

# Global Child Health

### RESEARCH AND TRAINING DETAILS



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Faculty	4
Joint Appointment Faculty	4
Support Personnel	11
Direct Annual Grant Support	\$3,795,113
Direct Annual Industry Support	\$280,346
Peer Reviewed Publications	9

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## Research Highlights

**Steven Black, MD**

### **The Risk of Narcolepsy following Adjuvanted Pandemic Influenza Vaccine**

In this U.S. Center for Disease Control and Prevention (CDC) funded study, [Dr. Steven Black](#), and colleagues, will evaluate the risk of narcolepsy following adjuvanted influenza vaccines. Three such vaccines were used during the 2009-2010 pandemic and one was associated with an increased risk of narcolepsy in children in several European studies. The goal of this project is to expand the scope of prior studies to include the other two adjuvanted vaccines by performing studies in Brazil, Taiwan, Canada, Israel, the Netherlands, Spain and Argentina. The results of this study will inform the future use

and selection of adjuvants for future pandemics.

### **Global Vaccine Safety Initiative Pilot Data Linkage Project**

This is a World Health Organization (W.H.O.) sponsored pilot to evaluate existing infrastructure regarding feasibility of a global consortium to evaluate vaccine safety concerns. Participating sites include eight sites in Latin America plus sites in Iran, Albania, India, Uganda, South Africa, Singapore, China and Australia.

### **Adekunle Dawodu, MBBS, FRCPCH**

#### **Maternal vitamin D supplementation alone to prevent vitamin D deficiency in breastfeeding mothers and their infants**

In this ongoing randomized controlled trial funded by [Qatar National Research Fund](#) to evaluate the effect of maternal vitamin D supplementation alone to prevent vitamin D deficiency in Qatari breastfeeding infants and their mothers, [Adekunle Dawodu, MBBS, FRCPCH](#), in collaboration with researchers in Doha, Qatar found a high prevalence of vitamin D deficiency in the first 60 consecutive enrolled mother-infant pairs. 76% percent of the mothers and 84% of the infants were found to be vitamin D deficient at enrollment in an environment with abundant sunlight. Vitamin D deficiency was associated with lack of sunlight exposure and inadequate vitamin D intake. This is an important finding because it supports a justification to evaluate a combined mother-infant vitamin D supplementation strategy to prevent vitamin D deficiency in this high-risk population.

### **Elizabeth Schlaudecker, MD, MPH**

[Dr. Schlaudecker's](#) research continues to focus on the immunologic responses to maternal immunization. After completing a comprehensive epidemiologic study of the etiology and seasonality of viral respiratory infections in rural Honduras, her interests have shifted to prevention of these infections with maternal immunization.

Her recent work has demonstrated an altered isotype profile in pregnant women compared to non-pregnant women consistent with a decreased response to the vaccine. She is working in [Dr. Sing Sing Way's](#) laboratory with the mentorship of [Dr. Fred Finkelman](#) in the [Division of Immunobiology](#), and with the support of a K12 Child Health Research Career Development Award from the National Institutes of Health (NIH). She is also investigating a novel respiratory syncytial virus (RSV) vaccine in pregnant women with Novavax, Inc., and the immunologic responses to immunization in breast milk with Cincinnati Children's NIH-supported Vaccine and Treatment Evaluation Unit (VTEU).

### **Mark Steinhoff, MD**

In tropical regions, influenza circulates for many months of the year, which makes the policy of using influenza vaccine during the flu "season" not feasible. [Mark Steinhoff](#), with colleagues at Johns Hopkins University, and in Nepal, have designed and are carrying out a prospective placebo-controlled trial of year-round influenza immunization in pregnancy. The study was carried out for two separate annual cohorts with a total of 3,600 women, and surveillance has just been completed. Preliminary evidence shows that the vaccine was effective at least part of the year and further analysis is being carried out.

Dr. Steinhoff's group was one of several groups involved in the evaluation of a new respiratory syncytial virus (RSV) vaccine designed for use in pregnancy to protect the newborn infant. The strategy of maternal immunization to prevent RSV is likely to be a new approach to reducing severe respiratory illness in infants.

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## **Significant Publications**

[Dawodu A](#), Davidson B, Woo JG, Peng YM, Ruiz-Palacios GM, Guerrero, ML. [Sun exposure and vitamin D supplementation in relation to vitamin D status of breastfeeding mothers and infants in the global exploration of human milk study](#). *Nutrients*. 2015 Feb 5;7(2):1081-93.

Vitamin D deficiency is common in breastfed infants and their mothers but a global comparison is lacking. This study which is part of the global exploration of human milk bioactive factors is one of the first to use a standardized protocol for global comparison of Vitamin D status of breastfeeding mothers and their infants. The prevalence of Vitamin D deficiency was found to be higher in a cohort of Mexican and Shanghai than Cincinnati mothers while Vitamin D deficiency was more common in Mexican and Cincinnati than Shanghai infants. Vitamin D deficiency in breastfeeding mothers and their infants appears to be a global problem and the prevalence in diverse population depends on sun exposure behaviors and Vitamin D supplementation. The findings suggest that when sun exposure is inadequate, greater attention to maternal and infant Vitamin D supplementation starting during pregnancy is warranted worldwide.

Chu HY, **Stein hoff MC**, Magaret A, Zaman K, Roy E, Langdon G, Formica MA, Walsh EE, Englund JA. **Respiratory syncytial virus transplacental antibody transfer and kinetics in mother-infant pairs in Bangladesh.** *J Infect Dis.* 2014 Nov 15;210(10):1582-9.

RSV is the most common cause of respiratory hospitalization in the first year of life in the USA. We carried out this study in Bangladesh to assess the transfer of RSV antibody from mother to infant, to estimate the duration of infant protection in this Asian population.

Omer SB, Richards JL, Madhi SA, Tapia MD, **Stein hoff MC**, Aqil AR, Wairagkar N; BMGF Supported Maternal Influenza Immunization Trials Investigators Group. **Three randomized trials of maternal influenza immunization in Mali, Nepal, and South Africa: Methods and expectations.** *Vaccine.* 2015 Jul 31;33(32):3801-12.

With colleagues in Nepal we have carried out a randomized placebo-controlled evaluation of influenza immunization in rural Nepal. This trial and similar trials in South Africa and Mali were supported by the Bill and Melinda Gates Foundation. We are participating in an analysis of all three trials to summarize the effects of maternal immunization in the three very different lower income regions.

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## Division Publications

1. Ahmed P, Babaniyi IB, Yusuf KK, Dodd C, Langdon G, Stein hoff M, Dawodu A. **Vitamin D status and hospitalisation for childhood acute lower respiratory tract infections in Nigeria.** *Paediatr Int Child Health.* 2015; 35:151-6.
2. Black S. **Safety and effectiveness of MF-59 adjuvanted influenza vaccines in children and adults.** *Vaccine.* 2015; 33 Suppl 2:B3-5.
3. Black S. **Potential long term vaccine benefits poorly translate in cost effectiveness modelling.** *BMJ.* 2014; 349:g6764.
4. Dawodu A, Davidson B, Woo JG, Peng YM, Ruiz-Palacios GM, de Lourdes Guerrero M, Morrow AL. **Sun exposure and vitamin D supplementation in relation to vitamin D status of breastfeeding mothers and infants in the global exploration of human milk study.** *Nutrients.* 2015; 7:1081-93.
5. Dawodu A, Zalla L, Woo JG, Herbers PM, Davidson BS, Heubi JE, Morrow AL. **Heightened attention to supplementation is needed to improve the vitamin D status of breastfeeding mothers and infants when sunshine exposure is restricted.** *Maternal and Child Nutrition.* 2014; 10:383-397.
6. Klopfer SO, Stek JE, Petrecz M, Reisinger KS, Black SB, Goveia MG, Nicholson O, Gardner JL, Grosso AD, Brown ML, Kuter BJ, Schodel FP. **Analysis of safety data in children after receiving two doses of ProQuad(R) (MMRV).** *Vaccine.* 2014; 32:7154-60.

7. Pereda MA, Chavez MA, Hooper-Miele CC, Gilman RH, Steinhoff MC, Ellington LE, Gross M, Price C, Tielsch JM, Checkley W. **Lung ultrasound for the diagnosis of pneumonia in children: a meta-analysis.** *Pediatrics*. 2015; 135:714-22.
8. Schlaudecker EP, Heck JP, MacIntyre ET, Martinez R, Dodd CN, McNeal MM, Staat MA, Heck JE, Steinhoff MC. **Comparison of a new transport medium with universal transport medium at a tropical field site.** *Diagn Microbiol Infect Dis*. 2014; 80:107-10.
9. Tielsch JM, Steinhoff M, Katz J, Englund JA, Kuypers J, Khatri SK, Shrestha L, LeClerq SC. **Designs of two randomized, community-based trials to assess the impact of influenza immunization during pregnancy on respiratory illness among pregnant women and their infants and reproductive outcomes in rural Nepal.** *BMC Pregnancy Childbirth*. 2015; 15:40.

## Faculty, Staff, and Trainees

### Faculty Members

**Mark Steinhoff, MD**, Professor  
 Leadership Division Director, Global Child Health  
 Research Interests Maternal immunization; infant infections.

**Steven Black, MD**, Professor  
 Research Interests Vaccine safety.

**Adekunle Dawodu, MD**, Professor  
 Leadership Director, International Patient Coordination  
 Research Interests Vitamin D supplementation.

**Elizabeth Schlaudecker, MD, MPH**, Assistant Professor  
 Research Interests Maternal immunization.

## Grants, Contracts, and Industry Agreements

### Grant and Contract Awards

Annual Direct

#### Black, S

##### Global Alignment of Immunization Safety Assessment

Bill & Melinda Gates Foundation (Brighton Collaboration Foundation)

3/30/2015-11/30/2016

\$30,000

##### Clinical Immunization Safety Assessment

Centers for Disease Control and Prevention

9/29/2013-9/28/2017

\$25,658

##### Enhanced Evaluation of Risk of Narcolepsy Associated with Pandemrix and Arepanrix

Centers for Disease Control and Prevention (Brighton Collaboration Foundation)

9/29/2012-9/28/2015

\$61,904

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**Dawodu, A**

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**Maternal Vitamin D Supplementation to Prevent Vitamin D Deficiency in Mothers and their Infants**

Qatar National Research Fund (Hamad Medical Corporation)

11/20/2013-11/19/2016

\$77,240

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**Staat, M**

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**Potential Mechanisms for Intussusception after Rotavirus Vaccine**

Centers for Disease Control and Prevention

9/29/2014-9/28/2016

\$334,578

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**Steinhoff, M**

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**Mother's GIFT Field Trial**

Bill & Melinda Gates Foundation

50274

12/11/2008-11/30/16

\$3,265,733

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**Current Year Direct**

**\$3,795,113**

**Industry Contracts**

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**Dawodu, A**

Procter and Gamble

\$280,346

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**Current Year Direct Receipts**

**\$280,346**

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**Total**

**\$4,075,459**

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# Efficient Transplacental Antibody Transfer From Mother to Fetus Crucial to Infant Health



Mark Steinhoff, MD

PUBLISHED NOV. 15, 2014

*The Journal of Infectious Diseases*

An international collaboration led by Mark Steinhoff, AMD, Director of the Division of Global Child Health, is advancing scientific understanding of how to protect infants from respiratory syncytial virus (RSV), the most important viral cause of infant pneumonia, though there is limited information from tropical regions.

The study, published Nov. 15, 2014, in *The Journal of Infectious Diseases*, is crucial research because, globally, pneumonia is the leading cause of childhood mortality.

The research team, which included colleagues in Seattle, WA, Rochester, NY, and Dhaka, Bangladesh, examined the role of maternal serum antibody in protecting infants from RSV. The team found that efficient transplacental transfer of RSV-specific antibody from mother to the fetus was documented in mother-infant pairs in Asia, and that higher cord-blood antibody titers were associated with infant protection from serologic RSV infection.

Findings were based on serial serum samples collected from mother-infant pairs in Bangladesh, from the third trimester of pregnancy to 72 weeks postpartum. They tested these using an RSV antibody microneutralization assay, and defined serologic infection as a four-fold increase in antibody titer (the highest dilution factor at which a positive reading is yielded). Maternal antibody half-life was calculated using infant antibody titers from birth to 20 weeks.

Researchers found that the ratio of infant cord blood to maternal serum RSV antibody titers in 149 mother-infant pairs was 1.01, and that there was a clear association between higher cord blood RSV antibody titers and lower risk of infant serologic infection.

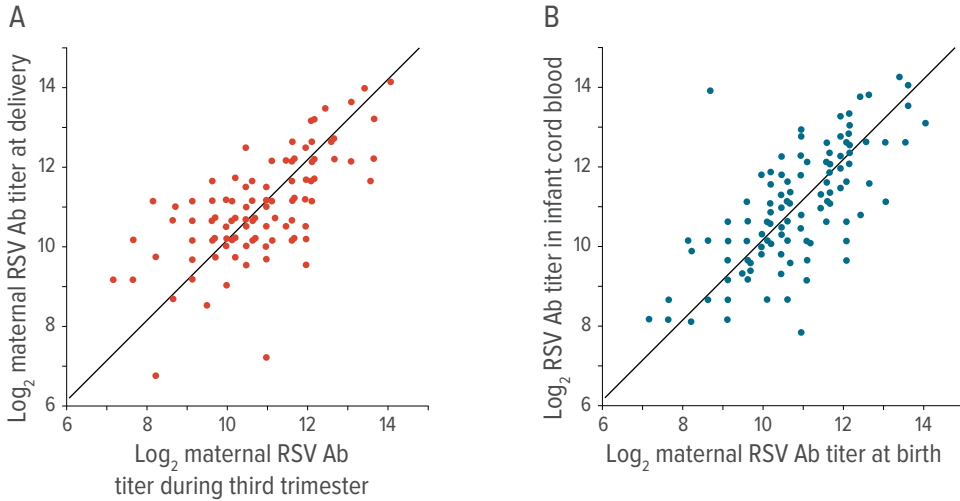
In addition to this major initiative in battling pneumonia in Bangladesh, Global Child Health also works to assess the disease risks and increase the availability of childhood vaccines for pneumococcal and influenza viruses in other countries with limited resources, including India, Sri Lanka, Indonesia and Nepal.

## RESEARCH AND TRAINING DETAILS

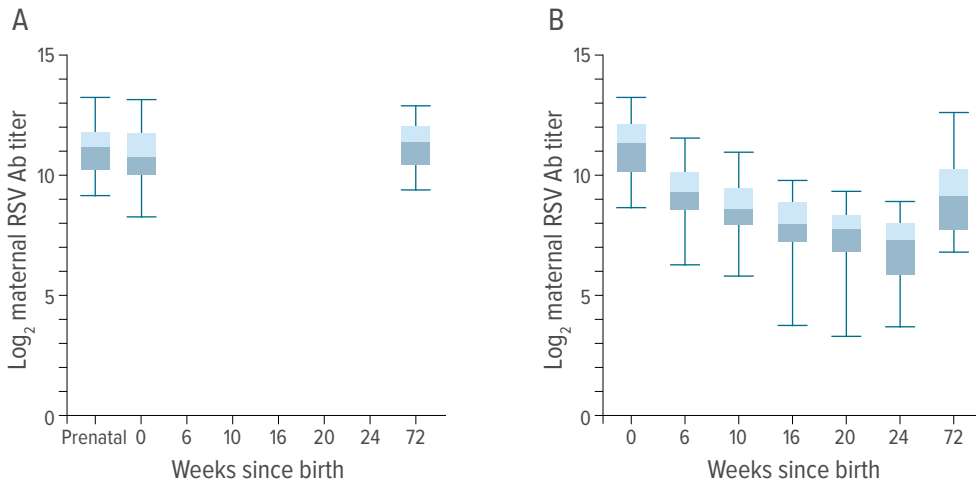
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Chu HY, Steinhoff MC, Magaret A, Zaman K, Roy E, Langdon G, Formica MA, Walsh EE, Englund JA. *J Infect Dis.* 2014 Nov 15;210(10):1582-9. doi: 10.1093/infdis/jiu316. Epub 2014 Jun 5.

COMPARISON OF LOG<sub>2</sub> MATERNAL RESPIRATORY SYNCYTIAL VIRUS (RSV) ANTIBODY (AB) TITERS IN THE THIRD TRIMESTER AND LOG<sub>2</sub> MATERNAL RSV AB TITERS AT BIRTH (R=0.68).



MATERNAL LOG<sub>2</sub> RESPIRATORY SYNCYTIAL VIRUS (RSV) ANTIBODY (AB) TITERS IN THE THIRD TRIMESTER, AT BIRTH, AND AT 72 WEEKS POSTPARTUM.



In a study examining the role of transplacental antibody transfer in infant health, these titer testing images show how mean maternal Ab titers in the third trimester were correlated with titers at birth and week 72 of the postpartum period (R = 0.68 and R = 0.47, respectively). The top charts compare the mother’s antibody titer to respiratory syncytial virus (RSV) in the third trimester (left) and at birth. The bottom charts show the levels at birth (left) and then 72 weeks later. The findings show a clear association between higher cord blood RSV antibody titers and lower risk of infant infection.