

- **Gene Expression Analysis:** Studies analysed the gene expression profiles following vaccination, identifying families of genes associated with immune responses. This helped understand the mechanisms behind vaccine-induced protection.
- **T-Cell Responses:** Research highlighted the importance of T-cell responses in preventing severe RSV disease, especially in older adults where immune senescence is a concern.

Epidemiological Insights

- **Hospitalisation Trends:** Data showed an increasing trend in RSV-related hospitalisations, particularly in infants and the elderly. Socioeconomic factors also influenced hospitalisation rates.
- **Burden of Disease:** Studies emphasised the significant burden of RSV, driving the need for effective vaccines to reduce hospital admissions and severe outcomes.

Current Vaccine Landscape

- **Maternal Vaccination:** The UK has introduced Pfizer's maternal RSV vaccine, which has shown high efficacy in preventing severe RSV disease in infants up to six months old.
- **Monoclonal Antibodies:** Monoclonal antibodies like nirsevimab have been developed to provide passive immunity to infants, showing high efficacy in preventing severe RSV disease.

Future Directions

- **Ongoing Research:** Continued research focuses on optimising vaccine formulations, understanding long-term immunity, and exploring new vaccine platforms.
- **Global Implementation:** Efforts are underway to ensure global access to RSV vaccines, particularly in low- and middle-income countries where the burden of RSV is highest.

Conclusion

The development of RSV vaccines has made significant progress, with several candidates showing promise in clinical trials. The introduction of maternal vaccines and monoclonal antibodies marks a major advancement in protecting vulnerable populations. Ongoing research and surveillance are essential to refine these vaccines and ensure their broad implementation.

Bacterial-Viral Interactions and Pneumococcal Challenge

Presenters: *Elena Mitsi and Gu-Lung Lin*

Overview: The team discussed the interactions between bacterial and viral pathogens, particularly focusing on pneumococcus and respiratory viruses.

Key Points:

- **Co-Infections:** Studies in young children and older adults have shown that viral infections, such as RSV and influenza virus, can increase the risk of pneumococcal colonisation and disease.
- **Infants with RSV Infection:** An additional virus can be detected in approximately one-quarter of infants with RSV infection. The presence of Haemophilus species in the nasopharynx has been associated with increased RSV severity, whereas the presence of Moraxella species has been correlated with reduced severity.
- **Human Challenge Models:** Co-infection models have been developed to study the interactions between pneumococcus and viruses in a controlled setting.
- **Impact on Vaccination:** Understanding these interactions is crucial for developing effective vaccination strategies that can address both bacterial and viral pathogens.

Elena Mitsi

Pneumonia and Vaccination in Nepal 2005 - 2024

Presenter: *Shrijana Shrestha*

Overview: Shrijana presented on the burden of pneumonia and the impact of vaccination programs in Nepal.

Key Points:

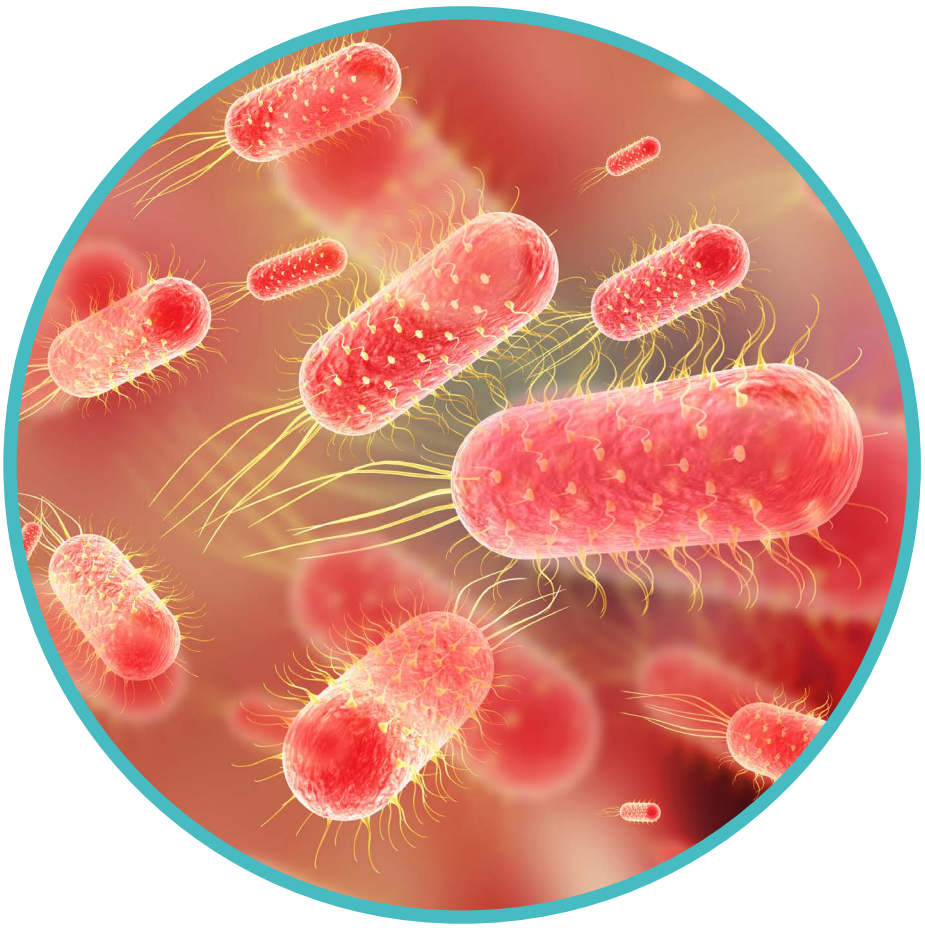
- **Disease Burden:** Pneumonia remains a leading cause of hospitalisation and mortality among children in Nepal.
- **Vaccine Impact:** Introduction of pneumococcal vaccine (PCV) has significantly reduced the incidence of pneumonia and invasive pneumococcal disease. However, an increase in the nasopharyngeal carriage of non-vaccine type pneumococcus has been observed among hospitalised children with pneumonia and also among the health cohort.
- **Research and Policy:** Local research has informed vaccine policy decisions, including the adoption of a two-plus-one schedule for PCV.
- **Challenges:** Ongoing challenges include access to healthcare, diagnostic facilities, and the need for continued surveillance for the serotype replacement and disease.

Shrijana Shrestha

Session Three

Typhoid and Paratyphoid

Session Chair: Daniela Ferreira



A Human Challenge Model for Typhoid

Presenters: *Claire Waddington, Tom Darton, and Christoph Blohmke*

Overview: The team discussed the development and implementation of a human challenge model for typhoid fever.

Key Points:

- **Background:** Typhoid fever remains a significant global health issue, particularly in areas with poor sanitation.
- **Challenge Model Development:** Inspired by earlier work at the University of Maryland, the team developed a challenge model using the Quailes strain of Salmonella Typhi.
- **Safety and Efficacy:** The model was shown to be safe and effective in replicating typhoid fever, with a 65% attack rate at the optimal dose.
- **Clinical Findings:** The model provided detailed insights into the clinical progression of typhoid fever and was used to test the efficacy of existing vaccines.

Claire Waddington

Tom Darton

Christoph Blohmke

Immunological Insights from the Typhoid Challenge Model

Presenters: *Malick Gibani, Amber Barton and Daniel O'Connor*

Overview: The presentation focused on the immunological findings from the typhoid challenge model.

Key Points:

Genetic Susceptibility: HLA-B27 was identified as a genetic variant associated with increased susceptibility to typhoid fever.

- **Gene Expression:** Early gene expression changes post-challenge highlighted the role of monocytes in the immune response.
- **Vaccine-Induced Immunity:** Studies identified molecular correlates of vaccine-induced protection, including interferon signalling and CD4 T-cell responses.

Malick Gibani

Amber Barton

STRATAA Case Study: The Case for Typhoid Vaccination

Presenters: *James Meiring and Firdausi Qadri*

Overview: The STRATAA study aimed to measure the real-world burden of typhoid disease and inform vaccination strategies in different endemic regions.

Key Points:

- **Study Design:** The study involved a demographic census of 100,000 people in Bangladesh, Nepal, and Malawi, with passive surveillance for febrile illness. We performed healthcare utilisation surveys and a large community-based serosurvey to capture sub-clinical typhoid cases.
- **Findings:** High incidence rates of typhoid fever were observed, particularly in children aged 5-9 years, with high rates of antibiotic resistance.
- **Policy Impact:** The data informed Gavi and WHO policy decisions, leading to the introduction of typhoid conjugate vaccines in several countries.

James Meiring

Firdausi Qadri

Long-Term Efficacy and Policy Implications of TCV

Presenters: *Mila Shakya and Xinxue Liu*

Overview: The presentation focused on the long-term efficacy of TCV and its policy implications.

Key Points:

- **Field Trials:** Large-scale field trials in Nepal, Malawi, and Bangladesh demonstrated high efficacy of TCV, with durable protection observed over several years.
- **Waning Immunity:** Data indicated waning immunity in younger children, suggesting the need for booster doses.
- **Policy Recommendations:** The findings are being used to inform WHO and national policy decisions on TCV vaccination schedules.

Mila Shakya

Xinxue Liu

Paratyphoid Challenge Model and Vaccine Development

Presenters: *Naina McCann and Margarete Vicentine*

Overview: The team discussed the development of a human challenge model for paratyphoid fever and the evaluation of a paratyphoid vaccine.

Key Points:

- **Challenge Model:** A challenge model for Salmonella Paratyphi A was developed, showing a 60% attack rate at the optimal dose.
- **Vaccine Evaluation:** The first evaluation of a live attenuated paratyphoid vaccine (CVD 1902) showed a vaccine efficacy of 73% in the challenge model.
- **Future Directions:** Ongoing studies aim to identify correlates of protection and evaluate other paratyphoid vaccines, including bivalent vaccines.

Naina McCann

Margarete Vicentine

Below is further detail on the development of the paratyphoid vaccine as discussed in the presentations:

Background on Paratyphoid Fever

- **Pathogen:** Paratyphoid fever is caused by Salmonella Paratyphi A, a bacterium that leads to enteric fever similar to typhoid fever.
- **Burden:** It accounts for a significant portion of enteric fever cases, particularly in South and Southeast Asia, and poses a risk of increasing incidence due to potential serotype replacement following typhoid vaccination.
- **Antimicrobial Resistance:** Rising antimicrobial resistance in Salmonella Paratyphi A underscores the need for effective vaccines.

Development of the Paratyphoid Challenge Model

- **Initial Steps:** The challenge model for Salmonella Paratyphi A was established in 2014 using a contemporary strain sensitive to relevant antibiotics.
- **Dose Finding:** The optimal dose for the challenge model was determined to be 1-5 × 103 CFU, with a 60% attack rate, ensuring a relevant endpoint for vaccine efficacy studies.
- **Tolerability:** The model was well-tolerated by participants, with lower symptom scores compared to the typhoid challenge model.

Evaluation of the First Paratyphoid Vaccine

- Vaccine Candidate: The first vaccine evaluated was a live attenuated oral vaccine, CVD 1902, developed by the University of Maryland.
- Study Design: Participants were randomized to receive either the CVD 1902 vaccine or a placebo, followed by a challenge with the wild-type Salmonella Paratyphi A strain.
- **Results:**
  - **Efficacy:** The vaccine demonstrated a 73% efficacy in preventing paratyphoid fever in the challenge model.
  - **Safety:** The vaccine was safe and well-tolerated, with low levels of symptoms and no vaccine-related serious adverse events.
  - **Immune Response:** Significant increases in IgG and IgA responses to the paratyphoid-specific O:2 polysaccharide were observed in the vaccinated group.

Future Directions and Ongoing Research

- **Correlates of Protection:** Ongoing research aims to identify immune correlates of protection, which are currently unknown for paratyphoid.
- **Bivalent Vaccines:** Development and evaluation of bivalent vaccines that combine typhoid and paratyphoid antigens are underway. For example, the Serum Institute of India has developed a bivalent vaccine that has shown promising phase one results.
- **Further Trials:** Additional trials are planned to evaluate other paratyphoid vaccines, including conjugate vaccines, in the challenge model.

Summary

The development of the paratyphoid vaccine has made significant progress with the establishment of a human challenge model and the successful evaluation of the first live attenuated vaccine. Ongoing research and future trials aim to further understand the immune responses and develop effective bivalent vaccines to combat both typhoid and paratyphoid fever.

Session Four

Endemics and Pandemics

Session Chair: Andrew Pollard

Endemics and Pandemics Overview

Presenter: *Teresa Lambe*

Overview: Tess discussed the approach to developing and testing vaccines against outbreak pathogens, emphasising the importance of collaboration and rapid response.

Key Points:

- The 2013 Ebola outbreak highlighted the need for preparedness.
- The WHO and other bodies created a list of priority pathogens.
- The development timeline for vaccines is typically 10-20 years, but the COVID-19 vaccine was developed in 11 months.
- The 100 Days Mission aims to prepare diagnostics, therapeutics, and vaccines for future pandemics.
- Current efforts include developing vaccines for multiple viruses using platforms like viral vectors and mRNA.

Teresa Lambe

Influenza 2009 and Ebola 2014/15

Presenters: *Matthew Snape and Claire Waddington*

2009 H1N1 Pandemic:

- The UK government needed data on paediatric vaccines.
- A collaborative effort led to a trial involving 1,000 children, providing crucial data for the vaccination strategy.

Ebola Outbreak (2014-2015):

- Multiple vaccines were tested, including viral vector vaccines.
- The Oxford Vaccine Group played a key role in the rapid development and testing of these vaccines.
- The experience highlighted the need for better preparedness and faster response times for future pandemics.

Case Studies:
Crimean-Congo Haemorrhagic Fever and Rift Valley Fever

Presenters: *Daniel Wright and Sandra Belij-Rammerstorfer*

Crimean-Congo Hemorrhagic Fever (CCHF):

- A tick-borne disease with high case fatality in humans.
- A vaccine candidate using the ChAdOx2 platform showed promising immunogenicity and safety in early trials.

Rift Valley Fever (RVF):

- A mosquito-borne disease affecting livestock and humans.
- The ChAdOx1 RVF vaccine is highly protective against disease and foetal loss in livestock and promising results in human trials.
- Efforts are ongoing to develop an mRNA vaccine for RVF.

Daniel Wright

Below is more detail on the development of a vaccine for RVF as discussed in the presentations:

Development of an mRNA Vaccine for Rift Valley Fever (RVF)

Background on Rift Valley Fever (RVF)

- **Pathogen:** Rift Valley fever virus (RVFV) is a mosquito-borne zoonotic virus that causes significant morbidity and mortality in both humans and animals.
- **Disease Impact:** RVF can lead to severe symptoms such as haemorrhagic fever, encephalitis, and retinitis in humans, and high rates of abortion and mortality in livestock.
- **Need for Vaccines:** There are currently no licensed RVF vaccines for human use, making the development of effective vaccines crucial for public health and the livestock industry.

Chadox1 RVF Vaccine

- **Development:** The Chadox1 RVF vaccine uses the same platform as the Oxford-AstraZeneca COVID-19 vaccine but targets RVF antigens (Gn and Gc proteins).
- **Efficacy:** Demonstrated 100% efficacy in small-scale trials with sheep, goats, and cattle. It also showed protection against disease and foetal loss in pregnant animals, a significant improvement over existing livestock vaccines.

mRNA Vaccine Development

- **Antigen Design:** The mRNA vaccine includes the Gn and Gc proteins, with a native leader sequence to ensure proper protein expression. Researchers explored adding a heterologous leader sequence (TPA) to improve antigen expression and immunogenicity.
- **Preclinical Trials:** Initial trials in mice showed promising results, leading to plans for trials in sheep. The mRNA vaccine aims to be rapidly deployable in the event of an RVF outbreak.

Collaborative Efforts

- **Global Collaboration:** The development involves collaborations with structural biologists and teams in the UK, Germany, and the US. This includes using AI and machine learning to predict optimal vaccine antigen design.

- **Investigative Immunology:** Integration of investigative immunology to understand the immune response and improve vaccine efficacy. This involves developing a suite of immunological assays against different proteins for various species.

Future Plans

- **Data Integration:** Combining human and livestock studies to assess immune responses and inform antigen design. This helps evaluate vaccine candidates and understand what protective immunity looks like.
- **Prototype Vaccines:** Developing prototype vaccines for potential future outbreaks, leveraging lessons learned from COVID-19 vaccine development.

Innovative Approaches

- **AI and Machine Learning:** Using these technologies to predict the best antigens to include in the vaccine.
- **Systems Biology:** Employing systems biology approaches to generate a playbook for optimal antigen design, assessed across multiple vaccine platforms.

The session emphasised the importance of a holistic approach to vaccine development, combining veterinary and human health perspectives to create effective and safe vaccines for outbreak pathogens like RVF.

Andrew Pollard, Sandra Belij-Rammerstorfer and Daniel Wright

Insights Into Immunity from the Lymph Node

Presenter: *Katrina Pollock*

Research Focus: Understanding how vaccines work by studying immune responses in lymph nodes.

Key Points:

- Lymph nodes are crucial for vaccine responses but are understudied.
- Fine needle aspirates from lymph nodes provide valuable data on immune cell populations and gene expression.
- The study showed significant changes in T follicular helper cells after vaccination, highlighting the importance of these cells in generating effective immune responses.

Katrina Pollock

Malaria Challenge Studies

Presenter: *Angela Minassian*

Overview: Development of next-generation vaccines for malaria, focusing on Plasmodium falciparum.

Key Points:

- The RTS,S and R21 vaccines target the CSP protein and have shown efficacy in preventing malaria.
- The RH5 protein is a promising target for blood-stage malaria vaccines.
- Clinical trials in the UK and Africa have shown promising immunogenicity and safety for RH5-based vaccines.
- A phase 2b trial in Burkina Faso demonstrated 55% efficacy for the RH5.1 vaccine.

Angela Minassian

Plague Vaccine Development

Presenters: *Arabella Stuart, Sagida Bibi and Young Kim*

Overview: Development of vaccines for plague, a historically significant and still relevant disease.

Key Points:

- Plague remains a threat in certain regions and has potential for bioterrorism.
- The ChAdOx1 platform was used to develop a plague vaccine targeting the F1 and V antigens.
- Phase 1 trials in the UK and Uganda showed promising immunogenicity and safety.
- Ongoing efforts include developing an mRNA vaccine for plague, which allows for multiple antigen targets and improved stability.

Arabella Stuart

Sagida Bibi

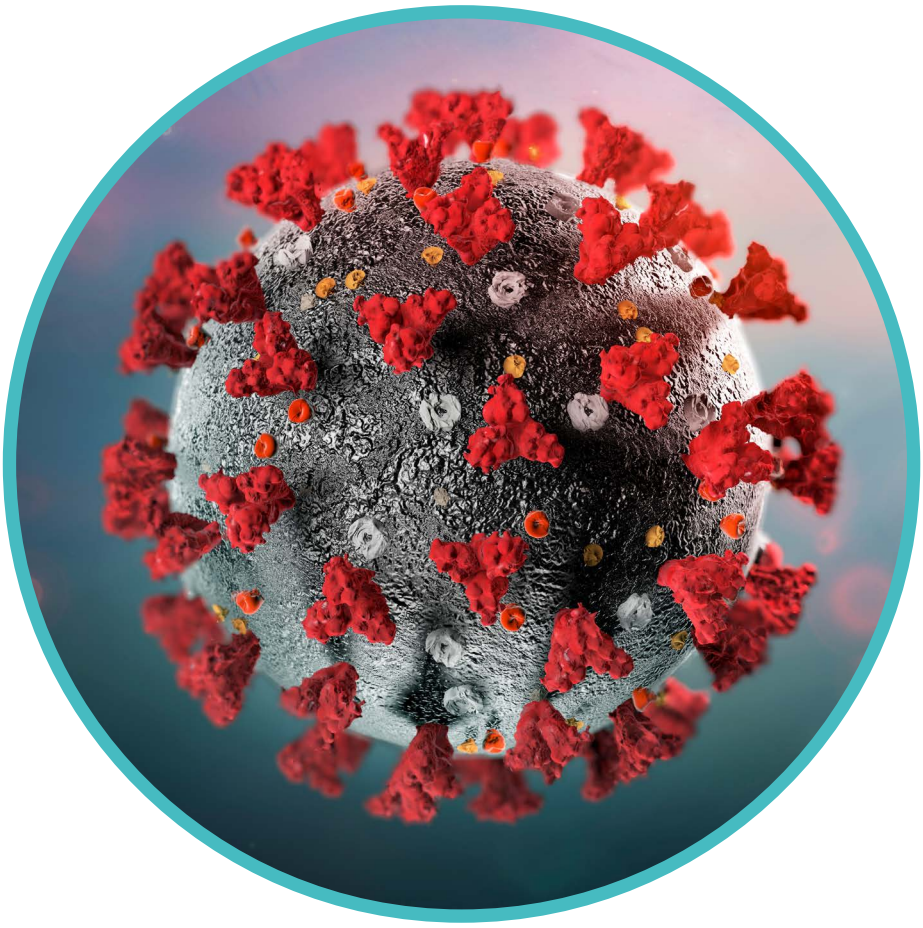
Young Kim

Session Five

Vaccines at Scale

Session Chair: Andrew Pollard

The session highlighted the significant contributions of the Oxford Vaccine Group to vaccine development, public health, and global vaccination efforts.



Clinical Development of the Oxford AZ Vaccine

Presenters: *Maheshi Ramasamy and Sue Ann Costa Clemens*

Overview: The session focused on the development, impact, and legacy of the Oxford COVID-19 vaccine.

Key Points:

- **Early Development:** The vaccine development began in January 2020, with the sequence of SARS-CoV-2 released by Chinese researchers. Tess Lambe and Sarah Gilbert started designing the vaccine using the Adenoviral vector platform.
- **Clinical Trials:** The phase one trial began in Oxford, followed by phase two trials involving older adults. Phase three trials were conducted in the UK, Brazil, and South Africa.
- **Global Collaboration:** The trials involved partnerships with multiple international sites and organisations, including AstraZeneca and the Serum Institute of India.
- **Impact:** The vaccine received emergency use authorisation in December 2020 and was rolled out globally. It significantly reduced hospitalisations and deaths, particularly among older adults.
- **Brazil's Role:** Brazil played a crucial role in the phase three trials and local production of the vaccine. The country produced over 200 million doses, contributing to global vaccination efforts.

Maheshi Ramasamy

Sue Ann Costa Clemens

Vaccine Effectiveness and Correlates of Protection

Presenter: Merryn Voysey, Elaine Shuo Feng and Khiyam Hussain

Overview: The presentation discussed the importance of correlates of protection in vaccine development and licensure.

Key Points:

- **Challenges:** Defining correlates of protection is challenging due to the lack of standardised assays, protocols, and consensus on data analysis methods.
- **Examples:** The presentation highlighted examples from COVID-19, Group B Streptococcus (GBS), and Ebola virus.
- **Statistical Methods:** Different statistical methods are used to model the relationship between antibody levels and disease risk. The choice of method can impact the interpretation of vaccine efficacy.
- **Research:** Ongoing research aims to identify the best methods for defining correlates of protection and to understand the role of T-cell immunity.

Merryn Voysey

Vaccines and the Public

Presenters: *Samantha Vanderslott and Charlie Firth*

Overview: The session focused on public engagement and communication strategies to promote vaccination.

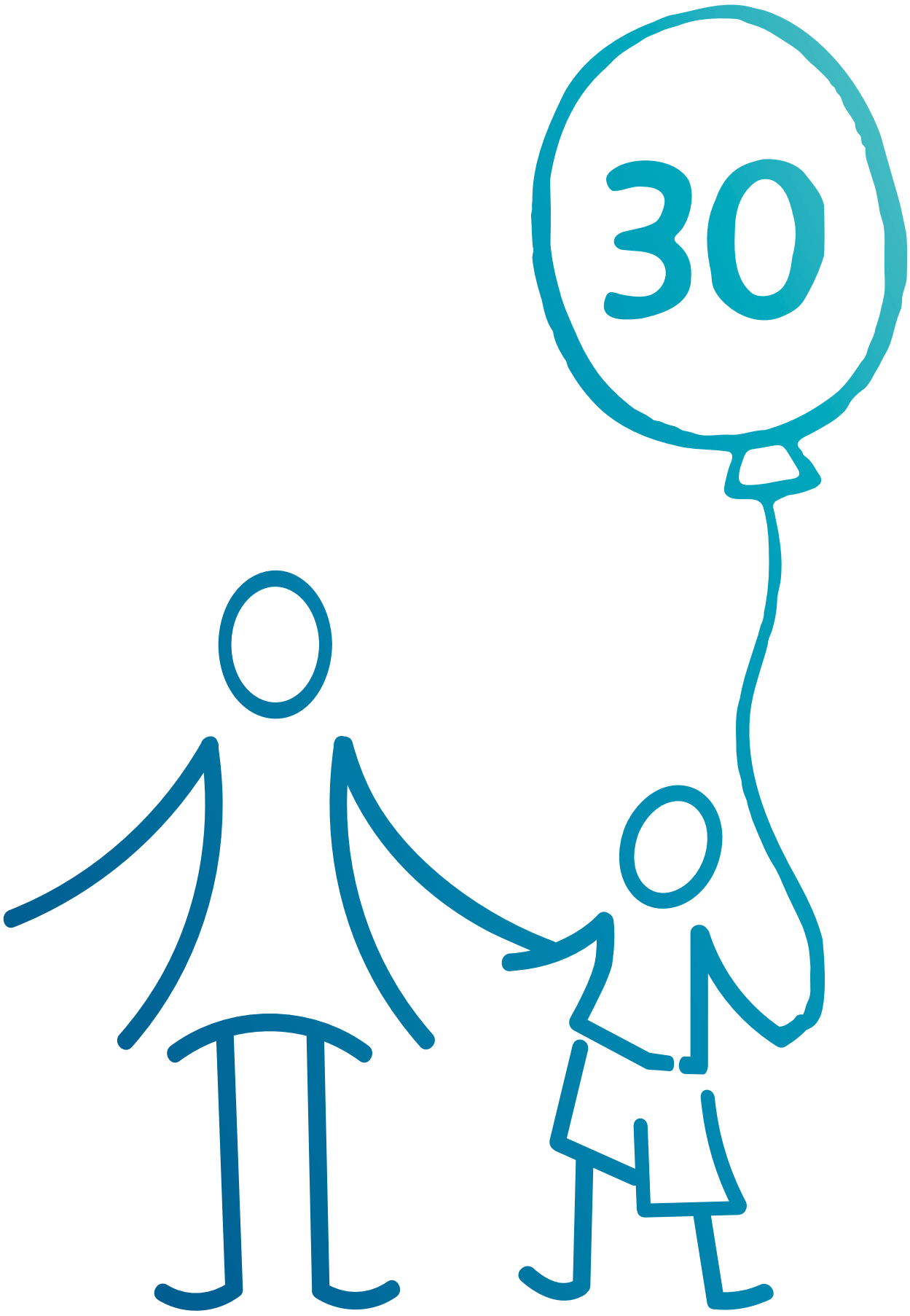
Key Points:

- **Vaccine Hesitancy:** Vaccine hesitancy is a significant issue, influenced by safety concerns, mistrust, and misinformation.
- **Community Engagement:** Engaging community leaders and healthcare workers is crucial for addressing vaccine hesitancy and improving vaccination rates.
- **Public Engagement Projects:** 'Vaccine Knowledge' provides reliable information about vaccines. Recent campaigns covered vaccine development and community immunity, with resources including a comic books and animations.
- **Impact:** The Vaccine Knowledge website has reached millions of users, providing valuable information, increasing vaccine confidence and countering misinformation.

Ongoing research and public engagement initiatives continue to improve public understanding and acceptance of vaccines.

Samantha Vanderslott

Charlie Firth


30

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