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Opening Welcomes

Syexwalia (Ann Whonnock)



Syexwalia /Ann Whonnock is an First Nations Health Authority Knowledge Keeper & Elder from Squamish Nation with strong Indigenous worldviews, ancestral knowledge and traditional teachings, widely respected and acknowledged for her work and energy commitment to her community.

Bonnie Henry



Dr. Bonnie Henry was appointed as British Columbia's provincial health officer February 1, 2018 following three years as the deputy provincial health officer. Preceding this, Dr. Henry served as the interim provincial executive medical director of the BC Centre for Disease Control (BCCDC) and was the medical director of Communicable Disease Prevention and Control and Public Health Emergency Management with the BCCDC and medical director for the provincial emerging and vector-borne diseases program as well as a provincial program for surveillance and control of healthcare associated infections.

She joined Toronto Public Health in September 2001 as associate medical officer of health where she was responsible for the Emergency Services Unit and the Communicable Disease Liaison Unit. In 2003, she was the operational lead in the response to the SARS outbreak in Toronto. Dr. Henry has worked internationally with the WHO/UNICEF polio eradication program in Pakistan and with the WHO to control the Ebola outbreak in Uganda.

She is a specialist in public health and preventive medicine and is board certified in preventive medicine in the U.S. She graduated from Dalhousie Medical School, completed a Masters in Public Health and residency training in preventive medicine at University of California, San Diego and in community medicine at University of Toronto.

Invited Presentation Abstracts

Opening Keynote

Protecting the next generation through neonatal and maternal immunization

Speaker: Dr. Shabir Madhi, University of the Witwatersrand, South Africa

Despite global progress in reducing under-5 childhood deaths as part of the Millennium Development Goals agenda (1990 to 2015), reductions in mortality rates during the neonatal period (-49%) lagged behind those in children 1-59 months of age (-62%). Furthermore, there has been limited focus on prevention of stillbirths, despite the stillbirth rate exceeding neonatal mortality rate in many low-middle income countries. The Sustainable Development Goal 3.2 aspire to prevention of all preventable deaths of newborns and children by 2030, including reduction of neonatal mortality to 12 per 1,000 live-births. In addition, the "Every Newborn Action Plan" aims to reduce stillbirth rates from

20 to 10 per 1,000 births by 2035. Universal coverage and access to reproductive health care services, and vaccines is core to the realisation of the SDG goals.

Quantifying the potential of maternal vaccines, or other prophylactic interventions, in reducing maternal morbidity, stillbirth rates and early-infancy deaths requires more in-depth and objective investigation (compared to imputation from verbal autopsy) of the causes of these deaths. Recent surveillance using minimal invasive tissue sampling (MITS), unmask the hitherto largely neglected contribution of infection as the dominant immediate cause of stillbirth and neonatal deaths, including in deaths usually attributed to premature birth. Such data are essential to inform the prioritisation of research and interventions aimed at reducing maternal and childhood deaths.

The potential of maternal immunization (coupled with other possible changes) in reducing neonatal mortality, is manifest by the near elimination of neonatal tetanus globally following recommendation of routine tetanus vaccine immunization of pregnant women. Furthermore, since the 2009 H1N1 influenza pandemic, there has been an acceleration of research on the value proposition of maternal immunization in improving maternal health, reducing adverse fetal outcomes and preventing infection-related morbidity and mortality during early infancy. This includes demonstrated effectiveness of acellular-pertussis vaccination of pregnant women in reducing severe pertussis during early infancy. Furthermore, randomized-controlled trials of seasonal influenza vaccination of pregnant women in low-middle income countries, provide evidence for vaccine-efficacy against seasonal influenza illness in the women and their young infants; and protection against other consequences of influenza infection in the mothers and infants. Also, the first efficacy trial of a RSV vaccine in pregnant women, demonstrated its potential for preventing the leading cause of severe lower respiratory tract infection during early-infancy, particularly in low-middle income settings. The prevention of RSV LRTI in early infancy could be augmented through the use of new-generation monoclonal antibodies that have an extended half-life; >75% efficacy against severe RSV LRTI in preterm babies. Another pathogen targeted in the maternal immunization program is Group B streptococcus (GBS), although a number of challenges exist in the licensure pathway of such as vaccine.

The successful adoption of the ever increasing number of potentially life-saving vaccines targeted at immunizing pregnant women, warrant integration into antenatal reproductive health programs. Future research on the potential of vaccines or monoclonal antibodies in reducing stillbirths and morbidity and mortality in young infants, need to be informed by systematic, biological investigation of the causes of such deaths.

Maternal tetanus vaccination as a platform for the implementation of maternal immunization in LMICs

Speaker: Dr. Philipp Lambach, World Health Organization, Switzerland

This talk, will summarize WHO activities to support maternal immunization platforms in LMICs. It will include efforts to support the introduction of future vaccines and findings of the Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) project, a collaborative effort between the WHO Departments of Immunization, Vaccines and Biologicals (IVB) and Maternal, Newborn, Child and Adolescent Health (MCA). MIACSA assesses current maternal tetanus vaccine service delivery strategies and factors associated with effective delivery in low resource settings. The session will discuss how maternal tetanus vaccine delivery strategies can be strengthened, and how countries can improve their delivery systems to be better prepared to consider the introduction of new maternal vaccines such as influenza, GBS (group B streptococcus) and RSV (respiratory syncytial virus).

Linking mothers and infants to assess the safety and effectiveness of maternal immunization.

Speaker: Deshayne Fell, University of Ottawa, Canada

Electronic health care data such as insurance claims, health administrative databases, registries, and electronic health records are being increasingly used to address important research on vaccine coverage, safety and effectiveness of maternal immunization. This presentation will highlight major advantages of using large, linked databases as well as commonly encountered challenges, illustrated by recent examples from research on maternal immunization.

Session 1 Oral Abstracts

Abstract O-1

Maternal pertussis vaccination during pregnancy and early childhood health outcomes in Ontario, Canada

Meghan Laverty, Natasha Crowcroft, Shelly Bolotin, Steven Hawken, Kumanan Wilson, Gayatri Amirthalingam, Anne Biringir, Jocelynn Cook, Vinita Dubey, Scott Halperin, Frances Jamieson, Jeff Kwong, Manish Sadarangani, Mark Walker, Deshayne Fell

Introduction/Background & Aims: Immunization with pertussis-containing vaccine is recommended to pregnant women in many countries worldwide to prevent pertussis infection in their young infants. Safety concerns are one of the main reasons for pregnant women not becoming immunized and can also affect health care provider willingness to recommend vaccination to their pregnant patients. The aim of this research was to assess the association between maternal Tdap (tetanus-diphtheria-acellular pertussis) vaccination and early childhood adverse health outcomes, both immune-related and non-immune related, in order to address evidence gaps about the longer-term safety of the vaccine in pregnancy.

Methods: We conducted a population-based retrospective cohort study in the province of Ontario, Canada, comprising 625,618 live births between April 2012 and March 2017. Infants were followed up until March 2018, for 1 to 6 years. We compared rates of outcomes between infants born to vaccinated ($n=12,045$ (1.9%)) and un-vaccinated women using adjusted incidence rate ratios (aIRR) estimated from Poisson regression or adjusted hazard ratios (aHR) estimated from Cox models. Propensity scores and inverse probability of treatment weighting were used to adjust for confounding.

Results: No association was found between vaccination and most immune-related outcomes in children (asthma: aHR 1.15, 95% CI: 0.86-2.37; upper respiratory infections: aIRR 1.05, 95% CI: 1.02-1.09; lower respiratory infections: aIRR 0.99, 95% CI: 0.94-1.05; otitis media: aIRR 1.06, 95% CI: 1.00-1.12), although we observed an inverse association between vaccination and gastrointestinal infections (aIRR 0.90, 95% CI: 0.84-0.97). No associations were observed with non-immune related morbidity outcomes (neoplasm: aHR 1.09, 95% CI: 0.50-2.39; vision or hearing loss: aHR 1.01, 95% CI: 0.48-2.13) or non-specific morbidity measures (urgent and in-patient health service utilization: aIRR 1.00, 95% CI: 0.98-1.02).

Conclusions: We did not observe any adverse association between exposure to Tdap vaccine during pregnancy and early childhood health outcomes, further supporting the long-term safety of Tdap administration in pregnancy.

Abstract O-2

Effectiveness of inactivated influenza vaccination in pregnant women for prevention of influenza-associated hospitalization in their young infants: a case-control study

Marta C. Nunes^{1,2}, Sibongile Walaza^{3,4}, Susan Meiring^{3,4}, Heather J Zar⁵, Gary Reubenson⁶, Sarona Lengana³, Raphaela Itzikowitz³, Kate Bishop³, Azwifarwi Mathunjwa³, Amy Wise⁷, Florette Treurnicht³, Orienka Helfferscee³, Pamela Sithole^{1,2}, Andrew Moultrie^{1,2}, Matt Laubscher^{1,2}, Nasiha Soofie^{1,2}, Natali Serafin^{1,2}, Clare L. Cutland^{1,2}, Shabir A. Madhi^{1,2}, Cheryl Cohen^{3,4}

¹Medical Research Council: Respiratory and Meningeal Pathogens Research Unit, University of the Witwatersrand, Johannesburg, South Africa; ²Department of Science and Technology/National Research Foundation: Vaccine Preventable Diseases, University of the Witwatersrand, Johannesburg, South Africa; ³Centre for Respiratory Disease and Meningitis, National Institute for Communicable Diseases, Johannesburg, South Africa; ⁴School of Public Health,

University of the Witwatersrand, Johannesburg, South Africa; 5Department of Paediatrics & Child Health, and SA-MRC Unit on Child & Adolescent Health, University of Cape Town, Cape Town, South Africa; 6Department of Paediatrics & Child Health, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa; 7Department of Obstetrics and Gynaecology, Rahima Moosa Mother and Child Hospital, University of the Witwatersrand, Johannesburg, South Africa.

Background: Influenza vaccination of pregnant women prevents influenza-associated illness in their infants. However, effectiveness of this strategy against influenza-associated hospitalization in settings with high maternal HIV-infection prevalence has not been investigated.

Aim: We assessed the effects of maternal vaccination in preventing influenza-associated hospitalizations in infants aged <6 months.

Methods: Before the anticipated onset of annual influenza epidemics during 2015-2018, influenza vaccination campaigns targeted at pregnant women were implemented at selected antenatal clinics (ANC) associated with four hospitals in two South African provinces. These campaigns were coupled with prospective hospital-based surveillance for acute-respiratory or febrile illness in infants <6 months old, including influenza PCR testing. A test-negative case-control study-design was used to estimate vaccine effectiveness (VE). Cases and controls were hospitalised infants whose mothers were eligible to have received vaccine and tested influenza positive or negative, respectively. For each case, 5 controls were randomly selected. Maternal vaccination status of cases and controls was assessed; infants were excluded from analyses if their mothers were vaccinated <14 days prior to delivery. Analyses were adjusted for year, site, and ANC with or without study-vaccine. Sub-analyses stratified by HIV-exposure, term or pre-term birth, and age at admission were performed.

Results: Maternal vaccination status was available for 80 of 84 potential cases, eight of whom were born to women who were vaccinated <14 days before delivery. Of 72 eligible cases, 55 (76%) were <3 months old, 17 (24%) were born pre-term and 18 (25%) were HIV-exposed. The mothers of 29% of cases and 36% of controls received influenza vaccine (adjusted-VE: 30.0%, 95%CI: -26.9, 61.4). When stratified by maternal HIV status and restricted to term infants, the adjusted-VE was 62.3% (95%CI: 0.05, 85.8) in HIV-unexposed and 54.1% (95%CI: -148.4, 91.5) in HIV-exposed infants aged <3 months.

Conclusions: Influenza vaccination during pregnancy was effective in preventing influenza-associated hospitalization among young, term, HIV-unexposed infants.

Abstract O-3

A multi-country cohort study investigating adverse birth outcomes among women hospitalized with acute respiratory infection during pregnancy

Regan A, Feldman B, Azziz-Baumgartner E, Naleway A, Williams J, Wyant B, Simmonds K, Effler P, Booth S, Ball S, Katz M, Fink R, Thompson M, Chung H, Kwong J, Fell D

Introduction/Background & Aims: Compared to the general population, pregnant women are at greater risk of severe complications associated with influenza, which may have adverse consequences for perinatal health. While studies have investigated the impact of pandemic influenza on perinatal outcomes, limited data exist for seasonal influenza.

Methods: A retrospective cohort of pregnant women in four high-income countries was established using administrative health data. Acute respiratory or febrile illness (ARFI) hospitalizations during pregnancy were extracted from hospital records based on International Classification of Diseases codes for the admission diagnosis. Laboratory testing data were used to identify women tested for influenza and test result (positive/negative). Birth records were used to identify women with no record of an ARFI admission during pregnancy (the comparison group). We matched hospitalized women to non-hospitalized women (1:4) based on timing of conception. Log-binomial logistic regression was used to estimate the adjusted relative risk (aRR) for preterm birth, small-for-gestational-age,

and low birthweight birth, controlling for pre-existing medical conditions, maternal age, and parity. A fixed effects meta-analysis was used to calculate pooled effect estimates across the four countries.

Results: 4,750 hospitalized pregnant women (Canada: 2,350; Israel: 1,025; United States: 815; Western Australia: 560) with testing results were matched with 19,000 non-hospitalized pregnant women. The risk of preterm birth was greater among women hospitalized with influenza-associated ARFI (pooled adjusted RR [aRR]: 2.12; 95% CI: 1.52-2.96) and non-influenza ARFI (pooled aRR: 3.11; 95% CI: 2.37-4.09) compared to non-hospitalized women. Similar results were observed for low birthweight for influenza-associated ARFI (pooled aRR: 1.70; 95% CI: 1.22-2.38) and non-influenza ARFI (pooled aRR: 2.62; 95% CI: 1.89-3.63). There was no association between ARFI and small-for-gestational-age birth.

Conclusions: Whether related to influenza or another respiratory pathogen, ARFI admission during pregnancy was associated with increased risk of preterm birth and low birthweight, suggesting potential perinatal benefits through prevention of severe respiratory disease.

Abstract O-4

A prospective study to evaluate the impact that method of gestational age determination has on the rates of key pharmacovigilance outcomes in The Gambia

Oluwalana C, Oko F, Kanteh E, Bah E, Bittaye M, Okoye M, **Clarke E**

Introduction/Background & Aims: Accurate determination of gestational age (GA) is critical to the identification of pre-term births (PTB) and small for gestational age infants (SGA) – hence for maternal vaccination pharmacovigilance. We report the impact that different levels of diagnostic certainty, based on GAIA Consortium definitions, have on the reporting of PTB and SGA in a maternal vaccination trial (n=600) in The Gambia.

Methods: GA was determined by ultrasound scanning (G-USS), measurement of the symphysis-fundal height (SFH) and reported last menstrual period (LMP). The resulting rates of PTB and SGA were compared.

Results: The mean (+/- standard deviation) GAs at delivery based on G-USS, SFH and LMP were 39.6 (+/-1.7) weeks, 39.1 (+/-3.7) weeks and 39.4 (+/-3.6) weeks respectively.

Compared to G-USS the use of SFH to identify PTB had a sensitivity, specificity, PPV and NPV of 76.5%, 69.6%, 13.1% and 98.0% respectively. This would result in 30.4% of term deliveries based on G-USS being mis-classified as PTB and 23.5% of PTB based on G-USS being mis-classified as term. Using SFH to identify SGA deliveries would result in 18.1% of non-SGA deliveries based on G-USS being mis-classified as SGA and 58.1% of SGA deliveries based on G-USS being mis-classified as non-SGA.

The use of LMP to identify PTB had a sensitivity, specificity, PPV and NPV of 63.6%, 78.7%, 10.5% and 98.2% respectively. This would result in 21.4% of term deliveries based on G-USS being mis-classified as PTB based on LMP and 36.4% of PTB based on G-USS being mis-classified as term. Using LMP to identify SGA deliveries would result in 26.7% of non-SGA deliveries based on G-USS being mis-classified as SGA and 45.0% of SGA deliveries based on G-USS being mis-classified as non-SGA.

Conclusions: Significantly greater variability in the accuracy of GA estimates based on either SFH or LMP data results in high levels of misclassification when assessing PTB and SGA.

Session 2

Translating research findings into government policy on maternal and neonatal immunization.

Speaker: Rolando Ulloa-Gutierrez on behalf of Maria Avila-Aguero

The 2015 Millennium Development Goals (MDGs) included improving maternal health and reducing child mortality. However, these goals have not been accomplished in many regions of the world, including the Americas. Each year, approximately 290,000 women worldwide die from complications related to pregnancy and childbirth. Additionally,

preventable diseases continue to be the main cause of deaths among children. Maternal and neonatal immunization (MNI) is a core component of the new immunization model in the Americas. A successful example of this is the application of pertussis vaccine during pregnancy, which can reduce the incidence of pertussis and mortality in young infants.

Strong evidence exists for political authorities to include MNI as a priority, a health intervention that has been proven to be cost-effective. Catalysts for MNI in the region have been political commitment, endorsement by scientific societies, an established “culture of vaccination,” widespread access to antenatal care, and context-specific communications. Vaccination in pregnant women should be complemented with a solid immunization program in the newborn. In 2017, PAHO published the guide [“Maternal and Neonatal Immunization Field Guide for Latin America and the Caribbean”](#), positioning the MNI at the highest political level and as a commitment for member states.

The challenges of the MNI program include achieving high coverage in the mother-child binomial, the cost of the program that requires permanent funds, reducing inequality in access to health services (prenatal care, delivery care and control of healthy children). The development of vaccines against RSV and GBS is vital, since both agents are associated with high morbidity and mortality. Continued efforts to integrate MNI with maternal and child health services will be critical to increase the strength of the strategy.

Session 2 Oral Abstracts

Abstract O-5

Motives For Maternal Vaccination Uptake In Urban And Rural Gambia

Penda Johm¹, Amie Ceesay¹, Heidi Larson² and Beate Kampmann^{1,3},

¹Vaccines and Immunity Theme, Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Fajara, The Gambia; ²Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, London, United Kingdom; ³The Vaccine Centre, Department of Clinical Research, London School of Hygiene and Tropical Medicine, London, United Kingdom

Background: Maternal immunization can protect the pregnant woman and her newborn from diseases. Tetanus toxoid (TT) is the only vaccine given to pregnant women in The Gambia by antenatal care providers as part of the Expanded Programme on Immunization (EPI). Although the coverage of TT is high (90%), no research has been published on determinants of TT acceptance, uptake or hesitancy. Given that additional vaccines are likely to be available soon, this is important to ascertain.

Aim: To explore factors influencing women in The Gambia’s acceptance and uptake of existing and potential maternal immunizations.

Methods: Qualitative focus group discussions and in-depth interviews were conducted across four regions of The Gambia identifying participants from both urban and rural settlements. We explored the knowledge and perceptions of 120 theoretically sampled women (pregnant or with infant) and 40 additional informants including health care workers (HCWs) towards maternal immunizations and its providers. NVivo 11 Software was used for management and thematic analysis of the data.

Results: Women’s motives for maternal immunization uptake were:

- Confidence in the qualifications of health care workers
- Incentives such as receiving the TT vaccine doses at no cost
- Results-Based Financing for Health (RBF) initiative, wherein they receive GMD300 twice for booking early and completing the required antenatal visits.

Acceptance of the TT vaccine was due to perceived safety of the vaccine and absence of side effects. Women would accept additional maternal vaccines if HCWs sensitize them about the risks and benefits. According to HCWs, none of

the women had ever refused or delayed taking up a maternal vaccine as a result of their sensitization messages on the importance.

Conclusions: Women in The Gambia's acceptance of maternal immunizations is based on their previous vaccination experiences and individual weighing of risks and benefits. Sensitization messages from trusted HCWs and monetary incentives increase uptake of maternal immunizations.

Abstract O-6

Healthcare provider interpretations of vaccine product monograph information regarding use in pregnancy

Top K, Manca T, Kervin M, MacDonald N, Graham J

Introduction/Background & Aims: Inactivated influenza vaccine (IIV) and tetanus-diphtheria-acellular pertussis (Tdap) are recommended during pregnancy. Yet, product monographs (PMs) for IIV and Tdap continue to contain precautionary language regarding effectiveness and safety. Using a multi-stage consensus methodology involving health professionals and other stakeholders, we developed evidence-based statements about use in pregnancy suitable for inclusion in PMs for IIV and Tdap. This study aimed to evaluate Canadian healthcare providers' perceptions of those revised statements.

Methods: A 30-item online survey with qualitative and quantitative components was distributed to healthcare providers via professional organizations and public health. After reading excerpts from current and revised IIV and Tdap PMs, participants indicated their perceptions of the safety and effectiveness of the vaccines described, whether they would recommend them during pregnancy and which statements they preferred.

Results: From June to August 2018, 449 healthcare providers completed the survey, including physicians (45%), nurses (24%), midwives (27%) and others (5%). After reading the current Tdap statement, 32% of respondents indicated they would recommend the vaccine, 25% would not, and 44% indicated "depends on circumstances". After reading our revised Tdap statement, 72% would recommend the vaccine, 8% would not and 20% indicated "depends". Responses to current and revised IIV statements showed a similar pattern. When asked which Tdap statement better explains the risks and benefits of the vaccine in pregnancy, 61% of respondents chose the revised statement, 16% chose the current statement and 23% were neutral. Results for IIV were 69%, 8%, and 23%, respectively. Midwives were less likely to recommend vaccines than physicians or nurses.

Conclusions: Canadian healthcare providers perceived the revised PM statements as providing clearer information on IIV and Tdap during pregnancy than current PMs. The revised PMs were associated with more positive vaccination recommendations. Analysis of qualitative data is ongoing. Clear, evidence-based PMs will help support vaccine uptake in pregnancy.

Abstract O-7

Beyond individual decision-making: The importance of policy and provider recommendation for maternal vaccine acceptance in a low- and middle-income setting

Sundaram N, Kowgi A, Sahu B, Murthy G, Larson H, Weiss M, Prost A, Tam C

Background & Aims: Maternal immunization is key to reducing the large disease burden among pregnant women and infants in low- and middle-income countries (LMICs). Our study aims to identify factors influencing individual acceptance of maternal vaccines in a LMIC setting by careful study of public, provider, policy-level and contextual elements anchored in the social-ecological model.

Methods: A cross-sectional, mixed methods research study was conducted in urban and rural districts of Bengaluru, India. In-depth interviews were conducted with currently and recently pregnant women (n=70) and their family members (n=11); healthcare providers (n=24) at government and private health facilities; and policy-makers (n=10). Three focus group discussions (n=30) with currently and recently pregnant women complemented the interviews.

Results: A majority of women indicated that healthcare decisions during pregnancy were made by family members, while under a fifth made their own decisions. Tetanus vaccines, which are prioritized through government guidelines, were widely recommended by providers and used by patients. Influenza vaccine was seldom used. However, most women anticipated taking it, as well as new maternal vaccines, if recommended to them and made available. Recommendations from doctors were the most valued information source on immunization and health, followed by advice from family, community and friends, and government guidelines. Doctors at government facilities mentioned relying exclusively on government guidelines for maternal vaccine recommendation, while state- and district-level policy-makers were largely reliant on national-level policy-makers to issue guidelines for maternal vaccine policy, which they would implement.

Conclusions: Community willingness to take maternal vaccines and trust in the health system in this context is high. Despite this, awareness of and access to vaccines other than tetanus are limited. The overwhelming influence of provider recommendations and policy guidelines on individual acceptance suggest the need to pay attention to factors beyond individual decision-making to broader system and policy environments in LMICs for effective maternal vaccine action.

Declaration of interests:

The authors have no competing interests to declare. Project funded by IMPRINT.

Abstract O-8

Lessons learned, knowledge and perceptions of maternal and neonatal immunization in Latin America

Vilajeliu A, Jauregui B, Omer S, Ropero-Alvarez A

Introduction/Background & Aims: Given the momentum that maternal and neonatal immunization (MNI) is gaining and the experience in the Americas Region, it is paramount to document lessons learned. The objectives of the study were to understand the current state of MNI policies, strategies and practices in Latin America, and to describe the knowledge and perceptions of pregnant women and health workers regarding MNI.

Methods: Mixed-methods study commissioned by the Pan American Health Organization in collaboration with Emory University and the Institute for Clinical Effectiveness and Health Policy of Argentina. Between 2017 and early 2018, missions to the capital cities of five countries (Argentina, Brazil, Peru, Mexico and Honduras) were conducted to: interview key informants from the Ministry of Health, the National Immunization Technical Advisory Group (NITAG), scientific societies, medical and nursing schools, and health workers (HW); focus groups with pregnant women; and observations at health centers.

Results: In the five country capitals we observed that greater integration on policy development between the National Immunization Program and the Maternal and Child Health Department enables a more successful implementation. Regarding vaccine confidence, results indicated that most pregnant women believe that vaccines are important, and they prioritize their babies' health over their own. No significant resistance to MNI was observed, although some fears were identified. The evidence showed that HW are a key factor influencing pregnant women's decision to be vaccinated and recommendations from scientific societies played also an important role. Explicit MNI training to HW as part of the academic curricula and the design of specific communication materials were identified as an opportunity to improve maternal vaccination uptake.

Conclusions: The lessons learned and best practices identified should enable the Region and other geographical areas to strengthen implementation of current maternal and neonatal vaccines and help prepare for the introduction of new maternal and neonatal vaccines in the pipeline.

Abstract O-24

Factors that influence vaccination decision-making among pregnant women: a systematic review and meta-analysis

Eliz Kilich BMCh1*, Sara Dada MSc1*, Mark R. Francis MSc1, John Tazare MSc1, R. Matthew Chico PhD2, Pauline Paterson PhD1, Heidi J. Larson PhD

Session 3

Systems immunology of the mother-infant dyad .

Speaker John Tsang, National Institutes of Health, USA

This presentation will cover developing and applying systems biology approaches— combining computation, modeling and experiments—to study the immune system at both the organismal and cellular levels. The move toward precision medicine has highlighted the importance of understanding biological variability within and across individuals in the human population. In particular, given the prevalent involvement of the immune system in diverse pathologies, an important question is how much and what information about the state of the immune system is required to enable accurate prediction of future health and response to medical interventions. Work on studying human immune states across health and disease, including the development of predictive models to uncover general indicators of immune responsiveness and exploring the connections between the maternal and infant immune systems will be presented.

Molecular and cellular basis of maternal antibody transfer.

Speaker: Madeleine Jennewein, Harvard University, USA

Despite the worldwide success of vaccination, newborns remain extremely vulnerable to infections because of immune system immaturity. Neonatal vaccination strategies have been hampered by maternal antibody-mediated dampening of immune responses and the enhanced regulatory and tolerogenic mechanisms of early life. The recent recommendation for maternal pre-natal immunization thus aims to boost neonatal immunity by increasing trans-placental antibody transfer to the fetus. However, emerging data suggest that antibodies are not transferred equally across the placenta and may vary based on antigen-specificity or other characteristics. To profile the types of antibodies transferred, we used systems serology, focusing on their Fc features and ability to mediate non-neutralizing functionality, to define the types of antibodies that are associated with enhanced transfer across the placenta. While there was efficient transfer of antibody titers across the placenta, the Fc-profile of neonatal and maternal antibodies differed, skewed towards the enhanced transfer of NK cell-activating antibodies. This selective transfer was linked to antibodies with digalactosylated Fc-glycans, antibodies that selectively bound FcRn and FCGR3A. This selectivity resulted in the increased transfer of antibodies able to efficiently leverage highly functional innate immune cells present at birth. Given emerging data that vaccination may direct antibody glycosylation, this research provides insights for the development of next-generation maternal vaccines designed to elicit antibodies that will most effectively bolster neonatal health.

Session 3 Oral Abstracts

Abstract O-9

Dissecting the Antibody-OME of Preterm and Term Newborns using Systems Serology

Sepideh Dolatshahi^{1,2}, Audrey Butler¹, Petter Brodin³, Douglas Lauffenburger^{2,4}, Galit Alter¹

¹Ragon Institute of MGH, MIT and Harvard, Cambridge, MA, 02139, USA; ²Department of Biological Engineering, Massachusetts Institute of Technology, Cambridge, MA, 02139, USA; ³Science for Life Laboratory, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden; ⁴MIT Center for Gynepathology Research, Cambridge, MA, 02139, USA

Introduction/Background & Aims: Premature newborns are more susceptible to infectious diseases at birth compared to full-term neonates. A recent study showed that preterm children receive comparable repertoires of maternal anti-viral IgG as full-term children, although at lower concentrations. To complement these studies, we defined the overall quantity as well as the Fc-mediated functional quality of native-antigen-specific antibody transfer across a wide range of vaccines, endemic pathogens, and common antigens.

Methods: Cord and peripheral blood from a cohort of 11 preterm and 12 full-term children were collected at birth through week 12. In a systems serology framework, we performed multiplexed measurements of antigen-specific antibody isotypes and subclasses, binding to Fc-receptors (FcR2A, FcR2B, FcR3A, FcR3B, and the neonatal FcRn), as well as Fc-mediated functional profiles of 24 antigen-specific antibody populations. Computational multivariate and network analyses were subsequently performed to uncover the differences in the temporal profiles of antibody properties in preterm and full-term children.

Results: Although higher antibody levels were present in full-term compared to preterm newborns across antigens, the overall functional profiles of antigen-specific antibodies were nearly equivalent across pre- and full-term neonates. Network analysis revealed that antigen-specific ability to drive phagocytosis through monocytes and neutrophils was more coordinated among preterm newborn antibodies, suggesting that antibodies transferred early in pregnancy may be functionally superior. While most antibody features were enriched among full-term newborns, as they have higher titers, preterm children for some antigens exhibited enhanced binding to Fc □R2A, the r involved in driving phagocytosis, suggesting that the placenta may sieve different antibody qualities at different stages of gestation.

Conclusions: The transfer of qualitatively distinct antibodies via the placenta may be driven by the differential role of FcRn partnered with Fc-receptors at different stages of gestation, with an enhanced role for FcR2A in early gestation, and a later dominant role for FcR3A in later pregnancy.

Abstract O-10

Functionality of antibody against *B. pertussis* in acellular versus whole cell pertussis-vaccinated infants born to mothers who received Tdap during pregnancy: a randomised trial

Nasamon Wanlapakorn^{1,2}, Kirsten Maertens³, Thao Mai Phuong Tran⁴, Sompong Vongpunsawad¹, Jiratchaya Peunpa¹, Niel Hens^{4,5}, Pierre Van Damme³, Anaïs Thiriard⁶, Dominique Raze⁶, Camille Locht⁶, Yong Poovorawan¹, Elke Leuridan³

¹Center of Excellence in Clinical Virology, Department of Pediatrics, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; ²Division of Academic Affairs, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand; ³Center for the Evaluation of Vaccination, Vaccine & Infectious Disease Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium; ⁴Interuniversity Institute for Biostatistics and statistical Bioinformatics, Hasselt University, Belgium; ⁵Centre for Health Economics Research & Modelling Infectious Diseases, Vaccine and Infectious Disease Institute, University of Antwerp, Belgium; ⁶Univ. Lille, CNRS, INSERM, Institut Pasteur de Lille, U1019 - UMR8204, Center for Infection and Immunity of Lille, France

Introduction/Background & Aims: Evaluation of the immune response to pertussis vaccines often relies on the measurement of serum IgG against *Bordetella pertussis* (*B. pertussis*) antigens. Although this is a widely-used method, it does not reflect functionality of the antibodies in mediating bacterial clearance. Serum IgG is opsonic and bactericidal, however, little evidence exists on the correlations between serum IgG to *B. pertussis* antigens and its bactericidal activity.

Methods: In a recent randomized controlled trial (NCT02408926) in Thailand which followed term infants born to tetanus-diphtheria-acellular pertussis (Tdap)-vaccinated mothers between 2015-2018, infants were randomized to receive either acellular (aP)-containing or whole cell pertussis (wP)-containing vaccine at 2, 4, 6 (primary vaccination) and 18 months of age (first booster). A comparison group comprised of wP-vaccinated children born to unvaccinated mothers. Blood samples were collected from women at delivery, and from infants at birth (cord), month 7, month 18

and month 19. Functionality of antibody against *B. pertussis* was measured by *B. pertussis* growth inhibition assay. Percentages of viable bacteria incubated with decomplexed sera were compared with that of bacteria alone.

Results: At one-month post-primary vaccination, antibodies of infants born to Tdap-vaccinated mothers appear to better reduce the bacterial load than that of infants born to unvaccinated mothers, regardless of vaccine types received during infancy. However, at month 18 and 19, the bactericidal activity was higher in infants vaccinated with wP compared to aP vaccines. No correlations between bactericidal activity and anti-PT, -FHA and -PRN IgG levels were found.

Conclusions: There were no obvious correlations between levels of antibodies to *B. pertussis* antigens and their bactericidal activities. Maternal immunization may enhance the agglutination of antibodies and *B. pertussis* at one-month post-primary vaccination regardless of the vaccine types received. Nevertheless, wP-vaccinated infants had higher sera bactericidal activity than aP-vaccinated infants at pre-booster and one-month post-booster.

Abstract O-11

The effect of pertussis vaccination during pregnancy on the cellular immune response after primary and booster infant vaccination

Marjolein R. P. Orije¹, Véronique Corbière², Kirsten Maertens¹, Ludo Mahieu³, Pierre Van Damme¹, Nathalie Cools⁴, Françoise Mascart² & Elke Leuridan¹

¹Center for the Evaluation of Vaccination, Vaccine & Infectious Diseases Institute, University of Antwerp, Belgium; ²Laboratory of Vaccinology and Mucosal Immunity, Université Libre de Bruxelles (U.L.B.), Faculty of Medicine, Belgium; ³Department of Paediatrics, Division of Neonatology, University Hospital Antwerp, Belgium; ⁴Laboratory of Experimental Hematology, Vaccine & Infectious Disease Institute, University of Antwerp, Belgium

Introduction/Background & Aims: Pertussis vaccination during pregnancy is a strategy to protect newborns against *B. pertussis*. There is, however, still a paucity of evidence on the cellular mediated immune (CMI) responses after infant vaccination in the presence of high maternal antibody titers. This study reports the CMI responses in term and preterm born infants of women vaccinated during pregnancy or not vaccinated for at least 5 years.

Methods: A convenience sample (N=79) was taken from a prospective cohort study (N=233, NCT02511327), including vaccinated (Boostrix[®]) and non-vaccinated women and their preterm or term born infants in Belgium. Infants were vaccinated and sampled ± 2 weeks before and one month after primary (8-12-16 weeks) and booster vaccination (13 or 15 months) (Hexyon[®]). The pertussis toxin (PT) specific lymphocytes (CD3⁺, CD4⁺ and CD8⁺blasts) were measured at these 4 time points with a flow cytometric assay on whole blood.

Results: Before primary vaccination $\pm 79.7\%$ of the infants did not respond to *in vitro* PT stimulation. In most infants specific PT CD3⁺blast and CD3⁺CD4⁺blast responses developed after completion of primary vaccination, and remained present following booster vaccination (Table 1). In term born infants of unvaccinated mothers CD3⁺CD8⁺ lymphocytes responses were detected ± 2 weeks before booster. Whereas, in the other cohorts CD3⁺CD8⁺ lymphocyte responses were generally absent at all time points.

Conclusions: Our study confirmed that both term and preterm infants are capable of inducing CMI responses against pertussis after vaccination. At this moment there is no evidence maternal pertussis vaccination influences these responses, this however should be confirmed on larger cohorts.

	T cell subset	Responders post vaccination	Responders pre booster vaccination	Responders post booster vaccination
Cohort 1 (N= 28)	CD3 ⁺	10/18 (55.6%)	9/21 (42.9%)	12/26 (46.2%)
Term born infants of vaccinated mothers	CD3 ⁺ CD4 ⁺	8/18 (44.4%)	9/21 (42.9%)	10/26 (38.5%)
	CD3 ⁺ CD8 ⁺	5/18 (27.8%)	5/21 (23.8%)	5/26 (19.2%)

Cohort 2 (N= 38) Preterm born infants of vaccinated mothers	CD3 ⁺	11/23 (47.8%)	9/36 (25%)	12/32 (37.5%)
	CD3 ⁺ CD4 ⁺	8/23 (34.8%)	9/36 (25%)	11/32 (34.4%)
	CD3 ⁺ CD8 ⁺	2/23 (8.7%)	5/36 (13.9%)	5/32 (15.6%)
Cohort 3 (N= 6) Term born infants of unvaccinated mothers	CD3 ⁺	2/4 (50%)	2/4 (50%)	3/6 (50%)
	CD3 ⁺ CD4 ⁺	2/4 (50%)	2/4 (50%)	1/6 (16.7%)
	CD3 ⁺ CD8 ⁺	1/4 (25%)	3/4 (75%)	1/6 (16.7%)
Cohort 4 (N = 7) Preterm born infants of unvaccinated mothers	CD3 ⁺	1/4 (25%)	2/4 (50%)	3/3 (100%)
	CD3 ⁺ CD4 ⁺	1/4 (25%)	2/4 (50%)	3/3 (100%)
	CD3 ⁺ CD8 ⁺	0/4 (0%)	0/4 (0%)	2/3 (66.7%)

Table 1:

Representation of the number of responders after *in vitro* PT stimulation.

Vaccine responders were defined as infants who produced 20% more blasts compared to the 95% confidence interval before primary vaccination.

Abstract O-12

Pregnancy-induced changes in antibody glycosylation and non-neutralizing functions

Pasetti M, Jennewein M, Noelette F, Boudreau C, Shehata C, Campbell J, Alter G

Introduction: During pregnancy, the body seeks to reduce systemic inflammation to allow coexistence of allogeneic tissue, healthy growth of the infant, and term delivery. Systemic immune changes occur, including alterations in immune cell frequency, function, and cytokine production, which leave pregnant women more vulnerable to infection. While research has focused primarily on the maternal-fetal immune interface, less is known about the immune changes and particularly humoral immune adaptations that take place during pregnancy. In light of the current recommendations for vaccination of pregnant women, understanding this immunomodulation and its influence on vaccine-induced antibody responses, may provide insights into the mechanisms associated with maternal vulnerability as well as reveal novel pathways that may be actively manipulated to enhance protection of both mothers and their newborns.

Methods: Serum samples from a matched cohort of 20 non-pregnant women and 20 pregnant women vaccinated against seasonal influenza were utilized to interrogate antibody glycosylation and non-neutralizing functionality.

Results: We found dramatic changes in antibody Fc-glycosylation between pregnant and non-pregnant women resulting in profiles associated with decreased inflammation. Fab glycosylation was distinct from Fc glycosylation and, likewise, differed between pregnant and non-pregnant women, evidencing specific structural domain-driven changes in antibody glycan profiles associated with pregnancy. However, despite these striking glycosylation differences, canonical Fc-functionality was not altered in pregnant women, suggesting that these glycan modifications may alter non-canonical antibody functions, including their ability to modulate inflammation during pregnancy.

Conclusions: Maternal antibody glycan modifications likely reflect the maternal pressure to control inflammation while maintaining the need to protect both mother and child from infection through efficient Fc involvement and function. This study points to non-canonical roles for both Fab and Fc glycosylation

changes during pregnancy and suggests unexpected and critical roles for post-translational antibody glycosylation associated with immunoregulatory or infant protection functions that have yet to be defined.

Session 4

Neonatal immunization: well begun is half done.

Speaker: Dr. David Goldblatt, University College London, United Kingdom

Neonatal vaccination is a strategy designed primarily to address infectious diseases that manifest in early life. It is designed to provide protection prior to the onset of immunity induced by vaccines given according to traditional schedules and has added strategic value in taking advantage of contact with health systems at birth. While the delivery of vaccines around the time of birth has included the use BCG, oral polio and Hepatitis B vaccine there is increasing interest in exploring the potential for providing protection to other pathogens such as *Bordetella Pertussis* and *Streptococcus Pneumoniae*. Issues that continue to confound the use of vaccines at or soon after birth include their relative safety, the impact of maternal immunity on vaccine responses especially in the context of maternal immunisation, their immunogenicity which is not generally optimised for inducing immunity very early in ontogeny and their ability to impact more generally on bystander immunity. Better models of early life immunity derived from systems biology might help rationalise the design and use of vaccines although an improved understanding of immunological protection on a pathogen by pathogen basis are also required.

Vaccination of Premature Infants, St Georges University of London, United Kingdom

Speaker: Dr. Paul t Heath

Globally, 13 million premature births occur each year. Premature infants have a higher risk of infections, including vaccine preventable infections. They are more likely to have lower vaccine responses compared to term infants but are often excluded from vaccination studies. They are also more likely to be under-vaccinated. There are often concerns about the potential for adverse events, especially in those that are still hospitalised at the time of vaccination.

In general, infants should be vaccinated according to chronological age, without correction for their prematurity. The optimum vaccine schedule may however, depend on the setting and the age at which they are at highest risk of disease.

Session 4 Oral Abstracts

Abstract O-13

Early pneumococcal conjugate vaccination primes mucosal immune responses to subsequent pneumococcal polysaccharide vaccine in Papua New Guinean children

Ford R, Orami T, Pomat W, Corscadden K, Thornton R, Kirkham L, van den Biggelaar A, Richmond P, Lehmann D

Introduction/Background&Aims: Pneumococcal disease remains a major cause of morbidity and mortality in Papua New Guinean infants. We studied the impact of accelerated priming with pneumococcal conjugate vaccine (PCV) on the induction of and subsequent pneumococcal serotype-specific antibody response to pneumococcal polysaccharide vaccine (PPV) responses in Papua New Guinean infants.

Methods: Children were randomized to receive 3 doses of 7-valent PCV (PCV7) in a 0-1-2-month (neonatal; n=41) or a 1-2-3-month (infant; n=51) schedule, or no PCV (control; n=39). All children received PPV at 9 months of age. Saliva was collected at ages 1, 2, 3, 4, 9, 10 and 18 months. Salivary IgA and IgG titres to PCV7 serotypes and serotypes 1, 3, 5, 7F, 19A were measured using bead-based immunoassays. Saliva samples were standardised by total protein; lactose-positive samples were excluded from IgA analyses.

Results: The neonatal and standard PCV immunization schedules induced similar mucosal polysaccharide antibody responses. At ages 3 and 4 months, geometric mean concentrations (GMCs) for salivary IgA to serotypes 4 and 14,

and salivary IgG for serotypes 4 and 18C were higher in the PCV-primed versus control children. One month post-PPV, salivary IgA GMCs for 5 of the PCV7 serotypes, and salivary IgG GMCs for all PCV7 serotypes were higher in PCV-primed than in control children. Pre-to-post PPV (9-10 month) mean fold increases in PCV7-serotype-specific IgA and IgG GMCs were 3.0 and 5.3 in PCV-primed children; and 1.0 and 1.2 in control children, respectively. By 18 months of age, all PCV7 serotype antibody levels declined to pre-PPV levels or below.

Conclusions: PCV7 had limited impact on development of mucosal antibody responses to vaccine serotypes, but both neonatal and infant schedules primed responses to subsequent PPV vaccination. This indicates that PPV immunization following PCV priming could improve protection against pneumococcal disease in Papua New Guinean children.

Abstract O-14 Abstract Withdrawn

The influence of maternal immunity on infant BCG vaccine response

Cranmer LM^{1,3}, **Sasser L2**, **Jaspan H6,9,11**, **Kagina B6**, **Khayumbi J4**, **Ongalo J4**, **Muchiri B4**, **Gillespie S1**, **Njuguna I7**, **Scriba T5,6**, **Nduba V4**, **Wamalwa D8**, ***John-Stewart GC9-11**, ***Day CL2** (*These authors contributed equally to this work)

Abstract O-15

Maternal pertussis vaccination and its effect on opsonophagocytic activity of infant pertussis specific antibodies up to 24 months of age: a randomised controlled trial

Daan Barug¹, **Daniëlle Hijdra**¹, **Betsy Kuipers**¹, **Rob Mariman**¹, **Nynke Y Rots**¹

¹Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, the Netherlands

Background: Maternal pertussis vaccination has been shown to result in increased pertussis specific total IgG antibody levels between birth and the first infant vaccine dose, but maternal antibodies interfere with infant vaccination responses. Pertussis specific antibodies protect the host by opsonizing *B. pertussis* and thereby facilitating its phagocytosis. We aimed to analyze the functionality of *B. pertussis*- specific maternal and infant antibodies using an opsonophagocytosis assay (OPA).

Methods: In a randomized controlled trial 58 women received a Tdap vaccination between week 30-32 of pregnancy and 60 women received the same vaccine within 48 hours after delivery. Their newborn children were vaccinated with a DTaP-IPV-Hib-HepB and PHiD-CV10 vaccine at age 3-5-11 months. Opsonizing and subsequent phagocytic capacity of pertussis antibodies present in pre- and post-vaccination serum samples was measured by flow cytometry using freshly isolated neutrophils, GFP expressing *B. pertussis* strain B0572 and PE-conjugated goat-F(ab')₂-anti-human-IgG.

Results: Opsonophagocytosis of *B. pertussis* was evaluated by a two-color flow cytometric assay that provides information on both the attachment and internalization of bacteria. The assay has been optimized to determine opsonophagocytic activity of antibodies pre- and post-vaccination. We showed phagocytosis of IgG-opsonized *B. pertussis* by freshly isolated human neutrophils. Preliminary results indicate that maternal vaccination results in presence of functional maternal antibodies in infants in their first months of life. Latest results will be presented with respect to maternal antibodies at birth and at 2 and 3 month of age before infant vaccination and for infant antibodies at 1 month post primary series and before and after booster vaccination.

Conclusions: We implemented an assay that can be used to determine functionality of maternal and infant pertussis specific IgG antibodies. Although the potential use as a functional correlate of protection needs to be established, this assay will help to monitor the effectiveness of maternal pertussis vaccination in protection against disease.

Abstract O-16

Licensed Bacille Calmette-Guérin (BCG) formulations differ markedly in bacterial viability, RNA content and innate immune activation

Asimenia Angelidou, MD, PhD^{a,b}; Maria-Giulia Conti, MD^{b,c}, Joann Diray-Arce, PhD^b, Christine S. Benn, MD, PhD^d, Frank Shann, MB, BS DMedSc^e, Mihai G. Netea, MD, PhD^{f,g}, Mark Liu, BS^b, Lakshmi Prasad Potluri, PhD^b; Robert Husson, MD^b; Al Ozonoff, PhD^b; Beate Kampmann, MD, PhD^{h,i}, Simon Daniël van Haren, PhD^{b*}; Ofer Levy, MD, PhD^{b*} (*These authors contributed equally to the study) Presented by Kinga Smolen.

^aDivision of Newborn Medicine, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA;

^bPrecision Vaccines Program, Division of Infectious Diseases, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, USA; ^cDepartment of Pediatrics, Sapienza University of Rome, Rome 00185, Italy ^dOPEN, Odense Patient data Explorative Network, Odense University Hospital/Institute of Clinical Research, University of Southern Denmark; 5000 Odense C, Denmark; ^eDepartment of Pediatrics, Royal Children's Hospital, University of Melbourne, Victoria 3052 Australia; ^fDepartment of Internal Medicine and Radboud Center for Infectious Diseases, Radboud University Medical Center, Nijmegen, Netherlands; ^gDepartment for Genomics & Immunoregulation, Life and Medical Sciences Institute (LIMES), University of Bonn, 53115 Bonn, Germany; ^hVaccine Centre, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, Keppel Street, London, WC1E 7HT, UK; ⁱVaccines & Immunity Theme, Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Fajara, PO Box 273, Banjul, The Gambia.

Background: Bacille Calmette-Guérin (BCG), the live attenuated tuberculosis vaccine, is manufactured under different conditions across the globe generating formulations that differ in clinical efficacy. Innate immune recognition of live BCG contributes to immunogenicity suggesting that differences in BCG viability may contribute to divergent activity of licensed formulations.

Methods: We compared BCG-Denmark (DEN), -Japan (JPN), -India (IND), -Bulgaria (BUL) and -USA in vitro with respect to a) viability as measured by colony-forming units (CFU), membrane integrity, and RNA content, and b) cytokine/chemokine production in newborn cord and adult peripheral blood.

Results: Upon culture, relative growth was BCG-USA > JPN >> DEN > BUL= IND. BCG-IND and -BUL demonstrated >1,000-fold lower growth than BCG-JPN in 7H9 medium and >10-fold lower growth in commercial Middlebrook 7H11 medium. BCG-IND demonstrated significantly decreased membrane integrity, lower RNA content, and weaker IFN- γ inducing activity in whole blood compared to other BCGs. BCG-induced whole blood cytokines differed significantly by age, vaccine formulation and concentration. BCG-induced cytokine production correlated with CFU, suggesting that mycobacterial viability may contribute to BCG-induced immune responses.

Conclusions: Licensed BCG vaccines differ markedly in their content of viable mycobacteria possibly contributing to formulation-dependent activation of innate and adaptive immunity and distinct protective effects.

Abstract O-17

Abstract O-17

BCG vaccination protects from neonatal sepsis through induction of emergency granulopoiesis.

Mr. Byron Brook, Mr. Danny Harbeson, Dr. Rym Ben-Othman, Dr. Bing Cai, Mr. Daniel He, Mr. Freddy Francis, Mr. Joe Huang, Dr. Natalia Varankovich, Mr. Aaron Liu, Ms. Winnie Bao, Ms. Nelly Amenogbe, M.D. PhD Tobias Kollmann

Introduction/Background & Aims: Neonatal sepsis is a major cause of infectious death with no vaccines and few treatments available. BCG vaccination, classically targeting tuberculosis, has been shown to reduce human neonatal mortality in randomized control trials, suggesting benefits extending beyond tuberculosis. The protective mechanism was not known.

Methods: Neonatal mice were challenged in an established model of neonatal sepsis and followed for survival, or bacterial burden. Flow cytometry was used to identify immune subsets. The ability to transfer protection was measured via purification and adoptive transfer of cell populations of interest.

Results: As in the human newborn, neonatal Bacillus Calmette-Guérin (BCG) vaccination reduced mortality. In newborn mice bacterial burden was also reduced, and this model allowed for identification of the relevant protective mechanism. Specifically, emergency granulopoiesis (EG)-supporting cytokines and the canonical EG marker, CEBP- β , were induced post-vaccination. Granulocyte (neutrophil) and monocyte progenitor cells (GMP) expanded within 2 days of vaccination, and these cells matured within the expected timeframe, leading to a doubling of mature neutrophils numbers in BCG-vaccinated mice. Mature neutrophils mobilized to fight infection, and the purification and adoptive transfer of this particular subset provided protection to a similar degree as the transfer of the entire spleen. Furthermore, purifying and increasing the number of cells transferred from a control mouse to match a BCG-vaccinated donor had similar degree of protection as cells from a BCG-vaccinated source; and a reduction of BCG-vaccinated donor cells to control levels impaired the ability to protect. This suggested that it was the simply quantitative increase in the number of mature neutrophils that provided the protection, not a change in their function.

Conclusions: Emergency granulopoiesis and the expansion of mature neutrophils induced by BCG vaccination was the protective factor against death from neonatal sepsis.

Abstract O-18

Malaria Antigen Shedding in Breastmilk of Mothers from a Region with Endemic Malaria

Dr Lieke van den Elsen, Prof Dr Valerie Verhasselt, Dr Thomas Egwang

Introduction/Background & Aims: More than 200 million cases of malaria occur yearly, with children under 5 years accounting for two thirds of all malaria deaths. Rodent and human data shows that the presence of foreign antigens in breastmilk can elicit strong immune responses in breastfed offspring. We propose that malaria antigens in breastmilk may stimulate antimalarial immune defences and reduce malaria risk in breastfed infants. As a first step to address this hypothesis, we investigated whether *Plasmodium falciparum* histidine-rich protein 2 (pHRP-2) and lactate dehydrogenase (pLDH) are detectable in breastmilk of mothers from Uganda.

Methods: Lactating Ugandan mothers (n=324) without clinical signs of malaria donated a breastmilk and blood sample. Asymptomatic malaria was diagnosed in blood by an ultrasensitive pHRP-2-based rapid diagnostic test (uRDT). The presence of malaria antigens in breastmilk was investigated by pHRP-2 and pLDH Quantimal CELISA with detection levels of 1.2 pg/ml and 4.8 U/ml respectively.

Results: Eighty-eight mothers (27%) harboured asymptomatic malaria. Among the breastmilk samples from these mothers, 7 had detectable pHRP-2 (7.9 %) with a median level (Q1-Q3) of 45.0 pg/ml (2.0 pg/ml-180.2 pg/ml) and 10 had detectable pLDH (11.3 %), 6.6 AU/ml (5.6 AU/ml-9.9 AU/ml). Overall, 14 samples (15.9%) were positive for either pLDH or pHRP-2 and 3 (3.4%) were positive for both pLDH and pHRP-2. Forty-four milk samples from malaria-negative mothers were used as controls and none of these showed detectable pHRP-2 or pLDH antigens. Our preliminary data indicated that blood levels of malaria antigens determine their levels in breastmilk.

Conclusions: This study shows for the first time that 15% of breastmilk samples from mothers with asymptomatic malaria contain malaria antigens. This landmark finding may have significant implications for susceptibility to malaria in infants, since malaria antigens in breastmilk may strongly influence the immune responses to natural malaria infections and to malaria vaccines in breastfed children.

Abstract O-23

The Influence of Pertussis-containing Vaccines in Pregnancy on Antibody Responses to Primary and Booster Immunizations in Infants: Individual Participant Data Meta-analysis

Bahaa Abu Raya,^{1*} Kirsten Maertens,^{2*} Flor M. Munoz,³ Petra Zimmermann,^{4,5} Nigel Curtis,⁴ Scott Halperin,⁶ Elke Leuridan,² Manish Sadarangani¹

¹Vaccine Evaluation Center, BC Children's Hospital Research Institute, University of British Columbia, Vancouver, British Columbia, Canada, ²Centre for the Evaluation of Vaccination, Vaccine and Infectious Diseases Institute, University of Antwerp, Belgium. ³Departments of Pediatrics and Molecular Virology and Microbiology, Baylor College of Medicine, Houston, Texas, US. ⁴Department of Paediatrics, The University of Melbourne and Infectious Diseases Research Group, Murdoch Children's Research Institute, Royal Children's Hospital Melbourne, Parkville, Australia. ⁵Department of Pediatrics, Fribourg Hospital HFR and Faculty of Science and Medicine, University of Fribourg, Switzerland. ⁶Canadian Center for Vaccinology, Departments of Pediatrics and Microbiology and Immunology, Dalhousie University, Izaak Walton Killam Health Centre, and Nova Scotia Health Authority, Halifax, NS, Canada. * **First co-authors**

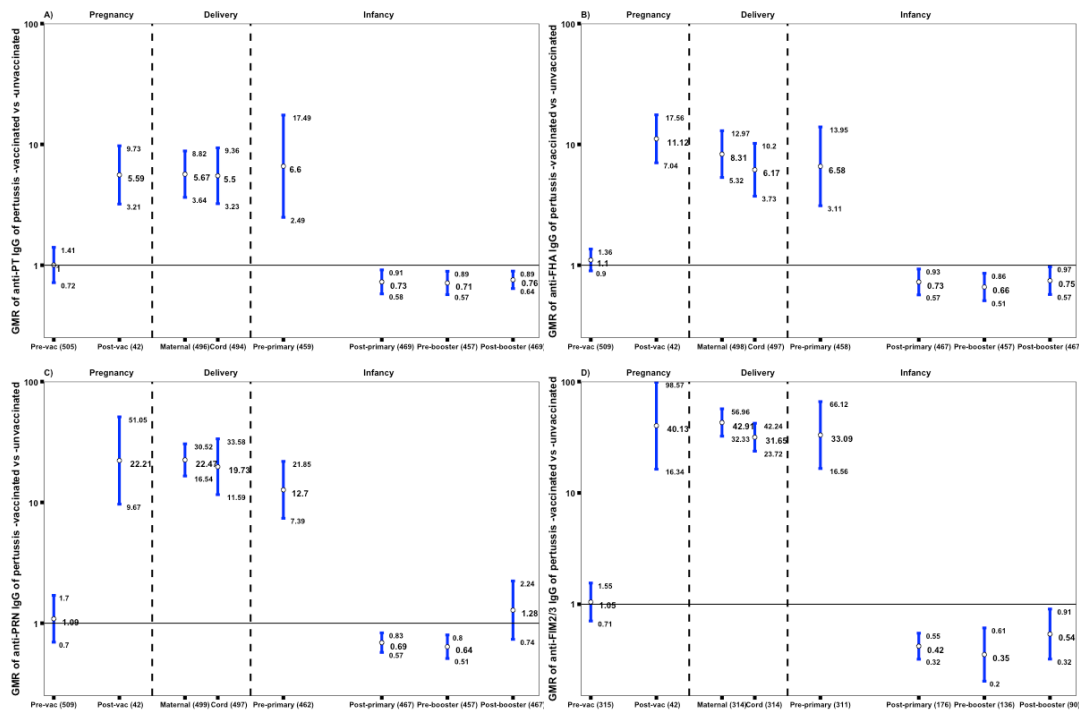
Background: Several countries recommend pertussis immunization in pregnancy. We aimed to determine the impact of pertussis immunization in pregnancy on infants' immune responses to routine vaccines and to identify factors influencing these.

Methods: We performed an individual-participant meta-analysis of antibody (Ab) levels to routine immunizations in infants of women who did or did not receive pertussis vaccine in pregnancy. Geometric mean ratios (GMRs) of pertussis-specific, tetanus toxoid (TT) and diphtheria toxoid (DT) Ab levels were calculated. Factors influencing Ab responses to primary immunizations in infants of immunized women were determined. Mixed-effects models were used. Seroprotection rates against TT, DT (≥ 0.1 IU/mL) and *Streptococcus pneumoniae* (SPN) (≥ 0.35 $\mu\text{g/mL}$) were calculated.

Results: 637 participants (4 RCTs, 1 non-RCT) were included. Maternally-derived antigen-specific Abs were higher in infants born to pertussis-immunized women at birth and at time of primary immunization. After primary immunization, infants of pertussis-immunized women had significantly lower pertussis toxin (PT) [GMR, 0.73; 95%CI, 0.58-0.91], filamentous haemagglutinin (FHA) [0.73; 0.57-0.93], pertactin (PRN) [0.69; 0.57-0.83] and fimbria (FIM) [0.42; 0.32-0.55] Ab levels but similar TT and DT levels. These low levels persisted at time of booster and after booster immunization (except PRN) (Fig. 1, 2). After primary immunization, seroprotection rates against DT and SPN5 (not TT and other SPN serotypes) were lower in infants of pertussis-immunized women (Fig. 3).

Antigen-specific Ab levels at primary immunization were associated with blunting of immune responses, with doubling Ab levels resulting in 46%-54% lower post-primary immunization levels. Timing of vaccination in pregnancy, age at initiation (7, 8 or 9 weeks) or spacing of vaccinations (2, 3, 4 vs. 2, 4, 6 months) did not affect post-primary immunization pertussis Ab levels (Fig. 4).

Conclusions: This large, international, longitudinal analysis demonstrates blunting to infants' immune responses to pertussis, diphtheria and some SPN serotypes, after maternal pertussis immunization. Factors affecting Ab levels at primary immunization, e.g. delaying primary immunization, might mitigate blunting and should be explored.



Session 5

Research needs for the next generation of maternal and neonatal vaccines: Lessons learned from the case study of maternal group B streptococcal disease.

Speaker: Stephanie Schrag, Centers for Disease Control and Prevention, USA

Programs to vaccinate pregnant women against tetanus, influenza and pertussis and newborns against hepatitis B pave the way for development and rollout of new maternal and neonatal immunizations. Globally, 11% of maternal and 23% of neonatal deaths are attributed to infection as a primary cause. Despite this, etiologies remain poorly characterized and vary by setting. This talk will discuss the next generation of neonatal and maternal vaccines such as Respiratory syncytial virus (RSV), monovalent pertussis, Zika virus, cytomegalovirus (CMV), hepatitis E, malaria and group B streptococcus (GBS). Challenges to the development and licensure are unique to specific vaccine candidates and disease targets and will be highlighted in this talk.

Tackling AMR through maternal and neonatal immunization

Speaker: Dr. Padmini Srikantiah, Bill & Melinda Gates Foundation, USA

Antimicrobial resistance (AMR) is a global public health problem that has the potential to contribute to increased morbidity and mortality particularly among the most vulnerable populations. In the case of neonatal infections, the etiologies of neonatal sepsis are increasingly reported to be multi-drug resistant organisms, including Gram negative bacilli that are conventionally considered nosocomial pathogens. These infections are associated with high mortality; and thus the threat of AMR underscores the importance of prevention of neonatal infections through novel interventions, including maternal vaccines targeted at Gram negative pathogens as well as passive immunization with monoclonal antibodies given at birth to a neonate.

Session 5 Oral Abstracts

Abstract O-19

Safety and Immunogenicity of a Hexavalent Group B Streptococcus Conjugate Vaccine in Healthy Nonpregnant Adults: A First-in-Human Study

Kimberly J. Center¹, Daniel A. Scott¹, Stan L. Block², James Peterson³, Ingrid Scully¹, Peter C. Giardina¹, Wendy J. Watson¹, Ed T. Buurman¹, William C. Gruber¹, Kathrin U. Jansen¹, Yahong Peng¹, Samantha Munson¹, Annaliesa Anderson¹, Judith Absalon¹

¹Vaccine Research and Development, Pfizer, New York, NY; ²Kentucky Pediatric/Adult Research, Bardstown, KY; ³J. Lewis Research, Salt Lake City, UT

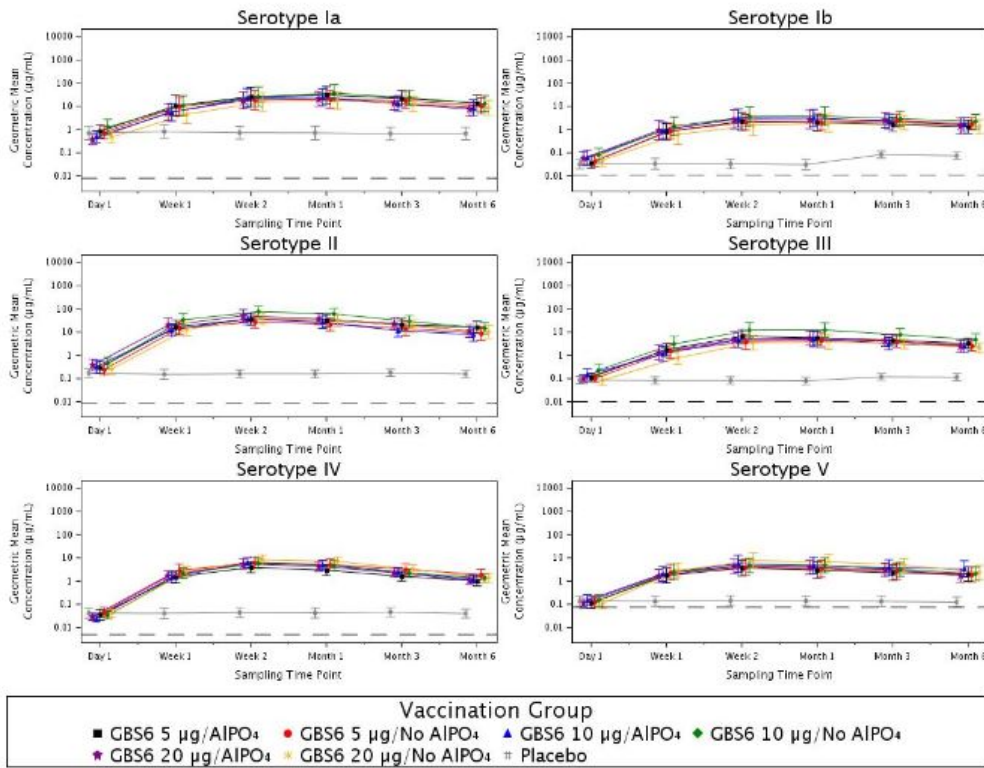
Introduction/Background & Aims: Group B streptococcus (GBS; *Streptococcus agalactiae*) is an important cause of invasive disease in young infants. Infants born to women with sufficient pre-existing anti-GBS capsular IgG antibodies are at reduced risk of GBS disease, making maternal immunization an attractive strategy for infant disease prevention. This Phase 1/2 study assessed the safety and immunogenicity through 6 months postvaccination of multiple 6-valent GBS-CRM₁₉₇ conjugate vaccine (GBS6) formulations in healthy adults age 18-49 years.

Methods: In this placebo-controlled, observer-blinded dose-escalation trial, subjects (N=365) were randomized to receive a single dose of GBS6, formulated with or without AlPO₄, or saline placebo. The primary objective was to describe the safety of GBS6, assessed by prompted local and systemic reactogenicity for 14 days after vaccination and unprompted adverse events (AEs) for 6 months. The secondary objective was to describe the immunogenicity as measured by GBS6 serotype-specific IgG geometric mean concentrations (GMCs) before and after vaccination.

Results: 364/365 randomized subjects were vaccinated; 348 (95.3%) completed follow-up. For GBS6 recipients (n=312), the most common injection site reaction was pain (highest in AlPO₄ formulations); the most common systemic reactions were fatigue and headache. Adverse events were reported by 21% to 48.1% of GBS6 recipients across groups compared to 38.5% of placebo recipients. GBS serotype-specific IgG GMCs are shown in the figure below.

Conclusions: GBS6 was well-tolerated in healthy adults and elicited robust immune responses for all ST at all dose levels and formulations that persisted through 6 months after vaccination. This study supports the evaluation of GBS6 in pregnant women.

Figure. Antibody Response Line Plot of IgG GMC Over Time, by Vaccine Group and Serotype



Abstract O-20

Safety and Immunogenicity and Efficacy of Third Trimester Immunization with an Respiratory Syncytial Virus F Protein Vaccine for the Protection of Infants Over the First 180 Days of Life.

L. Fries, I. Cho, D.N. Thomas, J. Wen, M. Spindler, A. Fix, J. Plested, G. Glenn (Novavax, Inc., Gaithersburg MD) and the Prepare Study Investigators.

Introduction/Background & Aims: Respiratory syncytial virus (RSV) is the leading viral cause of severe lower respiratory tract disease in infants worldwide, with severe disease occurring in the first months of life when active immunization may be slow to afford protection. We evaluated the efficacy of maternal immunization with an RSV F protein vaccine against RSV lower respiratory tract infection (LRTI) over the first 180 days of infant life.

Methods: Between 2015 and 2018, we recruited 4,636 women with low-risk singleton third trimester pregnancies in 11 countries to receive RSV F vaccine or placebo (2:1 ratio) in a randomized, observer-blind trial. Women were followed for 6 months post-delivery, and infants for ~364 days. Passive and active surveillance for RSV LRTI, identified by RT-PCR detection of RSV, physical examination, and pulse oximetry, was carried out for 180 days from delivery.

Results: The RSV F vaccine was well tolerated, with modest reactogenicity and no excess fever. There were no apparent negative impacts on pregnancy, delivery, or infant well-being. Immunogenicity was demonstrated by anti-F IgG, palivizumab-competitive antibody, and RSV/A and B neutralizing antibody increases, which were transferred transplacentally with >100% efficiency. Efficacy against RSV LRTI through 90 days of life was as follows:

Endpoint	Per-Protocol Population			Intent-to-Treat Population	
	Point Estimate	95% CI	97.52% CI	Point Estimate	95% CI
Medically significant RSV LRTI (SpO ₂ <95%)	39.4%	5.3, 61.2%	-1.0, 63.7%	32.2	- 4.2, 55.9%
RSV LRTI with severe hypoxemia (SpO ₂ <92%)	48.2%	-8.3, 75.3%	ND	44.4%	-14.9, 73.1%
RSV LRTI with hospitalization	44.4%	19.6, 61.5%	ND	48.1%	26.1, 63.5%

Efficacy against all-cause LRTI with severe hypoxemia (46.0%) or hospitalization (27.8%) in the ITT population was also noted, which persisted through 180 days of life.

Conclusions: RSV F vaccine in the third trimester was safe and had clinically-meaningful impacts on RSV and all-cause LRTI over the first 6 months of life.

Abstract O-21

Maternal-infant transfer of naturally-acquired antibodies for protection against *Shigella*

Ndungo E, Andronescu L, Laufer M, Pasetti M

Introduction/Background & Aims: *Shigella* is the second leading cause of diarrheal diseases, accounting for >200,000 infections and >50,000 deaths in children under 5 years of age worldwide. Disease incidence increases after the first year of life, possibly reflecting the contribution of maternally acquired immunity, which inversely correlates with disease incidence. The mechanisms of how placentally-transferred immune components and their functional capabilities protect against shigellosis are unknown.

Methods: Paired maternal and cord blood sera obtained from a longitudinal cohort study involving 100 mothers and their infants living in Malawi were tested for *Shigella*-specific antibody (class and subclass) levels against LPS and other virulent factors (IpaB, IpaC, IpaD and VirG). Antibody functionality was measured using serum bactericidal antibody and opsonophagocytic killing antibody assays. Efficiency of antibody transfer from mother to infant, and correlation analysis between antibody level and functional activity were also performed.

Results: We found elevated levels of *Shigella*-specific IgG in maternal sera that were transferred with high efficiency to cord blood ($\approx 60\%$ for anti-LPS, $\approx 100\%$ for anti-protein antigens). In contrast, functional antibodies were transferred less efficiently ($<20\%$). Depletion of antigen-specific antibody from sera showed that LPS was a target of functional activity. However, while functional activity correlated well with LPS IgG titers in cord blood, a similar correlation was not observed in maternal sera. Further analysis of antibody classes and IgG subclasses was performed to further characterize antibodies that were correlated with induction of bactericidal activity in maternal sera and those that were transferred through the placenta.

Conclusion: Our work characterizes the qualitative profile of maternally acquired antibodies induced by natural exposure to *Shigella*. This information would be useful to improve our understanding of functional antibody targets and for vaccine development to protect children after maternal immunity wanes.

Abstract O-22

Use of minimal invasive tissue sampling for determining the burden of neonatal mortality that is potentially vaccine-preventable.

Solomon F, Charwana R, Pathirana J, Bailie V, Izu A, Wadula J, Nakwa F, Velaphi S, Hale M, **Madhi S**

Introduction/Background & Aims: Post-mortem minimal invasive tissue sampling (MITS) is a potential alternative to the gold standard complete diagnostic autopsy for identifying specific causes of childhood deaths. We investigated the utility of MITS, interpreted with available clinical data, for attributing the underlying and immediate causes of neonatal deaths; and to ascertain the proportion of deaths from infectious diseases that are potentially preventable by vaccination.

Methods: This prospective, observational, pilot study enrolled neonatal deaths at Chris Hani Baragwanath Academic Hospital, Soweto, South Africa. The MITS included needle core-biopsy sampling for histo-pathology of brain, lungs and liver tissue. Microbiological culture and/or molecular tests were performed on lung, liver, blood, cerebrospinal fluid and stool samples. The “underlying” and “immediate” causes of death (CoD) were determined for each case by an international panel of 12-15 medical specialists.

Results: We enrolled 153 neonatal deaths; 106 aged 3-28 days. Leading underlying CoD included “Complications of prematurity” (52.9%), “Complications of intrapartum events” (15.0%), “Congenital malformations” (13.1%) and

“Infection related” (9.8%). Infectious causes were the immediate CoD in 70.4% (58/81) of neonates with “Complications of prematurity” as the underlying cause. Overall, 74.4% of 90 infection-related deaths were hospital-acquired; mainly due to multi-drug resistant *Acinetobacter baumannii* (52.2%), *Klebsiella pneumoniae* (22.4%) and *Staphylococcus aureus* (20.9%). *Streptococcus agalactiae* was the most common pathogen (5/15; 33.3%) among deaths with “Infections” as the underlying cause.

Conclusions: MITS has potential to address the knowledge-gap on specific causes of neonatal mortality. Included among the immediate causes of neonatal death were potentially vaccine preventable deaths due to GBS, for which vaccines is currently being developed for vaccination during pregnancy to protect their young infants. Also, passive immunization of preterm neonates, such as with yet to be developed monoclonal antibodies, could mitigate mortality against hospital acquired infections which was the immediate CoD in neonatal death with prematurity as an underlying condition.

Closing Keynote

The presumption of inclusion: maternal immunization against emerging infectious diseases

Speaker: Ruth A. Karron, Center for Immunization Research, Department of International Health, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD

In recent years, outbreaks of Zika, H1N1 influenza, and Ebola viruses have severely and uniquely affected pregnant women and their offspring. Pregnant women must be proactively considered in research agendas and deployment efforts for vaccines against emerging infectious diseases, yet these vaccines have rarely been designed or developed with pregnant women in mind. For this and other reasons, pregnant women have in some cases been denied vaccines that would have protected them and their offspring from severe epidemic threats. Recommendations to guide the development and deployment of appropriate vaccines in these situations did not exist. To address this need, we convened the Pregnancy Research Ethics for Vaccines, Epidemics, and New Technologies (PREVENT) Working Group - a multidisciplinary, international team of 17 experts specializing in bioethics, maternal immunization, maternal-fetal medicine, obstetrics, pediatrics, philosophy, public health, and vaccine research and policy, and consulted with over 100 additional experts in ethics, public health, vaccine science, maternal and child health, and regulatory affairs. We developed a guidance document that puts forth 22 recommendations across the domains of epidemic preparedness, vaccine R&D, and vaccine deployment. A key recommendation is the presumption of inclusion, which changes the default position such that pregnant women are included in vaccine development and deployment unless their exclusion can be justified from a scientific and ethical standpoint. The presumption of inclusion reframes decisions about investments in vaccine research, development, and delivery in ways that are profoundly important for public health and equity.

Importance: The PREVENT recommendations provide a framework for the fair inclusion of pregnant women in the development and deployment of vaccines against current and emerging epidemic threats. Many of the PREVENT recommendations may also be relevant as the inclusion of pregnant women is more broadly considered in the context of biomedical research.

Poster Abstracts

Poster 1

Safety and immunogenicity of reduced antigen-content diphtheria-tetanus-acellular pertussis immunization during pregnancy or post-partum, followed by hexavalent diphtheria, tetanus, acellular pertussis, poliovirus, Haemophilus influenzae type B conjugate hepatitis B virus primary immunization in infants

Halperin S, Perrett K, Nolan T, Tapiero B, Martínón-Torres F, Martínez Pancorbo C, Virta M, Cristobal Garcia I, Kostanyan L, Cheuvart B, Ceregido M, Meyer N, Kuriyakose S, Kokko S, Omenaca F, Carmona A, Marcos Fernandez M, Garcia-Sicilia Lopez J, Stranak Z, Rodríguez Zambrano M, Vanderkooi O, Kosina P, Garcia A, Merino J, Encinas Pardilla M, Cilleruelo Ortega M, Asenjo de la Fuente J, Camacho Marin M, Miranda M, Arias Novas B, Fernández-Miranda M, Ramos Amador J, Romero Espinar Y, Baca M, Marchisio P, Manzoni P, Mesaros N

Introduction/Background & Aims: Pertussis immunization during pregnancy reduces the risk of infection in newborns. Our aim was to assess the safety and immunogenicity of maternal pertussis immunization, transfer of antibodies to the newborn, and the effect on the infant's response to active immunization.

Methods: In an observer-blind, randomized, placebo-controlled trial (NCT02377349), women received dTpa or placebo at 27^{0/7}-36^{6/7} weeks of gestation and crossover immunization post-partum. In an open-label, non-randomized, uncontrolled trial (NCT02422264), their infants received a primary series (2 or 3 doses) of DTPa-HBV-IPV/Hib according to national schedules. Immune responses were assessed in women before and 1-month post-immunization, and in infants at birth (cord blood), before the first and 1-month post-last dose. Immune superiority of maternal immunization was defined as the lower limit of the 95% confidence interval of the GMC ratios in cord blood being ≥ 1.5 . In infants, the primary objective was the assessment of seroprotection/seropositivity rates for DTPa-HBV-IPV/Hib antigens 1-month post-primary vaccination. Solicited and unsolicited adverse events (AEs), serious AEs (SAEs), pregnancy and neonate AE's of interest were collected.

Results: 687 women (dTpa:341; control:346) and 601 infants (dTpa:296; control:305) were vaccinated. Superiority in cord blood for dTpa was demonstrated for all pertussis antigens (GMC ratios: 8.5-20.7). Post-primary series, 100% of infants for D and T, and >95% for polio, >98% for HepB, and >94% for Hib in both groups were seroprotected. For pertussis antigens, the response rate was 37.5-77.1% in the dTpa and 90.0-99.2% in the control group. AEs and SAEs rates were similar in both groups across studies.

Conclusions: dTpa during pregnancy leads to high levels of antibodies in newborns, but results in blunting of the response to pertussis, but not to other antigens, post-primary infant-series. The clinical significance of the lower responses is still unknown. The vaccines administered were well tolerated and no new safety concern was identified.

Poster 2

Assessing obstetrical and birth outcomes associated with maternal Tdap administration in Ontario, Canada

Romina Fakhraei, Natasha Crowcroft, Shelly Bolotin, Steven Hawken, Kumanan Wilson, Laura Gaudet, Gayatri Amirthalingam, Anne Biringer, Jocelynn Cook, Vinita Dubey, Scott Halperin, Frances Jamieson, Jeff Kwong, Manish Sadarangani, Mark Walker, Deshayne B. Fell

Introduction/Background & Aims: In February 2018, Canada's National Advisory Committee on Immunization (NACI) began recommending maternal immunization with pertussis-containing vaccine (Tdap) during every pregnancy, ideally between 27 and 32 weeks' gestation, as a strategy to prevent pertussis infection in young infants. The objectives of this study were to assess: (1) the characteristics of women who received Tdap immunization during pregnancy in the pre-policy time period; and, (2) the associations between maternal Tdap immunization with obstetrical and perinatal outcomes.

Methods: We performed a population-based retrospective cohort study of all live births in Ontario, encompassing 5 years of data prior to the 2018 NACI recommendation (April 2012 to March 2017). Tdap immunization during pregnancy was ascertained using pertussis-specific immunization fee codes. We used an extended Cox regression model with a time-dependent exposure variable to estimate adjusted hazards ratios (aHR) for preterm and very preterm birth. All other obstetrical and birth outcomes were assessed using log-binomial regression to generate adjusted risk ratios (aRR). We used inverse probability of treatment weights derived from propensity scores to adjust all estimates.

Results: Of the 630,351 women with a pregnancy ending in a live birth, 12,102 (1.9%) were vaccinated with Tdap. Women who were nulliparous, above 30 years of age, and living in a higher-income neighbourhood were more likely to be vaccinated. There were no significant increased risks (aHR/aRR [95% CI]) for preterm birth (0.99 [0.87-1.12]), very preterm birth (1.06 [0.72-1.56]), or small-for-gestational-age birth (0.96 [0.90-1.01]) in infants born to Tdap-vaccinated women compared with infants born to unvaccinated women. We did not observe any increased risk of chorioamnionitis with maternal Tdap vaccination (0.94 [0.79-1.13]).

Conclusions: No adverse obstetrical or perinatal outcomes were identified in association with maternal Tdap vaccination; however, on-going surveillance in Canada is needed as Tdap coverage among pregnant women will likely increase in the coming years.

Poster 3

The prevalence and clinical characteristics of pertussis-associated pneumonia among infants in Botswana

Sadarangani M, **Abu Raya B**, Arscott-Mills T, Cunningham C, Feemster K, Goldfarb D, Kelly M, Luinstra K, Patel M, Richard-Greenblatt M, Shah S, Smieja M, Steenhoff A

Background: There are scant data on the prevalence and clinical course of pertussis disease among infants with pneumonia in low and middle-income countries. While pertussis vaccination coverage is high ($\geq 90\%$) among infants in Botswana, human immunodeficiency virus (HIV) infection affects nearly one-third of pregnancies. We aimed to evaluate the prevalence and clinical course of pertussis disease in a cohort of HIV-exposed uninfected (HEU), HIV-unexposed uninfected (HUU), and HIV-infected infants with pneumonia in Botswana.

Methods: Children 1–23 months of age admitted to a tertiary care hospital (Princess Marina Hospital, Gaborone, Botswana) with pneumonia between April 2012 and June 2016 were included. Nasopharyngeal swab specimens obtained at enrollment were tested by a previously validated in-house real-time polymerase chain reaction assay that detects a unique sequence of the porin gene of *Bordetella pertussis*.

Results: *B. pertussis* was identified in 1/248 (0.4%) HUU and 3/110 (2.7%) HEU children 1-23 months of age. All pertussis-associated pneumonia cases occurred in infants <5 months of age (prevalence, 1.0% [1/103] in HUU and 4.8% [3/62] in HEU infants). *B. pertussis* was not detected from the 33 HIV-infected children with pneumonia. No HEU infants with pertussis-associated pneumonia were taking co-trimoxazole prophylaxis at the time of hospital presentation. One HUU infant required intensive care unit admission for mechanical ventilation, but there were no deaths.

Conclusions: The prevalence of pertussis was low among infants and young children with pneumonia in Botswana. Although vaccination against pertussis in pregnancy is designed to prevent classical pertussis disease, reduction of pertussis-associated pneumonia might be an additional important benefit.

Poster 4

Safety and immunogenicity of Tdap vaccine in pregnant women in Bamako, Mali

Flanon Coulibaly¹, Fadima Cheick Haidara¹, Djènèba Traoré¹, Milagritos D. Tapia^{1,2}, Samba O. Sow¹, Marcela Pasetti², Mat Makowski³, James Albert³, Karen Kotloff², Kathleen Neuzil²

1 Centre pour le Développement des Vaccins-Mali, Bamako, Mali; 2 University of Maryland School of Medicine, Center for Vaccine Development, Baltimore, MD, United States; 3 The Emmes Company, LLC, Rockville, MD, United States

Background: Young infants are at risk for severe pertussis infection. Pertussis vaccination programs for pregnant women have been highly effective in reducing morbidity in young infants in the UK and the US. Unfortunately, no such programs exist in low resource countries in Africa. Herein we evaluate the safety and immunogenicity of Tdap vaccine in pregnant women in Mali and measure immunity to pertussis in their infants.

Methods: Pregnant women (14-26 weeks gestational age) provided informed consent. Eligible women were enrolled and randomized 2:1 to Tdap or Td vaccine. Maternal blood samples were collected at baseline, 31 days post-vaccination and at delivery. Breast milk and infant blood samples were collected at birth, prior to 1st DTwP-HepB-Hib, prior to 2nd or 3rd DTwP-HepB-Hib and at 6 months of age. For women, solicited adverse events (AE) and unsolicited AE are collected until 7 days and 31 days after vaccination and serious AE (SAE) until 6 months post-partum. For infants, unsolicited AEs and SAEs are recorded for 6 months.

Results: From January 23, 2019 to July 25, 2019, 207 women were screened, 201 were randomized and 200 were vaccinated. Thus far, 30 women have delivered and 6 infants have received the first dose of DTwP-HepB-Hib. Mild pain was reported by 19 participants (9.5%) and mild swelling by 1 (0.5%). Five moderate unsolicited events have been observed. Fourteen unrelated SAEs have been recorded, including 1 stillbirth, 3 spontaneous abortions and 1 infant death secondary to an acute respiratory infection. (Results will be updated as data become available.)

Conclusion: Evaluating maternal immunization with Tdap will provide valuable information regarding the safety of this vaccine in pregnant women and their infants. Studying maternal and infant immunity to pertussis will yield information on the ability of this vaccine to protect infants in the first 6 months of life and on any effect it might have on immune responses to routine infant vaccination with DTwP-HepB-Hib.

This work is supported by the vaccine and treatment evaluation unit (VTEU) at University of Maryland (contract HHSN272201300022I). The network of VTEUs is supported by the National Institute of Allergy and Infectious Diseases, National Institutes of Health. ClinicalTrials.gov: NCT03589768.

Poster 5

Maternal immunization with Tdap in Latin America (LA): report from the 2017 Global Pertussis Initiative (GPI) Roundtable Meeting

Angela Gentile¹, **Rolando Ulloa-Gutierrez**² Lourdes Dueñas³, Cristina Mariño⁴, Luisa H Falleiros-Arlant⁵, Eitan Berezin⁶, Mónica Pujadas⁷, Abiel Mascareñas-de los Santos⁸, Maria G López⁹, Alfredo Guerreros-Benavides¹⁰, Fernando Ysern¹¹, Carl Heinz Wirsing von König¹², Tina Tan¹³, Kevin Forsyth¹⁴

¹Hospital de Niños Ricardo Gutiérrez, Buenos Aires, Argentina; ²Hospital Nacional de Niños “Dr. Carlos Sáenz Gutiérrez”, San José, Costa Rica; ³Hospital de Niños Benjamín Bloom, San Salvador, El Salvador; ⁴Hospital Militar Central, Bogotá, Colombia; ⁵Universidade Metropolitana, Sao Paulo, Brasil; ⁶Faculdade Ciências Médicas, Sao Paulo, Brasil; ⁷Universidad de la República de Uruguay, Montevideo, Uruguay; ⁸Hospital Universitario Jose E Gonzalez, Universidad Autónoma de Nuevo Leon, Mexico; ⁹Hospital de Niños JM de los Ríos, Caracas, Venezuela; ¹⁰Clínica Internacional, Lima, Perú; ¹¹Grupo Pediátrico de Caguas, Caguas, Puerto Rico; ¹²Medizin Krefeld MVZ, Krefeld, Germany; ¹³Feinberg School of Medicine, Chichago, IL; ¹⁴Flinders University and Flinders Medical Centre, Adelaide, Australia

Introduction/Background & Aims: The GPI Roundtable Meeting was convened in Cancun, Mexico (November 11–13, 2017), with participants from more than 14 countries. Discussed aspects included: a review of the current pertussis situation in The Americas and particularly LA, local epidemiology, current vaccination recommendations, obstacles and challenges for effective implementation, surveillance, and effectiveness data. Our main objective is to describe preliminary data presented by experts from representative LA countries that have introduced pregnancy Tdap immunization.

Methods: We analyzed data presented from 10 LA countries (2012-2017): Argentina, Brazil, Colombia, Costa Rica, El Salvador, Mexico, Peru, Puerto Rico, Uruguay, and Venezuela. Although maternal Tdap has been suggested and recommended by experts in most of these, we analyzed only those in which these programs have been introduced and maintained.

Results: Tdap immunization during pregnancy has been implemented nationwide in 6/10 countries: Argentina(2012), Costa Rica(2013), El Salvador(2014), Brazil(2014), Colombia(2014), and Uruguay(2015). Costa Rica had previous postpartum Tdap cocoon strategy and then switched to maternal immunization. Although post maternal-Tdap introduction preliminary impact data was promising, at the moment publications about nationwide impact were available only from Argentina, with an effectiveness of 77.6 (Tdap2nd trimester) and 82.7% (Tdap3rd trimester) in morbidity, and no deaths in a major reference hospital. Currently, the recommendations are inconsistent, implementation is suboptimal, and some countries lack good surveillance data, including percentage of maternal Tdap coverage. In Colombia, Tdap was started initially in Bogotá (2013) and then extended nationwide; in Uruguay it was reintroduced after an initial implementation only during a country outbreak.

Conclusions: Current available and published data for selected LA countries with maternal Tdap during pregnancy is scarce. Socioeconomical and political problems remain a significant barrier for some of these countries. Nevertheless, in LA countries where pertussis morbidity and mortality rates are high, maternal Tdap should be considered and implemented.

Poster 6

Timeline spread of a pertussis outbreak in a small country: The example of Costa Rica and the implementation of a nationwide postpartum maternal Tdap immunization strategy

Rolando Ulloa-Gutierrez¹, Ana Morice,² María L Avila-Agüero^{1,3}

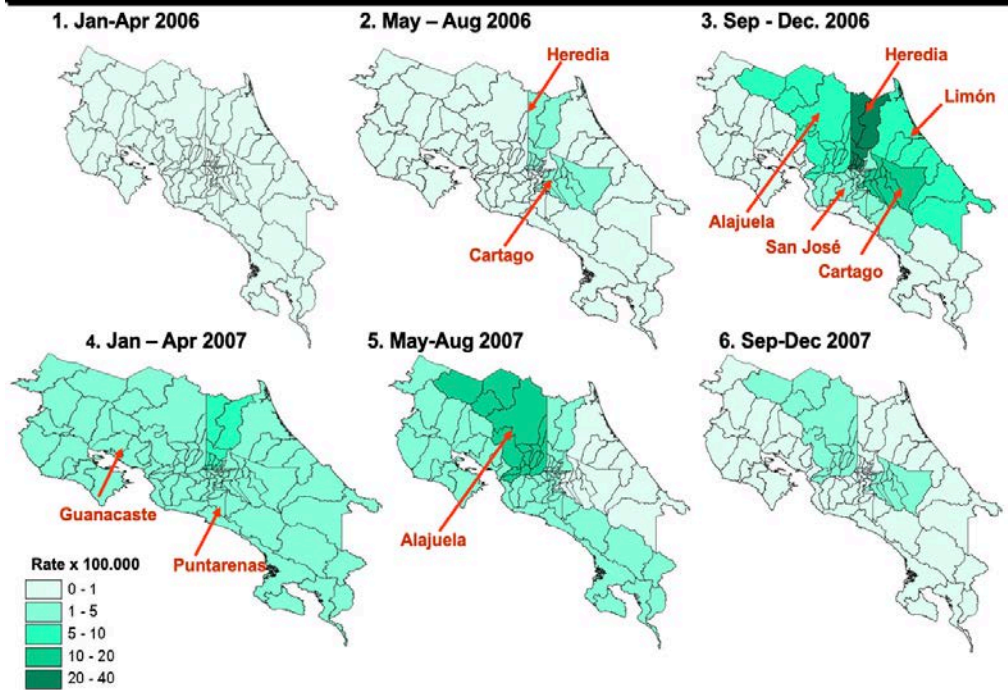
¹Servicio de Infectología, Hospital Nacional de Niños “Dr. Carlos Sáenz Herrera”, Centro de Ciencias Médicas de la Caja Costarricense de Seguro Social (CCSS); ²Independent Researcher; ^{1,2} San José, Costa Rica; ³Center for Infectious Disease Modeling and Analysis (CIDMA), Yale University; New Haven, CT, USA

Introduction/Background & Aims: Costa Rica (CR) is a small Central American developing country with a territorial extension of 51,100 km², a birth cohort of ~70,000 newborns annually, and a total population of 5,003,402 habitants (2018). A pertussis outbreak started in the country at the beginning of 2006, spread rapidly nationwide over the next months, and continued approximately until mid 2008. Our main objective is to describe part of the 2006 and 2007 rapid spread of pertussis in CR that justified and led for the first time ever in a country, to a nationwide postpartum maternal Tdap vaccination campaign strategy.

Methods: We analyzed incidence rates of pertussis per 100,000 habitants among the 7 provinces of CR: San José, Heredia, Alajuela, Cartago, Guanacaste, Puntarenas and Limón. Study period was: January 1st, 2006 to December 31st, 2007. Pertussis cases were detected and reported to the Ministry of Health, based on the clinical case definition, followed by DFA and PCR among the laboratory confirmed cases. We compared by annual quarters and geographically, the different incidences of pertussis pre, during, and soon after the cocoon strategy. Starting on 04/30/2007, universal Tdap vaccination was offered to all mothers within the first 24-48 hours postpartum, who delivered their babies at maternities or other hospitals. This represents around 98% of deliveries in CR, both in private and public services.

Results: As shown in Figure 1, the main province identified to be the original outbreak source was Heredia, which neighbors with San José, our nation’s capital and the most densely populated province.

Pertussis Incidence rates (per 100,000 habitants) by quarters Costa Rica, Outbreak of 2006 - 2007.



Conclusions: In countries with small geographical extensions as CR, local pertussis outbreaks can spread rapidly to other provinces and nationwide. Prompt public health interventions and vaccination strategies should be implemented. At that time, that was the best strategy available prior to the 2008 recommendations of maternal Tdap vaccination during pregnancy.

Poster 7

A phase IV, multi-centre, randomized clinical trial comparing two pertussis-containing vaccines in pregnant women in England and vaccine responses in their infants

Jones C, Calvert A, Southern J, Matheson M, Andrews N, Khalil A, Cuthbertson H, Hallis B, England A, Heath P, Miller E

Introduction/Background & Aims: Two pertussis-containing vaccines have been recommended in pregnancy in the UK - REPEVAX-IPV (2012-2014) and BOOSTRIX-IPV (2014 onwards). The aim of this trial was to assess antibody responses to pertussis antigens following primary immunisation in infants born to women receiving a pertussis-containing vaccine and infants born to unvaccinated women. Placental transfer ratios (PTRs) and concentrations of pertussis-specific antibodies prior to primary vaccination and at 13 months of age were also assessed.

Methods: Pregnant women were randomised to receive REPEVAX-IPV (DTaP₅-IPV) or BOOSTRIX-IPV (DTaP₃-IPV) at 28-32 gestational weeks. Blood samples were collected from mothers at delivery and infants at birth (cord or peripheral venous blood), 2, 5 and 13 months. A contemporaneous non-randomised control group of infants born to women who had not received a pertussis-containing vaccine in pregnancy was recruited postnatally.

Results: There was no difference in the PTR, according to maternal vaccine received. At 2 months of age, infants born to mothers vaccinated with DTaP₅-IPV (n=65) had lower geometric mean concentrations (GMC) of anti-PT and FHA IgG compared to infants born to DTaP₃-IPV vaccinated mothers (n=62) (geometric mean ratio [GMR] 0.64 [95% CI 0.43-0.94] and 0.48 [0.35-0.65] respectively) but higher GMCs of anti-FIM IgG (GMR 8.71 [5.2-14.58]).

Following infant primary vaccination, there was no difference in GMCs of anti-PT, FHA and PRN in those born to vaccinated women, however GMCs of anti-PT IgG in these infants was lower than that in infants born to unvaccinated mothers (GMR: 0.71 [0.56-0.90] and 0.78 [0.61-0.98], respectively).

At 13 months of age, GMCs of anti-PT, FHA and FIM were similar in those infants born to DTaP₃-IPV and DTaP₅-IPV vaccinated mothers.

Conclusions: Modest blunting of pertussis-specific antibody responses following primary vaccination occurs in infants born to vaccinated mothers, but with no difference according to the maternal vaccine received and with resolution by 13 months of age.

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Poster 8

Seasonality of *Bordetella Pertuissis* in Lusaka, Zambia

Gill C, Mupila Z, MacLeod B, Forman L, Mwananyanda L, Thea D. Presented by Rachel Pieclak

Background

Bordetella pertussis remains a cause of morbidity and mortality in infants and young children in Zambia, despite the availability of vaccines. There has been minimal surveillance for pertussis in Zambia due to limited diagnostics. It was against this background that the study aimed at looking at the trends in the seasonality of Pertussis in infants from a three cohort studies that measured the disease through nasopharyngeal swabs over a period of 7 years in Lusaka, Zambia.

Methods

We present counts of PCR diagnosed *B. pertussis* by calendar month of diagnosis from nasopharyngeal swabs. The samples came from three respiratory disease studies conducted in Lusaka from October 2011-October 2013; March 2015 to January 2016; and September 2017 to December 2018. The study populations for the three studies were 1) 1,154 children 1-59 months hospitalized with severe pneumonia sampled once; 2) a cohort of 939 healthy infants 1-13 weeks old sampled fortnightly, and; 3) 1,040 deceased infants 4 days to <6 months sampled within 48 hours of death.

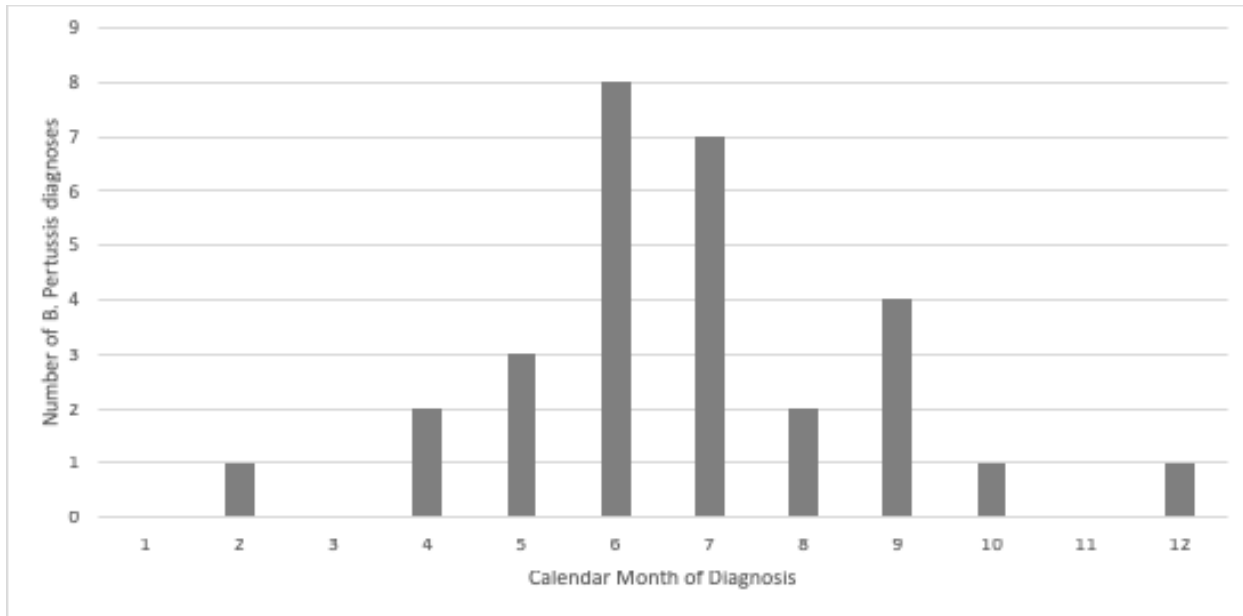
Results

Figure 1 shows the counts of pertussis diagnosis by calendar month. The count of pertussis cases was highest in the Southern hemisphere winter season in June and July. In the six months from September through March minimal amounts of pertussis was detected .

Conclusion

B. pertussis is circulating in Zambian infants and children and is more prevalent in Winter season. These findings will inform the policy makes and other stakeholders involved in devising interventions aimed at prevention and management of Pertussis.

Figure 1. Counts of PCR positive *B. pertussis* diagnoses by calendar month of diagnosis in Lusaka, Zambia



Poster 9

Risk of major structural birth defects associated with seasonal influenza vaccination during pregnancy

Minda Sarna^{1,2}, Damien Foo^{1,2}, Gavin Pereira¹, **Annette Regan**^{1,2,3}

¹School of Public Health, Curtin University, Bentley, Western Australia; ²Wesfarmers Centre for Vaccines and Infectious Diseases, Telethon Kids Institute, Nedlands, Western Australia; ³School of Public Health, Texas A&M University, College Station, Texas, USA.

Introduction/Background & Aims: Pregnant women and infants are at risk of severe influenza infection. Inactivated influenza vaccine (IIV) is recommended during pregnancy to protect both mothers and their infants. Few studies have evaluated the risk for major structural birth defects associated with prenatal administration of IIV.

Methods: We conducted a population-based cohort study using probabilistic data linkage. A cohort of births occurring between March 2012 and April 2016 in Western Australia were identified from state-wide birth records. This cohort was linked to the state’s register for developmental anomalies diagnosed among children up to five years of age and the state’s database for prenatal vaccination records. Vaccinated pregnancies were defined as those with a record of IIV in first trimester (week 2-13 of pregnancy). We estimated prevalence ratios (PRs) of any major structural birth defect. Inverse probability treatment weighting (IPTW) was used to factor for propensity for vaccination. Sensitivity analyses removed pregnancies where vaccination occurred after first trimester.

Results: Between 2012 and 2016, 146,935 births were identified; 16,043 (11%) had a record of IIV during pregnancy, of which 19% (n=3,072) received IIV in first trimester; 4% (n=6,071) of the cohort were diagnosed with a major structural defect: 4.2% of vaccinated births and 4.1% of unvaccinated births. We identified no association between first trimester IIV exposure and diagnosis of a major structural defect (unweighted PR: 1.02 [95% CI: 0.86-1.21]; IPTW PR: 1.03 [95% CI: 0.86-1.24]). We observed similar results after removing pregnancies where vaccination occurred after first trimester (IPTW PR: 1.05 [95% CI: 0.88-1.29]).

Conclusions: Results from this large, population-based cohort indicate that IIV exposure in the first trimester was not associated with an increased risk for major structural birth defects. These findings support the safety of IIV in first trimester, which may be used to inform vaccine decision-making in first trimester.

Poster 10

Paediatric health outcomes following antenatal influenza vaccination: systematic review and meta-analysis

Damien Foo a, Mohinder Sarna a, Hannah Moore b, Gavin Pereira a,c, Deshayne Felld e, Annette Regana b,f
a School of Public Health, Curtin University, Perth, Western Australia, Australia; b Wesfarmers Centre of Vaccines and Infectious Diseases, Telethon Kids Institute, Perth, Western Australia, Australia; c Telethon Kids Institute, Perth, Western Australia, Australia; d School of Epidemiology and Public Health, University of Ottawa, Ottawa, Ontario, Canada; e Children's Hospital of Eastern Ontario Research Institute Ottawa, Ottawa, Ontario, Canada; f School of Public Health, Texas A&M University, College Station, Texas, The United States of America

Introduction/Background & Aims: Pregnant women and infants under six months of age are two high-risk groups vulnerable to severe influenza infection. Antenatal influenza vaccination is the main strategy to prevent influenza infection in these vulnerable groups. To date, no reviews have investigated the longer-term paediatric health outcomes associated with antenatal influenza vaccination. The aim of this systematic review is to synthesise the current evidence for the association between antenatal influenza vaccination and paediatric health outcomes.

Methods: CINAHL Plus, Ovid/MEDLINE, Ovid/EMBASE, Scopus and Web of Science (from the inception of each database up to February 2019 with no restriction on geographic setting) were systematically searched for all peer-reviewed articles assessing health outcomes in children exposed to influenza vaccines during pregnancy. This review will include any health outcome occurring between the ages of six months to five years, including acute and chronic respiratory infections; atopic/allergic and sensory conditions; gastrointestinal diseases; endocrine, nutritional and metabolic diseases; mental, behavioural and neurodevelopmental disorders; diseases of the circulatory system; musculoskeletal diseases; neurological and immune conditions; cancers; and mortality. The search was limited to literature published in English and human subjects. Two independent reviewers screened the titles, abstracts and full-text articles for eligibility; and will assess the quality of observational studies and randomised controlled trials using the Newcastle-Ottawa Scale and the Cochrane Risk-of-Bias Tool, respectively. A third reviewer will resolve any disagreements between the two reviewers. If data permits, meta-analyses will be performed for each health outcome, otherwise a descriptive analysis will be conducted.

Results: Database searches conducted on February 26, 2019 yielded 7,193 citations. After the removal of duplicates, 3,532 unique citations were screened based on the title and abstract and 96 full-text articles met the criteria for full-text review.

Conclusions: This systematic review is ongoing and will provide a comprehensive summary regarding the childhood health impacts of influenza vaccination during pregnancy.

Poster 11

Immunogenicity and safety of a quadrivalent inactivated influenza vaccine in pregnant women: a randomized, observer-blind trial

Timo Vesikari, Miia Virta, Seppo Heinonen, Cécile Eymin, Nathalie Lavis, Anne-Laure Chabanon, Viviane Gresset-Bourgeois. Presented by Bruce Seet

Introduction/Background & Aims: Vaccination against influenza during pregnancy provides direct protection to pregnant women and passive protection for their infants. Although trivalent inactivated influenza vaccines (IIV3s) are safe and effective during pregnancy, quadrivalent inactivated influenza vaccines (IIV4s) have not been evaluated in pregnant women and their infants. We will report the results of a randomized phase IV study to evaluate the immunogenicity and safety of IIV4 vs. IIV3 in pregnant women.

Methods: Participants aged ≥ 18 years at weeks 20 to 32 of pregnancy were randomly assigned in a 2:1 ratio to receive a single dose of IIV4 (n=230) or IIV3 (n=116).

Results: Between baseline and 21 days after vaccination, hemagglutination inhibition (HAI) antibody titers increased in both groups by similar magnitudes for the two influenza A strains and single B strain common to IIV4 and IIV3. For

the additional B strain in IIV4, HAI titers were higher in IIV4 recipients than IIV3 recipients (post-/pre-vaccination geometric mean titer ratio, 6.3 [95% CI: 5.1–7.7] vs. 3.4 [95% CI: 2.7–4.3]). At delivery, in both groups, HAI antibody titers for all strains were 1.5–1.9-fold higher in umbilical cord blood than in maternal blood, confirming transplacental antibody transfer. Rates of solicited and unsolicited vaccine-related adverse events in mothers were similar between the two groups. Live births were reported for all participants and there were no vaccine-related adverse events in newborns.

Conclusions: These results suggest IIV4 is as safe and immunogenic as IIV3 in pregnant women, and that maternal immunization with IIV4 should protect newborns against influenza via passively acquired antibodies.

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Poster 12

Disease burden and maternal vaccination effectiveness in Australian infants hospitalized with influenza; a multisite, multiyear analysis

McRae J, Blyth C, Cheng A, Quinn H, Wood N, Macartney K

Introduction/Background & Aims: Infants less than 6 months of age are at high risk of severe hospitalized influenza. Unable to be vaccinated, best protection is afforded through maternal influenza-specific antibody transfer during pregnancy. This study explored risk factors for hospitalization and predictors for intensive care unit (ICU) admission as well as maternal vaccine coverage and effectiveness (VE) in Australian infants.

Methods: Data were captured using two active prospective Australian sentinel hospital surveillance networks: Influenza Complications Alert (FluCAN) and Paediatric Active Enhanced Disease Surveillance (PAEDS). Descriptive analysis for infants aged <6 months with laboratory confirmed influenza (LCI) was performed for 2011–2018, including assessment of factors predicting intensive care unit (ICU) admission. Using a test-negative design case control method, maternal VE against early infant hospitalization was estimated using multivariable logistic regression.

Results: Of 455 LCI cases from 2011–18, 70/451 (15.5%) were Indigenous Australians, 136/454 (30.0%) had an underlying medical condition (including prematurity), and 180 (39.6%) were aged <2 months. Influenza A accounted for 357 (78.5%) and influenza B for 94 (20.7%). Predictors of ICU admission (n=54, 12%) were medical comorbidities (OR 5.69, 95%CI: 2.78–11.64), oseltamivir use (OR 9.36, 95%CI: 4.38–19.99) and influenza B (OR 2.18, 95%CI: 1.00–4.74) over influenza A. Maternal vaccine coverage in controls in 2018 was 49.5%. In 2018 when influenza A/H1N1 dominated, maternal VE against infant hospitalization up to age 6 months was 77% (OR 0.23, 95%CI: 0.05–0.99); VE was much lower in 2017 (A/H3N2 dominant), consistent with all-age effectiveness.

Conclusions: Infants less than 6 months of age, 70% without risk factors, experience severe hospitalized influenza. Vaccination is effective at reducing infant disease. Improved uptake of maternal influenza vaccine to better infant health outcomes is a public health priority.

Poster 13

The impact of the maternal influenza vaccination programme on laboratory confirmed influenza in infants in England 2009–2017

Lopez Bernal J, Andrews N, Pebody R

Introduction/Background & Aims: The UK introduced a maternal influenza vaccination program in 2009. This has been shown to be effective at preventing influenza in infants born to vaccinated versus unvaccinated mothers, however, the overall impact of the program (incorporating direct and indirect effectiveness and coverage) has not been studied. This study aims to evaluate the population level impact (overall effect) of the maternal vaccination program on infant influenza. This is challenging because influenza is highly variable with dominant strains and overall burden changing each season, making pre- and post-program evaluations difficult. Furthermore, it is challenging to

disentangle the effect of the maternal program from indirect effects of the newly introduced child influenza vaccination.

Methods: We obtained data on all positive influenza samples submitted to Public Health England for 0-<24-month-old children between 2001-2017. Maternal antibodies against influenza remain in the infant circulation for 3-6 months. To estimate the impact of the maternal influenza program we examined the odds of positive samples coming from those aged <6 months compared to those aged 6-24 months in maternal vaccination years compared to non-vaccine years.

Results: There were 4,893 laboratory confirmed influenza cases aged 0-<24 months during the study period. Introduction of the maternal vaccination program was associated with a 26.7% (95%CI: 17.4-34.8%) reduction in the odds of positive samples coming from those aged <6 months and a 36.1% (95%CI: 26.0-44.8%) reduction in the odds of positive samples coming from <3 month-olds. There was significant evidence of an impact of the maternal influenza vaccine in all seasons apart from 2011/12, 2014/15, 2016/17 and 2017/18.

Conclusions: The maternal influenza vaccine has had a significant population level impact on infant influenza in England. Measuring case ratios according to the presence/absence of maternal antibodies is a valuable approach for estimating the impact of maternal vaccines while controlling for the effects of other vaccination programs.

Poster 14

Canadian National Vaccine Safety (CANVAS) Network Seasonal Influenza Safety Surveillance in Pregnant Women

Bettinger J, De Serres G, Coleman B, Top K, Kellner J, Valiquette L, Isenor J, Vanderkooi O, McCarthy A

Introduction/Background & Aims: The Canadian National Vaccine Safety (CANVAS) network, a sentinel network, was established in 2009 and now provides annual influenza vaccine safety information from >30,000 adults and children across Canada. To improve influenza vaccine safety monitoring during pregnancy, questions about pregnancy status and outcomes were added in 2016. Information on health events in pregnant women who are vaccinated during the seasonal influenza vaccination campaign and unvaccinated pregnant controls is now captured.

Methods: In 2016, 2017 and 2018 pregnant vaccinated participants completed an online survey at day 8 following vaccination. Unvaccinated pregnant controls completed an online survey on health events occurring over the past 7 days during the same years. Telephone follow up occurred for those who reported a medically attended event, both in the control and vaccinated groups.

Results: A total of 937 vaccinated and 474 unvaccinated pregnant women aged 15 to 49 years responded. Over the 3 years, 10.5% of vaccinated pregnant women and 13.4% of unvaccinated pregnant women reported a health event in the previous 7 days. The health event was severe enough to prevent work and/or require health care consultation for 4.1% of vaccinated and 4.6% of unvaccinated pregnant women. This compares to 5.0% of vaccinated women 15-49 years of age and 3.4% of unvaccinated non-pregnant women 15-49 years of age over the same time period. Among vaccinated pregnant women, malaise/myalgia/feeling unwell, respiratory and gastrointestinal symptoms were the most frequently reported symptoms with vaccinated pregnant women reporting slightly higher rates in all categories when compared with unvaccinated pregnant women. There were no pregnancy related adverse events in vaccinated women while one control reported miscarriage.

Conclusions: Severe event rates following influenza vaccination were lower among vaccinated pregnant women than unvaccinated pregnant women and non-pregnant vaccinated women. This suggested events in vaccinated pregnant women may be unrelated to influenza vaccination.

Poster 15

Respiratory illnesses during pregnancy: prevalence, aetiology, severity and associations with infant birth outcomes

Clarke M, Coat S, Riley K, Morello B, Marshall H

Introduction/Background & Aims: Respiratory illnesses during pregnancy have potential for significant consequence to the pregnant women and their infant. However, the true burden of respiratory illness in pregnancy is largely unknown. There is limited data on the aetiology, frequency or severity of these infections in pregnant women. This study aimed to estimate the frequency and severity of acute respiratory illness in pregnant women and describe the most common pathogens causing infection.

Methods: Pregnant women attending their first antenatal appointment at the Women's and Children's Hospital in South Australia between October 2017 and May 2018 were invited to participate if they were less than 20 weeks gestation at the time of consent. Participant's clinical and demographic factors, medical and vaccination history, household size, occupation and gestation at enrolment were collected. Participants were provided with swabs and instructions for self-collection of nasal swabs if they developed respiratory symptoms lasting at least 48 hours. Diary cards were provided to document clinical symptoms, duration and any medical advice sought. Infant birth details were collected from medical records. Laboratory testing of participants' swabs was undertaken using a routine respiratory pathogen polymerase chain reaction (PCR) panel.

Results: The study enrolled 135 women through the WCH antenatal clinics and obtained 21 nasal swabs collected during acute symptomatic respiratory illnesses. Of the 135 women enrolled, 119 (88%) completed the study to delivery. Of these, 17 mothers (14.3%) reported at least one respiratory illness. A pathogen was detected for 15/21 swabs, including rhinovirus (n=8), RSV (n=3) Influenza (n =3) and para influenza virus (n=1). Medical advice was sought for 5/21 respiratory illnesses (24%).

Conclusions: Respiratory illnesses in pregnancy are common and largely underreported. Whilst rhinovirus was the pathogen most commonly detected, illness due to significant pathogens such as RSV and influenza were also identified.

Poster 16

A new approach to deliver malaria prevention intervention to pregnant women at a community level in mukono district – Uganda

Fred Lwasampijja.¹, Skyler Jayden Dembe.¹, Halima Nakasaga.¹, Richard Lule.² Presented by emilly Tumheirwe Ndyomugyenyl

¹Grassland Community Initiatives Uganda (GCIU), Uganda; ² Makerere University, Kampala, Uganda

Introduction: To assess whether the new approach would increase assess and compliance to intermittent preventive treatment IPT to pregnant women.

Methodology: The study was conducted in 9 sub-counties and 25 parishes with 54,000 people. The new approach delivers IPT with sulphadoxinepyrimethamine (SP) through TBAs, drug shop vendors, CRHWs and adolescent peer mobilizers. The study assessed perception on malaria treatment and prevention, tested and evaluated the new approaches and assessed sustainable issues employing complementary methodologies using surveys, key informants and FGDs.

Results: There was lack of knowledge of who were mostly at risk of malaria and the impact of malaria on anaemia and LBW. People knew the benefit of using ITNs and perceived SP as an effective curative drug though its benefit in pregnancy was not known. With new approaches, 92.4% women received IPT during the second trimester and 67.5% had received two doses of SP compared to 39.9% at health units ($P < 0.0001$). IPT increased mean hemoglobin by 6.7 (PLO.0001), reduced severe anaemia from 5.7% to 3.1% ($P < 0.04$), parasitaemia was reduced from 24.5% to 16.3% ($P < 0.0001$) while parasite density reduced significantly ($P < 0.02$) after the first dose. Among women who got one dose of IPT, 7.6% had LBW babies Vs. 6.0% who got two doses ($P < 0.2$). LBWs were 8.3% at health units Vs 6.0% at the new approaches ($P < 0.03$).

Conclusion: The new approaches increased access and compliance to IPT, with an impact on anaemia, parasitiemia, LBW and were acceptable and cost effective.

Poster 17

Challenges of Introducing Hepatitis B Birth Dose in the African Region, 2018

Kabore H

Introduction WHO recommends that the hepatitis B birth dose (HepB BD) be administered within 24 hours after birth in countries with intermediate to high endemicity of Hepatitis B like in the African region. However, to date only 11 countries in the region have introduced the vaccine in their childhood vaccination schedule. We aimed to assess the barriers to the introduction of the vaccine.

Methods We conducted an online survey through SurveyMonkey from September 2018 through January 2019. To collect data, a memorandum with a link to access the survey was sent to the Expanded Program on Immunization (EPI) managers of the 36 countries in the region that have not yet introduced HepB BD.

Results Twenty-one countries responded to the survey representing a response rate of 58%. Among the respondents 67% had planned to introduce HepB BD in their Countries Multiple Year Plan (cMYP), however none of the countries implemented. The main reasons the vaccine was not introduced were the cost of introduction (71%) followed by the cost of the vaccine (64%) and lack of funding support from the Global Alliance for Vaccines and Immunization (GAVI) (50%). More than 2/3 of the countries (70%) that meet GAVI eligibility criteria would introduce the vaccine if funded by GAVI, while 30% do not know for sure.

Conclusions The progress of HepB BD introduction in the African region has been slow despite the prevalence of hepatitis B in the region. As most countries are relying on external funding to sustain routine children immunization, support with funding will boost the introduction and implementation of HepB BD to help the region move toward achieving the regional goal of achieving <2% prevalence of hepatitis B among children less than 5 years of age by 2020.

Poster 18 Abstract Withdrawn

Maternal Hepatitis B Infection Burden, Comorbidity and Pregnancy Outcome in a Low and Middle Income Population on the Nigeria –Benin Republic Border

Ogunsola O, AKINBODE S

Poster 19

Background incidence rates of adverse pregnancy outcomes in the Netherlands; data of 2006-2015.

Van Der Maas N, Quee F, Broeders L, Immink M, Bekker M, Groenendaal F, Kemmeren J, de Melker H

Background and aim Maternal vaccination can be an effective and safe intervention to protect newborns against infectious diseases in early life. We assessed background rates of adverse pregnancy outcomes, collected in The Netherlands Perinatal Registry prior to implementation of a maternal pertussis immunisation programme in the Netherlands, to distinguish legitimate safety concerns from events that are falsely assigned to the vaccination.

Methods The Netherlands Perinatal Registry is a joint effort of four professional organisations that provide perinatal care in the Netherlands and covers about 98% of all deliveries.

For 2006-2015, we analysed incidence rates (IR) per 10,000 births of several infant and maternal adverse pregnancy outcomes (Table 1).

Results In 2006-2015, birth cohorts ranged from 167,356 to 178,896. IRs of infant outcomes were highest for paediatric involvement (mean 2521 per 10,000) and lowest for neonatal mortality (mean 32 per 10,000)(Table 1).

IRs of maternal outcomes were highest for assisted delivery (mean 2521 per 10,000) and lowest for mortality (0.5 per 10,000) (Table 1).

Table 1. IRs per 10,000 of adverse pregnancy outcomes

	Mean IR per 10,000 (range) for 2006-2015
Newborn level	
Low Apgar score (<7 at 5m)	207(189-222)
Congenital disorders	296(253-340)
Prematurity <28w	68(64-70)
Prematurity <36w	705(668-736)
SGA <10percentile	859(749-979)
Involvement paediatrician	2521(2058-3151)
Resuscitation	256(195-306)
NICU admission	234(210-253)
Foetal mortality	59(51-70)
Neonatal mortality	32(30-36)
Perinatal mortality (1-7d)	88(78-106)
Maternal level	
Assisted delivery	2521(2450-2583)
Inducing childbirth	1744(1293-2113)
Fluxus	616(526-652)
Gestational diabetes	194(90-325)
pregnancy induced hypertension	801(735-877)
Mortality	0.5(0.3-0.8)

In general, case definitions and standards of care, e.g. in relation to very preterm infants, changed during the observation period and impacted IRs.

Conclusion Background rates provide important information to guide safety surveillance after implementation of maternal vaccination programmes in the Netherlands. Changes in routine care and case definitions should be taken into account when time series of adverse pregnancy outcomes are analysed.

Poster 20

A prospective study to evaluate the utility of applying the GAIA consortium case definitions for congenital anomalies and neonatal infections in a maternal vaccination trial in The Gambia

Bittaye M, Jadama B, Oluwalana C, Oko F, Okoye M, **Kanteh E**, Clarke E

Introduction/Background & Aims: The consistent reporting of safety outcomes in trials of maternal vaccinations and in post-licensure pharmacovigilance studies is essential if robust data are to be generated. To harmonize reporting, the GAIA Consortium has published a series of case definitions (CD) including for congenital anomalies and neonatal infections. The CD aim to be applicable in low-and-middle-income as well as high-income-countries. Levels of diagnostic certainty are used to account for the different resources available. The utility of the CD is assessed prospectively in a maternal vaccination trial in The Gambia.

Methods: All congenital anomalies and neonatal infections identified in the trial were assessed to determine the level of diagnostic certainty achievable. MRC Unit The Gambia has an ISO15189-accredited clinical laboratory and ultrasound/x-ray facilities. Paediatric medicine and general surgical expertise is available in The Gambia but little sub-specialization.

Results: Congenital anomalies were identified in 21 infants although 14 were judged to be minor (polydactyly [n = 13]; pre-auricular skin tags [n = 1]) and are not covered by the CD. There were five internal structural defects (three cardiac anomalies, one case each of posterior urethral valves and pyloric stenosis) and two external structural

abnormalities (one congenital talipes equinovarus and one complex of several anomalies). No functional defects were identified. The cardiac anomalies were confirmed with level 2/3 certainty based on echocardiography by a non-paediatric cardiologist. The other internal defects were diagnosed at with level 1 certainty based on imaging and/or surgical correction. Neonatal infections were diagnosed in 41 infants (invasive blood stream-34; meningitis-5; respiratory-2). Four (9.8%) achieved level one diagnostic certainty based on the identification of a recognized pathogen from a normally sterile site.

Conclusions: The CD for congenital anomalies and neonatal infections are readily applicable in a trial given adequate resources. Potential barriers to their use in post-licensure pharmacovigilance programmes in countries like The Gambia are considered.

Poster 21

Development of Surveillance Infrastructure for Monitoring Safety of Vaccine Exposure During Pregnancy

Azadeh Shoaibi a, Keran Moll b, Kathryn Fingar b, Minya Sheng b, Shayan Hobbi c, William Rosenfeld c, Tim Burrell b,d,e, **Hui-Lee Wong** a, Kristin A. Sepúlveda a, Kinnera Chada a, Joyce Obidi a, Barbee Whitaker a, Deepa Youssef b, Steven Anderson a

aU.S. Food and Drug Administration, Center for Biologics Evaluation and Research; bIBM Watson Health; cIBM Global Business Services; dUniversity of Louisville School of Medicine; eIndiana University School of Medicine

Introduction/Background & Aims Vaccine safety during pregnancy is a priority for the Food and Drug Administration Center for Biologics Evaluation and Research, which uses the Sentinel Post-Licensure Rapid Immunization Safety Monitoring and Biologics Effectiveness and Safety (BEST) systems to conduct active postmarket safety surveillance. BEST uses linked claims-electronic medical record (EMR) data to (1) develop an algorithm for gestational age and pregnancy outcomes using International Classification of Diseases, Tenth Revision (ICD-10) and Healthcare Common Procedure Coding System (HCPCS) codes on claims and (2) validate the algorithm through clinical EMR chart review, guided by Global Alignment of Immunization Safety Assessment in Pregnancy (GAIA) clinical standards for pregnancy outcomes.

Methods: We used the IBM® MarketScan® Explorys Claims-EMR Data Set (CED) to develop a hierarchical algorithm for determining gestational age at outcome and classifying pregnancy episodes as preterm births, full-term births, stillbirths, or spontaneous abortions on the basis of ICD-10 and HCPCS codes in claims data. Algorithms will be validated through semiautomated chart reviews using GAIA case definitions for outcomes mapped to structured components of the EMR as the reference method.

Results: Among 2.4 million individuals in the CED between August 1, 2016 and 2018, 33,000 pregnancy episodes were identified based on ICD-10 codes. Among them, 4,000 pregnancy episodes had EMR information on both outcomes and gestational age. We mapped GAIA elements to standardized medical terminology and laboratory observation codes in the EMR and developed a semiautomated chart abstraction tool. We will share findings comparing the claims-based algorithm with the semiautomated chart abstraction at the meeting.

Conclusions: ICD-10 code validity for determining gestational age and identifying live births, stillbirths, and spontaneous abortions is not well-known. Linked claims-structured EMR data offers opportunities to validate outcomes and gestational age by comparing claims data against those adjudicated by a clinician through semiautomated chart review of clinical information.

Poster 22

The 'Links2HealthierBubs' Cohort Study: Protocol for a record linkage study on the safety, uptake, and effectiveness of influenza and pertussis vaccines among pregnant Australian women

Sarna M 1, Andrews RM^{2,3}, Moore HC^{1,4}, Binks MJ², McHugh L², Pereira G¹, Blyth CC^{4,5}, Van Buynder P⁶, Lust K⁷, Regan A^{1,4,8}.

1School of Public Health, Curtin University, Western Australia, Australia; 2Menzies School of Health Research, Charles Darwin University, Northern Territory, Australia; 3National Centre for Epidemiology and Population Health, Australian

National University, Australian Capital Territory, Australia; 4Wesfarmers Centre of Vaccines & Infectious Diseases, Telethon Kids Institute, Western Australia, Australia; 5School of Medicine, University of Western Australia, Department of Paediatric Infectious Diseases, Perth Children's Hospital, Western Australia, Australia; 6Griffith University, Southport, Queensland, Australia; 7Royal Brisbane and Women's Hospital, Queensland, Australia; 8School of Public Health, Texas A&M University, College Station, Texas, United States of America.

Introduction/Background & Aims: Pregnant women and infants are at risk of severe influenza and pertussis infection. Inactivated influenza vaccine (IIV) and diphtheria-tetanus-acellular pertussis vaccine (dTpa) are recommended during pregnancy to protect both mothers and infants. In Australia, uptake is not routinely monitored but coverage appears sub-optimal. Evidence on the safety of combined antenatal IIV and dTpa is fragmented or deficient, and there remain knowledge gaps of population-level vaccine effectiveness. We aim to establish a population-based cohort of mother-infant pairs to measure the uptake, safety, and effectiveness of antenatal IIV and dTpa vaccines in three Australian jurisdictions.

Methods: 'Links2HealthierBubs' is an observational, population-based, retrospective cohort study established through probabilistic linkage of maternal, infant and child administrative health data in three Australian jurisdictions. The population-based cohort includes registered births between 2012 and 2017 in Northern Territory, Queensland and Western Australia. Linkage to jurisdictional vaccination registers will be used to identify antenatal vaccination status and the gestational timing of vaccination. Information on maternal, fetal, and child health outcomes will be obtained through linkage to hospitalisation and emergency department records, notifiable diseases databases, developmental anomaly registers, birth and mortality registers.

Results: The Links2HealthierBubs cohort will include ~607,605 mother-infant pairs from Queensland, Northern Territory, and Western Australia. Cohort data will be used to evaluate the effectiveness and the risk of adverse events associated with IIV and dTpa during pregnancy and at birth in Australian mothers and infants. Initial analysis of 134,698 West Australian mothers who gave birth between 2012 and 2016 showed 9.0% were vaccinated for influenza alone, 9.3% for pertussis alone, and 7.0% for both vaccines. Data collection in Northern Territory and Queensland is ongoing.

Conclusions: Links2HealthierBubs is the first national population-based study to evaluate the impact of antenatal vaccination programmes in Australia. Results will be used to guide national maternal immunisation policy.

Poster 23

Towards a strong maternal and neonatal immunization platform in Latin America and the Caribbean

Vilajeliu A, Ropero-Alvarez A

Introduction/Background & Aims: One of the goals of the Pan American Health Organization (PAHO) Regional Immunization Action Plan (RIAP) is achieving the expected results of the Sustainable Development Goals in reducing infant and maternal mortality and as part of the life course approach, it includes the establishment of a maternal and neonatal immunization (MNI) platform.

Methods: Descriptive study, including data from the RIAP progress report and the analysis of MNI related data from 2017 of the 52 countries and territories of the Americas, reported in the 2018 PAHO-WHO/UNICEF's Joint Reporting Form on immunization.

Results: During the last years, the PAHO's Technical Advisory Group (TAG) on vaccine-preventable diseases recommended the use of influenza, tetanus and pertussis-containing vaccines in pregnant women and hepatitis B birth dose in neonates. To support national policy decisions, 22 countries report having an active NITAG and a subregional Caribbean Immunization TAG (CiTAG) was launched in 2018. Currently, all countries recommend tetanus containing vaccine for women at childbearing age, 31 seasonal influenza at any gestational week, 14 pertussis containing vaccine, 23 vaccinate newborns with Hepatitis B birth dose (regional coverage 76%) and 31 with BCG (regional coverage 94%). Forty report having a passive surveillance system to monitor Adverse Events Following

Immunization (AEFI) and efforts are ongoing to establish a regional maternal vaccine safety network to assess outcomes in pregnant women and neonates.

Conclusions: The Region of the Americas is a leader in MNI, as seen by the elimination of the congenital rubella syndrome in 2015 and the achievement made in 2017, when Haiti was the last country in the Region to eliminate maternal and neonatal tetanus. A strong MNI platform can support the elimination of other diseases, such as perinatal transmission of hepatitis B, and the introduction of future maternal vaccines as respiratory syncytial virus that can significantly decrease neonatal morbidity and mortality.

Poster 24

Civil Society Organizations interventions to improve Perinatal and Neonatal conditions in Uganda

Luzinda L1, Kkisitwu F1, Burungi F1, Ssematya S.2 Presented by S Maxi Mbidde

1 Health and Care for Future Foundation Uganda (HCFU), Masaka, Uganda; 2 Health Informatics Initiatives (HII), Mukono, Uganda

Introduction/Background&Aims: A comprehensive review of the evidence base for impact of interventions on neonatal health and survival in Uganda has not been reported. This review of community-based antenatal, intrapartum, and postnatal intervention trials in Uganda aimed at identifying (1) key behaviors and interventions for which the weight of evidence is sufficient to recommend their inclusion in community-based neonatal care programs and (2) key gaps in knowledge and priority areas for future research and program learning.

Methods: Available published and unpublished data on the impact of community-based strategies and interventions on perinatal and neonatal health status outcomes were reviewed. Evidence was summarized systematically and categorized into 4 levels of evidence based on study size, location, design, and reported impact, particularly on perinatal or neonatal mortality. The evidence was placed in the context of biological plausibility of the intervention; evidence from relevant community studies; health care program experience in implementation; and recommendations from leading agencies.

Results: A paucity of community-based data was found from civil society organization studies on health status impact for many interventions currently being considered for inclusion in neonatal health programs. However, review of the evidence and consideration of the broader context of knowledge, experience, and recommendations regarding these interventions enabled us to categorize them according to the strength of the evidence base and confidence regarding their inclusion now in programs. This paper identifies a package of priority interventions to include in programs and formulates research priorities for advancing the state of the art in neonatal health care.

Conclusions: This study recommended an integrated approach to safe motherhood and newborn health and provided a foundation for policies and programs related to maternal and newborn health, emphasizing the importance of health systems research and evaluation of interventions.

Key words: Civil Society Organizations, Interventions, Perinatal & Neonatal conditions, Uganda

Poster 25

The WHO Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) project – understanding the mechanisms and barriers to immunization during pregnancy in low- and middle income countries.

Nathalie Roos¹, Philipp Lambach², Theresa Diaz¹, Joachim Hombach², Allisyn Moran¹.

1 World Health Organization, Department of Maternal, Newborn, Child and Adolescent Health (MCA), Geneva, Switzerland; 2 World Health Organization, Department of Immunization, Vaccines and Biologicals (IVB), Geneva, Switzerland

Introduction/Background & Aims: Maternal immunization (MI) is a safe and cost-effective strategy for preventing infectious diseases in mothers and their babies. To better understand the optimal strategies to deliver vaccines to pregnant women and the quality and capacity of antenatal care (ANC), we conducted the Maternal Immunization and Antenatal Care Situation Analysis (MIACSA) study in low- and middle income countries (LMICs).

Methods: This is a cross-sectional study carried out between 2016-2019 using a mixed methods approach. We collected qualitative and quantitative data in four phases in LMICs: a desktop review (n=137 countries); an online survey of LMICs (n=116); semi-structured telephone interviews with selected LMICs (n=26); and country visits that included key informant interviews and health facility observations (n=10). We assessed correlations between the MI delivery strategies and coverage of tetanus vaccine as a proxy measure of performance of MI.

Results: Most (76.6%) of (n=90) countries provided MI through ANC services. Mostly registered nurses or midwives provided vaccination to pregnant women, and mostly at the primary health facility level. Higher MI coverage was associated with the following: when vaccination was offered during an ANC visit as a “one-stop-shop” service, when there was a greater government financial contribution for immunization programs, when there was greater interaction between MNH and Immunization departments, and when pregnant women were contacted by community health workers or received written reminders.

Conclusions: The MIACSA study provides a first time, comprehensive global overview and analysis of existing MI delivery strategies in LMICs. These results should be used to better design MI services

Poster 26

A new tool to assess womens' satisfaction with maternal immunisation services

Khai Lin Kong¹, Suzie Ristevski², Sue J Lee³, Michelle Giles^{1,2}

1 Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia ; 2 Sunshine Hospital, Western Health, Melbourne, Australia; 3 Department of Infectious Diseases, Alfred Hospital

Introduction/Background & Aims: Understanding pregnant women's experience and satisfaction with maternal immunization services is crucial to ensure high vaccine uptake in pregnancy and consumer demand for the service. A validated questionnaire is useful to assess women's satisfaction with the maternal immunization service. In this study, we modified a questionnaire developed for the paediatric setting and trialed it in the maternity setting.

Methods: Sunshine Hospital is a metropolitan hospital with almost 6000 deliveries annually in Melbourne, Australia. All English-speaking pregnant women attending its Women and Children Immunisation Service for vaccines were invited to complete the questionnaire. Seventeen statements were ranked from 1 (very dissatisfied) to 5 (very satisfied), covering aspects of accessibility, friendliness and communication. Response rate, median score and proportion of missing responses were assessed and Bartlett's Test of Sphericity and the Kaiser-Meyer-Olkin measure of sampling adequacy (KMO) were calculated. Exploratory Factor Analysis (EFA) determined scale structure and Cronbach's alpha determined internal consistency reliability.

Results: From 22 Jan to 21 Mar 2019 (non-influenza season), 468/521 (90%) surveys were completed. Thirty-five (7.5%) had missing answers, 18 of them were due to a printing error. Median score was 5 (very satisfied) for each statement. KMO was 0.944 and Bartlett's test indicated the data were factorable ($p < 0.001$). EFA identified three underlying subscales explaining 73% of the variance. Cronbach's alpha indicated high internal reliability (0.942) with all item-total correlations >0.4 . Alpha-if-item-deleted did not increase alpha for any item.

Conclusions: High response rate, low proportion of missing answers, and high internal consistency reliability indicated that this survey is valid and reliable to assess pregnant women's satisfaction with maternal immunization service. With the potential expansion of maternal immunization in low and middle-income countries beyond tetanus vaccine, this tool may be applied to ensure patient satisfaction with the service.

Poster 27

To explore the experiences and sentiments towards vaccinating in pregnancy among pregnant and recently pregnant women globally

Dr. Eliz Kilich and Sara Dada (coauthors), Dr. Pauline Paterson (Assistant Professor) and Dr. Heidi Larson (Professor)

Introduction/Background & Aims: We aimed to explore the experiences and sentiments of pregnant or recently pregnant women on antenatal vaccination. Existing literature typically focuses on sociodemographic variables associated with vaccination however, we sought to highlight the factors that underpin confidence in vaccines during pregnancy.

Methods: We registered the study with the PROSPERO (#CRD42019118299). On 21st of November, researchers searched the following databases: MEDLINE, Embase Classic & Embase, PsycINFO, CINAHL Plus, Web of Science, IBSS, LILACS, AfricaWideInfo, IMEMR, and Global Health using a prior search query developed by (Wilson et al 2015). Studies were included following independent review by two authors based on pre-defined inclusion and exclusion criteria and were imported into EndNote (Clarivate Analytics). We developed a data extraction form using Microsoft Excel (Microsoft Corp, USA). Quality appraisal was independently performed (EK and SD) using the Joanna Briggs Institute qualitative quality assessment tool. Two authors (EK, SD) independently conducted a descriptive analysis in NVivo following code development and refinement based on researcher consensus.

Results: We extracted 17236 articles from our database search. One hundred and seventeen studies were included for content and validity analysis. The literature explored perceptions toward the Influenza vaccine (72), multiple vaccines (23), pertussis vaccine (13), Tetanus vaccine (7), and Hepatitis B vaccine (1) indicating similar barriers and facilitators. The majority of studies explored perceptions and experiences in the USA (32 articles).

Conclusions: Current literature provides a limited analysis of the interactions between pregnant women's sentiments and their personal history (such as a healthcare worker recommendation or previous vaccination) and their vaccination behavior. In addition, determining the necessity versus the sufficiency of these interacting beliefs and experiences in decision-making is under-examined. Some papers try to reconcile this issue, attempting to discriminate the weight of key variables, by adopting analytical strategies based on the health belief model or the theory of planned behavior.

Poster 28

Vaccination during pregnancy: Knowledge, attitudes and practices of maternity care providers in Canada

Dubé E, Gagnon D, Kaminsky K, Green C, Ouakki M, **Bettinger J**, Brousseau N, Castillo E, Crowcroft N, Driedger S, Greyson D, Fell D, Fisher W, Gagneur A, Guay M, Halperin D, Halperin S, MacDonald S, Meyer S, Waite N, Wilson K, Witteman H, Yudin M, Cook J

Introduction/Background & Aims: Many countries have implemented vaccination during pregnancy as a strategy to reduce the burden of influenza and pertussis. This study aimed to assess the involvement of Canadian maternity care providers in administration of vaccines in pregnancy. Providers' opinions regarding the pertussis vaccine were also assessed, but the survey was done prior to the statement of the National Advisory Committee on Immunization recommending pertussis vaccination during every pregnancy.

Methods: In 2017, a survey was distributed by email via organizational listservs to family physicians, obstetricians-gynecologists, midwives, pharmacists and nurses who care for pregnant patients. We used multivariable logistic regression to determine variables independently associated with offering vaccination services in pregnancy in providers' practice.

Results: A total of 1,135 participants were included. Overall, 64% (n=724) of the participants reported offering vaccines in their practice and 56% (n=632) reported offering vaccines to pregnant patients. The main reasons for not offering vaccination services in pregnancy were the belief that vaccination was outside of their scope of practice; logistical issues around access to vaccines; or lack of staff to administer vaccines. The majority of participants reported that the pertussis vaccine was safe in pregnancy (87% agreed) and effective in protecting the infant (83% agreed). In multivariable analysis, the main factors associated with vaccination of pregnant patients were: providers' confidence in counselling pregnant patients about vaccines, seeing fewer than 11 pregnant patients on average each week, and being a nurse or a family physician.

Conclusions: Although the majority of participants expressed strong support for vaccination during pregnancy, almost half were not offering vaccination services in their practice for reasons related to logistical barriers or vaccination not being part of their role. The barriers identified, and strategies to address them, are particularly relevant given the need to encourage uptake of the new recommendations on pertussis vaccination during pregnancy.

Poster 29

Obstetric Risk Assessment Tool: Evaluation of Selection Criteria for Vaccine Research Studies of Pregnant Women

Eckert L, Jones C, Kachikis A, Barjdaji A, Tavares Da Silva F, Absalon J, Rouse C, Khalil A, Cutland C, Kochar S, Munoz F

Introduction/Background & Aims: Determining exclusion criteria is a key challenge in designing maternal immunization (MI) trials. We developed an obstetrics risk assessment tool (ORAT), to evaluate and quantify obstetric risks in the current pregnancy based on medical and obstetric history.

Methods: We conducted a review of exclusion criteria in MI clinical trials using data published in ClinicalTrials.gov, reviewed obstetric risk referral guidelines, and literature. We developed a matrix of subject exclusion criteria and referral criteria, and created a matrix delineating their use frequency. Based on this, we assessed obstetric risk in pregnant clinical research subjects. We then reviewed the literature to quantify the risk that each of these factors and better understand how they can inform researchers in the selection of research subjects.

Results: We identified 67 MI studies (29 Phase I/II, 4 Phase III, 12 post licensure interventional, 22 post-licensure observational studies) and 6 practice guidelines. The number of exclusion criteria listed at least once was 119 for Phase I/II trials, 74 for Phase III and 48 for observational studies. Using a heat map, we identified the most commonly listed risk factors among the combined studies and guidelines. These included factors present during the current pregnancy (advanced or young maternal age, and alcohol or drug use), in the past obstetric history (congenital anomalies, hypertensive disease, perinatal death or stillbirth, prior preterm birth, spontaneous abortion, and maternal morbidity); and current maternal medical conditions (HIV or other immunodeficiency, bleeding disorders and psychiatric illness). For each of these risk factors we quantitated risk for adverse pregnancy outcomes in the current pregnancy.

Conclusions: We hypothesize that this consolidated evaluation and quantification of risk factors in pregnancy is a useful tool to help guide investigators in the selection of appropriate subjects in all development stages in MI clinical trials and may offer applicability for other interventions assessed in pregnant women.

Poster 30

“Pregnant women and vaccine hesitancy in Senegal:” determinants of vaccine acceptancy among pregnant women in Senegal

Nicole Nkoum¹, Elhadji Mbaye^{1,2} and Beate Kampmann^{1,3}

¹&² Social Sciences and Health Division, Institute of Health Research, Epidemiological Surveillance and Training, Diamniadio, Senegal; ³ Vaccines and Immunity Theme, Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Fajara, The Gambia; ²The Vaccine Centre, London School of Hygiene and Tropical Medicine, London, United Kingdom

Introduction/Background & Aims: Immunizing pregnant women is an increasingly accepted strategy to protect newborns against specific infections. The introduction of vaccines during pregnancy has significant challenges in term of acceptance and hesitancy, but there are no published data from Senegal. We evaluated what determines attitudes towards maternal vaccination in Senegal.

Methods: We carried out a qualitative study at 4 sites within 4 regions in Senegal (Kolda, Kaolack, Louga and Diamniadio). We conducted focus groups and in-depth interviews of pregnant women, family members, health care workers and institutional actors.

The data from 132 participants were analysed in two phases: raw data was processed in textual form and coded to

generate and / or identify analytical categories or themes for further analysis. Systematization and in-depth analysis were carried out with NVivo software.

Results: 3 main themes emerged :

- The trusting relationship between health care workers, in particular the midwives and pregnant women is one of the key determinant of the vaccine acceptance.
- Community health care workers named “Badienu goxx” (traditional matron/traditional midwives, kind of “cultural aunt” in the Senegal culture”) are the key actors for raising awareness around vaccines for women and link between community and official/institutional health care providers.
- Routine vaccine setting seem to be the appropriate way for the introduction of new vaccines for pregnant women
- inclusion in the ANC package is likely to enhance the acceptance, compared to vaccination campaigns

Conclusions:

- Although the level of vaccine uptake/acceptance in pregnant women in Senegal seem to be very high, it still remains a very fragile and complex process. Acceptancy is a constant dynamic process, hence needs continuous sensitization and engagement of the key community stakeholders.
- The specific needs for information of the wider community (husband, mother in-law, Iman, traditional leaders) have to be considered .

Poster 31

Canadian maternal healthcare providers’ experiences with recommending and providing pertussis vaccine during pregnancy

Mijović H, Gemmell E, Greyson D, Vivion M, Dubé È, Graham J, Bettinger J

INTRODUCTION/ BACKGROUND AND AIMS Immunization against pertussis during pregnancy has the potential to reduce disease burden among Canadian infants. In 2018 Canadian Society of Obstetricians and Gynecologists and the National Advisory Committee on Immunization made an official recommendation that pertussis vaccine should be offered in every pregnancy, irrespective of previous immunization history. We completed a qualitative study in order to identify barriers and facilitators of pertussis vaccine uptake encountered in clinical practice.

METHODS We conducted semi-structured, individual phone interviews with Canadian antenatal and perinatal healthcare providers. Data were analyzed using qualitative thematic analysis influenced by Interpretive Description. Initial deductive and inductive coding of interview transcripts was done with NVivo 12 software. This was followed by theme development and theory generation.

RESULTS We interviewed 38 healthcare providers (11 midwives, 6 nurses, 12 family physicians and 9 obstetricians) from 5 provinces (British Columbia, Manitoba, Nova Scotia, Ontario and Quebec). Providers across disciplines and provinces described routinely recommending pertussis vaccine in pregnancy. Providers’ ability to facilitate uptake was influenced by 1) provider level factors - including vaccine knowledge, vaccine confidence, and provider’s perceived role in vaccine counseling and follow-up 2) patient/client level factors – including provider’s assessment of women’s readiness to discuss the vaccine, and individual women’s confidence in vaccine safety and effectiveness and 3) health system level factors - including public funding for the vaccine, vaccine accessibility, and logistical and financial resources available to the providers.

CONCLUSIONS Despite healthcare provider recommendation of pertussis vaccine in pregnancy, several barriers to women receiving the vaccine persist. Further provider level, patient/client level and health system level interventions are needed to effectively implement pertussis vaccine recommendation and facilitate vaccine uptake in various clinical practice settings across Canada.

Poster 32

Pregnant women's knowledge and attitude to maternal vaccination including Group B Streptococcus (GBS) and Respiratory Syncytial Virus (RSV) vaccines

Assoc Prof **Michelle Giles** (corresponding author)^{1,2,4}, Professor Jim Buttery^{3,4}, Dr Mary-Ann Davey¹, Professor Euan Wallace¹

1. The Ritchie Centre, Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia; 2. Women's and Children's Health, Monash Health, Melbourne, Australia; 3. School of Public Health and Preventive Medicine and Department of Pediatrics, Monash University, Melbourne, Australia; 4. Monash Immunisation, Monash Health, Melbourne, Australia

Introduction Maternal immunization is an important strategy to reduce neonatal mortality and morbidity. New maternal vaccines such as Respiratory Syncytial Virus (RSV) and Group B streptococcus (GBS) are in development and/or clinical trials. However, little is known about pregnant women's knowledge about these diseases.

Methods Women attending antenatal clinics in Melbourne, Australia were invited to complete a questionnaire collecting demographic information, past vaccination history, understanding of risk of GBS and RSV disease in pregnancy and likelihood to accept these theoretical vaccines in the future.

Findings 495 women (48% born outside of Australia, from 48 different countries) completed the questionnaire. A large number of women had never heard of GBS (63%) or RSV (83%). Women over 35 years, born in Australia and women who had more than one child were more likely to have heard of GBS or RSV ($p < 0.001$). Women who had received influenza or pertussis vaccine in pregnancy were more likely to accept a RSV or GBS vaccine ($p < 0.001$).

Conclusions This study has shown that knowledge of GBS and RSV is poor. However, when provided with information about the two diseases, acceptance of a hypothetical vaccine for both diseases was high. This study highlights the enormous amount of work that needs to be done in educating pregnant women about the seriousness of these two diseases if a future vaccine is ever to be accepted and achieve high coverage among the target population.

Poster 33

Delay in receipt of birth doses of vaccines among infants attending immunization clinics in the Gambia

Nkereuwem O, Okomo U, **Kampmann B**

Introduction/Background & Aims: Current WHO guidelines recommend that all infants receive their birth doses of vaccines (BCG, HepB, and OPV) within the first 24 hours of birth. Delay in receipt of these vaccines may result in an infant being susceptible to Vaccine Preventable Diseases (VPDs), in particular Hep B. However, gaps in immunization infrastructure, health care workforce and logistical challenges are frequently associated with poor implementation of birth doses, which are usually administered by the EPI programs and teams.

Methods: In this cross-sectional descriptive study, we assessed the timeliness of receipt of birth vaccines among a cohort of women and their infants attending 15 Immunization clinics in four regions of The Gambia using an interviewer administered semi-structured questionnaire.

Results: Of the 113 mothers and their 114 infants (one set of twins) who were recruited, 100 (88.5%) were delivered in a clinic. However, only 10 (10.2%) infants received their birth doses of vaccines within 24 hours of birth, 19 (19.4%) within the first week of life. The majority (70.4%) received their birth doses of vaccines after one week of birth at a median time of 11.5 days of life (IQR 15.75).

The most frequently reported difficulties faced by new mothers were long distance from their home to the health center (47.1%), transportation difficulties (14.7%), and perceived poor attitude of health care workers by mothers (14.7%) for example starting clinic late, keeping mothers waiting and giving preference to some women over others.

Conclusion: Despite the high delivery rate in health facilities reported in this study, a substantial proportion of infants experienced delay in the receipt of their birth doses of vaccines. Alternative strategies to administer birth doses ought to be considered.

Poster 34

Assessing the impact of SMS delivered video messaging on the uptake of maternal influenza immunization

Khai Lin Kong¹, Paul Paddle², Michelle Giles¹

¹ Department of Obstetrics and Gynaecology, Monash University, Melbourne, Victoria, Australia ; ² Ears, Nose and Throat Department, Monash Health, Melbourne, Victoria, Australia

Introduction/Background & Aims: Influenza vaccination is recommended to all pregnant women as they are at high risk of severe disease. However Influenza vaccine uptake among pregnant women remains suboptimal despite vaccine availability and safety. In this study we aim to assess the impact of a video developed by the local antenatal care team and delivered via SMS directly to the woman's phone, on the uptake of maternal influenza immunization.

Methods: Northeast Health is a hospital at Wangaratta (rural Victoria, Australia) with 600-700 deliveries annually. In 2017 the coverage of antenatal influenza vaccine was 56%. To improve its maternal influenza vaccine uptake, we have developed a video featuring the Northeast Health antenatal team providing messages about the benefit and safety of influenza vaccine. The link for the video will be sent via SMS twice (early May and late June 2019) to all women booked to have their baby at the hospital. Pregnant women in antenatal clinic will be approached and invited to complete a questionnaire collecting the following information: (1) baseline demographics (2) recollection and feedback about the video, and (3) vaccination history and intention to receive vaccination. Information on duration and proportion of video watched will also be collected. The vaccine coverage data for Northeast Health will be assessed in August 2019.

Results: Data collection, quantitative analysis and overall vaccine coverage for the maternity service will be completed by end August 2019 given the influenza season in the southern hemisphere and timing of the intervention.

Conclusion: This study will be the first to explore the impact of a novel intervention (video with healthcare providers' recommendation delivered directly to the woman's phone) on uptake of influenza vaccine in pregnant women. It harnesses one of the most powerful predictors of uptake – healthcare provider recommendation- and delivers it personally to all women birthing at the same maternity service.

Poster 35

Anxiety, Access and Trust: communicating with new mothers about infant vaccination

Gemmell E, Greyson D, Bettinger J, Padhi S, Orth A

Introduction/Background & Aims: Information use in vaccination decision-making has evolved with the movement toward patient activation coupled with the arrival of online and social content sharing. Understanding the information seeking, assessment and use of specific vaccine-hesitant populations often requires in-depth qualitative investigation. This study applied ethnographic research methods to identified communities of low vaccine uptake in order to improve public health communication with new mothers at risk for vaccine hesitancy.

Methods: Semi-structured, in-depth interviews with new mothers and community service providers and ethnographic observation of community mother/baby groups were conducted between December 2016 and April 2018. Data were analyzed using qualitative thematic analysis influenced by grounded theory.

Results: Thirty-two interviews with new mothers, 8 with community service providers and 35 community group observations were conducted. Anxiety was a common theme and impacted information seeking and assessment. Online information-seeking was almost universal, but mothers were often confused about what information to trust. Public health and health care providers were generally well-trusted, but negative healthcare experiences undermined trust. Some mothers were dissatisfied with providers' ability to answer vaccine-related questions or reported feeling dismissed or stigmatized for raising questions. For mothers with low trust in the health system,

midwives were highly trusted information sources. Informal information sharing among social networks impacted vaccine uptake and confidence. Immigrant mothers sometimes experienced language, literacy or cultural barriers to accessing information and services.

Conclusions: Stress and anxiety impacts vaccine information seeking and assessment. Trust in public health and health care providers may be built or undermined by mothers' lifetime trajectory of health care experiences. Creating health care environments that are inclusive, safe and accessible to all mothers and building alliances with existing, trusted health information sources may increase vaccine confidence among new mothers.

Poster 36

The use of a Speaking Book in enhancing the knowledge of Primary Care Givers on vaccines in the Gambia.

Oluwatosin Nkereuwem, Oghenebrume Wariri, Mamanding Kinteh, Amie Ceesay, Sonali Kochhar, **Beate Kampmann**

Introduction/Background & Aims: The level of vaccine-related knowledge among Primary Care Givers (PCG) tends to be low in most settings. To fill this gap, we have developed and adapted to the local context an audio-visual educational tool, the *Speaking Book* (SB), which contains pre-recorded information explaining the routine vaccines in *Wolof* and *Mandinka* languages widely spoken in The Gambia. The aim of this project is to improve knowledge and assess the impact of the SB as a health education tool in the context of maternal and childhood vaccines.

Methods: This prospective cohort study is delivered in two phases: The Pilot Phase involved an iterative process of adapting the draft SB to reflect the local Gambian context. We collaborated directly with the Gambian EPI team and PCG attending EPI clinics using Focus Group Discussions (FGDs) to gain granular feedback that informed the final design.

The Implementation Phase involves handing out the SB to PCG including assessing PCGs knowledge on vaccines before, at one-month, and at three-months after receiving the SBs. Trained field workers conduct face-to-face interviews using an interviewer administered semi-structured questionnaires.

Results: Stakeholder feedback was essential for the final design of the materials. Currently in the implementation phase, we have recruited a total of 113 PCGs attending 15 Immunization clinics in four regions of The Gambia with their infants. Qualitative research shows high enthusiasm for this kind of tool at all levels. We are continuing to collect in-depth data on the impact of the SB on the vaccine knowledge of PCGs.

Conclusions: The SB is expected to address concerns, increase vaccine knowledge among PCGs and complement information provided by Health Care Workers. In addition to explaining EPI vaccines and increasing PCG knowledge and communication, a similar tool can be designed to address specific issues in maternal vaccination.

Poster 37

Vaccine Hesitancy and Compliance of mothers with neonatal immunization in the global south: Evidence from some Infant Welfare Clinics in Ondo State, Nigeria.

O Aladenola

Introduction/Background & Aims: The National Programme on Immunisation in Nigeria is designed to make available vaccines and create awareness on the need for mothers of neonates to vaccinate their children during the neonatal stage and proceed to complete the entire immunisation cycle. This critical period is short for a mother (or carer) who has doubt and does not trust the vaccine programme due to diverse reasons. This period also passes by quickly due to a flurry of adult-dependent activities that are embedded in cultural and social considerations. The study aim is to explore the factors responsible for vaccine hesitancy among mothers of neonates and identify the determinants of their compliance with immunisation uptake for their children using the SAGE Working Group on Vaccine Hesitancy Model and the Pen-3 Health Belief Model.

Methods: 300 mothers that visited the Infant Welfare Clinics in three Basic Health Centres in Akure were selected for the study. A self-administered questionnaire was utilized coupled with personal interview with those who did not fully complied with the immunization schedule. Data obtained were analysed using SPSS 22.

Results 60% of the mothers considered not accepting immunization for their children while 32% skip one or two of the vaccine while 12% did not make their children available for immunization in the first 28 days of life. Religious influence, family member opinion and peer influence by other mothers were the significant factors for converting potential rejection to acceptance. A curious correlation between trust in government and believe in government programmes was observed. Mothers that has no trust in government tend to doubt the initiatives of the government, including the Vaccine programme.

Conclusions: Health programmes that are important such as the neonatal vaccination must bear a community oriented face especially where lack of trust in government may constitute a limiting factor.

Poster 38

The impact of three different strategies to improve access and coverage of influenza vaccine in pregnant women (midwife led administration, pharmacist led administration or general practitioner led administration) across six maternity services.

Assoc Prof **Michelle Giles** (corresponding author)^{1,2}, Dr Khai Lin Kong¹, Ms Marg Angliss², Ms Karen Bellamy², Dr Sushena Krishnaswamy³, Professor Beverley Vollenhoven^{1, 4}

1. The Ritchie Centre, Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia; 2. Monash Immunisation, Monash Health, Melbourne, Australia; 3. Department of Infectious Diseases, Monash Health, Melbourne, Victoria, Australia; 4. Womens and Newborn Program, Monash Health, Melbourne, Victoria, Australia

Introduction Despite national recommendations and a funded program for maternal influenza coverage remains suboptimal particularly compared to maternal pertussis vaccine.

Previous work suggests that access at the point of antenatal care is critical to high uptake. The aims of this project were to implement three different delivery models and evaluate change in coverage, the barriers and facilitators to implementation of each and an economic evaluation of each delivery strategy for the 2019 influenza season (southern hemisphere).

Methods Six maternity services in the state of Victoria were approached to partner on the project. A landscape analysis was undertaken at each service and a delivery model designed with the healthcare providers at that site to integrate into existing infrastructure, within the capacity of existing resources with a key goal of sustainability beyond the project.

Vaccine coverage data is collected for every pregnant woman who births in Victoria. Coverage data comparing 2017/2018 to 2019 will be analysed and a full economic evaluation undertaken at the completion of influenza season 2019.

Findings The six maternity services participating ranged from level 2 facilities (normal and low complexity pregnancies) to level 6 facilities (complex pregnancies birthing at any gestation) in both metropolitan and regional/rural centres. In total, these maternity services cover approximately 11,000 births. The largest metropolitan hospital has integrated a pharmacist led model, four regional hospitals have integrated midwife led models and one regional centre are not vaccinating at the time of antenatal care but through their primary care network of general practitioners. Seasonal influenza vaccine will be available at the start of April 2019.

Conclusions This study will contrast three different models of influenza vaccine service delivery including an assessment of the barriers and facilitator to successful implementation according to different models, magnitude of impact and the cost associated with each model.

Poster 39

MatImms: Bringing Vaccines to Pregnant Women

Helen Skirrow¹, Beth Holder², Anna Bosanquet³, Alison Meinel⁴, Evelyn Narh⁴, Sara Barnett³, Beverly Donaldson³, Lena Choudary-Salter⁵ & Beate Kampmann⁶

¹Speciality Registrar, London Public Health Medicine Specialist Training Program, Imperial Healthcare NHS Trust; ²Lecturer in Maternal and Fetal Health, Institute of Reproductive and Developmental Biology, Department of Surgery and Cancer, Imperial College London; ³Research Midwife, Imperial College London; ⁴Midwife, Immunisation Team, Imperial College Healthcare NHS Trust; ⁵Director, Mosaic Community Trust; ⁶Professor of Paediatric Infection & Immunity, Director of the Vaccine Centre & Scientific Director (Theme Leader) for Vaccinology research at the MRC Unit The Gambia, London School of Hygiene and Tropical Medicine. Visiting Professor, Department of Medicine, Imperial College London.

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Introduction/Background & Aims: Pertussis and Seasonal Influenza Vaccines are offered to pregnant women in England. Previous work at Imperial Healthcare NHS Trust found low maternal pertussis vaccine awareness and uptake, with lowest uptake among Black, Afro-Caribbean women. Following introduction of maternal pertussis vaccination, the MatImms App was developed to improve vaccine information. Traditionally, vaccines are delivered through general practice, though from 2016, some antenatal midwife-led services began offering maternal vaccines. Several collaborative projects with local midwives were undertaken to assess service changes and local women's maternal vaccine attitudes and experiences.

Methods:

1. Reassessment of maternal vaccine uptake, 2017-18, through auditing convenience sample of 110 women postnatally. **2.** Service evaluation of midwife-led, antenatal vaccination service to describe demographic characteristics of service-users, differences in those receiving or declining vaccination alongside undertaking qualitative in-depth interviews. **3.** Public involvement in partnership with a women's community group, Mosaic Community Trust, based in a locally deprived area explored maternal vaccine understanding including feedback on the MatImms App.

Results: **1.** The 2017/18 MatImms audit found uptake had improved since the 2013/4 study and reported higher maternal vaccine uptake than regional estimates. **2.** Between 1.4.2017-31.3.2018 the midwife-led service vaccinated 42% of all women delivering at the hospital with one or two maternal vaccines (1501/3147). More Black Afro-Caribbean women (30%) declined vaccination compared to other ethnicities (10%). In-depth interviews with 10 women found reassurance from midwives, risk perception and beliefs were key factors in maternal vaccine decisions. **3.** Public involvement 'vaccine conversation' events found vaccine misconceptions persist locally. Women wanted simple, easily understood maternal vaccine information which was consistent with MatImms app feedback.

Conclusions: Midwives are key to both maternal vaccine delivery and the provision of simple, understandable vaccine information for women. Maternal vaccine uptake figures must include antenatal service delivered vaccines to ensure accuracy. Consistent with previous work, ethnicity remains a predictor of maternal vaccine receipt.

Poster 40

Neonatal herd immunity – A strong counselling tool for maternal flu vaccine

Gemawat N

INTRODUCTION Infants are 33% less likely to be hospitalized for respiratory illness in first 6 months when mothers are vaccinated for influenza during third trimester. Because infants cannot be vaccinated earlier, maternal vaccination is only

protection they have against virus which offers mothers extra incentive to get vaccinated, but maternal vaccination against influenza is not well taken because of various psychosocial, economic and religious beliefs in developing countries. Educating mothers about herd immunity can increase proportion willing to vaccinated for influenza, We studied result of counseling about herd immunity and acceptance of influenza vaccine during third trimester as Mothers were less likely to get vaccinated to protect themselves but willing for protecting their babies.

METHOD Total 15 young to be mothers in third trimester attending the clinic were studied with their attitude towards influenza vaccine. and were on vaccine counseling session.

RESULT Our study showed that only 2 mothers were willing for the vaccine initially but after vaccine counseling session, understanding importance of herd immunity resulted in acceptance of flu vaccine by all for protecting newborns with effective herd immunity as a tool for maternal flu vaccination.

CONCLUSION Present study reveals that mothers may differ vaccinations for themselves but with herd immunity for prevention of influenza infection to newborns results in well acceptance for maternal vaccination. Many parents lack basic knowledge of how vaccines work, as well as access to accurate information explaining herd immunity health education as a tool is well accepted.

Poster 41

Vitamin D And Compliance On Neonatal And Maternal Vaccination

Gemawat S

Immunization is an essential part of care for pregnant women, and newborns are at greater risk of maternal morbidity and mortality in addition to fetal morbidity, congenital anomalies, preterm birth, low birth weight and compromised immunity. Subsequent immunisation of the newborn represents overcoming morbidity and mortality due to infection in early life include poor immunogenicity, tolerogenicity or hypo-responsiveness to concomitant antigens administered at birth or in the subsequent months. Understanding reasons for vaccination from the parental perspective is critical for designing vaccination campaigns to increase vaccination uptake. Vitamin D, a potent immunomodulatory agent, deficiency is thought to be common among pregnant women and neonates. We observed that vitamin D supplementation during maternal and neonatal vaccination schedule increases compliance regarding success of maternal and neonatal vaccination program.

16 pregnant mothers and 14 newborn who were attending our immunization clinic with post vaccination concern of fever, pain, swelling, nutritional, physical and immunological outcome, were advised vitamin D as 1000iu/day for mothers and 400iu/day for neonates during 2nd, 3rd trimester and 1st month of age.

We observed that all pregnant mothers and neonates were well perceived with positive compliance for the vaccinations with safe pregnancy period and neonatal period.

Our observation has shown the effective compliance during maternal and neonatal vaccination. Vitamin D benefits include inherent innate and adaptive immunity and herd immunity, Vitamin D has strong compliance for the success of maternal and neonatal vaccine. More large scientific studies may be done.

Poster 42

Introduction of Maternal Immunization- Regulatory, Ethical, Programmatic and Safety Considerations

Kochhar S, Edwards K, Alvarez A, Moro P, R. J

Background: Maternal immunization programs reduce infectious disease-related morbidity and mortality in pregnant women and their infants. However, the uptake of current maternal vaccines e.g. influenza vaccine, has been well below recommended levels. With new maternal vaccines in advanced stages of clinical development e.g. respiratory syncytial virus (RSV) and group B streptococcus (GBS), it is critical to plan for their successful introduction.

Methods: Extensive literature review was done then consensus was reached among the authors on the most important aspects of the introduction plan. The draft plan was piloted with the available details of RSV, GBS, and other maternal vaccines.

Results: Important pre-requisites for the successful introduction of new vaccines for maternal immunization include in-country political commitment and adequate financial resources; trained, committed and sufficient numbers of healthcare workers to deliver the vaccines; adequate logistics for vaccine acquisition, storage, administration and monitoring; close integration of immunization programs with antenatal care (ANC) and Maternal and Child Health services; adequate access to ANC by pregnant women in the country (especially in LMIC); and a high proportion of births occurring in health facilities (to ensure maternal and neonatal follow-up).

The framework needed to advance a vaccine program from product licensure to successful country-level implementation includes establishing and organizing data collection for anticipated vaccine program impact, developing supportive policies, and translating policies into local action. Measures to address the challenges which exist in using the ANC platform to deliver vaccines, especially in LMIC, barriers to healthcare workers provision of vaccines during pregnancy and vaccine hesitancy in pregnant women are detailed.

Conclusions: International and national coordination efforts; proactive planning from conception to implementation of the programs (including country-level policy making, planning, and implementation, regulatory guidance, pharmacovigilance) and country-specific, cultural and local factors must be considered during successful introduction of vaccines for pregnant women

Poster 43

Effect of Maternal Education on immunization: A population based study

Dr DHARMENDRA KHATRI

Introduction/ Background & Aims: Infants can be protected against a wide variety of dangerous infections early in life through immunity transferred from their mothers. Vaccination during pregnancy and post birth to neonates can offer protection against severe infectious diseases for the mother, for the newborn, or both. Hence, in the present cross sectional study on knowledge of immunization affects both mother and infants immunity.

Methods: A population based study was done on a total 120 mothers and were interviewed using questionnaires on Knowledge, Attitudes, Perceptions. Data on children aged 12 to 24 months were examined for their vaccination history.

Results: The results of present study showed that the immunization statuses of all the children (120) were varied. Only 47% of children had received full immunization while 40% received only partially and rests (23%) were not immunized. Taken as a whole immunization exposure with traditional vaccines (DTP, polio, Hib, HBV, 1st dose MMR) was found to be satisfactory while booster doses were not given on time or even not take. Almost all the children were found that they had received polio vaccine during polio vaccine program. Almost all the mothers showed their positive approach towards polio vaccine but not for all vaccine immunization program run by Government of India.

Conclusions: The findings of present study highlights that the maternal knowledge about vaccination and vaccination programme need to be improve. This can be achieved by regular visit of primary healthcare centres and updates on next immunization dose by the healthcare professional and NGO are required.

Poster 44 Abstract withdrawn

Urbanisation and tackling of vaccine hesitancy and rejection in developing countries: Evidence from a post-natal GSM-based information service system

Mr Olufemi Aladenola, DR OLUMIDE FALANA

Poster 45 Abstract Withdrawn

The impact of mobile health care services on the uptake of antenatal care by expectant mothers

Kabogoza J. 1, Mutawe E.1, Nampungu R.2

1 Giving Children Hope Initiative (GCHI)-Mityana, Uganda ; 2Task Force for Child Survival and Development (TFSD), Jinja, Uganda; 2Makerere University, Kampala, Uganda;

Poster 46 Abstract Withdrawn

Insights and factors influencing the utilization of tetanus toxoid vaccination among reproductive-age women in Central Uganda

Lugemwa M.1, Ssemambo N.1, Mukwaya J.2, Mbatudde E.2

1 Save the Women and Children Health Organisation (SWCHO), Mpigi, Uganda; 2Makerere University, Kampala, Uganda;

Poster 47

Mapping social media sentiments towards maternal vaccines

Dr. Sam Martin (presenter), Dr. Eliz Kilich, Dr. Per Egil Kummervold, Sara Dada and Chermain Denny (coauthors) Dr. Pauline Paterson (Assistant Professor) and Dr. Heidi Larson (Professor)

Introduction/Background & Aims: We aimed to map the global social media sentiment towards vaccinating in pregnancy. Existing literature typically focuses on general sentiment on social media towards vaccines, however we sought to highlight factors covering sentiment to a range of maternal vaccines.

Methods: From 1st November 2018 to 31st April 2019, researchers mined 19192 social media posts using the Meltwater Media Monitoring platform (Meltwater (UK) Ltd.). Posts were included following independent review based on pre-defined inclusion and exclusion criteria and were imported into Microsoft Excel (Microsoft Corp, USA), and manually coded. Sentiment was categorized into four vaccine-related categories: Promotional; Ambiguous; Neutral; or Discouraging. We used Google BERT (Bidirectional Encoder Representations from Transformers) to train a machine learning algorithm on a sample of 6228 tweets. Authors independently conducted a descriptive analysis on key themes found in the social media samples in NVivo.

Results: While overall posts were positive or neutral, the USA had the greatest overall number of negative posts (23% of USA posts). Negative tweets focused on mistrust of the safety of maternal vaccine trials. A key spike in February 2019, came from the USA, when 13 countries tweeted about a US lawsuit that reported the FDA admitted a lack of safety data in their antenatal vaccines. This created a retweet pattern of a greater proportion of negative tweets in South Africa (7 (Nov-Dec)-28% (Jan-Feb)), South Korea (0% (Nov Dec)- 32% (Jan-Feb) and Germany (5% (Nov-Dec)- 15% (Jan-Feb)). Lack of clear information created a vacancy for mistrust to spread on social media.

Conclusions: Current literature provides limited analysis of the nuances of sentiment expressed on social media with regards to maternal vaccines. Determining the range of sentiment expressed, and how this can influence the overall attitude towards uptake of maternal vaccines is important, and especially key public health planning can provide ethical interventions.

Poster 48

"Flu vaccines for pregnant women and children?! Absurd" – An analysis of maternal vaccination discourse on social media

Sara Dada, Dr. Eliz Kilich, Dr. Sam Martin, and Chermain Denny, Dr. Pauline Paterson (Assistant Professor) and Dr. Heidi Larson (Professor)

Introduction/Background & Aims: We aimed to explore the experiences and beliefs of pregnant or recently pregnant women on antenatal vaccination by assessing social media posts over two months.

Methods: We extracted the data using Meltwater®, a media intelligence system which sources media content from a wide range of news and social media outlets, for 15 countries over a period of 2 months. We imported country specific data into Nodus Labs for automated discourse analysis to identify influential topics used in discussions on social media. Word frequency analysis was performed on the dataset to provide insight into the most frequent and weighted sub-topics of conversation in each country to provide a more detailed content review of topics.

Results: We exported 8236 social media posts (from 16 languages) obtained between 1st November 2018 and December 31st 2018. We sorted the extracted data by country of which 5909 of the exported data was specific to our selected 15 countries. Discouraging posts were most common in Italy (28%), the United States (19%), and Canada (12%). Forty-one posts in the USA referred to the CDC of which twenty-four posts (59%) referred to them as corrupt or untrustworthy. Nine posts in Italy highlighted mistrust of the ASL in association with vaccines in pregnancy. Tweets incorrectly linked vaccines with causing different diseases despite evidence of variable causation. However, disability united all the diseases mentioned in posts (Congenital Zika Syndrome, Moebius syndrome, mercury related neurological deficit, and autism).

Conclusions: Posts relating to maternal vaccination from November to December 2018 ranged significantly in terms of content and sentiment between countries, however ten topics identified were common across countries (the promotion of the flu vaccine, pertussis vaccine, vaccines for protection, inclusion of women in vaccine research, the safety and risks of vaccines, disability and vaccination, scientific evidence/updates, mistrust of health institutions, free vaccines, and vaccine recommendations).

Poster 49

Time of flight mass cytometry (CyTOF) reveals age- and adjuvant-dependent functional plasticity of human blood mononuclear cells

Soni D, Schüller S, Ramirez J, Daley J, Levy O, Dowling D

Introduction: Immune ontogeny leads to age-dependent functional differences in immune system and perhaps important, to designing effective approaches to enhance immunity. Most ontogeny studies are limited in terms of high-throughput functional analysis of complex plethora of peripheral blood mononuclear cells (PBMCs). We utilized an advanced tool i.e. time of flight mass cytometry (CyTOF), a cell-by-cell analysis technique employing elemental tags thereby enabling simultaneous measurement of upto 42 different expression markers, to characterize age-dependent functional differences of human PBMCs.

Methods: Immune responses were evaluated post-stimulation with candidate pattern recognition receptor (PRR) agonists relevant for vaccine development in neonatal cord blood MCs (CBMCs) compared to adult- and elderly PBMCs *in vitro*, respectively. Freshly isolated CBMCs and PBMCs (n=10) were stimulated with Alum hydroxide (inflammasome), MPLA (TLR4), R848 (TLR7/8), ODN 2216 (TLR9) and 2',3'-cGAMP (STING) for 18 hours. Samples stained with isotope-conjugated antibodies were processed by Helios mass cytometer. A 40-parameter-panel was applied to identify the functional responses of 19 immune cell populations. Data were analyzed with a combination of tools developed for the visualization of high-dimensional data.

Results: We demonstrate that the cellular composition as well as the functional diversification of MCs shows an age-dependent pattern in neonates, adults and elderly. The t-distributed stochastic neighbor-embedding algorithm (visNE) revealed a functional plasticity of immune cells in response to single PRR stimuli, which was less pronounced in neonates compared to adults and elderly. Age-specific signatures of maturation and functional diversification in CBMCs and PBMCs identified by CyTOF corresponded with multi-cytokine measurements in the supernatant of treated cells.

Conclusions: This study highlights the utility of CyTOF in evaluating age-specific immune responses by identification of multi-parametric immune signatures in response to PRR-agonist stimulation. Hence, our data provides a high-

resolution reference map of the cellular composition and functional organization of the human MC system that may also inform adjuvanted-vaccine development.

Poster 50

To study expansion of proinflammatory cytokines, autoantibodies and regulatory T cells in infants of mothers with type 1 diabetes

Kumar P, Sharma V

Introduction/Background & Aims:

Maternal transmission of islet autoantibodies to children born to mothers with type 1 diabetes (T1D) has been shown to protect from autoantibodies and diabetes development later in life.

To evaluate the hypothesis that exposure of the offspring to maternal insulin therapy induces regulatory mechanisms in utero, we compared the FOXP3 expressing regulatory T cells, proinflammatory cytokines and autoantibodies in cord blood (CB) of infants born to mothers with or without T1D.

Methods: Cord blood mononuclear cells (CBMCs) from 20 infants with maternal T1D and from 20 infants with an unaffected mother were analyzed for the numbers of CD4+CD25+FOXP3+ cells ex vivo and after in vitro stimulation with human insulin by flow cytometry. The mRNA expression of FOXP3, NFATc2, STIM1, interleukin (IL)-10, and transforming growth factor (TGF)- β was measured by RT-PCR.

Results: The percentage of FOXP3+ cells in CD4+CD25(high) cells was higher in the CB of the infants with maternal T1D when compared with the infants of unaffected mothers. After in vitro insulin stimulation an increase in the percentage of FOXP3+ cells in CD4+CD25 cells as well as upregulation of FOXP3, NFATc2, STIM1, IL-10, and TGF- β transcripts in CBMCs for all was observed only in the offspring of mothers with T1D, in whom the disease-related PTPN22 allele was associated with reduced STIM1 and NFATc2 response in insulin-stimulated. The results are consistent with early priming of the fetal immune system only in children born to mothers with T1D. Levels of interleukin (IL)-1beta, tumour necrosis factor (TNF)-alpha and IL-8, as well as the frequency of CD4(+) CD25(+) T cells were significantly increased, and the increased levels correlated positively with anti-GAD65 autoantibody levels.

Conclusions: We suggest that maternal insulin treatment induces expansion of regulatory T cells and proinflammatory cytokines in the fetus, which might contribute to the lower risk of diabetes in children with maternal vs. paternal diabetes.

Poster 51

Safety, Immunogenicity and Transplacental Antibody Transfer of Polysaccharide and Conjugated Pneumococcal Vaccines Administered to Pregnant Women Living with HIV (WLHIV)

Adriana Weinberg, M.D., Marisa M. Mussi-Pinhata, M.D., Geraldo Duarte, M.D., Petronella Muresan, M.S, Lauren Laimon, M.S., Stephen I. Pelton, M.D., David Goldblatt, MB.Ch., Ph.D., F.R.C.P., F.R.C.P.C.H, Terry Fenton, Sc.D., Bonnie Zimmer, Frederic Bone, Lassallete Newton, Esau C. Joao, M.D., Breno R. Santos, M.D., Elizabeth S. Machado, MD, PhD., Adriana F. R. Coimbra, Pharm. D., Jennifer Canniff, Nahida Chakhtoura, M.D.

Introduction/Background & Aims: Vaccination during pregnancy may protect both mother and infant against infections. PCV-10 and PPV-23 are recommended for WLHIV, but are seldom used during pregnancy. We compared the safety, immunogenicity and transplacental antibody transfer of PCV-10 with PPV-23 and placebo administered to pregnant WLHIV on antiretroviral therapy. The study was powered to show 20% higher seroresponses in PCV-10 compared with PPV-23 recipients.

Methods: 347 Brazilian anti-pneumococcal vaccine-naïve WLHIV were randomized to receive PCV-10, PPV-23 or placebo at 14-32 weeks of gestation. Maternal antibodies against pneumococcal serotypes 1, 5, 6B and 14, common to both vaccines, were measured at entry, 4 weeks post-vaccination, delivery and 24 weeks post-partum using Mesoscale Discovery arrays. Antibodies against the same serotypes were measured in infants at birth, 8, 16 and 24 weeks of life. Seroresponse was defined by ≥ 2 -fold antibody concentration increases from pre- to post-vaccination; seroprotection was defined by serum antibodies ≥ 0.35 $\mu\text{g/ml}$.

Results: At enrollment, women were mean (SD) 27.6 (6.1) years of age; 25.5 (5) weeks gestation; had 582 (266) CD4 cells/ μ l and 674 (4730) HIV RNA copies/ml. Grade \geq 3 maternal and infant adverse events were similar among treatment groups.

Magnitude, persistence, transplacental transfer and effect of maternal antibody responses to PCV-10 and PPV-23 on infant seroprotection

<i>Seroresponse/seroprotection against 4 vaccine serotypes</i>	<i>Maternal Treatment Arm</i>		
	<i>PCV-10</i>	<i>PPV-23</i>	<i>Placebo</i>
<i>Maternal seroresponders (%; 95% CI) at 4 weeks post-vaccination</i>			
• To \geq 1 serotype	96; 90-99*	95; 89-98*	3; 1-8
• To all serotypes	32; 24-42*	34; 25-43*	1; 0-5
<i>Maternal seroprotection: median; Q1-Q3 number of serotypes/woman</i>			
• Pre-vaccination	3; 2-4	3; 2-4	2; 1-4
• 4 weeks post-vaccination	4; 4-4*	4; 4-4*	2; 1-4
• Delivery	4; 3-4*	4; 3.5-4*	2; 1-4
• 24 weeks post-partum	4; 3-4*	4; 3-4*	3; 2-4
<i>Infant seroprotection: median; Q1-Q3 number of serotypes/infant</i>			
• Birth	4; 2-4*	4; 2-4*	1; 1-2
• 8 weeks of life (pre-1 st childhood PCV)	2; 1-2*	2; 1-3*	0; 0-1
• 16 weeks of life (8 weeks post-1 st and pre-2 nd childhood PCV)	3; 2-4 [§]	3; 3-4* [§]	3; 2-4
• 24 weeks of life (8 weeks post-2 nd and last childhood PCV)	4; 3-4* [§]	4; 4-4 [§]	4; 4-4

* p<0.05 vaccine compared with placebo groups; [§]p<0.05 between vaccine groups

Chi-square test was used for % seroresponders; Student's t-test was used for number of serotypes.

Conclusions: PCV-10 and PPV-23 had similar safety; magnitude and persistence of antibody responses; and antibody transplacental transfer in WLHIV on antiretroviral therapy. Maternal anti-pneumococcal immunization conferred seroprotection until the initiation of childhood PCV against \geq 50% vaccine serotypes tested, while infants born to placebo recipients had seroprotection against 0-25% serotypes. Administration of PCV-10, but not PPV-23, during pregnancy may decrease infant antibody responses to childhood PCV.

Poster 52

Understanding of Streptococcus agalactiae CC17 virulence and disease mechanisms using comparative genomics and in vivo models

Hajar AlQadeeb¹, Adrian Casarez-Lopez¹, Murielle Baltazar¹, Paul Roberts², Timothy Neal², Aras Kadioglu¹, Neil French^{1, 3}, Marie Yang¹

¹Institute of Infection and Global Health, University of Liverpool, Liverpool, UK; ²Royal Liverpool and Broadgreen University Hospitals NHS Trust; ³College of Medicine, Blantyre, Malawi

Background. Group B *Streptococcus* (GBS) is a leading cause of sepsis and meningitis worldwide, associated with high rates of mortality and morbidity, especially in infants. Here, we place emphasis on GBS clonal complex (CC)-17 for its persistence as a neonate invasive isolate and its association with high disease incidence. We hypothesized that a CC found prevalently in humans has undergone distinct genomic and phenotypic changes in response to their environmental niches that will impact on their potential to cause invasive disease. These evolutionary adaptations may hold the key towards developing novel preventative and therapeutic strategies.

Methods. We carried out whole-genome illumina-sequencing (WGS) and analysis of n=40 GBS clinical isolates serotype III, CC17 archived at the Royal Liverpool Hospital between April 2015 and December 2018. These 40 neonate invasive isolates were carefully selected as representative strains on the basis of patient information and disease outcome. Phenotypic characterisation of these isolates was also conducted using complement-binding and opsonophagocytosis killing assays, capsule thickness analysis and antibiotics MIC testing.

Results. A subset of 9 vaccine gene candidates were identified on the basis of their conserved expression across CC-17 and bacterial cell-wall association, and further shortlisted to 3 genes on the basis of their non-similarity to human

proteins, predicted B-cell and T-cell immunogenicity. GBS mutant strains deficient for these genes will be generated and tested in murine models of vaginal colonisation and vertical transmission models. We are in the process of further comparing our dataset against a comprehensive collection of 2,364 publicly available human GBS genomes originating from America (USA, Latin America, Canada), Africa (Kenya), Asia (Singapore, Thailand), and Europe (UK and the Netherlands).

Conclusion. Inferring genome-wide associations, particularly within the same serotype provide unique insights into GBS virulence mechanisms and help identifying targets for novel and robust antimicrobial and vaccine targets.

Poster 53

Humanised FcRn mouse model: a novel tool for preclinical testing of vaccine-induced immune correlates and maternofetal transfer of humoral immunity.

Shadia K, Yang M, Le Doare K, Phiri E, Saha S, Weeks A, Kadioglu A, French N

Introduction/Background & Aims: The success of maternal immunisation for neonatal protection lies in the efficient transfer of vaccine-induced immunity to the offspring. As the maternofetal interface is a complex and dynamic functional component, a robust pre-clinical model is needed which can predict functional immune outcomes as closely as possible to the human. The aim of our study is to develop an '*in vivo*' bio-assay for testing the effectiveness of antibody transfer from mother to offspring in providing protection against neonatal Group B Streptococcal (GBS) disease.

Methods: We have developed a murine 'maternofetal transfer model' using transgenic humanised FcRn (neonatal Fc receptor) mice of C57BL background. The mice are genetically modified to replace the 'mouse FcRn' receptor by its human homologue. Human FcRn receptor in the mouse placental tissue binds exclusively with human IgG within a realistic range comparable to human.

Human maternal serum from women of childbearing age from three countries; Malawi, UK & Bangladesh with naturally acquired anti-GBS antibodies will be used to investigate differences in anti-GBS immunity that might explain heterogeneity in GBS risk in these country settings.

Pregnant mice will be administered with the sera, and the pups will be challenged with a lethal dose of wild type GBS (serotype III, CC17 clinical isolates). Then the pups will be monitored for the sign of disease or protection. Blood samples will be collected from the pups to determine human anti-GBS IgG titers (Luminex®) as a measure of placental transfer.

Results: We have recently acquired and successfully started breeding our transgenic mouse colony and have started the process of validating the model using human serum containing anti-GBS antibody. We will present this data at the INMIS conference.

Conclusions: Our transgenic maternofetal transfer model offers clinically relevant bio-assay and surrogate of protection for the vaccine-induced immune response in human studies.

Poster 54

Understanding the interaction between Maternal IgG and Neonatal Innate Immune Cells

Alansana Darboe, Lamin Sillah, Saikou Keita, Abdoulie Njie, and Beate Kampmann.

Medical Research Council Unit The Gambia at The London School of Hygiene & Tropical Medicine.

Background & Aims: Neonatal and early infant deaths now contribute over 45% of all deaths observed in children under 5 years of age with the majority caused by infections. Maternal immunization can be used to protect these neonates against some vaccine-preventable infections early in life. However, the effects of maternal antibodies on the neonate's immune responses is not well elucidated, especially with regards to their potential to activate neonatal innate cells. Thus, we aim to generate an *in vitro* model for the evaluation of innate immune responses in neonates who were exposed to maternal vaccines.

Methods: To investigate whether maternal antibodies might affect the immune response of innate cells in the newborn, we will pursue two approaches using available neonatal cord blood samples in two sets of experiments:

Firstly, we will investigate whether tetanus toxoid (TT) antigen can induce the activation of innate cells expressing the FcR in the presence of maternally derived TT antibodies. The activation of classical, intermediate/ non-classical monocytes will be examined using flow cytometry with the following markers CD40/CD86/ICOS-L/MHCII, whilst, the induction of cord blood natural killer cells will be observed using CD107a/IFN-g/TNF-a/IL-10/CD25.

Secondly, we will study functional differences and epigenetic changes in cord blood monocytes that are exposed to vaccine antigens and were subjected to “training” by prior exposure to BCG or b-glucan in vitro, compared with non-trained control monocytes. We will use ATAC-Seq methodology to investigate differences in methylation and acetylation patterns between varying conditions of such “trained” monocytes. We will subsequently validate the models using cord blood samples collected from a clinical trial of pertussis immunization in pregnancy. The results of these experiments aim to indicate key innate pathways affected by maternal antibody.

Conclusions: The availability of this in vitro neonatal cord blood model could be beneficial for the early evaluation of a range of upcoming vaccines to be administered in pregnancy.

Poster 55

Effect of neonatal malnutrition on immune responses in male rats

Kumar P, Khanna R, Sharma V

Introduction/Background&Aims: Neonatal malnutrition induces metabolic and endocrine changes that have beneficial effects on the neonatal in the short term but, in the longer term, these alterations lead to maladaptations. We investigated the effect of neonatal malnutrition on immune responses in adult rats submitted or not to an aggressiveness test.

Methods: Male Wistar rats were distributed to one of two groups according to their mothers' diet during lactation: the well-nourished group (group C, n = 42, receiving 23% of protein) and the malnourished group (group MN, n = 42, receiving 8% of protein). After weaning, all rats received normoproteic diet. Ninety days after birth, each group was subdivided into three subgroups: control rats (n = 14, respectively), aggressive rats (n = 14, respectively) and rats receiving foot shock (FS; n = 14, respectively). Plasma corticosterone concentration was measured after FS sessions. Leukocyte counts and humoral immunity were evaluated.

Results: In neonatal malnourished animals, FS-induced stress reduced plasma corticosterone concentration. Intraspecific aggressiveness induced alterations in leukocyte counts and antibody titers 7 and 15 days after immunization. Neonatal malnourished animals showed no changes in the immune parameters evaluated.

Conclusions: Expression of intraspecific aggressiveness activates the immune system. Neonatal malnutrition seems to have a long-lasting effect on components of both neuroendocrine and immune functions.

Poster 56

Development of multi-epitope driven subunit vaccine in secretory and membrane protein of Plasmodium falciparum to convey protection against placental malaria infection

Mr Rajan Kumar Pandey

Introduction/Background & Aims: Placental malaria is the severe health concern for a long time which targets the pregnant woman regardless of previous acquired immunity. This severe pathological condition is mediated by the VAR2CSA, a Plasmodium antigen that interacts with the placental chondroitin sulfate-A (CSA). As per the WHO reports, the malarial infection causes huge mortality all around the world and is incomparable with any other infectious diseases. The absence of effective treatment options and increasing drug resistance to the available therapeutics like artemisinin and other derivatives demand an efficient alternative to overcome this death burden.

Methods: We performed the literature survey and sorted the *Plasmodium falciparum* secretory and membrane proteins including VAR2CSA to design multi-epitope subunit vaccine using an adjuvant, B-cell- and T-cell epitopes including cytotoxic T-lymphocytes (CTL) and helper T-lymphocytes (HTL) epitopes. Every helper HTL epitope was IFN- γ positive and IL-4 non-inducer. The physicochemical properties, allergenicity, and antigenicity of designed vaccine were analyzed for the safety concern. Homology modeling and refinement were performed to obtain the functional tertiary structure of vaccine protein followed by its molecular docking with the toll-like receptor-4 (TLR-4) immune receptor. Molecular dynamics simulation was performed to check the interaction and stability of the receptor-ligand complex.

Results: Multi epitope subunit vaccine of 704 amino acid residues was designed having its entire component as mentioned above including CTL, HTL, B-cell epitopes, adjuvant and linkers.

Conclusions: Immunoinformatics evaluation revealed the immunogenic and stable nature of designed subunit vaccine while, its experimental validation may confirm its ability to enhance the maternal immunity against placental malaria infection. This way, we designed the multi-epitope subunit vaccine to serve the maternal health living in the global endemic zone.

Poster 57

STAT3 transfection restores lack of Th17 differentiation in neonatal CD4+ T cells

Ms. Zohreh Sharafian, Ms. Rache Da Silva, Dr. Ashish Sharma, Dr. Hamid Razzaghian, Dr. Colin Ross, Dr. Pascal Lavoie

Introduction/Background & Aims: *Candida* is a common cause of oral thrush and diaper rashes in newborns. T helper 17 CD4 cells (Th17) play an important role in controlling mucosal *Candida* invasion. Neonatal naïve CD4 T cells lack capacity to differentiate into IL-17-producing effector cells. Signal Transducer and Activator of Transcription 3 (STAT3) is required for Th17 differentiation, through the IL-6 receptor. In this study, we performed a comparative systems-level analysis of neonatal and adult naïve CD4 T cells to understand the molecular basis for their lack of Th17 differentiation.

Methods: Comparative genome-wide gene expression analysis was performed between neonatal and adult naïve CD4 T cells isolated from umbilical cord blood and healthy adult peripheral blood, respectively. To test the role of STAT3, the corresponding gene was cloned into a pIRES2-eGFP plasmid and over-expressed in primary neonatal naïve CD4 T cells by electroporation. Transfected cells were stimulated for 3 days (CD3/CD28) in the presence of Th17-polarizing cytokines (IL-1 β , IL-6, IL-23 \pm TGF- β). IL-17/IL-22 production was measured by ELISA.

Results: Our gene expression analysis demonstrated an age-related reduction of STAT3 and perturbation within TGF- β signaling in neonatal T cells, paralleled to a reduction in STAT3 phosphorylation. Without exogenous STAT3, neonatal T cells activated in Th17-differentiating conditions produced high levels of IL-22 instead of IL-17. Transfection of *STAT3* restored IL-17 secretion in neonatal naïve CD4 T cells.

Conclusions: In the absence of sufficient STAT3, neonatal T cells are skewed towards non-stereotypic Th17 responses characterized by a predominant production of IL-22 rather than IL-17. Given that IL-22 is not essential against *Candida* invasion, the lack of Th17-differentiation capacity of neonatal T cells may explain infants' susceptibility to mucocutaneous infections. On the other hand, preferential IL-22 production by neonatal T cells may help protect from pathogenic effects of IL-17 at this age.

Poster 58

The half-life of maternal transplacental antibodies against diphtheria, tetanus, and pertussis in infants after maternal immunization: an individual participant data meta-analysis

Leuridan E1, Barug D2, Dang DA3, Halperin S4, Hoang HT3, Holder B5, Kampmann B6, Langley JM4, Madavan N7, Maertens K1, Munoz FM8, Pollard AJ9, Rots N2, Wanlapakorn N10, **Voysey M9**,
1University of Antwerp, Belgium; 2Institute for Public Health and the Environment (RIVM), The Netherlands;
3National Institute of Hygiene and Epidemiology, Hanoi, Vietnam; 4Dalhousie University, Canada; 5Imperial College

London, United Kingdom; 6London School of Hygiene and Tropical Medicine, United Kingdom; 7University of Exeter, United Kingdom; 8Baylor College of Medicine, USA; 9University of Oxford, United Kingdom; 10Chulalongkorn University, Thailand

Introduction/Background & Aims:

We calculated the half-life of vaccine induced maternal antibodies against diphtheria (D), tetanus (T) and pertussis (P) in infants born to women who received tetanus, diphtheria, acellular pertussis (Tdap) vaccine during pregnancy, and determined whether antibody decayed at different rates according to vaccine received, maternal age, gestational age, birthweight, sex, and country.

Methods: De-identified individual participant data from infants born to women who participated in studies of maternal Tdap vaccination conducted in 7 countries were meta-analysed. Data from blood samples taken prior to the administration of any DTP-containing vaccine (cord blood and 2 months of age), were \log_2 -transformed and the antibody decay rate estimated for each antigen.

Results: Infants from 548 women who received Tdap vaccines containing 3 (n=354) or 5 (n= 194) pertussis antigens at a median age of 30.4 years (IQR 16-44), and 32 (IQR 30-34) weeks gestation were included. Half-lives are shown in Table 1.

Table 1: Half-life of maternal antibodies for 5 antigens

Antigen	Half-life (days)	95% CI	
Pertussis Toxoid	29.4	24.2	37.4
Pertactin	32.8	29.7	36.7
Filamentous haemagglutinin	36.2	30.8	43.7
Diphtheria toxoid	30.5	23.7	42.7
Tetanus toxoid	34.1	24.3	57.3

Half-lives differed between countries. There was no effect of maternal age or vaccine product. Higher birthweight was associated with slower decay for PT and FHA. Female sex and later gestational age at vaccination were associated with slower decay for FHA and TT respectively.

Conclusions: Differences in vaccination histories and laboratory methods may account for some of the variation seen between studies in our results. Results from further studies will be incorporated in the near future and additional analyses conducted on unvaccinated pregnancies, and comparisons between low and high income settings.

Poster 59

Antibody levels in breast milk after maternal pertussis vaccination are not influenced by preterm delivery

Marjolein Orije 1, Ludo Mahieu², Pierre Van Damme¹, Leni Waeterschoot¹, Margot Wouters¹, Kirsten Maertens ¹ & Elke Leuridan ¹

¹Center for the Evaluation of Vaccination, Vaccine & Infectious Diseases Institute, University of Antwerp, Belgium;

²Department of Paediatrics, Division of Neonatology, University Hospital Antwerp, Belgium

Introduction/Background & Aims: Maternal pertussis immunization increases pertussis specific antibody levels in breast milk, potentially offering mucosal immunity against pertussis when breastfeeding. However, it is not known whether preterm delivery has an effect on breastmilk composition. This study looks at potential differences in breastmilk composition between lactating women who delivered at term or prematurely after maternal pertussis immunization.

Methods: Total and anti-pertussis toxin (anti-PT) immunoglobulin (Ig) A and G were measured in breast milk samples of lactating women at 72 hours (colostrum), 4, 8, 12 weeks postpartum.

Results: 463 samples of 150 women were available for analysis. After immunoassay validation, no differences were detected in anti-PT IgA, anti-PT IgG and total IgA levels in colostrum samples of women who delivered at term or

prematurely (Figure 1). Total IgG levels in colostrum, however, were higher in women who delivered at term compared to women who delivered prematurely ($p=0.09$). This difference persisted four weeks after delivery ($p=0.008$). Eight weeks postpartum total IgA levels were significantly higher in breastmilk of women who delivered prematurely ($p=0.04$). At twelve weeks no differences were detected between the groups. Furthermore, PT IgA to total IgA and PT IgG to total IgG ratios were comparable between both groups at all time points. Additionally, antibody levels naturally declined over time.

Conclusions: Premature delivery did not significantly alter PT antibody levels in breastmilk, showing that there is no compensation via breastmilk for immature transplacental transport of pertussis specific antibodies. However, significant differences were detected in Total IgG and Total IgA levels.

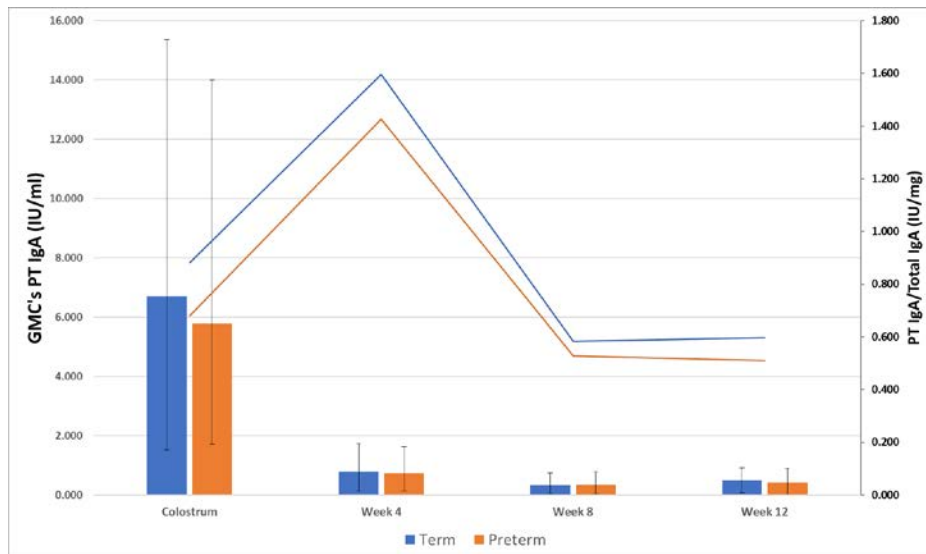


Figure 1: Representation of the GMCs of anti-PT IgA (bar graph, left axis) and the ratio of the anti-PT IgA to total IgA (line graph, right axis) at the 4 time points. No significant differences were detected between mothers who delivered at term and mothers who delivered prematurely.

Poster 60

Does maternal Tdap vaccination modulate innate immune responses in mothers and infants?

Rice T, Diavatopoulos D, Guo Y, Barnett S, Donaldson B, Holder B, Kampmann B

Introduction/Background & Aims: Maternal infection during pregnancy can impact the infant immune system and susceptibility to childhood infection. However, little is known about the impact of vaccination during pregnancy on maternal and infant immune responses, particularly the potential for heterologous vaccine effects. We therefore assessed innate cellular responses in maternal and cord PBMC from pertussis vaccinated and unvaccinated pregnancies.

Methods: Maternal and cord blood PBMC were collected at birth from vaccinated and unvaccinated pregnancies. To investigate pathogen-specific responses, cord PBMCs were stimulated for 4h with heat-killed wild-type pertussis bacteria or a cocktail of pertussis vaccine antigens (pertussis toxin, FHA and pertactin). Phenotype of innate cell populations including NK cells, dendritic cells and monocytes was measured by flow cytometry. To investigate potential heterologous effects, maternal and cord blood PBMC were stimulated overnight with a panel of microbial ligands followed by IL-6 and IL-1beta ELISAs.

Results: PBMCs from vaccinated women showed reduced IL-6 and IL-1beta production in response to stimulation with fungal ligands compared to PBMCs from unvaccinated women. A similar effect was observed in cord blood samples, with infants from vaccinated pregnancies showing reduced IL-6 responses. There was no effect of vaccination on responses to the other ligands. Cord PBMC from female infants in the unvaccinated group had

elevated IL-1beta to bacterial and viral ligands compared to male infants, but this trend was reversed for IL-6 responses. Multiparameter flow cytometry of innate cell populations following pertussis bacteria and antigen stimulation was performed on cord blood PBMC from vaccinated (n=10) and unvaccinated (n=10) pregnancies. Analysis is underway.

Conclusions: Innate immunity is important in fighting pertussis infection. Continued monitoring of the impact of pertussis vaccination during pregnancy on maternal and infant innate immune responses, as well as potential non-specific effects of pertussis vaccination during pregnancy, is required.

Poster 61

Characterisation of $\gamma\delta$ T cells in Infants During Primary CMV Infection

PhD Candidate Jessica Tuengel, PhD Candidate Maria Papadopoulou, Mr. Gurpreet Aulakh, Miss Alexandra Maslova, MD Peter van den Elzen, PhD David Vermijlen, MPH, PhD, MD Soren Gantt

Introduction/Background & Aims: Congenital cytomegalovirus (cCMV) infection is the most common congenital infection in the world and can cause deafness and intellectual disability. A CMV vaccine is a high public health priority but better understanding of protective immunity against cCMV disease is needed. Gamma-delta ($\gamma\delta$) T cells develop early in gestation and may be important for controlling CMV infection before alpha-beta T cell immunity develops. Indeed, a “public” (shared among many individuals) $\gamma\delta$ T cell receptor (TCR) clone has been associated with cCMV and may represent an important early response to the virus. In this study we aimed to comprehensively characterize $\gamma\delta$ T cell responses to CMV infection in early life.

Methods: Following a birth cohort of 32 Ugandan infants and their mothers during their first year of life, we captured 2 cCMV infections and 21 infant postnatal CMV infections. Using flow cytometry, we characterized $\gamma\delta$ T cells, CD8/CD4 T cells, invariant natural killer T cells (iNKT) and natural killer (NK) cells. From a subset of these samples we extracted RNA and sequenced the $\gamma\delta$ TCR regions.

Results: Total $\gamma\delta$ T cell numbers were correlated with age and CMV infection (p-values 0.001, 0.016). Expression of CD16, CD57 and NKG2C were also higher after CMV acquisition (p-values 0.002, <0.000, 0.010), indicating $\gamma\delta$ T cell activation. Neither total $\gamma\delta$ nor any of the other markers were correlated with EBV infection. The relative abundance of $\gamma\delta$ subtypes (V δ 1, V δ 2, V δ 3 and V γ 9+, V γ 9-) by CMV infection status did not differ between CMV-infected and uninfected infants. We detected the public $\gamma\delta$ TCR clone in 4/12 early (<120 days old) postnatal CMV infections and in 0/13 CMV negative infants.

Conclusions: Our findings support the notion that $\gamma\delta$ T cells are involved in the immune response to CMV infection in early life, providing insight for novel new vaccine designs to more effectively prevent CMV-related disease.

Poster 62

IMPACT OF HIV INFECTION ON ANTIBODY AND MEMORY B CELL RESPONSES TO TDAP IMMUNIZATION DURING PREGNANCY

Taton M, Konopnicki D, Cogan A, Martin C, Goetghebuer T, De Wit S, **Marchant A**, Willems F, Dauby N

Background: Maternal immunization with tetanus-diphtheria-acellular pertussis (TDaP) vaccine decreases the incidence and severity of post-natal Bordetella pertussis infection. The influence of maternal HIV infection on the immunogenicity of pertussis immunisation has not been reported.

Methods: HIV-infected and uninfected pregnant women were immunized with TDaP vaccine, mostly during the second trimester of pregnancy. Maternal serum and peripheral blood mononuclear cells were collected before, 7-10 days and 30 days after immunization and at delivery. Serum from cord blood was collected. Pertussis specific IgG levels were measured by ELISA. Memory B-cells were enumerated by ELISPOT.

Results: All HIV-infected women were on antiretroviral therapy (ART) at the time of vaccination. Median CD4 count was 706/ μ L and all but one woman had undetectable viral load. Mean time between vaccination and delivery was

17.5 weeks for HIV-infected women and 16 weeks for uninfected women. Geometric mean concentrations (GMC) of PT IgG were similar in HIV-infected and uninfected women before and 7-10 days after vaccination. At 30 days, PT IgG levels tended to be lower in HIV-infected as compared to uninfected women (GMC: 63 IU/mL (95% CI, 40.5-98) vs 96.5 IU/mL (95% CI, 71-131)). Expansion of PT-specific memory B cells was detected 30 days after immunization in the two study groups. HIV-infected women had a more rapid decay of PT IgG than uninfected women. At delivery, maternal PT IgG GMCs were 16 IU/mL (95% CI, 4-65) in HIV-infected and 47 IU/mL (95% CI, 34-65) in uninfected mothers. PT IgG levels were lower in HIV-exposed (GMCs: 45 IU/mL (95% CI, 25-81)) than in unexposed newborns (86.5 IU/mL (95% CI, 60-124.5)).

Conclusions: Our results indicate that PT IgG responses to Tdap immunization are impaired in HIV-infected pregnant women on ART. This reduced immunogenicity could limit the efficacy of maternal immunization in this population.

Poster 63

The effect of HIV and malaria in pregnancy on maternal and infant immune responses and trans-placental antibody transfer: A systematic review

Marbán-Castro E, Pantoja E, Phadke V, Aguado T, Menéndez C, Omer S, **Bardají A**

Introduction/Background & Aims: Maternal infections may alter trans-placental antibody transfer. We did a systematic review, using PRISMA guidelines (PROSPERO CRD42018089307), on the effect of maternal HIV and/or malaria in pregnancy on maternal and infant immune responses and placental passage of antibodies, against vaccine preventable infections the aim of identifying key data gaps to help direct future maternal immunization research.

Methods: We searched MEDLINE, SCOPUS (PubMed/EMBASE), Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials and Clinicaltrials.gov for published studies from 1970 to February 2018. Human studies reporting data on maternal and cord/neonatal/infant antibody levels, and/or placental antibody transfer, against vaccine preventable infections according to HIV and malaria infection in the mother were included.

Results: A total of 4717 articles were identified through database search and 36 articles were included (24 articles that reported effect of HIV, 12 articles of malaria, and 3 that reported both effect of HIV and malaria). The majority of studies were observational (n=32) with the exception of 2 clinical trials. Maternal HIV infection and/or placental malaria were associated in most studies with reduced placental transfer of antibodies to various pathogens (tetanus, pertussis, group B Streptococcus, influenza, Pneumococcus, and Haemophilus influenzae type b); though results were inconsistent for the effect of placental malaria on respiratory syncytial virus antibodies. Few studies reported data on responses following infant routine vaccination or correlation with clinical outcomes. Heterogeneity in measurement of immune outcomes and trans-placental antibody transfer was a limitation for comparability of studies.

Conclusions: Substantial gaps exist on the understanding of maternal vaccines in countries heavily affected by HIV and malaria. Filling these gaps is vital to guide future maternal immunization policies in these settings and protect most vulnerable populations.

Poster 64

Cord Blood Passive Antibody against Protein and Polysaccharide Antigens in Human Immunodeficiency Virus (HIV) - Exposed and Unexposed Infants

Choudhury S, Ladson G

Introduction: Little clinical evidence exists regarding the placental transfer of polysaccharide versus protein antigens from HIV-infected and -uninfected mothers to their infants. The placental transfer of IgG1 (protein) versus IgG2 (polysaccharide) antibodies from mother to infant is known. The purpose of the study was to examine whether maternal HIV infection has an impact on the placental transfer of protein versus polysaccharide antigens in HIV-exposed infants when compared with their HIV-unexposed counterparts.

Methods: Antibody levels to polysaccharide antigens (*Haemophilus influenzae* type b [Hib], *Streptococcus pneumoniae* [SPN]), and protein antigens (tetanus toxoid [TT], measles, and varicella) were evaluated in a group of HIV-infected

and uninfected mothers during pregnancy and in the cord blood of their infants. Protective antibody levels were defined for the respective antigens. Antibody assays for *SPN*, *Hib*, tetanus, and measles were performed using an enzyme-linked immunosorbent assay (ELISA) and for varicella using an indirect immunofluorescent antibody (IFA).

Results: Antibody levels in cord blood were found to be considerably lower for polysaccharide antigens (*Hib*, *SPN*) and higher for protein antigens (TT) than those in maternal blood. The ratio of cord blood to maternal blood antibody levels (reflecting placental transfer) was significantly ($p=0.05$) higher for protein antigens (TT) compared with polysaccharide antigens (*Hib* and *SPN*) in both HIV and control groups. Within the HIV-exposed group, maternal CD4 counts lower than 500/mm³ were associated with a considerably ($p=0.06$) lower placental transfer of protein antigens (TT) compared against those with CD4 counts >500/mm³.

Conclusions: There is significantly lower passive antibody transfer against polysaccharide antigens compared with protein antigens not only in HIV-exposed infants, but also in those not exposed to HIV. Larger prospective studies may need to be performed to replicate these findings. Maternal immunization during pregnancy may be a strategy for boosting passive antibody levels to polysaccharide antigens, thus protecting neonates and young infants in vulnerable populations.

Poster 65

Effect of maternal immunisation on infant T cell responses to pertussis vaccination

Dr Nasamon Wanlapakorn, Dr Shamsheer Ahmed, Prof Elke Leuridan, Prof Yong Poovorawan, **Dr Qibo Zhang**

Background and aims: Pertussis causes serious disease particularly in infants. Current efforts are made to protect young infants through immunizing pregnant mothers. However, there has been concerns on the potential blunting effect of maternal immunisation on subsequent development of antibody response in infants. Animal studies suggest a critical role for T cell immunity e.g. Th1 and Th17 in protection against pertussis. It is therefore valuable to study how maternal immunisation may modulate vaccine-induced T cellular immunity in infants. **Methods:** we studied infants T cell responses following immunization with pertussis vaccines (acellular(aP) or whole cell (wP)). Infant T cell responses were analysed following *in vitro* stimulation of PBMC with inactivated pertussis toxin (PT) or anti-CD3 antibody, followed by cytokine profile analysis using cytokine beads array(13 cytokines). We compared the responses between infants born to Tdap-vaccinated mothers during pregnancy (received aP or wP, thus aP- and wP-group infants) and those born to non-Tdap-vaccinated mothers and received wP (Expanded Program on Immunization(EPI)-wP group). **Results:** we demonstrate significant differences in Th1 response(IFN γ & TNF α) in PBMC from infants at 7-months(following primary immunization) and 18-months(before booster). Th1 response was strongest in aP-group, higher than wP- and EPI-wP group infants, with EPI-wP group showing lowest at 7-months. At 18-months, Th1 response in wP-group was lower than EPI-wP and aP groups. This appeared to be associated with a marked increase in Th1 response in EPI-wP group but a decrease in wP-group as compared to 7-months. Overall, Th2 response was also shown stronger in aP-group than wP groups, although no such pattern was seen in Th17 cytokines. **Conclusion:** we show maternal immunization has a significant effect on infant T cell response to pertussis vaccines. Different profiles of T helper cell(Th) responses following aP and wP vaccination may impact on antibody response and protective immunity which warrants further study.

Poster 66

B. pertussis specific IgG B-cell responses in infants before and after 11 months booster vaccination and the influence of maternal Tdap immunization

Daan Barug¹, Lisa Beckers¹, Anne-Marie Buisman¹, Alina Nicolai¹, Elisabeth A.M. Sanders^{1, 2}, Cecile A.C.M. van Elsland¹, Nynke Y. Rots¹

¹ Centre for Infectious Disease Control, National Institute for Public Health and the Environment, Bilthoven, the Netherlands; ² Department of Paediatric Immunology and Infectious Diseases, Wilhelmina Children's Hospital, Utrecht, the Netherlands

Introduction Despite a growing body of data on interference of maternal tetanus, diphtheria and acellular pertussis (Tdap) vaccination on infant pertussis vaccine-induced antibody responses, little is known about impact on infant B-cell responses in the first year of life. We compared B-cell responses in infants pre- and post- booster vaccination at 11 months of mothers who received Tdap (maternal Tdap group) compared to control infants.

Methods In a randomized controlled trial with DTaP-primed infants at 3 and 5 months, 41 blood samples were collected before- and 38 blood samples 1 week after booster DTaP vaccination at age 11 months. Mothers of these infants either received Tdap vaccination at 30 to 32 weeks of pregnancy (maternal Tdap group) or within 48h after delivery (control group). After stimulation of PBMCs with CPG +R848+IL2 for 5 days, we enumerated B-cells specific for pertussis vaccine antigens PT, FHA and Prn by ELISpot assays.

Results An overall significant B-cell response after booster vaccination at age 11 months was observed for all antigens (Mann-Whitney p-value<0.01). The numbers of Prn specific IgG producing B-cells were dominant in both groups before and after booster vaccination (ranging from 44-76% of total PT, FHA and Prn specific IgG producing B-cells). Based on our pre- and post-booster samples, we have got no evidence for differences between the maternal Tdap group and the control group for antigens PT, FHA and Prn specific IgG producing B-cells/10⁵ CD19+ cells.

Conclusions In very young infants with expected low frequencies of PT, FHA and Prn specific IgG producing B-cells/10⁵ CD19+ cells, clear B-cell responses to *B. pertussis* before and after booster vaccination were observed. Whereas infant vaccine-induced humoral immune responses were lower after maternal Tdap vaccination compared to controls, B-cell responses did not seem to be affected by maternal Tdap vaccination both pre and post-booster vaccination.

Poster 67

Antibody responses to primary and booster immunizations in infants born to women immunized with pertussis-containing vaccines in pregnancy versus unimmunized women: Systematic review and meta-analysis

Abu Raya B, Halperin S, Leuridan E, Maertens K, Munoz F, Sadarangani M

Background: Several countries have recommended pertussis immunization in pregnancy. We aimed to determine if pertussis immunization in pregnancy modifies the active immune response to primary/booster infant immunizations.

Methods: A systematic review and meta-analysis of studies reporting antibody levels to primary/booster immunization in infants born to women immunized against pertussis in pregnancy vs. unimmunized women was performed. The geometric mean ratios (GMRs) of anti-tetanus toxoid (TT), anti-diphtheria toxoid (DT), anti-*Streptococcus pneumoniae* (SPN) and anti-pertussis antibodies in infants born to women immunized in pregnancy vs. unimmunized women were calculated (random-effects model).

Results: 8 studies (3 RCTs) were included. After primary immunization, infants born to women immunized in pregnancy had significantly ($P<0.05$) lower anti-pertussis toxin (PT) [GMR, 0.72; 95% CI, 0.59-0.86], anti-pertactin (PRN) [0.65;0.54-0.77], anti-fimbriae 2+3 (FIM2+3) [0.46;0.37-0.56], anti-DT [0.67;0.53-0.83], anti-SPN1 [0.65;0.46-0.91], anti-SPN3 [0.44;0.24-0.79], anti-SPN4 [0.69;0.59-0.79], anti-SPN5 [0.58;0.49-0.68], anti-SPN6A [0.57;0.46-0.70], anti-SPN7F [0.76;0.64-0.88], anti-SPN19A [0.75;0.61-0.90] antibody levels, but not significantly lower anti-TT [1.09;0.82-1.44], anti-SPN6B [1.08;0.88-1.32], anti-SPN9V [0.62;0.37-1.03], anti-SPN14 [0.68;0.35-1.30], anti-SPN18C [0.89;0.74-1.06], anti-SPN19F [0.85;0.71-1.01], anti-SPN23F [0.89;0.72-1.10] antibody levels compared with infants born to unimmunized women.

After booster immunization, infants born to women immunized in pregnancy had significantly ($P<0.05$) lower anti-PT [0.79;0.68-0.92], anti-FHA [0.75;0.64-0.86], anti-FIM2+3 [0.43;0.32-0.58], anti-DT [0.86;0.75-0.98] antibody levels, but not significantly lower anti-PRN [1.02;0.81-1.28] nor anti-TT [1.58;0.72-3.43] antibody levels, compared with infants born to unimmunized women. Results remained significant in sensitivity analysis restricted to RCTs except for anti-PT and anti-DT antibodies post-primary and post-booster immunization, respectively.

Conclusions:

This is the first meta-analysis supporting interference of pertussis immunization in pregnancy with infants' active immune responses. These findings support the need for enhanced surveillance of pertussis, diphtheria and pneumococcal diseases after primary and booster vaccinations in infancy to determine the clinical significance of this effect.

Systematic Review Registration: PROSPERO CRD42017079171.

Poster 68

Whole Exome Sequencing among Thai Children with Bacille Calmette-Guérin-Induced Diseases following Neonatal BCG Immunization

Lapphra K, Srijareonvijit C, Satproedprai N, Phongsamart W, Wittawatmongkol O, Rungmaitree S, Mahasirimongkol S, Chokephaibulkit K

Background: Bacille Calmette-Guérin (BCG)-induced diseases (BCG-ID) have been increasingly reported in many countries. Host genetic susceptibility to BCG-ID following neonatal BCG vaccination has not been well studied.

Aim: To determine the candidate genetic variants related to host susceptibility to BCG-ID by whole exome sequencing (WES).

Methods: WES accompanied with filtering strategy were used to analyze the genetic variants among children under 3 year of age who were diagnosed with BCG-ID; i.e. lymphadenitis that required medical attention, osteitis, or disseminated infection, at a tertiary care center in Bangkok, Thailand, from January 2008 to December 2017. The primary immunodeficiency (PID) genetic variants were classified into three groups: (I) variants associated with congruent reported as "Pathogenic" in ACMG and ClinVar or have been reported in publications, (II) variants associated with conflicting significance or any deleterious mutations, and (III) other variants potentially involved in BCG-ID.

Results: Of 60 children with BCG-ID; 42 (70%) were male, and the median age at onset was 2.5 (IQR1-8) months. Of these, 16 (26.7%) were suspected (defined as ipsilateral regional lymphadenitis near the vaccination site, or with other clinical features compatible with BCG-ID), 27 (45.0%) were probable; (defined as suspected cases with microbiologic or histologic evidence of mycobacteriosis), and 17 (28.3%) were molecular confirmed BCG-ID. Overall, 48 (80.0%) children had regional lymphadenitis, 9 (15.0%) osteitis, and 3 (5.0%) disseminated infections. We identified three candidate genetic variants in 9 (15%) patients, including Wiskott Aldrich syndrome (WAS), complement component 9 (C9), T-box 1 transcription factor gene (TBX1). Of these, one with confirmed disseminated BCG-ID had 13-base pair frameshift mutation of WAS gene (c.181_193del GCTGAGCACTGGA, p.Ala61ProfsTer11) and had compatible clinical manifestations with WAS.

Conclusion: Mutations that may associated with host susceptibility were found in a small proportion of patients with BCG-ID. Further study is needed to elucidate other factors related to BCG-ID.

Poster 69

The response to pertussis-containing combination vaccines in infants after maternal immunization with reduced antigen content tetanus-diphtheria-acellular pertussis vaccine

Klein N, Abu-Elyazeed R, Chevart B, Mihalyi A, Janssens W, Mesaros N

Introduction/Background & Aims: Maternal pertussis immunization during pregnancy offers protection to women and their newborns but may interfere with immune responses of infants to primary and/or booster immunization. We assessed the effect of maternal reduced antigen content tetanus-diphtheria-acellular pertussis (Tdap) vaccination on infant responses to DTaP-based combination vaccines.

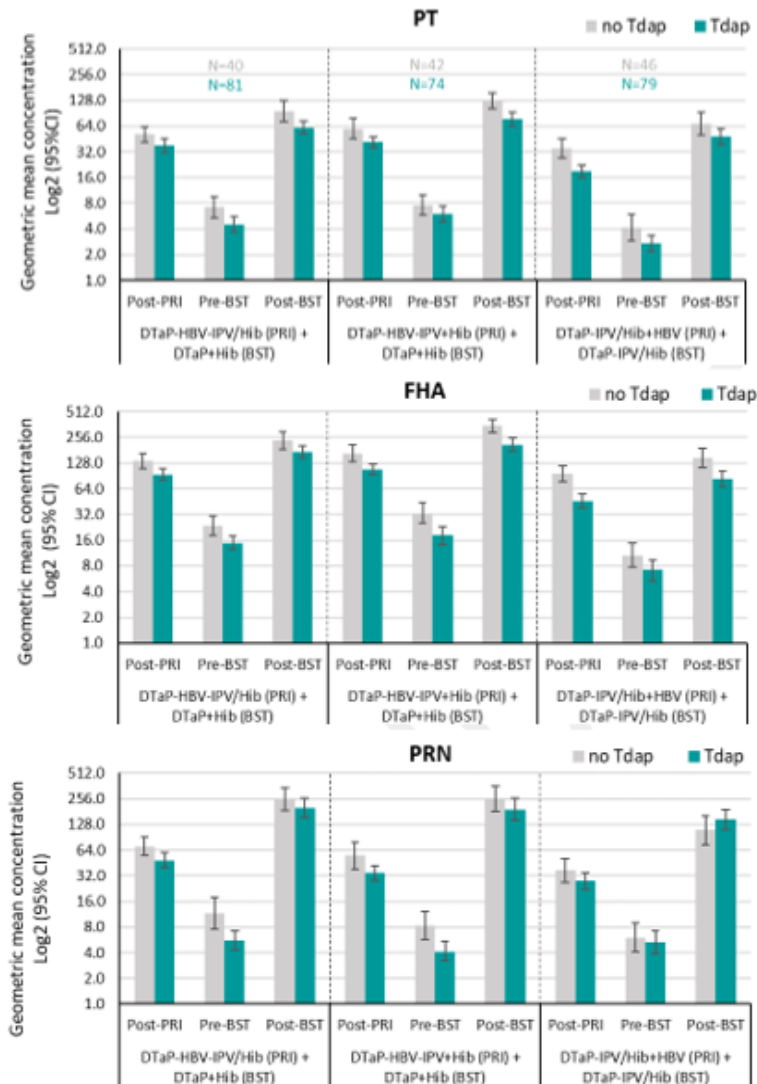
Methods: In this phase III, open-label, randomized, controlled study (NCT02096263), we randomized infants (1:1:1) to receive primary and booster vaccination with DTaP-based combination vaccines at 2-4-6 and 15-18 months (M) of

age. We assessed antibody geometric mean concentrations (GMCs) for pertussis toxoid (PT), filamentous hemagglutinin (FHA) and pertactin (PRN) using enzyme-linked immunosorbent assays at 1M post-primary, pre-booster and 1M post-booster vaccination. We performed an exploratory analysis on a subgroup of infants for whom maternal Tdap immunization was known.

Results: Maternal Tdap vaccination status was known for 379/466 (primary) and 339/408 (booster) evaluable infants. Antibody GMCs for PT, FHA and PRN were observed to be lower post-primary and generally post-booster if mothers had received Tdap during pregnancy (Figure).

Conclusions: This exploratory analysis found that maternal Tdap vaccination lowered infant responses to pertussis immunization. These data are consistent with other studies conducted to date but should be interpreted with caution as no formal statistical comparison was performed and potential confounders were not adjusted for. Other studies will be needed to better understand this phenomenon. The clinical relevance of immunological interference remains unknown and has not been reported to impact DTaP effectiveness.

Figure. Pertussis antigen responses (PT, FHA, PRN) post-primary, pre-booster and post-booster in infants in the 3 study groups, stratified by maternal Tdap immunization status (no Tdap/Tdap)



CI, confidence interval; BST, booster; FHA, filamentous hemagglutinin; PRI, primary; PRN, pertactin; PT, pertussis toxin; no Tdap, the subgroup of infants whose mothers did not receive the reduced antigen content tetanus, diphtheria, acellular pertussis (Tdap) vaccine during pregnancy; Tdap, the subgroup of infants whose mothers received Tdap during pregnancy; N, maximum number of infants with available results in each group and for each antigen, by maternal Tdap status in the primary and booster according-to-protocol cohort for immunogenicity. DTaP-HBV-IPV/Hib, hexavalent diphtheria, tetanus, acellular pertussis, hepatitis B, inactivated poliovirus and *Haemophilus influenzae* type b (Hib) vaccine; DTaP-HBV-IPV, diphtheria, tetanus, acellular pertussis, hepatitis B, and inactivated poliovirus vaccine; DTaP-IPV/Hib, diphtheria, tetanus, acellular pertussis, inactivated poliovirus and Hib vaccine; DTaP, diphtheria, tetanus, acellular pertussis vaccine; Hib, monovalent Hib conjugate vaccine; HBV, hepatitis B vaccine

Poster 70

Effects of maternal or neonatal immunization with Prevenar13™ on infant cellular responses: induction of immunological tolerance or early priming?

Sophie Roetyncck¹, Mustapha Jaiteh¹, Amadou Faal¹, Fatoumatta Foon¹, Michael Okoye¹, Claire Oluwalana¹, Mustapha Bittaye¹, Ebrima Bah¹, Ebrima Kanteh¹, Francis Oko¹, Ed Clarke¹

¹Vaccines and Immunity Theme, Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine, Fajara, The Gambia

Background: Maternal and neonatal vaccination represent important strategies to protect infants from life-threatening infections but their effects on T cell development and subsequent vaccine responses remain unknown. Foreign antigen exposure prenatally or immediately after birth has long been thought to induce lifelong tolerance. Yet, neonates can mount significant T cell responses to vaccine antigens. Although controversial, it is possible that, similarly to exposure to maternal infection *in utero*, vaccination during pregnancy may also prime the foetal immune system.

Methods: These data are generated in a blinded trial, exploring the effect of maternal (28-34 weeks gestation) or neonatal (within 1 week of life) Prevenar13™ vaccination on infant pneumococcal carriage up to 9 months of age. To determine how both regimens could affect infant cellular immunity, T cell responses to the protein carrier (diphtheria toxoid (DT)) are analysed at time points up to the end of their primary series. IFN-g (Th1) and IL-5 (Th2) secreting T cells following *in vitro* stimulation with DT and tetanus toxoid (TT) are enumerated in the blood of mothers at delivery and their infants at birth, 2 and 5 months of age, using a FluoroSpot assay. All expectant mothers receive TT vaccination and all infants receive TT and DT according to the national EPI schedule; hence TT is used as a control antigen.

Results: A mixture of Th1 and Th2 TT-specific T cell responses was observed in all maternal samples, while weaker DT-specific (predominantly IFN-g+) responses were detected. Infant TT and DT-specific responses were weak, Th2-biased and increased with age, suggesting immunity rather than anergy. Some antigen-specific responses were detected in cord blood, possibly resulting from prenatal *in utero* priming.

Conclusion: These preliminary blinded data confirm our ability to detect antigen-specific T cells in this cohort. These responses will be compared between vaccination regimens and ultimately correlated with infant pneumococcal-specific humoral responses.

Poster 71

Factors associated with seropositive vaccine responses following influenza vaccination during pregnancy.

Clarke M, Marshall H, Giles L, Sullivan S, Barr I

Introduction/Background & Aims: Influenza vaccination is recommended for pregnant women, offering the dual benefit of protecting pregnant women and their newborn infants. This study aimed to investigate factors affecting vaccine responses following influenza vaccination during pregnancy.

Methods: Pregnant women attending antenatal clinics at the Women's and Children's Hospital in South Australia during 2014-2016 were enrolled. Participant's clinical and demographic factors including height, weight, age and gestation at vaccination were recorded prior to administration of licensed seasonal influenza vaccination. Receipt of prior influenza vaccines (during last 12 months) was recorded. Pre- and 1 month post- vaccination blood samples were collected to measure antibody responses by haemagglutination inhibition (HI) assay. Seropositivity was defined as a post vaccination HI titre ≥ 40 . Chi-squared or Fisher's exact tests were used to compare proportions between groups.

Results: Most pregnant women (72/90, 80%) demonstrated seropositive antibody titres to all three influenza vaccine strains (H1N1, H3N2 and B) following vaccination. More women were seropositive following vaccination in 2014 (39/43, 91%) compared with 2015 (19/29, 66%) and 2016 (14/18, 78%) ($p=0.031$). Seropositivity was comparable amongst women of high versus normal body mass index (BMI) (22/24, 92% vs 50/68, 74%; $p=0.09$). Women

vaccinated during their second trimester were more likely to achieve seropositivity to all three vaccine antigens (47/53, 88%) compared with women vaccinated during the first trimester (7/12, 58%); $p=0.024$). There was little evidence of any association of seropositivity with maternal age or prior receipt of influenza vaccination.

Conclusions: Maternal age or BMI did not affect likelihood of achieving seropositive antibody responses to influenza vaccination in pregnant women. Variability by year vaccinated was apparent. Gestation at vaccination may be an important consideration for optimising vaccine protection for pregnant women and their newborns; however, larger studies assessing first trimester vaccine responses are warranted.

Poster 72 Withdrawn

Stimulants of infant responses to vaccines in presence of maternal immunoglobulins

Nalubega R.¹, Muyonjo N.¹, Kimsitu F.X¹, Nakatudde R.¹, Katubwe .J²

Poster 73

Demographic and health factors associated with infant respiratory deaths in Lusaka, Zambia

Gill C, Forman L, MacLeod B, Mwananyanda L, Thea D

Introduction / Background & Aims: Infants in low income countries die from respiratory diseases at a high rate. From data collected in our ZPRIME study in Lusaka Zambia, which assessed medical circumstances of all infant deaths, we sought to correlate maternal demographic, socioeconomic, and health history characteristics with respiratory mortality. We hypothesized that identifiable demographic and health characteristics of infant respiratory deaths would differ systematically among non-respiratory deaths.

Methods: By chart and death certificate review and in-depth query of family members about the pre-death events of children who died at University Teaching Hospital in Lusaka, Zambia, three physicians individually classified deaths as due to respiratory or non-respiratory causes and then adjudicated the differences. We used log binomial regression to calculate prevalence ratios and 95% CI for descriptive characteristics.

Results: Of 308 in-hospital deaths among children 4 days to 6 months, seen over 17 months, 86 (28%) were classified as respiratory, compared to 66% non-respiratory and 6% with no consensus. The proportion of infant respiratory deaths increased with age: 12% among 4 day to <1 month infants and 66% among 1 to <6 month of age infants. (PR: 5.50; 95% CI (3.73-8.13)). Infant respiratory deaths were more likely to have HIV positive mothers (1.91 (1.34, 2.72)). Other factors with suggested associations to respiratory death included: parental secondary education (1.39 (0.85, 2.27)), employment (employed vs. not, 1.19 (0.71, 1.99)), facility birth (1.17 (0.64, 2.13)), and birth complications (0.70 (0.36, 1.33)). Household size (1.00 (0.94, 1.06)) was not associated.

Conclusion: Respiratory death increased in frequency from the neonatal to the post-neonatal period of infancy, when it becomes far more common. A partial explanation is the preponderance of deaths due to prematurity and birth complications during the early neonatal period. Respiratory deaths also appeared more common among infants of mothers infected with HIV.

Poster 74

Vaccination-induced, cell mediated immunity in peripheral blood of young infants in the Gambia

Dr Julia Strandmark, Dr Alansana Darboe, Prof Beate Kampmann, EPIC-HIPC Consortium

Introduction/Background & Aims: Anti-Hepatitis B virus (HBV) surface antigen antibodies are a well-established correlate of protection in response to HBV vaccination. In contrast, T-cell responses are poorly understood and have not been assessed in detail in the neonate.

CD4+ T-cells can contribute to immunity following vaccination both by supporting the development of humoral immunity and/or by providing alternative pathways of protection. Efforts to investigate these possibilities have been hampered by the challenges involved with measuring antigen specific T-cell responses, especially in the small

volumes of blood available from neonates.

Here we present a cell mediated immune assay that allows us to quantify antigen specific T-cell responses in vaccinated infants and determine the relationship between CD4+ T-cell immunity and antibody titres early in life.

Methods: PBMCs were isolated from vaccinated neonates enrolled in the EPIC-HIPC study in the Gambia. Following *in vitro* re-stimulation with HBV and BCG, CD40L (CD154) was used to detect antigen specific CD4+ T-cells. Activation, as well as memory cell markers were additionally included to further dissect T-cell functionality.

Results: Low levels of HBV and BCG specific CD4+ T-cells were detectable in vaccinated infants one month following vaccination. Completion of full vaccination schedule increased frequencies of antigen specific T-cells.

Conclusions: This assay can be used to detect antigen specific CD4+ T-cells in the blood of neonates as young as one month old. The data collected will help us understand the relationship between T-cell immunity and development of protective antibodies early in life.

Poster 75

Infant immune responses to diphtheria-tetanus-acellular pertussis and 13-valent pneumococcal conjugate vaccines are comparable in children whose mothers received a first or subsequent Tdap booster during pregnancy

Miss Sonia McAlister, Dr Anita van den Biggelaar, Miss Camille Gibson, Mrs Karli Corscadden, Dr Ruth Thornton, Assoc. Professor Peter Richmond

Introduction/Background & Aims: Maternal pertussis immunizations protect infants against severe pertussis disease before they can receive their own vaccinations, but have been associated with blunting of infant antibody responses to some antigens in the primary vaccination series. We investigated if this effect was enhanced in infants whose mothers received a repeated Tdap immunization during pregnancy.

Methods: Infants (n = 62) were recruited in Perth, Australia, before receiving their primary immunizations with diphtheria-tetanus-acellular pertussis vaccine (DTPa; 2, 4 and 6 months) and 13-valent pneumococcal conjugate vaccine (PCV13; 2 and 4 months). Maternal pertussis immunization status was assessed retrospectively. IgG responses to diphtheria toxoid (DT), tetanus toxoid (TT), pertussis toxin (PT), filamentous hemagglutinin, pertactin, fimbriae, and PCV13-serotypes were measured before and after completion of primary vaccination (age 7 months). Seroprotection was defined as PCV13-IgG ≥ 0.35 $\mu\text{g/mL}$, and TT- and DT-IgG ≥ 0.1 IU/mL, and PT-IgG ≥ 5 IU/mL as seropositive.

Results: Twenty women had received a first, and 42 a subsequent Tdap dose in this pregnancy. The average time between subsequent doses was 3.3 years (range 0.8 – 8.6).

GMCs and seropositive/seroprotective rates for DTPa and PCV13-specific IgG responses after primary vaccinations were comparable for infants whose mothers had received a first or subsequent Tdap booster, regardless of whether the recent dose was within two years or longer since the previous dose. Infant PT-IgG titers before and after primary vaccinations were inversely correlated (R=-0.6, p<0.0001), and the same was found for DT-IgG (R=-0.5, p<0.0001).

Conclusions: These preliminary results imply that repeated Tdap vaccination in pregnancy does not lead to greater interference of childhood immunization responses. Maternal transfer of higher antibody titers may provide better protection in the first weeks of life but may reduce infant responses to childhood vaccines. These findings support administering maternal Tdap boosters during subsequent pregnancies to protect vulnerable infants.

Poster 76

Juno: a global genomic survey of *Streptococcus agalactiae* to inform disease prevention strategies and vaccine development

Dorota Jamrozy¹, Arie van der Ende^{2,3}, G Gopal Rao^{4,5}, Stephen D Bentley¹, Juno Consortium

¹ Wellcome Sanger Institute; ² Department of Medical Microbiology, Academic Medical Center, University of Amsterdam, Amsterdam Infection & Immunity, Amsterdam, Netherlands; ³ Netherlands Reference Laboratory for Bacterial Meningitis, Amsterdam, Netherlands; ⁴ Departments of Microbiology, Northwick Park Hospital, Harrow, UK; ⁵ Faculty of Medicine, Imperial College, London, UK

Introduction/Background & Aims: Group B *Streptococcus* (GBS), also known as *Streptococcus agalactiae* is an opportunistic pathogen and a leading cause of infant invasive disease worldwide. A great deal of scientific investment has been focused on the development of maternal GBS vaccine for prevention of infections in newborns. This can be supported by improving our understanding of GBS diversity, transmission and the role of GBS genetics in development of disease.

Methods: We use whole genome sequencing to study GBS from diverse sources, focusing on isolates from infant disease and maternal carriage. With support from the Bill and Melinda Gates Foundation, we have launched **Juno**, an international collaboration to perform a global genomic survey of GBS, and we are actively seeking further project partners.

Results: We are currently in the process of building a global GBS sample collection for genomic analysis, aiming to sequence at least 10,000 isolates. Using results from previous GBS studies we can demonstrate the value of genomics for studying GBS as a pathogen and a colonizer. We performed a genomic analysis of a nationwide collection of 1345 infant invasive disease isolates, collected between 1987 and 2016 in the Netherlands. Using genomic data, we were able to identify a correlation between temporal changes in population structure of GBS and rise in the disease incidence over time. In another study of 536 UK GBS isolates from maternal carriage in an ethnically diverse community, we identified a high level of genetic diversity but low prevalence of rare serotypes that were limited to specific GBS genotypes.

Conclusions: Through **Juno**, we will build a large genomics data resource for GBS. We believe this will lead to new major insights into the genetics and evolution of GBS and serve to inform global vaccine coverage and infer possible impact of vaccine implementation on the pathogen population.

Poster 77

Defining the timing for delivery of a maternal respiratory syncytial virus vaccine using antenatal care gestational age data among pregnant women in Kilifi, Coastal Kenya.

Joyce U. Nyiro¹, Elizabeth Bukusi^{2,3}, Dufton Mwaengo³, Patrick Munywoki⁴, David Walumbe¹, Amek Nyaguara¹, Nancy Otieno⁶, Bryan Nyawanda⁶, James A. Berkley¹ and D James Nokes^{1,4 5}

¹. Kenya Medical Research Institute (KEMRI)-Wellcome Trust Research Programme, Centre for Geographic Medicine Research-Coast, Kilifi, Kenya; ². Kenya Medical Research Institute (KEMRI), Centre for Microbiology Research, Nairobi, Kenya; ³. University of Nairobi, Institute of Tropical and Infectious Diseases, Nairobi, Kenya; ⁴. Pwani University, Kilifi, Kenya ⁵. School of Life Sciences and Zeeman Institute (SBIDER), University of Warwick, Coventry, UK ; ⁶. Kenya Medical Research Institute (KEMRI), Centre for Global Health Research, Kisumu, Kenya

Introduction/Background & Aims: Maternal Immunisation to boost respiratory syncytial virus (RSV) specific antibodies in pregnant women is being considered a realistic approach to protect infants and postpone the first natural RSV infection. Despite progress towards licensure of a leading candidate maternal RSV vaccine, Kenya has no data on gestational age distribution of pregnant women attending antenatal care (ANC) or the proportion of women attending ANC during the proposed window period for vaccination to inform appropriate delivery of this vaccine.

Methods: This cross-sectional study conducted within the Kilifi Health and Demographic Surveillance System (KHDSS) included a random sample of 1000 women registered pregnant in the years 2017 and 2018. By the time of data

collection they had a birth outcome. They were tracked to their homes, if willing, consented for participation in the study and records of their antenatal attendance during pregnancy abstracted from their ANC booklet.

Results: Of the 1000 women selected, 553 (55%) with ANC booklets were available for interview. Median age was 28 years. The median gestational age measured by fundal height at attendance for ANC1 to ANC5 was 26 weeks (Interquartile Range IQR: 21-28), 29 (IQR: 26-32), 32 (IQR: 28-34), 34 (IQR: 32-36) and 36 (IQR: 34-38), respectively. The median gestational age at birth was 38 weeks (IQR: 36-40). The proportion of women attending ANC during the proposed World Health Organization (WHO) window of vaccination (28-32 weeks) was 64% (354), compared to the observed proportion for a vaccination window at 26-33 weeks of 71% (391).

Conclusions: If delivery of the maternal RSV vaccine is scheduled at 26-33 weeks of gestation, the coverage will be 71% of the women attending ANC in Coastal Kenya, which is higher than the proposed window. However, widening the vaccination window requires incorporating data on RSV antibody kinetics in pregnant women to inform vaccine efficacy.

Poster 78

Adverse outcomes associated with invasive pneumococcal disease during and pregnancy and the postpartum period

Z. Amin¹, S. Collins¹, C. Sheppard², D. Litt², N. Fry¹, S. Ladhani¹

¹ Immunisation and Countermeasures Division, Public Health England, London, UK; ² Respiratory and Vaccine Preventable Bacteria Reference Unit, Public Health England, London, UK

Introduction/Background & Aims: The risk and burden of invasive pneumococcal disease (IPD) during pregnancy and the post-partum period remains largely unknown. Here, we describe the clinical characteristics, serotype distribution and outcomes of IPD in pregnant women and their infants in England over a 4 year-period.

Methods: Public Health England (PHE) conducts enhanced surveillance of IPD in England. The 13-valent pneumococcal conjugate vaccine (PCV13) was introduced into the UK immunisation schedule in 2010. For this analysis, all confirmed IPD cases in women aged 15-44 years who were reported to be pregnant within 30 days of IPD diagnosis between 01 July 2014 and 30 June 2018 were included.

Results: During the 4-year surveillance period, 48 women with a median age of 34 (IQR 26-35) years had laboratory-confirmed IPD during pregnancy or the post-partum period. Where gestational age was known (n=43), 6 (14.0%) developed IPD during the first trimester, 10 (23.3%) in the second trimester, 20 (46.5%) during the third trimester and the remaining 16.3% postpartum. Only 10/48 women (20.8%) had an underlying comorbidity and the most common clinical presentation was pneumonia (28/47, 59.6%). Ten women delivered at time of IPD and, where known (n=6), all had emergency caesarian section. Seven women required intensive care and one died before giving birth. Eight of the 48 reported cases (16.7%) were due to PCV13 serotypes, 29/48 (60.4%) due to the additional PPV23 serotypes and 11/48 (22.9%) due to non-PPV23 serotypes. Adverse foetal outcomes associated with IPD included miscarriage (n=4), ectopic pregnancy (n=1), stillbirth (n=1), termination of pregnancy (n=1), and premature birth (n=7). Only one infant died because of a severe congenital abnormality and unrelated to infection.

Conclusions: IPD during pregnancy is mainly due to vaccine-preventable serotypes and is associated with significant morbidity for the mother, the foetus and the newborn infant.

Poster 79

How much of neonatal invasive pneumococcal disease (IPD) is vaccine-preventable? A prospective observational cohort study, 2014-18

Z. Amin¹, S. Collins¹, C. Sheppard², D. Litt², N. Fry¹, S. Ladhani¹

1 Immunisation and Countermeasures Division, Public Health England, London, UK; 2 Respiratory and Vaccine Preventable Bacteria Reference Unit, Public Health England, London, UK

Introduction/Background & Aims: Invasive pneumococcal disease (IPD) is a major cause of morbidity and mortality worldwide, but is rare among neonates. Here, we describe the clinical characteristics, serotype distribution and outcomes in infants, focusing particularly on early-onset and late-onset disease, over the past 4 years.

Methods: Public Health England (PHE) conducts enhanced IPD surveillance in England and provides a national reference service for serotyping of invasive isolates. The 13-valent pneumococcal conjugate vaccine (PCV13) was introduced into the UK immunisation schedule in 2010. Confirmed IPD cases in infants (<1-year-olds) between 01 July 2014 and 30 June 2018 were included in the analysis. Early-onset was defined as cases diagnosed within 7 days of birth and late-onset as those diagnosed at 7 to 89 days of age.

Results: Of the 504 IPD cases in infants, 458 (90.1%) isolates were serotyped. There were 46 (10.0%) early-onset, 86 (18.8%) late-onset and 326 (71.2%) cases in infants aged 90 days to one year. Comorbidity prevalence was 13% (n=6), 12% (n=10) and 19% (n=61), respectively. Bacteraemia (23/46, 50.0%) was the most common clinical presentation among early-onset cases, compared to meningitis (39/86, 45.4%) among both late-onset and older infants (142/326, 43.6%). Among the three groups, 29 (63.0%), 11 (12.8%) and 55 (16.9%) were reported to be born prematurely (<37 weeks). Serotype distribution also varied, with 47.8% (n=22), 25.6% (n=22) and 7.4% (n=24) of IPD cases due to PCV13 serotypes and 39.1% (n=18), 44.2% (n=38) and 54.4% (n=193) due to one of the additional 13 serotypes covered by pneumococcal polysaccharide vaccine (PPV23). CFR was 6.5% (3/46) in early-onset, 7.0% (6/86) in late-onset and 3.4% (11/326) among older infants.

Conclusions: Almost one-third of IPD cases in infants occur prior to routine infant immunisations. Early-onset cases were associated with a high prevalence of premature births. Most cases in young infants were due to vaccine-preventable serotypes.

Poster 80

Evaluating the Effectiveness of CMV Vaccination on Preventing the Occurrence of Congenital Abnormalities

Byrne C, Gantt S

University of British Columbia

Introduction/Background & Aims: Cytomegalovirus (CMV) congenital infection is a major cause of permanent neurodevelopmental damage. Thus, the development of a CMV vaccine has long been a top public health priority. Despite CMV's high prevalence, CMV has been shown to be very inefficient at establishing infection; thus, we hypothesize the probability of transmission is driven primarily by the frequency and viral load of exposures. A vaccine that can even modestly reduce the viral load of shedding in the donor, and/or viral spread in the recipient, should greatly reduce transmission and disease burden. Using mathematical modelling, we aimed to determine what vaccination strategies may effectively reduce the occurrence of CMV congenital infection.

Methods: We developed a mathematical model to accurately describe the current CMV transmission dynamics within the population. Parameters governing the major routes of CMV transmission, namely transmission between mothers and babies and transmission among children in daycare, were informed by pre-existing data on the prevalence and dynamics of CMV infection. Using our model, we next analyzed the effects of vaccines when given to different age groups and to different proportions of the population.

Results: We found that vaccines that provide sterilizing immunity were not essential for reducing the incidence of congenital CMV infection. Rather, imperfect vaccines that sufficiently decrease susceptibility, reactivation and/or viral shedding in an individual, and are given to a high enough proportion of the population were sufficient. Vaccines

targeting young children, who are the largest spreaders of CMV, proved most effective at reducing the burden of CMV in the population.

Conclusions: Up until now, invoking sterilizing immunity against CMV has been thought to be the only way of effectively reducing the burden of CMV on the population. Our results, however, suggest that imperfect vaccines, perhaps even ones which have already been developed, should be re-evaluated and may prove equally effective.

Poster 81

The epidemiology of respiratory syncytial virus (RSV) among the hospitalized paediatric population aged 0-16 years in Canada, 2017-2018

Bettinger J, Sandhu S, Shane A, Vaudry W, Embree J, Bancej C, Killikelly A, Tunis M, House A, Le Saux N, Langley J, Lebel M, Morris S, Papenburg J, Robinson J, Sadarangani M, Tran D, Halperin S

Introduction/Background and Aim(s) RSV is the leading cause of hospitalization for acute lower respiratory infection among infants in North America. Candidate vaccines intended for use in pregnant women, children and the elderly are in clinical trials. To consider recommendations for future RSV vaccines licenced in a Canadian market, Canada's National Advisory Committee on Immunization (NACI) requires up-to-date and comprehensive data on the burden of RSV disease in Canada. This surveillance pilot was initiated to describe the epidemiology of Canadian children hospitalized with RSV from 2017 to 2018.

Methods RSV surveillance was conducted in 11 of the 12 hospitals participating in the Canadian Immunization Monitoring Program ACTIVE (IMPACT), a national paediatric hospital-based surveillance network representing approximately 90% of all tertiary care paediatric beds in Canada. Demographic, health care utilization and outcome data were collected between November 1, 2017 and June 30, 2018 on all patients 0-16 years of age positive for RSV. Descriptive analyses were conducted using SAS EG 5.1.

Results 2178 patients with RSV were identified during the surveillance period. Hospitalizations peaked the week of December 24-30, 2017. Median age was 6 months (IQR: 1-19 months), with the largest proportion (16%) among 1 month olds, and 52% aged ≤ 6 months. 54% of the cases were male. Median length of hospitalization was 3 days (IQR: 2-6 days), 22% were admitted to the ICU and 2 deaths were reported.

Conclusions The highest burden of disease in the pediatric hospitalized population is in young infants (0-6 months). The pilot continues through 2018/19 and has expanded to include data on underlying health conditions, clinical manifestations, indicators of severity, co-infection, virus subtyping and partial genome sequencing. These data will inform vaccine guidance development.

Poster 82

A road less traveled: mapping the maternal RSV vaccine journey ahead—from development through delivery

Jessica Fleming¹, Philipp Lambach², Nathalie Roos², Sadaf Khan¹, Evan Simpson¹, Deborah Higgins¹
1PATH, Seattle, WA, US; 2WHO, Geneva, Switzerland

Background: While vaccines are one of the most powerful disease prevention interventions in global health, achieving protection via active immunization often requires multiple doses given over time, leaving infants susceptible to some life-threatening diseases that occur in the first months of life. Maternal immunization (MI) could address a number of infectious disease threats that disproportionately affect young infants in low- and middle-income countries (LMICs), including respiratory syncytial virus (RSV) and Group B *Streptococcus*. Despite a safe and effective track record against several diseases, MI's full potential has yet to be tapped and its availability in LMICs is limited. Charting a clear path to enable efficient, well-informed decisions around MI introduction in LMICs is needed.

Methods: The Advancing Maternal Immunization (AMI) collaboration, led by PATH in collaboration with WHO, aims to enable efficient, well-informed decisions around RSV MI introduction in LMICs. In 2017-18, AMI engaged cross-sectoral experts to identify activities required to inform evidence-based global and country decisions around if and how to implement MI against RSV in LMICs. AMI conducted a gap analysis to identify information needs related to

RSV disease, maternal vaccines, health economics, and vaccine delivery specific to LMIC contexts. These findings informed the development of a roadmap.

Results: *A Roadmap for Advancing RSV Maternal Immunization* outlines priority activities and timeframes to meet information needs related to RSV MI. The roadmap complements existing guidance documents and takes a broad view of activities required to inform the vaccine development to delivery continuum.

Conclusions: A strategy for preventing infectious diseases during infancy is urgently needed, particularly in LMICs. AMI's roadmap outlines priority activities to ensure meaningful vaccine impact against one of these diseases, RSV. While specific for maternal RSV vaccines, many of the activities described are applicable to all maternal vaccines and the roadmap can be used to inform a broader maternal immunization platform.

Poster 83

Respiratory syncytial virus associated hospitalisations in Australian infants: Essential data to inform future maternal vaccination strategies

Saravanos G, Sheel M, Homaira N, Quinn H, Dey A, Wang H, Britton P, Macartney K, Wood N

Introduction/Background & Aims: Respiratory syncytial virus (RSV) disease is a leading cause of infant hospitalisation. One maternal vaccine candidate recently reported 44% efficacy against RSV lower respiratory tract infection hospitalisation for infants <90 days of age. Assessing RSV-associated early infant hospitalisations will inform the assessment of potential maternal vaccine impact.

Methods: We estimated rates of RSV-associated hospitalisation in Australian infants aged <6 months by month of age, sex and Indigenous status for 2011-2015 using International Classification of Diseases version 10 Australian Modified (ICD-10-AM) diagnosis codes (RSV bronchiolitis (J21.0), RSV pneumonia (J12.1), RSV bronchitis (J20.5) and RSV organism (B97.4), as well as unspecified bronchiolitis-coded hospitalisations (J21.9). We also described length of stay (LOS), in-hospital deaths and procedure codes. In addition, clinical review was undertaken on ICD-coded and RSV-test positive infant deaths at a single Sydney Hospital over a 20 year period.

Results: We identified 18,006 principal RSV-coded hospitalisations nationally, the majority coded as RSV bronchiolitis (98.2%). The hospitalisation rate was 2369 per 100,000 population aged <6 months; the highest rate was at 1 month of age (3805 per 100,000). Median LOS was 3 days (IQR 2-4) and an invasive ventilation procedure code was recorded in 1.6% of episodes. Hospitalisation rates were higher in males than females (IRR 1.2 [1.2-1.3]) and Indigenous than other infants (IRR 1.9 [1.8-2.0]). There were an additional 20,842 unspecified bronchiolitis-coded hospitalisations most coinciding with RSV seasons. In total, nine in-hospital deaths were recorded nationally. Data on clinical review of RSV-associated deaths will be presented.

Conclusions: This analysis of national hospitalisations provides valuable insight into severe RSV-associated disease in Australian infants. However, analysis of RSV-coded hospitalisations alone likely represents minimum rate estimates. Indigenous infants appear at higher risk from RSV disease compared with other infants. Maternal vaccination has the potential to substantially reduce the burden of RSV disease in Australia.

Poster 84

Group B streptococcus neonatal invasive infections in Belgium 2010-2017, and characterization of isolated strains

Melin P, Sacheli R, Lambotte O, Hayette M, Descy J, Huynen P, Meex C

Introduction/Background & Aims: Where intrapartum antibiotic-prophylaxis (IAP) is given to pregnant women colonized with Group B Streptococcus (GBS), the incidence of neonatal early-onset disease (EOD) has been successfully reduced; nevertheless, GBS is still the leading cause of severe disease among newborns, notably because the incidence of GBS late-onset disease (LOD) is not affected by IAP. Another strategy such as maternal immunization for prevention of both EOD/LOD is highly desirable worldwide.

Aiming to describe GBS epidemiology and characterization of relevant epidemiological markers for vaccine development, surveillance of isolates causing neonatal disease is needed.

We provide here results from the Belgian surveillance organized by the National Reference Centre(NRC).

Methods: A total of 292 strains of GBS isolated from blood culture/cerebro-spinal fluid of newborns with invasive disease (149 EOD; 143 LOD) were sent to NRC by laboratories of a surveillance network, through years 2010-2017. Capsular-polysaccharide (CPS)-typing and pili-typing were performed with multiplex PCR assays. Multilocus sequence-typing and assignment to the hypervirulent clonal-complex (CC)17 was determined.

Results: CPS type III isolates were responsible for 38.9% (n=58) of EOD cases, followed mainly by types Ia, V and II (22.1%, 18.1%, 8.1%). LOD cases were mainly caused by type III isolates (n=107, 74.8%), followed by types Ia (12.6%), V, Ib, IV and II (4.2%, 3.5%, 2.8%, 2.1%). These distributions did not vary during the study period. A pili type was assigned to all isolates: at least one pili gene, PI2a, PI2b, or a combination of genes PI1-PI2a and PI1-PI2b. In 2016-2017, the hypervirulent-clone CC17 accounted for 33.3% of EOD (70.4% of type III) and 67% of LOD (89% of type III).

Conclusions: The Belgian CPS distributions of isolates from EOD/LOD were similar to European data. One or 2 of 3 pilus-genes were detected in all isolates.

CPS type III was predominant in both EOD/LOD and was mainly represented by CC-17 strains.

Poster 85

Aptitude of Verbal Autopsy (VA) tool for discerning respiratory symptoms among deceased infants tested for Respiratory Syncytial Virus (RSV) in Lusaka, Zambia.

Gill C, Wagh O, MacLeod B, Forman L, Mwananyanda L, Thea D

Introduction/Background & Aims: The Zambia Pertussis RSV Infant Mortality Estimation (Z-PRIME) study analyzes data of deceased infants to determine the burden of preventable infant mortality due to *Bordetella Pertussis* and RSV. A Verbal Autopsy tool (VA), created and validated by the Population Health Medical Research Council (PHMRC) group, was used to collect clinical data on infant deaths which occurred outside of a hospital setting, and to categorize them as respiratory, non-respiratory or unknown. In order to determine the accuracy of the verbal autopsy, we evaluated it on 2 criteria:

1. Usefulness of the VA tool in classifying respiratory vs. non-respiratory death.
2. Ability of the VA tool to successfully determine the etiology (i.e. RSV status) of deaths.

Methods: The total number of subjects who died outside of a hospital setting and were adjudicated as respiratory deaths was 234. Nasal swabs for these subjects were collected and analyzed for RSV. Descriptive statistics for respiratory symptoms, stratified by RSV status, are presented below.

Results:

Symptoms	Respiratory symptoms among infant respiratory deaths					
	RSV Positive (n = 20)			RSV Negative (n = 214)		
	Yes	No	Don't know	Yes	No	Don't know
Cough	13(65%)	6(30%)	1(5%)	85(40%)	126(59%)	3(1%)
Difficulty breathing	14(70%)	5(25%)	1(5%)	75(35%)	131(61%)	8(4%)
Fast breathing	1(5%)	17(85%)	2(10%)	42(20%)	146(68%)	26(12%)
Grunting sound	1(5%)	16(80%)	3(15%)	40(19%)	152(71%)	22(10%)

Conclusions: The verbal autopsy tool is a useful way to determine death due to respiratory causes. However, as a stand-alone tool, the VA tool is not suitable for identifying the underlying etiology (i.e. RSV status) of these deaths, as some respiratory symptoms do not clearly divide according to RSV status.

Poster 86

Immunity by proxy: protection of neonatal mice from HSV challenge mediated by passive antibody therapy of their mothers

Backes I, Patel C, Taylor S, Ackerman M, Leib D

Introduction/Background & Aims: Neonatal herpes (nHSV) infections commonly have high mortality and morbidity despite aggressive antiviral therapy, leaving many survivors with lifelong neurological sequelae. Neonatal infection is most likely to be transmitted during birth by a newly-infected, HSV seronegative mother. However, epidemiological and animal studies have demonstrated that maternal antibodies protect neonates from clinically evident nHSV infections. We propose to utilize administration of monoclonal antibodies (mAbs) to the maternal circulation during pregnancy to protect vulnerable neonates.

Methods: Using a mouse model we investigated the ability of mAbs to prevent nHSV-associated morbidity and mortality. Expecting dams or 1-2 day old pups were infused with HSV-specific mAbs. Pups were subsequently challenged with HSV and monitored for nHSV-associated morbidity and mortality. Dissemination of nHSV was assessed via a luciferase-expressing HSV, which allows for real time infection monitoring. Neurological morbidity was assessed via the open field test, which has been validated to assess anxiety-like behavior.

Results: Administration of mAbs to expecting dams protects mouse pups from nHSV-associated morbidity and mortality. Disseminated disease was significantly reduced in pups treated with HSV-specific antibodies, particularly in groups where mAbs were maternally transferred. In addition, pups treated with HSV specific mAbs display reduced anxiety-like behavior when compared to isotype control-treated controls.

Conclusions: Maternal administration of HSV specific mAbs is a promising strategy to protect neonates from HSV. Addition of mAbs to existing antiviral therapy may help overcome the challenges in preventing the mortality and neurological morbidity associated with disseminated and CNS disease. Looking forward, the versatility of mAbs to be engineered presents an opportunity to further optimize maternal administration for neonatal protection from disease.

Poster 87

Seasonality of Respiratory Syncytial Virus Infection in infants and young children in Lusaka, Zambia

Gill C, Nakazwe R, MacLeod B, Forman L, Mwananyanda L, Thea D. Presented by Rachel Pleciak

Introduction: Respiratory Syncytial Virus (RSV) is a significant cause of respiratory infections with high morbidity and mortality in young children, affecting about 60 – 70% of children before the age of 1 year, globally. To improve the management RSV infections it is helpful to understand the timing of RSV outbreaks in local settings. We looked at the trends in the seasonality of RSV in infants from three cohort studies that measured the disease via nasopharyngeal swabs over a period of 7 years in Lusaka, Zambia.

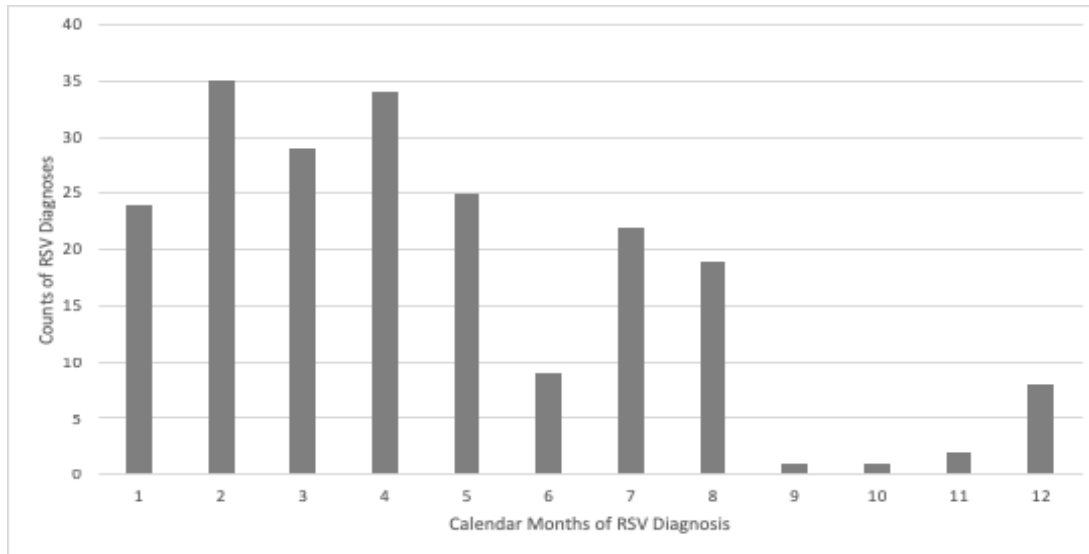
Methods: We present counts of PCR diagnosed RSV by calendar month of diagnosis from nasopharyngeal swabs. The samples came from three respiratory disease studies conducted in Lusaka from October 2011–October 2013; March 2015 to January 2016; and September 2017 to December 2018. The study populations for the three studies were 1) 1,141 children 1-59 months hospitalized with severe pneumonia sampled once; 2) a cohort of 797 healthy infants 1-13 weeks old sampled fortnightly, and; 3) 987 deceased infants 4 days to <6 months sampled within 48 hours of death.

Results: Figure 1 shows the counts of RSV was highest in the rainy season (summer) peaking in February through April. Counts of RSV infection declined into the cool dry season in the months of May to August. The lowest counts of RSV infection occurred in the hot dry season months of September to November.

Conclusions: These findings demonstrate the seasonality of RSV infection. This knowledge is important for informing public health in timely and effective management of RSV.

KEYWORDS: Respiratory Syncytial virus, immunization, seasonality, public health

Figure 1. Counts of PCR positive B. pertussis diagnoses by calendar month of diagnosis in Lusaka, Zambia



Poster 88

CRISPR Mediated vaccine: An aid for HIV Infection

Sharma V

Background: Human Immunodeficiency Virus (HIV) causes one of the world's most serious public health challenges. As per the Global Burden of Disease Study 2015, HIV/AIDS is the leading cause of death among reproductive age women. Approximately, 5% of global pregnancy related deaths were due to HIV/AIDS. Till now all over the world not a single vaccine or any stable cure is developed which can control the virus merging or expression in human genome.

Hypothesis/Methods/Results: We proposed to prevent HIV infection in our society by implementing CRISPR based vaccination approach as we know that CRISPR based mechanism is exploited by bacteria to protect themselves from virus infections. By using this mechanism we will be able to target the HIV genomic RNA at the initial stages before it can express or overpowered the host genome. By transforming CRISPR-Cas9, we propose to design a DNA vaccine by performing vector engineering. Here, we aim to design a novel vector carrying sequences for guide RNA, Cas9 and HIV antigen to develop the memory cells and immune response. It will work simultaneously to inhibit the entry of HIV by killing viruses and at the same time it may also generate the immunity according to developed memory cell against HIV antigens inserted in to the vector.

Conclusion: CRISPR/cas9 makes a RNA-DNA hybrid and this nuclease enzyme detect the specific **PAM sequences** of the viral DNA and selectively degrade the only DNA part. Therefore, by inserting a crisper gene with cas9 enzyme gene and HIV antigenic proteins, this will lead to generate memory cell. We will also add the proteins which initiates the targeting of T-helper cells. So, whenever the virus infects us the very next time the memory cell and crisper RNA is ready to degrade the viral-DNA.

Poster 89

Rectovaginal group B streptococcus colonization among pregnant women in Nicaragua: a systematic review and meta-analysis

Dr. Nadja Vielot, Mr. Christian Toval-Ruiz, Dr. Rachel Weber, Dr. Sylvia Becker-Dreps, Dr. Teresa Aleman Rivera

Introduction/Background & Aims: Maternal colonization with group B Streptococcus (GBS) is a predictor of neonatal sepsis. In Nicaragua, neonatal sepsis is a major cause of hospitalization, but it can be prevented with intrapartum antibiotic prophylaxis (IAP). We undertook this study to estimate the pooled prevalence of rectovaginal GBS colonization among pregnant women 35-40 weeks gestation in Nicaragua, and sensitivity of GBS isolates to various antibiotics.

Methods: We systematically searched electronic databases of peer-reviewed and unpublished literature using pre-specified search terms. We included English- and Spanish-language studies of rectovaginal GBS colonization and/or antibiotic sensitivity of GBS isolates that followed internationally-recognized diagnostic standards, from various sites and years. Two reviewers independently abstracted data and assessed the risk of bias in each study, pertaining to recruitment of pregnant women; validity of the information; validity of the clinical and laboratory procedures; and method of estimating GBS colonization prevalence. We then estimated the pooled prevalence of rectovaginal GBS colonization and antibiotic sensitivity of GBS isolates. We performed subgroup analyses by geographic location of the study site, urban residence of the study participants, and study risk of bias.

Results: Prevalence of rectovaginal GBS colonization from 13 samples in 11 studies was 0.14 (95% CI: 0.09, 0.20). Effect size heterogeneity was identified between coastal (0.12 [95% CI: 0.07, 0.18]) and central study sites (0.23 [95% CI: 0.18, 0.28]), and between predominantly rural (0.06 [95% CI: 0.02, 0.10]) and urban (0.28 [95% CI: 0.19, 0.37]) samples of pregnant women. We observed no effect size heterogeneity between studies with high and low risk of bias. GBS sensitivity to penicillin, the first-line IAP treatment, was 0.88 (95% CI: 0.71, 0.99) based on data from eight studies.

Conclusions: Maternal GBS colonization was substantial in some sites. Most GBS isolates are sensitive to recommended antibiotics, and IAP may effectively prevent neonatal sepsis in Nicaragua, absent a maternal vaccine.

Poster 90 Abstract withdrawn

Using Guthrie Cards for a Sero-Surveillance Study of Maternally-Derived Antibody against Group B Streptococcus Erick Auma

Poster 91

Maternal immunization with a replication defective herpes simplex vaccine candidate prevents memory loss in offspring following neonatal infection.

Chaya Patel¹, Sean Taylor¹, Jailene Paredes¹, Iara Backes¹, David Knipe², Margaret Ackerman³ and David Leib¹

1. Department of Microbiology and Immunology, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire, USA; 2. Department of Microbiology and Immunobiology, Harvard Medical School, Boston, MA, USA; 3. Thayer School of Engineering, Dartmouth College, Hanover, USA

Introduction/Background & Aims: Neonatal herpes simplex virus (nHSV) infections cause devastating morbidity and mortality in infants and maternal immunization could provide protective antibodies during this window of vulnerability. In surviving infants, nHSV often results in lifelong neurological deficits. Consistent with this pathology, there is increasing evidence to suggest a link between HSV infection and neurodegenerative diseases. Thus, we hypothesized that maternal immunization against HSV could not only prevent nHSV, but also prevent the neurological sequelae that frequently follows. HSV vaccine candidates have, to date, been unsuccessful in preventing horizontal spread in adults. Vaccine efficacy against other outcomes, such as nHSV and subsequent cognitive decline, has not been tested. In murine models, HSV infection leads to anxiety-like behavior following neonatal infection. The aim of the current study is to identify the long-term effects of HSV infection on memory and cognition, and the mechanisms by which these pathologies occur.

Methods: Using a murine model, we assessed memory, cognition, neurodegeneration, and neuroinflammation in adult and aged mice following nHSV challenge. We subsequently tested whether maternal immunization with a replication-defective vaccine candidate, HSV-2 *d/5-29*, could protect against these immunological and behavioral changes.

Results: We observed considerable and permanent impacts of nHSV infection on behavior, memory, and neurodegeneration in adult mice. Even clinically-inapparent nHSV infection accelerated memory and cognition decline over time. Importantly, these cognitive and neuropathological changes were prevented by maternal immunization with the *d/5-29* vaccine candidate.

Conclusions: This study demonstrates a novel and unexpected benefit of immunization in preventing the loss of memory and cognition that follows nHSV. These findings also support the broad notion that maternal immunization could prevent other neurotropic neonatal infections and their unsuspected impact on neuropathology and behavior.

Poster 92

Isolation of a ZIKV-neutralizing IgM from a pregnant woman in Brazil as a candidate antibody-based prophylaxis during pregnancy

Tulika Singh, Kwan Ki-Hwang, Kan Luo, Josh A. Eudailey, Helen S. Webster, Cesar A. Lopez, Premkumar Lakshmanane, Robert J. Edwards, Camila Giuberti, Summer Zhang, Morgan A. Gladden, Maria Dennis, Reynaldo Dietze, Aravinda de Silva, Helen M. Lazear, Eng Eong Ooi, Sallie R. Permar*, Mattia Bonsignori*

*Shared senior authorship

Introduction: Congenital transmission of Zika virus (ZIKV) in ~7-14% of infants born to ZIKV-infected mothers may lead to lifelong morbidity with symptoms like microcephaly, neurodevelopmental defects, visual impairment, and motor dysfunction. Without licensed vaccines, passive administration of immunoglobulin to pregnant women may be a valuable prophylactic option. We sought to isolate affinity matured neutralizing antibodies from ZIKV-specific memory B cells in a pregnant Brazilian woman with prolonged viremia.

Methods: PBMCs were collected 30 days after viremia cleared. ZIKV-specific memory B cells (CD14-/CD16-/CD3-/CD19-/IgD-) were sorted using fluorescently-labelled UV-inactivated ZIKV, stimulated with EBV and plated at limiting dilution in presence of CD40L-expressing MS40L cells, ODN2006, IL-21 and CHK2-inhibitor for 14 days. A B cell line was derived from a ZIKV+/IgM+ B cell clone, and purified monoclonal antibody (mAb) was tested for ZIKV and dengue virus (DENV) serotypes 1-4 binding and neutralization.

Results: Subject B1_0037 had high titers of ZIKV and DENV1-4 neutralizing antibody. Six of 14 Ig+ culture supernatants (5 IgG and 1 IgM) confirmed reactivity with ZIKV ($OD_{450} > 1$). From one immortalized ZIKV+/IgM+ B cell line, we isolated mAb DH1017.IgM. DH1017.IgM potently neutralized ZIKV ($FRNT_{50} = 6.57$ ng/mL), bound to ZIKV ($AUC = 153.7$), E protein dimer ($E_{80} = 228$ ng/ml) and weakly to E protein monomer ($E_{80} = 934$ ng/ml), but not to E domains I and III. DH1017.IgM did not bind or neutralize DENV1-4.

Conclusions: From a memory B cell, we isolated a ZIKV type-specific and strongly neutralizing mAb DH1017.IgM, which appears to bind to a quaternary structure epitope displayed on the E dimer. Since IgM cannot be transferred across the placenta, this mAb would not facilitate fetal disease by transcytosis of ZIKV, nor increase risk of severe DENV infection for the newborn. These characteristics suggest a role of IgM memory B cells in protection against ZIKV infection and posit DH1017.IgM as a suitable candidate for a prophylactic ZIKV intervention during pregnancy.

Poster 93

Antibody response to primary cytomegalovirus infection during pregnancy

Sharma S1, Weiner J2, Fornara C3, Wolf DG4, Wine Y5, Lilleri D3, Ackerman ME2, Marchant A1, for the CYMAF consortium

1Institute for Medical Immunology, Université libre de Bruxelles (ULB), Gosselies; 2Thayer School of Engineering, Dartmouth College, Hanover, NH; 3Fondazione IRCCS Policlinico San Matteo, Pavia, Italy; 4Hadassah University Medical Center, Jerusalem, Israel; 5Tel Aviv University, Tel Aviv, Israel.

Introduction/Background & Aims: Antibodies play a key role in controlling cytomegalovirus (CMV) infection. Recent studies indicate that, beyond neutralisation, antibodies mediate CMV control by stimulating innate immune responses, including monocyte phagocytosis. The potential of IgG to stimulate innate immune responses critically depends on their subclass and binding to Fc

IgG response to primary CMV infection and to define the impact of pregnancy on this response.

Methods: IgG responses were studied in pregnant women with primary or chronic CMV infection and in non-pregnant patients with primary or chronic infection (n=30 per group). CMV antigens included the envelope glycoproteins gB and pentamer as well as immunodominant polypeptides of tegument proteins pp52 and pp150. Antigen specific IgG subclass and binding to Fc

Antibody-dependent cellular phagocytosis (ADCP) was measured using antigen-coated beads and the THP-1 monocyte cell line.

Results: Overall, IgG response profiles were very distinct in primary and in chronic CMV infection and were much more similar in pregnant and non-pregnant patients. Primary CMV infection was characterized by lower ADCP responses to envelope glycoproteins than in chronic infection whereas ADCP responses to tegument proteins were similar in both groups. The low ADCP responses to envelope glycoproteins in primary infection were associated with low titers of IgG3 and low binding to Fcγ receptors II and III.

Conclusions:

Primary CMV infection in pregnancy is associated with a limited capacity of envelope glycoprotein-specific IgG to promote cellular phagocytosis. This defect may reduce CMV control and contribute to the risk of viral transmission to the fetus.

Poster 94

Sublingual vaccine administration in pregnancy: a possible route for maternal immunisation against neonatal Group B streptococcus infection?

Dr Mohamed Yousif, Dr Fatme Mawas, Dr Seanette Wilson, Dr Sudaxshina Murdan

Introduction/Background & Aims: Group B streptococcus (GBS) is a leading cause of neonatal sepsis, and current prevention and treatment strategies are not universally applicable and/or successful. A maternal vaccine is urgently needed. Indeed, several injectable vaccines have been/are being tested in clinical trials. It is expected that following immunisation of the pregnant woman, maternal IgG will be generated and transferred trans-placentally to the foetus, and this would protect the newborn against GBS infection.

We proposed an alternative route, i.e. sublingual vaccine administration in pregnancy. The main advantage would be that in addition to systemic immune responses (which would transfer trans-placentally to the foetus), sublingual immunisation would also generate mucosal immunity in the vagina, which would prevent mother-to-baby GBS transmission during vaginal birth. Our aim was therefore to investigate whether both mucosal and systemic immunity are generated following sublingual administration of a GBS vaccine.

Methods: Mice received sublingual administrations (5 per group, at weekly intervals) of: i) GBS polysaccharide (serotype III) with cholera toxin B subunit as an adjuvant, or ii) GBS polysaccharide-tetanus toxoid conjugate (serotype III, The Biovac Institute) with cholera toxin B-subunit. The positive control mice received GBS conjugate

□ receptors

□ receptors

subcutaneously. The mice were bled and serum IgG levels were determined by ELISA. Mucosal IgA from vaginal washes and from intestinal samples were also measured.

Results: Sublingual administration of GBS conjugate with cholera toxin B subunit generated: i) serum IgG titres that were equivalent to the subcutaneous administration, and ii) intestinal and vaginal mucosal IgA levels that were considerably higher than following subcutaneous administration. As expected, the GBS polysaccharide (i.e. without conjugation) was much less immunogenic than the GBS conjugate.

Conclusions: The sublingual route is promising for maternal immunisation against neonatal GBS.

Abstracts on Promoting Academic Research Networks and Education Activities

Poster 95

The effect of maternal immunization with PPV23 on the quantity/ function of antibodies to 23 serotypes of *SPN* in infants in Dhaka, BD

Shahana Choudhury

Meharry Medical College, Nashville, TN

We demonstrated that younger infants with bacterial pneumonia more likely suffer morbidity than their older counterparts in Dhaka, Bangladesh (BD). (HSOA Journal of Clinical Studies and Medical Case Reports. 2017; 4 (1): 045; DOI: [10.24966/CSMC.8801/100040](https://doi.org/10.24966/CSMC.8801/100040)); additional pneumonia studies in progress (**self-funded**). Pneumonia accounts for twenty-six percent of neonatal deaths in BD (52.5 vs 6.8/ 1,000 infant births in the US). *Streptococcus pneumoniae* (*SPN*) remains a major cause. We have also demonstrated decreased placental transfer of *SPN* (polysaccharide) compared to protein antigens in cord blood samples. (INMIS 2019 abstract). Our **goal** is to reduce neonatal death in BD; current standard of care in BD (PCV10 at 6, 10 and 14 weeks of age)- does not cover neonatal period and may not provide adequate coverage of circulating *SPN* serotypes. Our **objective** is to examine the effect of maternal immunization with PPV23 on the quantity/ function of antibodies to 23 serotypes of *SPN* in infants. We, here at Meharry Medical College (USA) will execute our objectives via collaboration with multi-centers in Dhaka, BD (**if funding becomes available**), the following specific aims: We will determine- **Aim 1**- immunogenicity of PPV23 in mothers (pre-and post vaccination) during 3rd trimester pregnancy; **Aim 2**- antibody levels in cord blood and peripheral blood of infants (6 months of age), respectively; **Aim 3**- immunological and clinical outcomes -at 12 and 24 months of age. Our study will involve collecting blood, urine and nasopharyngeal swabs for immune response studies from a cohort of 400 Bangladeshi women and their infants.

Poster 96

Research capacities at ISGlobal to conduct vaccine trials and clinical studies in support to maternal immunization research in Mozambique

Azucena Bardají

ISGlobal, Hospital Clínic-University of Barcelona, Barcelona, Spain; Centro de Investigação em Saúde de Manhiça (CISM), Manhiça, Mozambique

The **Barcelona Institute for Global Health (ISGlobal)** is a leading international institution aimed at improving global health and promoting equity through excellence in research. The **Fundação Manhiça/Centro de Investigação em Saúde de Manhiça (FM/CISM)**, is one of the leading centres of excellence for biomedical research in Africa, and the main collaborating centre for ISGlobal since 1996.

The Manhiça District, a semi-rural area in Southern Mozambique, is a resource-constrained setting and a **malaria endemic area** of moderate intensity. **HIV prevalence in pregnancy** is high (**30%**), and **40% of admitted children** at the Manhiça District Hospital (MDH) are **HIV positive**. Group B *Streptococcus* (GBS) is the second cause of neonatal sepsis, and acute respiratory infections and malaria are major causes of infant mortality.

FM/CISM runs continuous **Demographic Surveillance** (\approx 200.000 people), and a round-the-clock **Morbidity Surveillance** at the MDH. **Microbiological Surveillance** is routinely conducted for all admitted children. **Routine Pneumonia Surveillance** is available for *Streptococcus pneumoniae*, respiratory syncytial virus (RSV) and other viral pneumonias. FM/CISM has recently **expanded research activities to newly-established locations within the country**, increasing capacities to perform clinical trials. FM/CISM has excellent laboratory infrastructure run according to GCLP and QA/QC systems.

Work on maternal immunization (MI) conducted so far/ongoing include preparatory/feasibility studies for MI trials, disease burden studies (RSV pneumonia and mortality, pertussis burden, GBS characterization), and the effect of HIV and malaria on placental transfer of Ab.

ISGlobal has a **well-established and ongoing network of collaborators** and has coordinated several consortiums involving African countries. We are willing to explore further collaborations/networking opportunities with groups working on maternal immunization.

Poster 97

Opportunities for collaboration at established research sites in Malawi

This abstract presents the potential clinical and research capability of Malawi Health Care Centers led by Dr. Miriam Laufer and Dr. Matt Laurens. Dr. Laufer is Professor and Associate Director for Malaria Research at the Center for Vaccine Development and Global Health (CVD) at the University of Maryland, Baltimore (UMB) and has been Principal Investigator in numerous epidemiological studies and clinical trials in Malawi since 2002. Dr. Laurens is Associate Professor and Director of International Clinical Trials Unit at the CVD. Dr. Laufer and her team of collaborators from UMB, the University of Malawi College of Medicine, and other international institutions conduct longitudinal studies of infectious diseases and long-term child health outcomes in multiple sites in Malawi. The sites include an urban health center in Ndirande, a peri-urban township of approximately 200,000 people on a mountainside adjacent to Blantyre, the largest city and economic center of Malawi. This site provides opportunities to conduct vaccine trials and evaluation of the impact of HIV on infant health and development. Community and facility-based studies have been conducted and are on-going that focus on malaria in infants and children. A study of the impact of malaria in pregnancy on infant susceptibility to malaria recently closed and large cohort studies are underway as part of the International Center of Excellence in Malaria Research (ICEMR).

Poster 98

Maternal Immunization: a text book

Elke Leuridan¹, Marta Nunes² and Chrissie Jones³

1 Vaccine & Infectious Diseases Institute, University of Antwerp, Belgium; 2Vaccine Preventable Diseases Unit, Faculty of Health Sciences, University of the Witwatersrand, South Africa; 3 University of Southampton and University Hospital Southampton NHS Trust, UK

Maternal vaccination is a proven strategy to prevent infection in both the mother and the young infant and there is an increasing focus from all stakeholders to harness this approach to better protect these vulnerable groups. The book **“Maternal Immunization” will be published by Elsevier in late 2019 and aims** to provide a contemporary global overview of vaccines to be used in pregnancy and post-partum. The book will provide in-depth insights valuable to all those engaged with vaccination of women planning pregnancy, whilst pregnant and post-partum. It will be available as a printed text as well as downloadable chapters.

Topics include: History of maternal vaccination, immunobiology, clinical trials in pregnancy, implementation of maternal immunization programmes, vaccine acceptance, vaccination in women planning pregnancy and postpartum women, tetanus, influenza, pertussis, vaccines recommended in special circumstances, respiratory syncytial virus, group B streptococcus, cytomegalovirus, Zika and malaria.

The text book is co-authored by international experts from multiple disciplines including: Helen Chu, Clare Cutland, Patrick Duffy, Linda Eckert, Kathy Edwards, Janet Englund, Deshayne Fell, Paul Heath, Heidi Larson, Elke Leuridan, Chrissie Jones, Philip Lambach, Shabhir Madhi, Arnaud Marchant, Flor Munoz, Karin Nielsen-Saines, Marta Nunes, Saad Omer, Mark Schleiss, Ajoke Sobanjo-Ter Meulen, Milagritos Tapia, Nick Wood.

This book is the first textbook to focus on maternal immunization will benefit the reader who wishes to become informed and become up to date with new developments in this rapidly evolving field. It will be wide interest and applicability to INMIS delegates.

Poster 99

Introducing the OpTIMUM study

A. Calvert, N. Andrews, B. Hallis, A. England, C. Jones, K. Karampatsas, A. Khalil, K. Le Doare, M. Matheson, **P. Heath**

Background: Pertussis is a highly infectious respiratory illness which can cause significant morbidity and mortality in infants. Along with many high income countries, the UK has seen a dramatic increase in cases which led to the pertussis vaccination in pregnancy being introduced as an outbreak measure in 2012. This intervention is safe and effective, but there remains uncertainty about the best time to offer the vaccination in pregnancy to provide optimal protection to the newborn infant at birth.

Aims: The OpTIMUM study will investigate the impact of timing of maternal pertussis vaccination on antibody concentration in the newborn at birth.

Methods: We will recruit 354 women from across 6 UK sites who will be randomised into three timing groups: $\leq 23+6$ weeks, 24-27+6 weeks and 28-31+6 weeks. Participants will receive the Boostrix-IPV[®] vaccine according to their allocated timing period. They will be asked to complete a diary card for one week after receiving the vaccination. Blood samples from the participant will be obtained prior to vaccination, 14 days following vaccination and at delivery, a cord sample will also be taken at delivery and an infant sample will be collected 28-42 days after the third set of immunisations (at around 5 months of age). The concentration of IgG antibodies against Pertussis Toxin, Filamentous haemagglutinin and Pertactin will be quantified by ELISA.

Timelines: Recruitment opened at the first site in May 2019. We hope to complete recruitment by February 2020, complete follow up by November 2020 and have initial results by early 2021.

Poster 100

African Leadership in Vaccinology Expertise (ALIVE): University of the Witwatersrand

Clare Cutland

ALIVE, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

The development of new vaccines and strengthening of immunization programs rank high among global and African public health priorities. Nevertheless, there is limited capacity in Africa to conduct research in vaccinology, take informed policy decisions and improve program implementation.

The 'African Leadership in Vaccinology Expertise' (ALIVE) consortium, established in 2016, is the South African National Research Foundation (NRF)-supported Flagship research entity of the University of the Witwatersrand. Helen Rees and Shabir Madhi spearheaded and coordinated the development of ALIVE and serve as co-directors.

Mission

- to create African expertise and leadership in vaccinology research and advocacy to significantly reduce vaccine preventable diseases over the next 15 years.

Vision:

- become a unique South African and African resource, which will inspire innovation in this important field of vaccinology research spanning basic and clinical sciences, implementation science and public health expertise.

Objectives

- create new opportunities for African global research leadership and advocacy
- build capacity in African vaccinology research
- connect and expand on an African network of vaccinology expertise

Limited training opportunities in the field of vaccinology are available in Africa. In order to fill this gap, ALIVE has established a biennial 9-day African Advanced vaccinology course (Afro-ADVAC, next course September 2020) and a Masters in the field of Vaccinology. (www.wits-alive.ac.za)

The ALIVE consortium's work focuses on vaccine development, implementation and advocacy for key pathogens (CMV, GBS, HPV), selected for their public health importance and their potential to serve as models for optimising delivery and evaluating impact of future maternal and adolescent vaccines.

Poster 101

A cloud-based biostatistical and bioinformatics data and analytic infrastructure for the Expanded Program on Immunization Consortium

Dr. Joann Diray-Arce, **Ms. Sofia Vignolo**, Ms. Kerry McEnaney, EPIC-HIPC Consortium, Dr. Al Ozonoff

Introduction/Background & Aims: The overarching goal of the Expanded Program for Immunization Consortium - Human Immunology Project Consortium (EPIC-HIPC) is to identify and characterize vaccine-induced neonatal responses and define biomarkers that may predict immunogenicity. Key to this effort is the establishment of the Data Management Core (DMC) to provide reliable clinical data and bioinformatic infrastructure for centralized curation, storage, and analysis of multiple 'omics datasets.

Methods: The DMC established a cloud-based platform to track, store, and share data according to set standards using Amazon Web Services (AWS) server. In our clinical core sites, biosamples collected and shipped across sites are tracked using ItemTracker via AWS Elastic Compute Cloud while their associated clinical data are captured using Research Electronic Data Capture. Multi-omic datasets are stored in access-regulated AWS Simple Storage Service (S3) for file version control. All data must complete quality control (QC) processes by the site generating said data, which is then exported to the DMC for quality assurance (QA). Data integration is performed using RStudio Server Pro which directly imports the data files from AWS S3 in a controlled R computing environment. The DMC deposits QC/QA'd data onto public repositories to be shared openly upon publication.

Results: Key benchmark for success includes the curation and deposition of primary enrollment 'omic datasets of the Medical Research Council - The Gambia. Subsequent benchmarks will include regular data quality performance audits, user feedback, HIPC-wide outputs upload to ImmPort, and peer-reviewed manuscripts publication describing vaccinology results.

Conclusions: Completion of our goal will provide the resources, planning, and scientific expertise to make this discovery platform possible. Robust DMC operations will allow rapid sharing of integrative results across the entire team. Maintenance of standards and public deposition of high quality 'omics data will further advance scientific progress for the benefit of vaccine development and public health.

Travel Bursary Awardees

- **Olajumoke Aladenola**, Ondo State Ministry of Health, Nigeria
- **Alansana Darboe**, MRC Unit the Gambia at the London School of Hygiene and Tropical Medicine, The Gambia
- **Rebecca Ford**, PNG Institute of Medical Research, Paupa New Guinea
- **Narendra Gemawat**, Hindustan chamber Chikitsalaya, India
- **Suresh Gemawat**, Madan Mohan Medical and Counselling Centre, India
- **Penda Johm**, MRC Unit the Gambia at the London School of Hygiene and Tropical Medicine, The Gambia
- **Joseph Kabogoza**, Giving Children Hope Initiative (CGHI), Uganda
- **Hyacinte Kabore**, World Health Organization, Congo
- **Dharmendra Kumar Khatri**, Dr. D. Y. Patil Institute Of Pharmaceutical Sciences And Research, India
- **Pardeep Kumar ShriMaha Maya Vaishnav Devi Mandir Research Institute**, India
- **Keswadee Lapphra**, Faculty of Medicine siriraj Hospital, Mahidol University, Thailand
- **Ssyenondo Max Mbidde**, Health and Care for Future Foundation Uganda (HCFU), Uganda
- **Emilly Tumuheirwe Kadooko Ndyomugenyi**, Grassland Community Initiatives Uganda (GCIU), Uganda
- **Marta Nunes**, University of the Witsatersrand, South Africa
- **Joyce Nyiro**, Kemir-Wellcome Trust Research Programme, Kenya
- **Ebrima K Kanteh**, MRC Unit the Gambia at the London School of Hygiene and Tropical Medicinent, The Gambia
- **Rajan Kumar Pandey**, Central University of Rajasthan, India
- **Sophie Roetyncck**, MRC Unit the Gambia at the London School of Hygiene and Tropical Medicine, The Gambia
- **Shilpee Sharma**, Institute for Medical Immunology, (trainee from India)
- **Vinita Sharma**, Central University of Rajasthan, India
- **Julia Strandmark**, MRC Unit the Gambia at the London School of Hygiene and Tropical Medicine, The Gambia
- **Nasamon Walapakorn**, Chulalongkorn University, Thailand

Scientific Organizing Committee

- **Manish Sadarangani**, INMIS2019 Co-Chair *Vaccine Evaluation Center, BC Children's Hospital Research Institute, University of British Columbia, Canada*
- **Tobias Kollmann**, INMIS2019 Co-Chair *Telethon Kids Institute, Perth Children's Hospital, University of Western Australia*
- **Bahaa Abu Raya**, *Vaccine Evaluation Center, BC Children's Hospital Research Institute, University of British Columbia, Canada*
- **Gordean Bjornson**, *Vaccine Evaluation Center, BC Children's Hospital Research Institute, University of British Columbia, Canada*
- **Surasith Chaithongwongwatthana**, *Division of Infectious Disease in Gynecology and Obstetrics (InDiGO), Faculty of Medicine, Chulalongkorn University, Thailand*
- **Ed Clarke**, *Medical Research Council Laboratories The Gambia, The Gambia*
- **Clare Cutland**, *Respiratory and Meningeal Pathogens Research Unit (RMPRU), African Leadership in Vaccinology Expertise (ALIVE), University of Witwatersrand, South Africa*
- **Ener Dinleyici**, *Eskişehir Osmangazi University, Turkey*
- **Paul Heath**, *St George's University of London, UK*
- **Beate Kampmann**, *Medical Research Council Laboratories The Gambia, The Gambia and Imperial College, London, UK*
- **Elke Leuridan**, *Centre for the Evaluation of Vaccinations, Vaccine & Infectious Diseases Institute, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium*
- **Ofer Levy**, *Precision Vaccines Program Boston Children's Hospital & Harvard Medical School,*
- **Arnaud Marchant**, *Université Libre de Bruxelles, Belgium*
- **Flor Munoz**, *Baylor College of Medicine, USA*
- **Pierre Van Damme**, *University of Antwerp, Belgium*

IMPRINT Fellowship: Understanding interactions between Maternal IgG and Neonatal Innate Immune Cells (MINIC)

Summary

Whether vaccines given to women in pregnancy (maternal immunization) have an effect on the developing immune system of the newborn baby are still not well understood. However, this knowledge is important to make sure that current and future vaccines used in pregnancy can be used in the most efficient and protective way. Whilst we have better insights into the effect of the maternal vaccines on the antigen-specific, acquired immune responses in the newborn, but there remains a gap in knowledge about effects of maternal vaccination on infant natural defense cells (innate immunity) and any potential modification of these cells.

This project will use cord blood samples collected within an ongoing large-scale observational study of neonatal vaccine responses to develop a prototype of assays in the lab that will allow us to investigate the effects of maternal antibody on the natural defense cells in the newborn. Initially we will use the model of tetanus vaccination, given that this vaccine is already routinely given to pregnant women in The Gambia. This model can then serve to assess the potential impact of other maternal vaccines on neonatal innate responses, such as pertussis or future vaccines. In addition, we will examine in another lab assay whether "training" of specific cells generated from cord blood (monocytes) by BCG -another vaccine used in the newborn- can induce changes in gene expression. We will also have the opportunity to measure if the early natural cellular responses have an influence on the antibody levels measured in response to vaccines the baby receives in the first few months of life.

This knowledge will help us to estimate if there is potential for clinical impact on longer term antigen-specific immunity in the infants or not.

The fellowship is embedded in an existing strong research partnership between the three research sponsors in Gambia, Vancouver and Brussels and will provide the fellow with the opportunity to develop an independent complimentary aspect of the research around one of the key challenges identified by the IMPRINT network.

Project lead

Dr Alansana Darboe

Vaccine & Immunity Theme Medical Research Council Unit The Gambia at the London School of Hygiene and Tropical Medicine

IMPRINT Fellowship: Towards the understanding of anti-Group B Streptococcus (GBS) protective immunity: characterisation of maternal sera in high- vs. low- GBS prevalence countries using humanised mice

Summary

Pregnant women sometimes carry a bacterium called Group B Streptococcus (GBS) in their vagina or rectum. During pregnancy or upon delivery, GBS may be transmitted to the baby resulting in the death of the baby in the womb or go on to cause infections such as sepsis or meningitis soon after birth. GBS disease is more serious in some low- and middle-income countries (LMICs) where pregnant women do not have access to proper antenatal care and antibiotics. A solution would be to vaccinate mothers against GBS, so they can produce antibodies protective proteins (antibodies) that can be transferred to the baby through the placenta and protect them from developing an infection in the first place. Interestingly, LMICs situated in South-East Asia report a low GBS disease burden while high GBS disease rates are documented on the African continent, in countries such as Malawi or South Africa.

In this project we aim to collect the blood of GBS-colonised mothers from high vs. low GBS disease burden countries (U.K. vs. Malawi vs. Bangladesh) and compare how the immune system of the women reacts to GBS by measuring anti-GBS antibody concentrations, the ability of the antibody to kill the bacteria, as well its ability to bind to factors present on the surface of the GBS bacteria. We also aim to examine how effectively the antibodies are transferred across the placenta and give protection to babies.

By comparing the properties of antibodies collected from high- vs low- disease burden countries, we hope to understand the criteria that are essential for the optimal transfer of GBS protective antibodies from mother to baby. Altogether this knowledge will significantly help towards the design of more efficient and safe vaccines to protect new born babies from life-threatening GBS disease.

Project lead

Dr. Shadia Khandaker

Department of Clinical Infection, Microbiology and Immunology
Institute of Infection and Global Health, University of Liverpool, United Kingdom

IMPRINT Fellowship: Innovations for vaccine safety monitoring and improved maternal and neonatal immunization in rural Uganda (InVxSIM)

Summary

The InVxSIM project will setup a vaccine safety monitoring system in rural Uganda within the Iganga Mayuge health and demographic surveillance system (HDSS). It will focus on maternal and neonatal vaccine acceptability and safety. This project will be implemented in a population of over 90,000 individuals of which 18% are women in reproductive age. The HDSS demographic updates data that we routinely collect will be linked to the health facility electronic health records system which captures antenatal care for the mother and vaccinations in mothers and children.

The InVxSIM project will first assess the ability to measure obstetric and neonatal outcomes as defined in the GAIA project. It will also monitor the safety of maternal immunization to ensure that potential concerns are addressed rapidly. Lastly, we will build a system for identification, follow-up and delivery of reminders to get immunized to pregnant women. We hope that the project will improve information on vaccine safety, uptake and coverage, and thereby facilitate to maintain and improve trust in the maternal and neonatal immunization programs by being able to provide requested information rapidly. This may ultimately reduce mortality and morbidity because of better prevention of vaccine preventable diseases and be an example for other LMIC that may have similar fragmented information systems.

Project lead

Dr Dan Kajungu

Centre Leader & Executive Director

Iganga Mayuge HDSS & Makerere University Centre for Health and Population Research, Uganda

IMPRINT Fellowship: Understanding the influence of public, provider, policy and contextual factors on maternal vaccine acceptance

Summary

Vaccination during pregnancy, also known as maternal immunization, has the potential to prevent disease and death among mothers and their infants. Maternal immunization can have tremendous impact in low and middle-income countries (LMICs) where burden of disease is very high and access to adequate healthcare can be problematic. However, not everyone is willing to accept vaccines, especially during pregnancy, due to safety and other concerns. Available maternal vaccines are safe and effective in preventing disease. Not taking vaccines puts the women and their children at risk of what can often be severe disease and this poses a significant public health challenge that needs to be addressed.

Our research project aims to identify factors of practical value that may affect individual vaccine acceptance during pregnancy. We will consider individual concerns and priorities, and factors beyond individual decision-making. This would include the influence of healthcare provider recommendation, facilitators and barriers to healthcare provider recommendation and the influence of policies and policy-maker priorities on vaccine acceptance. We also seek to understand the influence of contextual social, cultural, historical, political, economic, religious and media-related factors on vaccine acceptance.

We think that it is important to take a broad approach. Focussing on individual factors alone without considering wider influences of provider-level, policy/programme-level and contextual factors on vaccine acceptance is akin to studying diet and nutrition as determined purely by individual choice without consideration of social, cultural or financial circumstances.

We will conduct this research in India using a number of methods, including in-depth interviews, focus groups discussions and document review. Research participants will include pregnant women and new mothers, public and private healthcare providers, and policy-makers and key stakeholders. As a study outcome we will develop a comprehensive framework that looks at the relationship between public, provider, policy, structural and contextual factors on individual vaccine acceptance in order to identify ways to maximise access to and acceptance of safe and effective maternal vaccines.

Project lead

Dr. Neisha Sundaram

Department of Infectious Disease Epidemiology, London School of Hygiene and Tropical Medicine, United Kingdom

IMPRINT Pump Priming Project: Unravelling maternal protection: Factors affecting transplacental transfer of antibody from mother to infant

Summary

Young infants are more susceptible to infection than individuals at any other life stage. Their immune systems are inexperienced and they are too young to benefit from infant vaccination, most of which are given several weeks after birth. In the first weeks of life, babies rely on protective proteins called antibodies, which are transferred across the placenta from the mother to the baby whilst still in the womb. In some cases, the amount of antibody transferred to the baby is not sufficient to protect the baby from infections, such as whooping cough. Vaccines given in pregnancy aim to increase the amount of antibody in the mother's blood, so that more antibody is transferred across the placenta to the baby so that the infant is protected until they are old enough to receive infant vaccines.

Antibody is transferred across the placenta by binding to specialised receptors on the surface of placental cells. In this project, we aim to study each part of the antibody-receptor interaction, namely:

- Functional changes in the antibody
- The amount and location of the antibody receptor
- The strength of the binding between the antibody and the receptor

We aim to understand how these factors change throughout pregnancy, by testing stored blood and placental samples. We will also look at how vaccination in pregnancy can affect these factors.

In developing countries, a significant proportion of pregnant women are affected by HIV infection. This can affect how well antibody is transferred across the placenta. We aim to understand how HIV affects the maternal antibody and how well it binds to the receptor in the placenta.

We hope that this project will help us understand more about the way babies are protected by vaccines in pregnancy and in the future, help us design vaccines that are more effective at protecting the mother and infant.

Project lead

Dr Chrissie Jones

Associate Professor and Honorary Consultant in Paediatric Infectious Diseases Clinical and Experimental Sciences

Room LF102, F Level, South Academic Block University Hospital Southampton NHS Foundation

Trust Tremona Road

Southampton SO16 6YD, United Kingdom

IMPRINT Pump Priming Project: Evaluating the Field Performance and Validating Novel Case Definitions Designed to Harmonize Safety Monitoring for Immunization in LMIC

Summary

Giving vaccines to pregnant women is a useful public health measure. It will help to reduce death and disease among pregnant women and newborn infants from infectious diseases. This will be most important in low- and middle-income countries (LMIC). New vaccines are being developed for use in pregnant women e.g. for Group B streptococcus, respiratory syncytial virus and cytomegalovirus. The safety of vaccines administered to pregnant women is most important for pregnant women, healthcare providers, researchers, regulators, ethics committees, vaccine developers and communities. There is a need for a global coordinated approach to determine the safety of vaccines used for pregnant women and for Maternal and Child Health (MCH) studies. The GAIA (Global Alignment of Immunization safety Assessment in pregnancy) project has developed 21 globally consistent tools (case definitions of key terms) to determine the safety of vaccines in pregnancy. These can also be used for MCH studies. Assessment of these tools in LMIC is required. This study will assess key case definitions and terms using data from clinical studies conducted in South Africa and The Gambia. The study will determine how possible it is to utilize the case definitions,

the quality and accuracy of the data collected, the challenges and advantages of using the case definitions and collection of any possible edits to the case definitions that would make them easy to use in LMIC.

Project lead

Sonali Kochhar, MD
Medical Director, Global Healthcare Consulting
Scientific Researcher, Department of Public Health
Erasmus University Medical Center, Rotterdam, The Netherlands

IMPRINT Pump Priming Project: Elucidating the effect of maternal immunisation on the subsequent development of T cell response following pertussis vaccination in infants

Summary

Whooping cough can cause serious disease, particularly in young infants. In the UK, and other countries around the world, it is recommended that pregnant women receive the whooping cough vaccine in order to protect mothers and infants against whooping cough. Antibodies (protective proteins) are transferred across the placenta from the mother to the infant and protect the infant in the first months of life, before the infant is protected by infant whooping cough vaccination. There are concerns that high levels of maternal antibody in the infant at birth may prevent the infant from producing such a good response to their own vaccines.

There is a type of blood cell in the circulation called “T Follicular Helper” cells (or TFH cells for short.) These cells are thought to be important for how well the body produces the protective antibody proteins in response to vaccination. It is important to understand if vaccination in pregnancy can affect how well these specialised cells develop in the infant’s blood stream and therefore how well the infant responds to their own vaccines. Other specialised cells that are important to how well the infant responds to infections like whooping cough, such as “T” cells, may also potentially be affected by vaccination in pregnancy.

In this study, we will work with partners in Thailand who are already carrying out studies looking at whooping cough vaccination in pregnancy. We will work with samples that have already been collected, from infants born to vaccinated mothers and infants born to unvaccinated mothers. This will allow us to compare the infant’s cellular response to vaccination in these different groups of infants.

We hope that this study will improve our understanding of infant immunity and inform future vaccination strategies.

Project lead

Dr Qibo Zhang
Senior Lecturer in Immunology, Institute of Infection and Global Health
University of Liverpool, Southampton, United Kingdom

IMPRINT Pump Priming Project: Using in vitro mycobacterial growth inhibition assays as a tool to assess functional immune responses induced by VPM1002 vaccination in infants

Summary

Tuberculosis (TB) is a disease caused by a germ that can affect the lungs and in severe cases, the blood and the brain. Almost one million children, mostly from the tropics, suffered from TB in the year 2015. A vaccine called BCG is used to prevent this disease. It is given to babies and is able to prevent severe forms of TB that involve the blood and the brain but does not provide adequate protection from the lung form which is the most common. New vaccines that are able to do a better job at preventing TB in babies are needed. VPM1002 is a vaccine that has been developed to work better than BCG. It has been tested in adults and babies and the results show that it is safe, however we need to know how well it is able to kill TB germs. This study aims to use a tool in the lab to show how well the new vaccine, VPM1002 works in babies from Uganda, an African country where TB is common.

Project lead

Mr Simon Gwapa Kimuda

Associate Scientist, Immunomodulation and Vaccines

Medical Research Council/UVRI Uganda Research Unit on AIDS, Entebbe, Uganda

IMPRINT Pump Priming Project: Oral vaccines which generate immune responses in the vagina and prevent mother-to-baby transmission of infections during birth

Summary

The ultimate aim of our work is to develop vaccines that will be taken by pregnant women and which will then protect babies from catching infections caused by, for example, HIV, hepatitis B and Zika, during birth. The vaccines will be taken by mouth, but will have their effects in the mother's vagina. The oral route of vaccine taking has been chosen as this route is expected to have higher acceptability and be cheaper than injections, which have to be sterile, need to be given by medically-trained personnel and can be painful. The cost factor is especially relevant in LMIC, for poorer people and where healthcare costs are largely borne by individuals, rather than the state.

For oral vaccines to have an influence in the vagina, they have to be prepared using specific chemicals, such that once a vaccine is swallowed, it is only processed in the large bowel (and nowhere else in the gut). In this project, we will: i) identify those chemicals, ii) prepare the vaccines, and iii) test whether the prepared vaccines will be processed in the large bowel following swallowing.

The results of this study will be used to apply for follow-on funding to determine whether such vaccines will have an influence in the mother's vagina and protect newborns during birth.

Project lead

Dr Sudaxshina Murdan

Reader in Pharmaceutics, UCL School of Pharmacy

University College London, London, United Kingdom

IMPRINT Pump Priming Project: The human placental perfusion model: advance in knowledge of maternofetal antibody transfer

Summary

During pregnancy, the placenta is the interface between mother and baby. Its' specialised structure allows nutrients and protective molecules such as antibodies to be transferred to the developing baby. These antibodies help protect the infant in the first weeks of life, when the infant is exposed to viruses and bacteria for the first time. In several countries, we now vaccinate women against certain diseases, which increases the amounts of specific antibodies passed to the baby, therefore protecting them against disease.

Surprisingly, despite the importance of trans-placental antibody transfer, there is lots we still do not know about this process. This includes how the antibody crosses all the different cell layers between the mother's and baby's bloodstream, how changes in the mother's immune system may affect antibody transport, and how differences in the structure of antibodies can increase or decrease their transport to the baby. Understanding these issues will help us to optimize maternal vaccination programmes to protect infants in early life.

One way to address some of these gaps in our knowledge is through use of placental perfusion. This technique uses a piece of the human placenta donated after birth, which is kept in a warm chamber and bathed in fluids to copy how it functions during pregnancy. We can therefore track the movement of different types of antibodies across the human placenta in the laboratory, without the need for animal models. This will help us understand what regulates how well

certain antibodies are passed to the baby. Our project brings together a placental biologist and an expert in antibody function, in order to answer pressing questions around how infants are protected from early-life infections, and how we can develop new vaccines in order to improve this.

Project lead

Dr Beth Holder

Research Associate, Department of Pediatrics

London School of Hygiene and Tropical Medicine, United Kingdom

IMPRINT Pump Priming Project: How does iron influence infant immune development? A systems immunology RCT sub-study in Bangladeshi infants

Summary

Infections and nutritional deficiencies, including iron deficiency, affect millions of young children in Low- and Middle-Income Countries (LMICs). Moreover, iron deficiency has recently been reported as the most common cause of preventable death and disability in such settings. Recent evidence indicates that iron is essential for effective immune responses, so iron deficiency could therefore contribute to impaired immunity leading to poor responses to vaccines and infection susceptibility in infants. However, the ways in which iron deficiency, and treating infants with iron supplements, influence infant immunity in LMIC settings remains poorly explored.

This proposal will address this issue by applying a state-of-the-art immunological method termed CyTOF to blood samples obtained from infants participating in a large clinical trial of iron supplementation in Bangladesh; this trial is investigating the relative pros and cons of iron treatments for infants. CyTOF will enable us to study how iron affects the array of different types of white blood cells in circulation, and the functioning of these different immune cell types. We will link this information with data collected concurrently from the same infants including their immune responses to the measles-rubella vaccine, the diversity of microorganisms found in their intestine, as well as data on infection, growth and developmental.

Together, the study will advance understanding of how nutrition can shape development of the immune system in infants in settings where the ability to mount competent immune responses to immunisations and infections is of great importance. The data will also inform global health policy makers in developing guidelines regarding the use of iron treatments in infants in infection-susceptible populations.

Project lead

Dr Andrew Armitage

Senior Postdoctoral Scientist, MRC HIU, MRC WIMM

University of Oxford, United Kingdom

IMPRINT Pump Priming Project: Maternal transplacental antibody decay rates: an individual participant data meta-analysis

Summary

Babies have more protection against some diseases (e.g. whooping cough, tetanus) in the first few months of life if their mothers are vaccinated during pregnancy. Vaccines given to mothers produce antibodies that fight disease. These 'maternal' antibodies are passed on to babies before birth and protect them whilst they are too young to be vaccinated themselves.

Naturally, over time, maternal antibodies in babies decline. It is therefore important that, at some point, babies receive their own vaccinations to keep them protected. Timing is important. If maternal antibodies still exist in babies

when they receive their first vaccinations, they may have a lower antibody response. This may mean that they are not protected as well as they could be.

In planning vaccine programmes, therefore, it is important to understand how quickly maternal antibodies decline in babies.

Currently, there is little information about the rate at which maternal antibodies decline in babies for some common vaccines. Antibody levels may decline at different rates for different vaccines. Until we know more, it is difficult to find out the best time to vaccinate babies.

We can find out more by using information from studies that have already finished. We will collect data from studies that have looked at antibody levels in two blood samples in babies. We will work out the rate at which maternal antibody levels decline in them. Combining data in this way means that we will have enough data for accurate calculations without taking any further blood samples.

Our project will provide information that will help improve the planning of vaccine programmes in order to provide the best protection for babies against disease.

Project lead

Dr Merryn Voysey

Senior Statistician

Nuffield Dept Primary Care Health Sciences, University of Oxford, United Kingdom

IMPRINT Pump Priming Project: Assessing community acceptancy and health facility preparedness for implementation of maternal immunisation programs in urban and rural South Africa

Summary

Vaccines have prevented millions of child deaths; however, 45% of remaining under-5 deaths occur during the neonatal period, when infants are vulnerable to disease. Immunisation of pregnant women with tetanus toxoid to protect mother and newborn from tetanus has been widely implemented and accepted.

Maternal immunisation has the potential to reduce or prevent stillbirths and neonatal deaths from other diseases including influenza, pertussis, Group B streptococcus and Respiratory Syncytial virus. Pregnant women have not been included in clinical trials for most vaccines and medicines, due to concerns about potentially detrimental side effects on foetus/ infant and mother.

It is important to understand knowledge, perceptions and acceptance of maternal immunisation programs in different countries, especially low- middle income countries, where the vast majority of stillbirths, neonatal infections and deaths occur. Additionally, understanding of the suitability of and resources available at local health care facilities to implement large-scale maternal immunisation programs is important to enable smooth and effective roll-out of maternal immunisation programs.

South African sites have been involved in vaccine-preventable disease (VPD) surveillance programs and maternal immunisation trials, and the large burden of VPD in new-borns encourages rapid roll-out of MI programs.

In this study, we aim to first describe the perceptions about and acceptability of maternal immunisation amongst communities in urban (Soweto, Johannesburg, Gauteng) and rural (Somkhele, Mtubatuba, KwaZulu-Natal) communities in South Africa; second to understand the social and cultural factors which impact on the acceptability of maternal immunisation; and third to assess health care worker and facility preparedness for roll-out of MI programs. In order to fulfill these outcomes, we will conduct interviews and group discussions with community members, and an electronic survey of health care workers.

Project lead

Dr Clare Cutland

Director Deputy, Respiratory and Meningeal Pathogens Research Unit, Wits Health Consortium
University of the Witwatersrand, Johannesburg, South Africa

IMPRINT Pump Priming Project: IMPROVE - IMMunology of PRObiotics supplementation on Vaccine outcomes in Early life

Summary

Globally each year more than 1 million infants die from infections, and most of these deaths occur in low-income countries. The time that children are at highest risk of serious infections is during the first few months after birth.

A large study conducted in India found that supplementing newborns during the first 10 days of life with probiotics, which are live, harmless bacteria, lowered the risk for sepsis, diarrhoea and lower respiratory tract infections. The beneficial effect of probiotics on preventing respiratory tract infections in particular was unexpected and intriguing, suggesting that the effect of probiotics goes beyond that of a healthy gut.

Infants in Papua New Guinea (PNG) have one of the highest risk in the world for severe respiratory infections caused by *Streptococcus pneumoniae* (pneumococcus), including pneumonia. Before the pneumococcus causes disease, it first colonises the infant's nose. In PNG, almost all infants have been colonized with pneumococci by the age of 1 month.

The aim of this project is to conduct a pilot study to test two probiotic supplementations for safety and possible effects on early pneumococcal colonization and pneumococcal vaccine responses in PNG infants. This pilot study will support the implementation of a subsequent large clinical trial that will aim to study in PNG infants the direct and indirect impacts (by improving vaccine responses) of probiotics on serious infections including severe pneumonia, blood poisoning and meningitis. If proven to be efficient, probiotics supplementation could be a simple, safe and affordable intervention to save infants' lives.

Project lead

Dr William Pomat

Acting Director, Papua New Guinea Institute of Medical Research, Papua New Guinea