

# **CELEBRATING 30 YEARS OF THE OXFORD VACCINE GROUP**



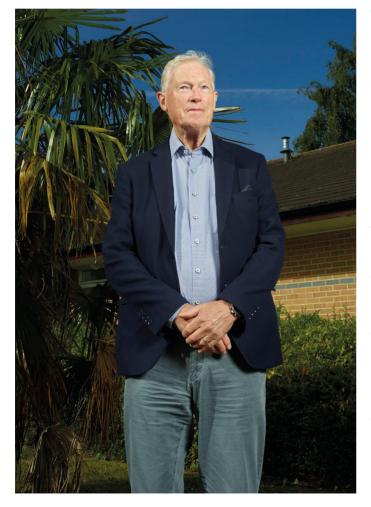
# CELEBRATING 30 YEARS OF THE OXFORD VACCINE GROUP

## Our mission

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

## Foreword

*Professor Richard Moxon* Founder of the Oxford Vaccine Group



"The Oxford Vaccine Group is a testament to the importance of determination and resilience in the pursuit of a dream"

The Oxford Vaccine Group (OVG) was an inspired idea I had over 30 years ago, borne out of opportunity and necessity, but that has now grown and flourished into the success story for global health outcomes that we are celebrating today. While a dedicated vaccine research group now seems like a no-brainer, setting up the OVG was not a straightforward process.

I came to Oxford in 1984, after fourteen years in the US – four years in Boston training in infectious diseases and ten years as a faculty member at the John Hopkins Medical School in Baltimore. My work at the time was focused on bacterial meningitis including the development of vaccines to prevent this devastating childhood disease. Vaccines against bacterial meningitis were in the early stages of clinical development at the time and so it was an opportune moment to translate my research from the laboratory to the clinic. For six years, between 1984 and 1990, my research group, including Gareth Tudor-Williams, Robert Booy and Paul Heath, undertook the necessary epidemiological and clinical



studies that set the stage for a definitive efficacy trial of a vaccine to prevent Haemophilus influenzae type b (Hib) meningitis.

And following the successful conclusion of this trial in 1991, the UK Department of Immunisation rolled out the Hib vaccine in a nationwide programme the following year with spectacular success. Encouraged by the impact of our research on this vaccine, the time seemed right to set up a dedicated vaccine research group that became OVG. Oxford had many strengths in epidemiology, microbiology, immunology and public health, and I envisaged an entity that would amalgamate this collective expertise, based within the Department of Paediatrics, and recognised by the University as a separate entity for funding purposes.

- carry out translational, multi-disciplinary research for existing and future vaccines;
- develop the required laboratory-based microbiology and immunology to facilitate and monitor vaccine implementation;
- provide a resource for education, advocacy and training in vaccinology including a referral unit for vaccine complications;
- establish, over time, a dedicated building (Vaccine Centre) for these activities.

In the 1990s this was ground-breaking territory. Oxford University, as we know, treads carefully into the unknown, and it took many months to persuade the University's General Board to approve our plan. The committee had concerns about how the OVG

The aims of OVG were to:



Richard Moxon (centre) at the launch of the Moxon Building, 2013

would be funded; what the University's liability for undertaking clinical trials would be as well as the risks of adverse reactions; and the extent to which our success would be dependent on contracts with vaccine developers.

In 1994 the Board finally gave their seal of approval for a model we had developed that secured longterm funding, including investment into the building of a dedicated vaccine centre. OVG required upfront financing to fund research doctors, nurses, laboratory personnel, statistical expertise and many other essential activities and thankfully, negotiations with several major vaccine manufacturers secured the contracts and necessary investment. These contracts had a special emphasis on the newlyhatched childhood Combination Vaccines and the development of immunisations against invasive meningococcal infections. And in 1999, the UK government's Joint Infrastructure Fund, together with substantial investment from the Wellcome Trust, provided financial support for the building of the Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) on the Churchill site, which was officially opened in 2003.

Today, OVG is still based in the CCVTM, and it has facilitated the development of many successful vaccines over the course of its 30-year story: from those preventing meningitis to respiratory syncytial virus, typhoid, pneumonia, Marburg and Ebola and of course covid-19. The Oxford Vaccine Group is a testament to the importance of determination and resilience in the pursuit of a dream that, with a little bit of luck and a whole lot of hard work, became a reality.

## Introduction

*Professor Sir Andrew Pollard* Director of the Oxford Vaccine Group



elebrating 30 years since the foundation of the Oxford Vaccine Group (OVG) is a very special moment. Every person who has been part of this journey in OVG, and all those who have facilitated our research at Oxford, can be truly proud of what we have achieved, what we are and the way in which we have conducted ourselves in science and in service to public health and one another. In those three decades OVG has made major contributions to understanding immunity, to vaccine innovation, championing human challenge models, the development, testing and deployment of vaccines, as well as clinical service and immunisation education, all aimed at achieving our mission "to improve human health through immunisation". We did just that.

In this short brochure, we reflect on some of those achievements – from discovery and translation to policy impact in the fight against meningitis, pneumonia, typhoid, outbreaks of influenza, Ebola, and many other bacteria/viruses and even a pandemic. We have been in a constant battle against the microbial world which continues to challenge us, but through it all, OVG has been part of the astonishing story of vaccines and vaccination that has demonstrably saved lives and improved the health of populations around the world. This is remarkable.

Of course, OVG is not just about science and impact. OVG is very much about a team of talented people from a wide variety of disciplines and backgrounds who work together with a shared mission and are connected through the years. The OVG environment in which we work is unique, with an extraordinary research infrastructure that enables what we do and has been expertly built over the decades. And central to that is our focus on working as a collective of researchers with our knowledge and wisdom, as well as with integrity and kindness, where everyone has a part to play, all are valued, and indeed every person is critical to our success. There is a strong sense of a shared responsibility because what we do is so important. In a recent review, OVG was commended for its positive culture and ethos, and reputation for creating a collaborative work environment. I am sure you will agree that this is an extraordinary reflection on who and what OVG aspires to be.

Since the outset of our global expansion about 20 years ago, we have had the honour to work

"OVG has the vision, wisdom and dedication to continue to change the world."

with terrific colleagues across South Asia, Africa and Latin America, to address important questions of relevance to those regions but also of global importance. Those collaborators and our experiences with them have enriched OVG and directed our work to the scientific questions that matter most.

Today, our alumni, those who have studied or trained with us over those 30 years, are spread across the globe with roles in science, medicine, and industry making their own contributions to patients, research and policy, and the future of our health. The reach of OVG is far beyond Headington. Past staff and students remain an important part of our group and it is fitting that many of them join us for the 30th anniversary symposium and celebration in reunion.

Whilst it is the right moment to look back and reflect on the past and to ponder admiringly on our many successes and what has made OVG, we cannot linger too long here as there is much still to do. The next 30 years will bring new challenges but I am confident that OVG has the vision, wisdom and dedication, underpinned by excellence in science, to continue to change the world.

## **Our Principal Investigators**



Professor Sir Andrew Pollard Ashall Professor of Infection and Immunity Director of the Oxford Vaccine Group Consultant in Paediatric Infectious Disease and Immunology Fellow of St. Cross College Chair of UK Department of Health and Social Care's Joint Committee on Vaccination and Immunisation Chair of the WHQ TAG on Salmonella vaccines



#### Associate Professor Angela Minassian

Chief Investigator, Malaria Vaccine Clinical Trials Programme Honorary Consultant in Infectious Diseases Lead for Equality, Diversity and Inclusion in Medical Education Research Fellow at Wolfson College



#### Associate Professor Brian Angus

Director of the Oxford Centre for Tropical Medicine and Global Health Associate Professor of Infectious Diseases Chair of the National Advisory Committee on malaria prevention Chair and Lead Examiner FRCPath examination board



### Associate Professor Daniel O'Connor

Head of Bioinformatics Elective Module Lead – MSc Genomic Medicine Course Tutor – Continuing Education



#### Professor Daniela Ferreira

Professor of Vaccinology and Mucosal Immunity Director of the Liverpool Vaccine Group Visiting Professor at the Universidade Federal de Minas Gerais and National Centre for Vaccines



### Associate Professor Dominic Kelly

Clinical Lead for Paediatric Infectious Disease and Immunology Deputy Director of Postgraduate Diploma in Paediatric Infectious Diseases BRC Consultant in Paediatrics and Vaccinology



## Associate Professor Katrina Pollock

Associate Professor and MRC Clinician Scientist in Vaccinology Honorary Consultant in Sexual Health Honorary Clinical Senior Lecturer in Vaccinology



### Associate Professor Maheshi Ramasamy

Consultant Physician, Acute General Medicine & Infectious Diseases Florey Lecturer and Fellow in Clinical Medicine Deputy Director Graduate Entry Medicine



Professor Merryn Voysey Head of Statistics in Vaccinology



Associate Professor Samantha Vanderslott Head of Vaccines & Society Unit University Research Lecturer Social Sciences Researcher



#### Dr Simon Drysdale

Senior Lecturer in Paediatric Infectious Diseases Consultant in Paediatric Infectious Diseases and Immunology



## Professor Sue Ann Costa Clemens CBE

Chair of Global Health and Clinical Development Professor of Paediatric Infectious Diseases, Vaccinology Director and Founder of LATAM Research Group



#### Professor Teresa Lambe

Professor of Vaccinology and Immunology Calleva Head of Vaccine Immunology



Associate Professor Xinxue Liu

Associate Professor of Medical Statistics and Epidemiology Head of Statistics in Clinical Trials

## History of the Oxford Vaccine Group

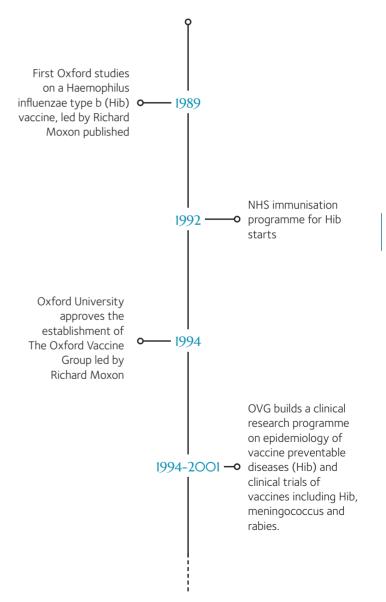
## THE EARLY YEARS

#### 1994

The Oxford Vaccine Group was established in 1994 at Oxford University by Professor Richard Moxon, Head of the Department of Paediatrics at the time. Prior to the formal approval of its name, studies on Hib vaccine had been conducted by Professor Moxon's team which had provided important data for the introduction of the vaccine to the UK immunisation schedule in 1992. As a result, the case was made to the University on the importance of vaccines in public health and the anticipated developments in technology that would advance vaccine development and evaluation.

The original terms of reference for the group in 1994 were to:

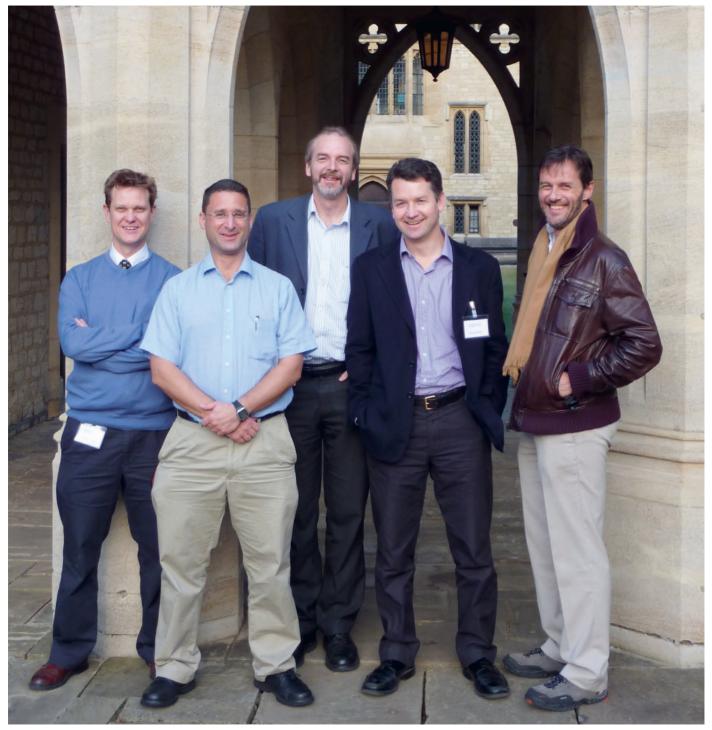
- 1. Provide a scientific resource for research into the development and implementation of vaccines.
- 2. Undertake basic and applied research on diseases for which there is no vaccine: meningococcal sepsis, AIDS, malaria.
- 3. Be a clinical referral service for adverse events and immunisation in special circumstances.



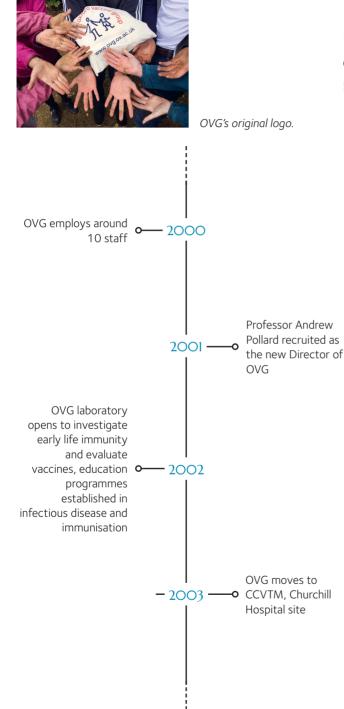
# The UK Paediatric Vaccine Group (UKPVG)

The UKPVG is an independent network of research institutions which, through collaboration, aims to further education, training and high-quality research in the field of paediatric vaccines. Founded in 2001, the group includes the Oxford Vaccine Group, Bristol Children's Vaccine Centre, University of Southampton Wellcome Trust Clinical Research Facility, Public Health England and St. George's Vaccine Institute. Its trials have examined a range of vaccines including acellular pertussis, diphteria, and tetanus vaccine as well as the safety and immunogenicity of the influenza vaccine in UK children aged 6 months to 12 years.

Over the course of the last 23 years, thousands of children have been recruited to clinical trials of relevant and important vaccines. It has been a long-lasting, successful and sustainable collaboration built on shared interests, values, mutual respect, a competitive spirit and above all, a good sense of humour.



From left to right: Matthew Snape, Saul Faust, Andrew Pollard, Paul Heath, Adam Finn



Undertake basic and applied research on diseases for which there is no vaccine: meningococcal sepsis, AIDS, malaria.

- One of the OVG's original terms of reference.

- 4. Conduct phase II safety and immunogenicity trials and develop a resource for phase I trials
- 5. Develop laboratory expertise in microbiology and immunology
- 6. Provide a platform for education and advocacy
- 7. Establish a new building at the Churchill Hospital site

OVG was originally run from an office on level 4 of the John Radcliffe Hospital, and employed a small team of research fellows and nurses who conducted epidemiological studies and ran clinical trials in children focussing on Hib and meningococcal vaccines.

### 2001

In 2001, Andrew Pollard was recruited to lead OVG and take on the clinical trials activities of the team. He was keen to expand the capabilities of the research group and set up an OVG laboratory made possible by the recently vacated physical space of a laboratory near to the trial office, which aimed to use cutting edge immunology to understand the development of immunity in babies and young children, and using vaccines as a tool to explore the immune system.

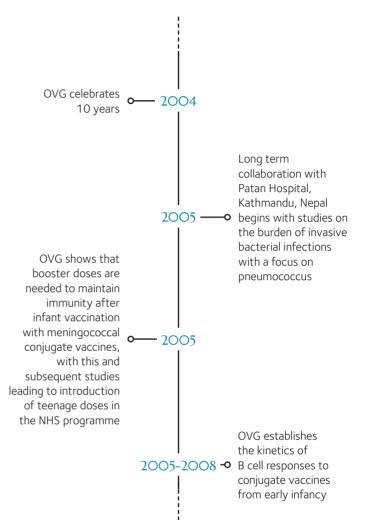
## 2003

OVG moved to the newly built Centre for Clinical Vaccinology and Tropical Medicine (CCVTM) at the Churchill Hospital site, in 2003. It initially shared about one third of the space with the Department of Medicine (who also hosted Tropical Medicine in the building at that time) however today, OVG occupies the majority of the office space and the entire laboratory.

## 2004

Following a European Directive, new clinical trials regulations came into force in 2004 but thanks to its investment in facilities and infrastructure, OVG was already in a good position to meet the new standards around clinical trial management and governance.

The group also became the only UK Clinical Research Collaboration (UKCRC – established 2007) registered clinical trials unit (CTU) focussed on vaccines (registration number: 52). The CTU runs as a collaborative with the University's Primary Healthcare Department and the Jenner Institute.





Team OVG in 2005

## Education and training

VG has had a major focus on training over the past 25 years, with an annual immunisation seminar provided for health professionals across the Thames Valley and training courses for practice nurses provided by OVG nurses. The group also runs an annual course on infection and immunity in children (IIC – the Oxford Course) aimed at trainees in paediatric infectious disease. OVG also hosts the Oxford University postgraduate certificate, diploma and Msc in Paediatric Infectious Disease and will continue to grow its education and training offering with the

opening of the Clinical Trials Training Centre in Rio de Janeiro in 2024.

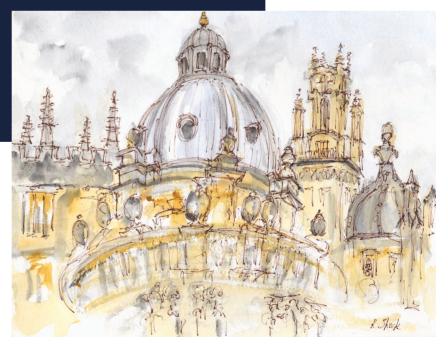
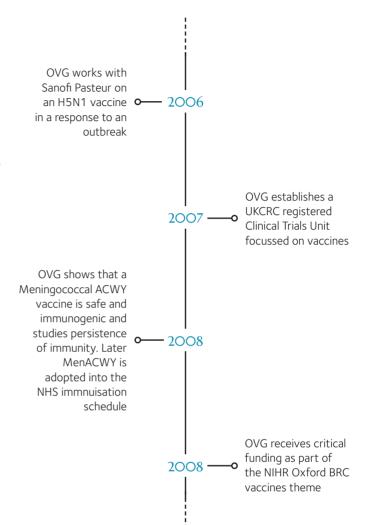


Illustration of the Radcliffe Camera from IIC course materials

## 2008

In 2008 Oxford was awarded funding by the UK Department of Health for a National Institute for Health Research (NIHR) Biomedical Research Centre (BRC), which included a vaccines theme. Originally co-led by Professor Adrian Hill and Professor Andrew Pollard it is now directed by Professor Eleanor Barnes alongside Professor Sir Andrew Pollard. At the same time the NIHR set up a national Clinical Research Network which provided additional funding to support clinical research across the UK. Together, these initiatives enabled the recruitment of key staff and led to a substantial increase in capability, research activity, trial recruitment and output.

Vaccsline was another initiative set up in 2008. This aimed to provide vaccine advice for medical staff across the Thames Valley region. It was run as a service funded by OVG in collaboration with regional public health services and a team of vaccine nurses who operated the telephone and email consultation service before the entire provision was incorporated into the UK Health Security Agency, shortly prior to the pandemic.





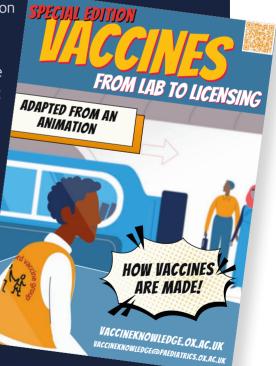
The expanding Team OVG in 2009

## Vaccine Knowledge

The Vaccine Knowledge Project was established in 2011, rebranded to Vaccine Knowledge in 2023. It is an online source of independent, evidence-based information about immunisation and infectious diseases, designed to help the general public to make informed decisions about vaccine-related issues.

The Vaccine Knowledge Project is a comprehensive resource on complex topics and since July 2016, it has been a member of the World Health Organization's Vaccine Safety Net, a global network of websites providing reliable information on vaccine safety. This means that this website has been judged to meet the World Health Organization's criteria for providing good quality information about vaccine safety issues.

Visitors to the site are predominantly healthcare professionals including health visitors, school nurses, GPs and paediatricians and all medical content is personally reviewed by Professor Sir Andrew Pollard, Director of Oxford Vaccine Group, to ensure its currency and accuracy.



Above: Cover of Vaccines: From Lab to Licensing comic book



Left: Andrew and colleagues at IIC in 2009. Right: OVG away day, 2009

## 2010

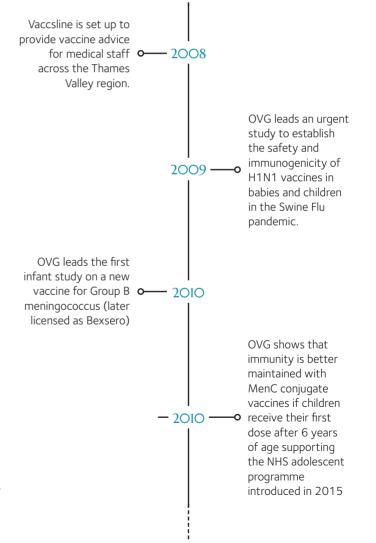
By 2010 OVG had grown from fewer than 10 researchers in 2000 to over 60 research staff (including medical doctors, scientists, nurses and trials administration) based in CCVTM and it has continued to expand with over 200 staff and students in 2024.

## **SINCE 2011**

#### Vaccines

Prior to the covid pandemic, OVG's main focus was on childhood vaccines against encapsulated bacteria with a particular focus on meningococcus, pneumococcus and typhoid. Through its research, it has made major contributions to national and international policy and understanding of the nature of immunity induced by these vaccines.

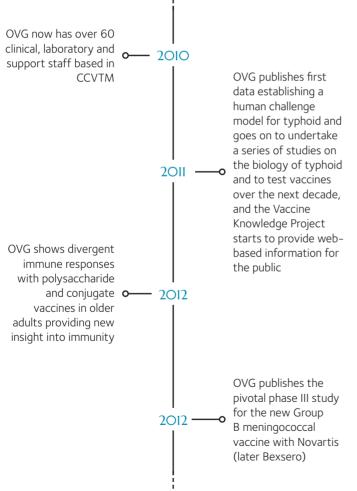
The expertise it acquired over the course of these clinical trials also led to studies on vaccines for other pathogens including influenza, RSV, Ebola, and rabies. Several new vaccines were developed in the OVG laboratory during the period between 2011 and 2020 and tested in phase I human trials. These included two group B meningococcal vaccines (outer membrane vesicles and viral vectors) and a vaccine against plague.







Left: OVG in 2011 Right: Blenheim Palace, 2012



## Human Challenge Models

OVG has also pioneered the use of human challenge models to support vaccine development for typhoid and paratyphoid, work which since 2022 has expanded to include pneumococcus, RSV, and plans for influenza and malaria. The typhoid vaccine was rolled out following WHO guidance in 2018 and since 2022 some 60 million doses have been deployed. Since 2014, OVG has also hosted the National Immunisation Schedules Evaluation Consortium (NISEC, initially led by Professor Matthew Snape and now by Professor Maheshi Ramasamy) funded by the Department of Health to conduct research to support UK policy.

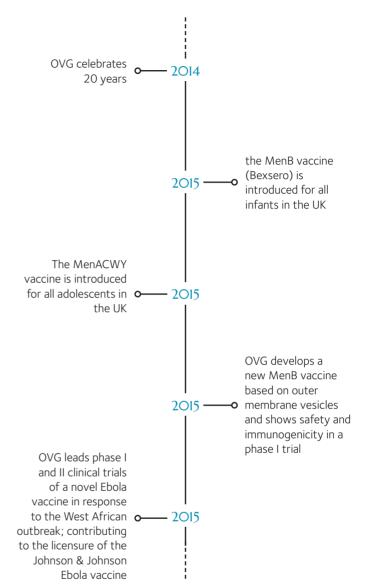
## Outbreak pathogens

OVG's capabilities have been important in the response to outbreaks. Its research has contributed to the production of the H5N1 vaccine with Sanofi Pasteur (2006), an evaluation of H1N1 vaccines for children funded by UK Government (2009), and research on novel Ebola vaccines funded by the European Community (2015/16) in response to the West Africa outbreak, which contributed to the licensure of the Johnson and Johnson Ebola vaccine. In 2020, OVG took on leadership of the clinical development of the Oxford-AstraZeneca COVID19 vaccine and led a team, with collaborators, of some 2000 researchers across UK, South Africa and Brazil which provided the pivotal data for the global licensure of the vaccine (initially registered in 180 countries) with over 3 billion doses deployed. The vaccine is said by AirFinity to have saved 6.3 million lives in 2021 alone.

Since the pandemic, OVG has developed an expanded portfolio with new investigators joining the team. The current programme led by individual Principal Investigators includes research on vaccines for bacterial diseases and viral outbreak pathogens, vaccines for childhood diseases, human challenge studies (respiratory, enteric and malaria), all of which is underpinned by cutting edge immunology.

Additional laboratory space was acquired in 2022 within the Institute for Developmental and Regenerative Medicine, and an expansion in clinical space in CCVTM was opened in 2023.

Social sciences research, ethics and philosophy have all featured in OVG's portfolio since 2001, but this was formalised under the leadership of Professor





OVG away day, 2013



OVG staff, 2013

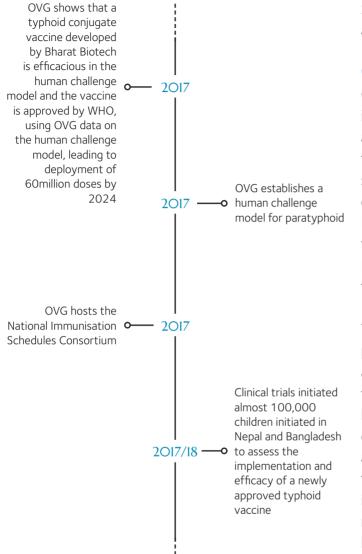
## Vaccines and Society

The Vaccines and Society Unit (VAS) is a multidisciplinary research centre hosted by the Oxford Vaccine Group. It produces theoretical and empirical research in social sciences aimed at giving the public a better understanding of health issues generally. Its research covers a wide range of public health topics including issue prioritisation, disease history, and social mobilisation although its main focus is the study of attitudes and behaviour towards vaccination in society.

VAS draws on a variety of disciplines from sociology, history, behavioural science, health economics, and public policy to combine a wide set of tools and literatures. As it is hosted by OVG, it also has unrivalled access to vaccinologists, epidemiologists, immunologists, and clinicians.



A patient gets vaccinated as part of the TyVac Nepal Study in Wolku Ward in Lalitpur, Nepal in November 2017.



Samantha Vanderslott who coordinates the Vaccines and Society unit launched in 2023.

### **Global Studies Team**

OVG has a Global Studies Programme which began in 2005 as a collaboration with Patan Hospital to assess the burden of pneumococcal disease. Over the past 19 years, the programme has expanded significantly, incorporating additional global collaborators. The number of OVG-based Principal Investigators has increased from one to seven, and the scope of projects now includes Clinical Trials of Investigational Medicinal Products (CTIMPs), large field efficacy studies, and social science research.

The Oxford based team has grown from a single part-time nurse to a full-time team that includes a clinical programme director, three research fellows, and several PhD students. We leverage high-level support from all OVG teams, including data management, grants and finance, quality assurance, and statisticians. To date we have trained and supported over 100 staff at partner institutions including research fellows, nurses, data managers, staff new to QA activities, community health workers, lab assistants and grant managers at collaborating sites.



Left: OVG, 2016 Right: Nursing staff, 2018

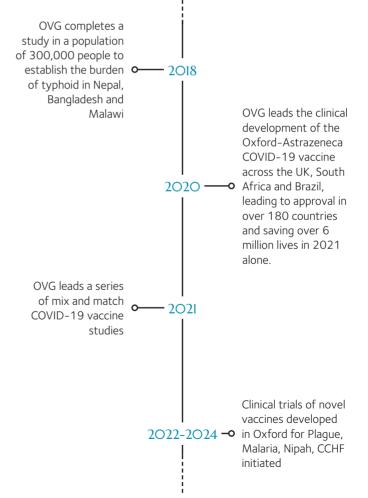


Left: Andrew with a framed cover of the Sun on Sunday, 2021 Right: Matt Hancock meeting the OVG team, 2021

Currently collaborators span three continents with partners in over six countries to facilitate highquality clinical research, thereby impacting the global vaccine landscape. Our work spans early-phase novel vaccine trials, evaluations of different vaccination schedules, and social science research on vaccine beliefs. In addition to the research activities, we aim to build confidence, competence, and capacity within our partner organisations, helping them establish local research facilities capable of delivering independent and impactful research.

We provide oversight, support, training, and mentorship to all staff at collaborating institutions and offer guidance as needed to the Oxford based teams working on malaria trials, emerging pathogens, and TB studies.

Whilst our operations extend worldwide, we have particularly strong and longstanding relationships with organisations in Brazil, Nepal, Uganda and Bangladesh with whom we work closely. New partnerships are being established for projects in Pakistan, Ghana, Nigeria and Malaysia.



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## **Clinical Trials Global Network**



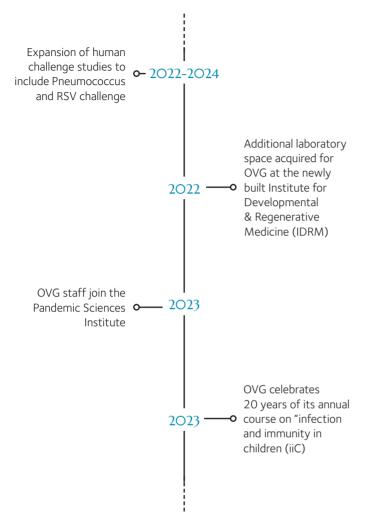
Political World Map, by Jonasz, colours desaturated. Licensed under CC.BY.3.0 Source: https://en.m.wikipedia.org/wiki/File:World\_map\_blank.svg

OVG staff were able to respond to the Covid-19 pandemic in 2020 by establishing excellent infrastructure and partnerships in South Africa and Brazil.

An important expansion of OVG's activities over the past 30 years has been the development of collaborative international research. The model used is one of partnership with local leadership: OVG staff in Oxford support research efforts and help to obtain funding and training, but the programmes are led by a local PI with travel at regular intervals to the site. Oxford clinical staff visit external sites for periods of a few days to a few months but do not live-in country.

The capability and capacity developed in large scale clinical studies (about 300,000 people in non-UK epidemiological studies from 2015) and trials (over 100,000 children in clinical trials since 2017) meant that OVG staff were able to respond to the Covid-19 pandemic in 2020 by establishing excellent infrastructure and partnerships in South Africa and Brazil. Some of our long-standing partnerships are mapped on the figure opposite. Examples of projects are:

- 1. Study of invasive bacterial diseases in children at Patan Hospital, Nepal (2005–2024) and various vaccine studies in the population (Hib and pneumococcus)
- 2. Population incidence of typhoid and paratyphoid in Nepal, Bangladesh and Malawi (2015–2024)
- 3. RCT of typhoid conjugate vaccine in Nepal and Bangladesh (2017-current)
- 4. Phase I trial of plague vaccine in Uganda (2022-2024)
- 5. Study in schedules of immunisation in infants in Nepal and Uganda
- 6. Early measles vaccine use in infants in Uganda
- 7. Covid-19 vaccine development in Kenya, South Africa and Brazil



## Typhoid and Paratyphoid studies

Assessing incidence and prevalence of typhoid and paratyphoid, along with the immune response following infection and vaccination has allowed teams to establish the burden in endemic countries (Nepal, Malawi and Bangladesh) and establish the efficacy and effectiveness of the typhoid conjugate vaccine in different settings. Surveillance of culture positive typhoid continues in these cohorts aiming to monitor medium- and long-term efficacy of the vaccination. Data from these studies has supported the introduction of the typhoid conjugate vaccine into the national schedule in Nepal from 2015, and Bangladesh as planned for 2024.

## Childhood Immunisation Schedule studies

A multisite study looking to establish the optimal strategy for childhood immunisation by establishing the immune response to differing timings and number of childhood vaccinations given. This study further plans to evaluate reasons for participation in clinical trials and attitudes towards vaccination



Left: OVG team at Patan Hospital, Nepal Right: Typhoid challenge study

schedule changes to support future trials in these settings. A measles vaccine study assessing the timing of first and second doses of measles, the first dose given at 6 or 9 months of age and boosted at 12 or 15 months of age.

## Improving diagnostics for febrile illness

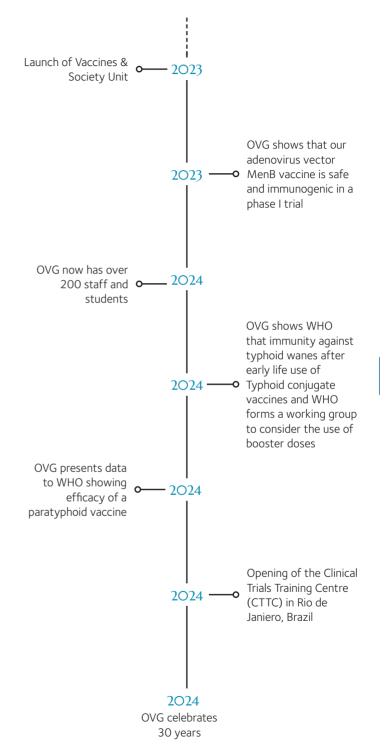
DIAMONDS is an EU Horizon2020 project to develop a molecular test for the rapid diagnosis of serious infectious and inflammatory diseases using personalised gene signatures. It recruits febrile patients across a spectrum of diseases to enable the development of a transcriptomic diagnostic signature, and the validation of this signature. The majority of sites are based in Europe, with Kathmandu being only one of two in Asia – providing invaluable data for illnesses prevalent within this continent, including dengue and typhoid.

## **Covid Studies**

The global studies team has supported Covid vaccine trials in Kenya, Brazil and South Africa; Estimating the vaccine effectiveness of various Covid-19 vaccines as well as identifying different variants of SARS CoV-2 circulating during the studies.

## **Emerging Pathogens**

Early phase vaccine studies for a variety of emerging and outbreak pathogens in a number of countries globally including Bangladesh, Ghana, Uganda and Malaysia, evidencing both their safety and immune response.



## Pandemic Sciences Institute

The Oxford Vaccine Group's outstanding contribution in the trial and rollout of the Oxford/AstraZeneca COVID-19 vaccine has led to new interdisciplinary research collaborations.

With the pandemic transforming many of the University of Oxford's historic ways of working, the OVG team developed new partnerships with researchers across the breadth of the University, working in fields of epidemiology, therapeutics, ethics and beyond.

Building on these partnerships, in 2022 OVG Professors Teresa Lambe OBE and Sir Andrew Pollard were instrumental in establishing the Pandemic Sciences Institute (PSI), a new interdisciplinary research institute dedicated to confronting the challenge of epidemic and pandemic infectious diseases.

Led by Professor Sir Peter Horby, PSI is hosted by the Nuffield Department of Medicine and brings together researchers from across all four divisions of the University of Oxford: Medical Sciences; Mathematical, Physical and Life Sciences; Social Sciences; and Humanities.

PSI's vision is a world where people and societies are better protected from infectious diseases. The Institute is working with academia, industry and public health organisations across the world to create science-led innovations, accelerate understanding, and develop new diagnostics, treatments, vaccines and disease control tools.

Current work to develop vaccines for Marburg virus, Junin virus and Crimean–Congo haemorrhagic fever are just a few examples of OVG/PSI research collaboration that is preparing the world for future pandemic threats.



## Impact case study Meningococcal and Pneumococcal Vaccines

The Oxford Vaccine Group has produced research over the past 30 years to support major developments in the childhood immunisation programme, particularly informing global policy on pneumonia and meningitis programmes, the scheduling of vaccines and the use of combination vaccines for infants and toddlers.

Studies on anti-meningococcal immunity initially identified poor quality antibody responses in young children (Pollard & Levin, Lancet 2000) and then provided new insight into immunity after vaccination with polysaccharide and conjugate vaccines (Kelly et al, Blood 2006), with the first descriptions of the nature and kinetics of the plasma and memory B cell response to polysaccharide and conjugate vaccines in infancy.

We also conducted intricate studies to show the relationship between germinal centre priming in infants and the magnitude of the immune response, suggesting that strategies that favour production of memory B cells, rather than antibody-producing plasma cells, might lead to better magnitude and persistence of immune responses in infancy. Evaluation of the group C meningococcal vaccine demonstrated poor persistence of immunity after early childhood and that young children had become susceptible again, leading to a change in policy and introduction of meningococcal booster vaccines for adolescents in many countries including the UK.

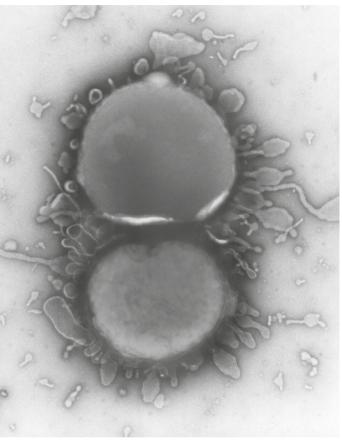
We also contributed to understanding of the role of nasopharyngeal colonization, the potential for control of transmission and induction of herd immunity with meningococcal and pneumococcal vaccines. Studies on scheduling vaccination showed that reduced dose schedules were as immunogenic as standard schedules, leading to a reduction in the numbers of doses administered for infants.

The OVG led the first global infant trials of a quadrivalent meningococcal vaccine, a combination Haemophilus influenzae type b-serogroup C meningococcal vaccine, and a serogroup B meningococcal candidate vaccine (MenB, Bexsero, GSK vaccines), supporting the eventual licensure of each of these products. The group also led the pan-European phase 3 study of the MenB vaccine which supported its introduction for all infants in the UK in 2015. We also showed how immunity to this vaccine persists through early childhood but fades by adolescence and provided novel insight into the genetic control of vaccine reactions and persistence of immunity using GWAS.

Around 600,000 infants each year receive meningococcal vaccines from the NHS which prevent up to 1,000 cases of meningitis per annum in the UK alone, directly linked to OVGs research. We have designed two entirely novel meningococcal vaccines through preclinical development to ongoing early phase studies in humans.

Furthermore, the OVG led ground-breaking studies on epidemiology, immunity and immunisation against pneumococcus, responsible for nearly 300,000 paediatric deaths globally. The work has predominantly been conducted in the UK and Nepal, where we run surveillance for invasive bacterial disease, funded by WHO and Gavi for 18 years, embedding intervention studies in the programme to assess vaccine impact, informing global policy.

Our work on interchangeability of different pneumococcal vaccines as a booster for toddlers is also cited in WHO guidance. Extensive international studies conducted by OVG have shown the impact of vaccines on nasopharyngeal carriage of pneumococci documenting changes in serotype distribution



Electron microscope photograph of a meningococcus photographed by Andrew Pollard as a PhD student in the 1990s

and informing vaccine programmes. Our work has contributed to an extensive series of host and bacterial genetic studies showing genes associated with meningitis and molecular epidemiology of S. pneumoniae. Furthermore, in an extensive series of laboratory studies, we investigated immunity to polysaccharide and conjugate vaccines and showed that antigen-specific B cells were depleted by plain polysaccharide vaccines but not conjugate vaccines, reducing responsiveness to subsequent vaccine doses.

## Impact case study Typhoid

The OVG's work on typhoid has been hugely influential, changing our understanding of the biology and the potential of vaccination to control the disease. Since typhoid occurs only in humans, it cannot be studied in animals, and so the decision to use human challenge studies, built on an ethical and scientific framework, was a game changer, enabling a new understanding of the pathogenic mechanisms driving the disease, and an evidence-based approach to evaluate interventions like vaccines.

e showed that a small oral dose of 10,000 Salmonella Typhi bacteria resulted in clinical typhoid in two thirds of volunteers. We analysed transcriptional, cytokine and antibody responses during acute disease, identifying an unexpected asymptomatic transcriptional and cytokine signature in all individuals within 24 hours of challenge. Further immunological and transcriptional analyses showed that clinical symptoms were associated with a type I/II interferon signatures that correlated with disease progression. The human challenge model also identified a central role for host tryptophan metabolism in the pathogenesis of typhoid fever, as well as providing new data on diagnosis, antibiotic performance, and immune correlates. The typhoid model is now referenced in the WHO guidelines for vaccine manufacturers, an exemplar for its utility for vaccines development against other diseases.

We also led ambitious large-scale studies on the burden of typhoid in Nepal, Bangladesh and Malawi. These trials, involving 300,000 people, resulted in exquisite analysis showing a higher-than-expected burden of the disease in children after adjusting for healthcare seeking behaviour, phlebotomy rates and blood culture sensitivity. This in turn provided key evidence for WHO decision-making on vaccine use.

In these populations we implemented field vaccine safety and efficacy trials involving 100,000 children across the study sites. An interim analysis of 20,000 children in Nepal showed that the typhoid conjugate vaccine provided 82% efficacy. We corroborated these data using a novel technique for estimating efficacy using serological markers from another trial in India. Working with colleagues in Bangladesh, we



verified these findings in a landmark paper showing protection with a single dose even in children under two years of age (Qadri et al, Lancet 2021). The safety data from these field trials were referenced in a review by WHOs Global Advisory Committee on Vaccine Safety (Typhoid vaccines (who.int)).

The work proved instrumental in driving the impetus to use the typhoid conjugate vaccine to protect children in endemic areas and control outbreaks of multiple antibiotic resistant S. Typhi. 10 million doses were used at the end of 2019 to contain an outbreak of extraordinarily resistant (XDR) typhoid in Pakistan, and since then there have been introductions in seven countries with 60 million children already protected amid an ongoing roll out.

We have now begun work on the disease caused by the genetically distinct pathogen, Salmonella Paratyphi A, identifying pathways for pathogenesis, antigenic targets and opening up routes for vaccine development using a new controlled human infection model, with a vision for comprehensive control of enteric fever by driving development of a bivalent typhoid-paratyphoid vaccine.

# Outbreaks Ebola

The OVG led the clinical trials of the Oxford coronavirus vaccine, leading challenging urgent international studies in a pandemic with 25,000 volunteers enrolled in 2020 – an extraordinary achievement in setting up rapid and efficient global clinical development through to global licensure despite the limited resources of a university research team and a global lockdown.

In the first Covid-19 vaccine trials in Europe, we assembled a team of more than 1000 researchers from early February 2020 to develop the clinical programme at unprecedented speed and scale with the first volunteer vaccinated in Oxford on 23rd April 2020. The subsequent pivotal efficacy trials across England, Scotland, Wales, South Africa and Brazil, led to authorisation of the vaccine in the UK on 30th December 2020. It required judicious, innovative methodology to capture key data on protection, laboratory correlates of protection, and dosing, Further analyses showed protection with a single dose, the improved immune responses and efficacy with longer dose intervals, impact on transmission against early variants, protection against subsequent variants and the first analysis of novel correlates of protection (see full publications list).

We assessed the profile of vaccine-induced antibody responses, using systems serology, and T cell responses (papers in Nature Medicine) showing the breadth of immune responses to Covid-19 vaccines including neutralising and non-neutralising antibodies with Ec-mediated functions. The vaccine was licensed in over 180 countries, with more than three billion doses distributed, a major contributor to Covax and estimates that it saved more lives (6.3 million) than any other vaccine in 2021. OVG led global trials of a Beta-variant vaccine showing the profile of neutralizing antibody against ancestral and subsequent viral variants, studies of mixed schedules of vaccine products in LMICs and evaluation of the original vaccine in children. We worked with the CEPI on guidelines on enhanced disease, and advised international governments and global organisations throughout the pandemic.

We made major contributions in science communication by providing information to the public about the pandemic with numerous appearances in the global broadcast and written media and an ongoing podcast series. Our contributions in the Covid-19 pandemic were recognised by the award of Royal Honours to various members of the team and receipt of the Royal Society's prestigious Copley medal (awarded to the Oxford vaccine team) in 2022.

Our work on Covid-19 vaccines built on prior outbreak response experience. OVG led the UK paediatric clinical trials of vaccines against the H1N1 pandemic virus in Autumn 2009 enrolling 943 children in five weeks, and enabling immunisation recommendations by the Department of Health for three million children under five years of age and informing global policy. We had previously evaluated H5N1 vaccines, showing poor responses to standard non-adjuvanted vaccines, which informed development in the 2009 pandemic. We led an expedited phase II clinical trial of an adenovirus/MVA Ebola vaccine Ebola (contributing to approval by the European Medicines Agency in 2020) in response to the huge 2013 West African outbreak.

This is one of only two licensed Ebola vaccines and was recently deployed for outbreak control in the Democratic Republic of Congo (DRC). During the recent filovirus outbreaks in 2022-2023 in Equatorial Guinea, Tanzania and Uganda, two vaccines designed and tested by OVG (Lambe) were selected by the WHO Technical Advisory Group (TAG CVP) for inclusion in ring vaccination trials. In just 60 days, the Serum Institute of India manufactured approx. 400,000 doses with 40,000 doses deployed to Uganda during the outbreak.





Oxford Vaccine Anthem The Oxford Colloquy Podcast Umbrella of Protection Animation The Deadly Six Art Installation

The following pages detail four artistic responses to the work of the Oxford Vaccine Group in celebration of their thirty years battling some of the world's most deadly diseases.

# Oxford Vaccine Anthem

#### Words and music by Professor Christopher Wood MB B Ch, MD, FRCSEd, FLSW, LMRCO

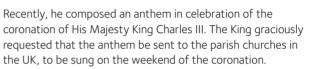
his anthem has been composed specifically to commemorate the 30th anniversary of the Oxford Vaccine Group. Both the words and music have been created by Professor Christopher Wood, who also composed the anthem for the Coronation of King Charles III in 2023. The music conveys firstly the fear and despair that outbreaks of serious infectious diseases bring, followed by the shock of illness, and then the hope that comes with the provision of life-saving vaccines. While the pandemic is a contemporary backdrop to the words, the anthem is written to highlight the breadth of vaccine discoveries that keep us all healthy, as well as OVG's ground-breaking research.

It will be premiered for the first time in Keble College Chapel, Oxford, on the evening of 26th September, 2024 and a recording will be available on the Oxford Vaccine Group website. Our world, our ordered world was filled with fear. For death, in dark and sudden form came near. It brought despair and dread, As swift the microbe spread. So many lives were lost, And at what sad and awful cost; But at a time of great despair We saw the best of human care. The darkest hour when hope was gone The light of human kindness shone. For then as one we stood, United for the common good; And in our deepest pain, We saw the best of us again; And kindness was life's soft refrain.

New hope, fresh hope sprang up to show the way. New dawn then broke for us, a brighter day. For science took control, To play a central role, And find the vital lead, An answer for our desperate need. From Oxford's dreaming spires there came A finding of such great acclaim. And novel vaccines now protect From our disease's worst effect. To those who found new ways To them we give due praise. Their works for ever stand With grateful tribute from our land. Professor Christopher Wood was born in Wales and graduated in Medicine from the Welsh National School of Medicine. He trained as a surgeon, becoming a consultant surgeon at the Royal Postgraduate Medical School at Hammersmith Hospital, London and an honorary Professor at Imperial College, London. He holds a postgraduate M.D. from the University of Wales School of Medicine and is a Fellow of the Royal College of Surgeons of Edinburgh. He was made a Fellow of the University of Wales Trinity St David and a Fellow of the Learned Society of Wales for his contribution to medicine. In 2020 he was given the Freedom of the City of London for his achievements in medicine and the Arts. In 2021 he was given a lifetime Achievement Award by the Scottish Life Sciences Association for his accomplishments in the field of medicine.

Christopher Wood has gained an international reputation for his ability to identify, develop and commercialise innovative medicines. His first successful venture was a biotech business he co-founded and which became a public listed company on the London Stock Exchange. This was one of the first (if not the first) biotech company to go public in the UK. Then he founded a biopharmaceutical company, Bioenvision Inc, that he took public on NASDAQ and which, as Chairman and CEO, he led to a successful acquisition. At Bioenvision, Christopher developed the first new drug to be approved for childhood leukemia in over 30 years, and for which he was given a lifetime achievement award by the Leukemia and Lymphoma Society in the USA. He was a co-founder of NuCana PLC and served as Executive Chairman until 2020. taking the company public on the NASDAQ exchange in the U.S. He is also the founder and chairman of Thirty Group Ltd, MedAnnex Ltd and aTen Therapeutics Ltd - companies developing new medicines to treat cancer, autoimmune disease, lung infections and Alzheimer's disease. Chris also founded Edixomed Ltd, a company in which he developed a technology to combat antibiotic resistance, and which was recently acquired by one of the world's leading advanced wound care companies.

Christopher Wood is also known for his contribution to music and the arts. He has composed several major choral works, including *Requiem*, Easter Oratorio (*Holy Week*) and *Warrior Trilogy*. His orchestral works commemorating the 50<sup>th</sup> Anniversary of the Aberfan disaster and the D-Day landings have been performed at the Last Night of the Welsh Proms. *Aberfan* was first broadcast on Classic FM as part of the Full Works Concert in August 2017. It was also performed by the Royal Philharmonic Orchestra at Cadogan Hall in April 2018 and the Britten Sinfonia in King's College chapel, Cambridge in July 2023.



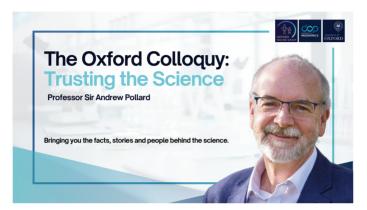
He was appointed a Trustee of the Royal College of Organists and served as chair of the council for 3 years. In recognition of his services to the RCO he was granted an honorary lifetime membership of the College. He now serves as chair of the RCO Foundation and has made substantial donations to the Foundation to fund the ambitious project of placing organs in 700 state schools in the UK.

Christopher is also chair of the Campaign Committee at the Guildhall School of Music and Drama. The aim of the committee is to establish a legacy fund to give financial support to talented individuals who are unable to meet the tuition costs. Chris has fronted this programme by providing the funds for a Scholarship for gifted students from deprived backgrounds. Roderick Williams, a rising star in the operatic world, who studied at the Guildhall School and who sang at the coronation, kindly agreed to add his name to the grant, thereby giving extra kudos for the recipients of the award. The Scholarship will provide funding for a student a year for the next 10 years.

Christopher has recently been appointed Chair of the St Alban's International Organ Festival, one of the world's leading organ competitions, and a trustee of the Oxford Philharmonic Orchestra.

In addition, Christopher has made substantial philanthropic donations to the Royal Philharmonic Orchestra, the Welsh Proms, the Welsh International Academy of Voice, and for the music at his local church in Christchurch.

# The Oxford Colloquy



To celebrate the 30th anniversary of the Oxford Vaccine Group, Professor Sir Andrew Pollard has recorded a second series of The Oxford Colloquy – his discourses dedicated to exploring the world of science by delving into the fascinating facts, stories, and people that make it all possible.

This series is called Trusting the Science and each episode delves into a conversation on the crucial role that science plays in our understanding of health and immunity. The Professor interviews leading global experts – starting with Anthony Fauci, Chief Scientific Advisor to seven US Presidents – on their scientific discoveries, and their thoughts on how we build and maintain the public's trust in scientific knowledge at a time of misinformation and cynicism. Episodes in the series:

- Anthony Fauci, former Chief Scientific Advisor to the President of the US, about dedication to a life of service, delivering the largest and most impactful public health endeavour, and using science to lead his decision-making throughout his career.
- 2. **Dame Sally Davies**, former government Chief Medical Officer and UK Special envoy on AMR, talks about her journey into medicine, legislating for public health, and the complexities of tackling antimicrobial resistance.
- 3. **Dr Ananda Bandyopadhyay**, Deputy Director of Technology, Research and Analytics in the Polio Team at the Bill & Melinda Gates Foundation on his drive to eliminate preventable disease, the decline of trust in scientific interventions and the frontline workers in his Global Health Olympics.
- 4. **Professor Peter Doherty**, Nobel laureate, immunologist and Australian National Treasure, on his controversial discovery of killer T cells, ensuing notoriety, and the accidental tweet that actually made him famous.

5. **Fiona Fox OBE**, Honorary Fellow of the Royal Society and Chief executive of the Science Media Centre, on improving the quality of the science in our news, the politics of the truth and the importance of good communicators in the media.

- Scottish-born **Professor Ian Fraser**, founding CEO and Director of the Translational Research Institute in Brisbane, on the painstaking work involved in ground-breaking research, difficulties of securing funding and the development of a vaccine for the prevention of HPV infection and precancer.
- 7. **Matt Hancock**, former MP and Secretary of State for Health from 2018 to 2021, on the communication of public health policy and the role and impact of social media on it.
- 8. **Heidi Larson**, founding director of the Vaccine Confidence Project at the London School of Hygiene and Tropical Medicine, on the cultural,

Exploring the world of science by delving into the fascinating facts, stories, and people that make it all possible.

political, social and economic impacts on immunisation programmes and the drivers behind regional differences in trust in science.

- 9. **Professor Margaret Stanley OBE**, Emeritus Professor of Epithelial Biology at the University of Cambridge, on the immune system, the development of an HPV vaccine and the impact of communication on local and global vaccination programmes.
- 10. **Professor Andrew Steer**, Director of Infection, Immunity and Global Health at the Murdoch Children's Research Institute and Paediatric Infectious Disease Specialist at Royal Melbourne Children's Hospital, on the link between childhood sore throats and adult cardiology, and the controversial drug Ivermectin as "a terrible drug for COVID, but fantastic drug for parasites".

Episodes will be released on the last Thursday of every month. Available on www.podcasts.ox.ac.uk

#### **Umbrella of Protection Animation**

E stablished by Professor Sir Andrew Pollard in 2011, Vaccine Knowledge is an independent, free, online source of evidence-based information about vaccines and infectious diseases. The site provides clear information on complex topics, supported by references to reliable research.

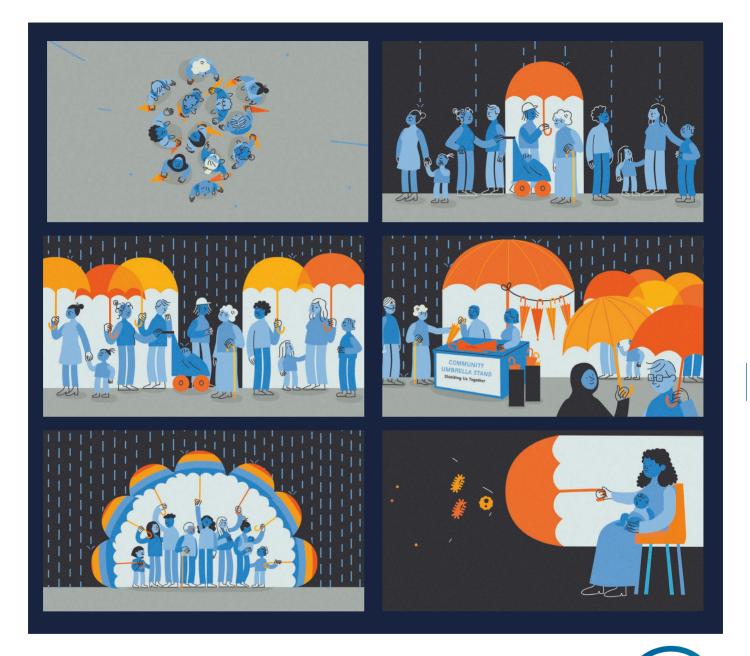
To coincide with the 30<sup>th</sup> anniversary of the Oxford Vaccine Group, and the 16<sup>th</sup> year since the project's inception, Vaccine Knowledge is launching a new animation and graphic booklet, to emphasise the power and importance of herd immunity, in particular focusing on the critical role of maternal vaccines. The animation uses a simple yet powerful analogy: umbrellas in the rain. Just as a group of people raising umbrellas can shield others from the rain, vaccines protect communities by reducing the spread of disease. The narrative illustrates how vaccination creates a protective shield, ensuring that even those who cannot be vaccinated directly, like newborns, are safeguarded.

The accompanying illustrated booklet also explores these concepts, offering the same visual aids to reinforce the importance of maintaining high vaccination levels within communities, and inform the public about how vaccines can protect entire communities, and not just individuals. Both the animation and booklet are available on the Vaccine Knowledge website, alongside a comprehensive collection of information on vaccines and the infectious diseases they prevent.

All content created by Vaccine Knowledge Project is aimed at the general public and designed to help them make informed decisions about vaccinerelated issues. Its resources are frequently cited by healthcare professionals including school nurses, GPs and paediatricians.

Vaccine Knowledge is managed by the Oxford Vaccine Group, and updated regularly to make sure information is as accurate as possible. All medical content is reviewed by Professor Pollard.

Since July 2016 Vaccine Knowledge has been a member of the World Health Organization's Vaccine Safety Net, a global network of websites providing reliable information on vaccine safety. This means that this website has been judged to meet the World Health Organization's criteria for providing good quality information about vaccine safety issues.



A new animation and graphic booklet, to emphasise the power and importance of herd immunity, in particular focusing on the critical role of maternal vaccines

### The Deadly Six

A cclaimed Scottish sculptor Angela Palmer, has created a stunning woven display of super-sized bacteria, viruses and parasites to mark the 30th anniversary of the Oxford Vaccine Group (OVG).

Palmer, whose work features in permanent collections of museums worldwide – including the Smithsonian Air and Space Museum in Washington, and the National Galleries of Scotland – was asked to create a visual representation of six key vaccines OVG had developed over the course of its 30-year history. These are:

Pneumonia (*Streptococcus pneumoniae*) Meningitis (*Neisseria meningitidis*) Typhoid (*Salmonella* Typhi) Coronavirus (SARS-Cov2) Ebola (Ebola) Malaria (*Plasmodium falciparum*)

Palmer originally planned to use the same technique she had used for her glass sculpture of the coronavirus, now on permanent display in London's Science Museum. However, it soon became clear that aside from the covid virus, none had been modelled in 3D and so she found herself at a loss. "While I was battling to find an alternative concept" she explains, "I came across a collection of strange, three-dimensional shapes woven in straw at a restaurant while on holiday in Corsica. One particular shape reminded me of the meningitis bacteria form which I had recently been researching for the project.

It struck me that I could explore creating the entire installation in willow – a tree that is native to the UK and a material imbued with historical medicinal associations, dating back over 3,500 years when willow bark was used by Sumerians and Egyptians as a painkiller and antipyretic. Indeed, Hippocrates recommended an extract of willow bark for fever, pain and child birth."

Her research then led her to two of the foremost and talented weavers in the UK, Jenny Crisp and her daughter Issy Wilkes, based in Worcestershire. In spite of the breakneck speed required to complete the project, they readily accepted the challenge.

Issy and Jenny then pored over scientific illustrations and drawings of how Palmer visualised the elements. These included electron microscope photographs forwarded by Professor Pollard of a meningococcus, as well as an image of the malaria parasite invading



"Willow [is] a tree that is native to the UK and a material imbued with historical medicinal associations, dating back over 3,500 years"

a red blood cell taken by Simon Draper, Professor of Vaccinology and Translational Medicine.

Palmer's vision was to loosely interpret each form in willow but dramatically upscaled, and then to suspend them as an installation from the ceiling. Issy and Jenny then embarked on an intense period of experimentation in their workshop, interpreting the structures using a multiplicity of weaves, including the pili of some bacteria and flamboyant flagella on the Salmonella. They resolved to weave the coronavirus into a sphere with protruding corkscrews in white stripped willow.

Within the element representing malaria – a teardrop form resembling the shape of the parasite sent by Professor Draper – Palmer has introduced the sound of one of the deadliest mosquitoes in the world and a recording will be played, on a loop, within the woven vessel. The sound will pause for a few seconds every minute to reflect the fact that one child under the age of five dies every minute from malaria. The recordings were provided by Dr Marianne Sinka, co-principal investigator of HumBug, an Oxford University programme which uses lowcost smartphones to detect the flight tones of the deadliest mosquitoes, helping to understand the presence of malaria vectors using real-world acoustic data. For the malaria vessel, the artist sought the expertise of a third willow weaver, Mel Bastier, based in the Vale of Glamorgan in Wales.

To help realise the sound element, Palmer consulted Professor Ron Roy, head of the University's Department of Engineering, who in turn introduced her to associate engineering professor, James Kwan, part of the Physical Acoustics Lab, who generously agreed to offer his guidance.

The installation will be on display at the Museum of Natural History in Oxford until early 2025.



The Oxford Vaccine Group, July 2023