RESULTS: RSV F protein-specific IgA and IgG levels in breast milk, but not total IgA and IgG or RSV G protein-specific antibodies, were significantly higher in women who received RSV F vaccine than in placebo recipients. Both background levels and vaccine-stimulated levels were markedly higher in colostrum, as expected, but RSV-specific antibodies also persisted in vaccine recipients for 180 days (p≤0.0003 for both RSV-specific IgA and IgG at all post-delivery time points). RSV/A-specific neutralizing antibodies were 3-fold higher in the colostrum of RSV F vaccine recipients relative to controls (p=0.0333); precision of the neutralization contrasts at later timepoints was limited by technical limitations and small sample size, although point estimates were higher for at least 35 days. Geometric mean concentrations in ELISA were 28 to 31 units/mL for specific IgA in vaccinees, versus 9 to 13 in controls. Geometric mean concentrations in ELISA were 227 to 360 μg/mL for specific IgG in vaccinees, versus 40 to 107 in controls.

CONCLUSION: Sustained high levels of specific anti-RSV antibodies in breast milk suggest that breastfeeding may provide local mucosal protection against RSV to the infant. Additional studies are needed to determine the immunologic impact of breast milk-mediated protection following maternal RSV immunization.

LEARNING OBJECTIVES: Learners will be able to identify the potential impact of anti-RSV antibodies in breast milk following maternal RSV immunization.

11 Safety of third trimester immunization with a respiratory syncytial virus F protein vaccine and protection of infants over the first 180 days of life against all-cause lower respiratory tract infection

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OBJECTIVES: The Pneumovirus family includes two human pathogens: human metapneumovirus (HMPV) and respiratory syncytial virus (RSV), that cause respiratory disease in infants. We studied the impact of maternal immunization with RSV F protein nanoparticle vaccine on pneumovirus and all-cause severe lower respiratory tract infection (LRTI) in the first 90 to 180 days of infant life.

METHODS: We recruited 4,636 women with low-risk singleton 3rd 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 safety for 6 months post-delivery, and infants for 1 year. Surveillance of infants for LRTI, with virus detection by RT-PCR, physical examination, and pulse oximetry, was carried out for 180 days from delivery.

RESULTS: Results: The RSV F vaccine was well tolerated in women, with modest reactogenicity and no apparent negative impacts on pregnancy, delivery, or infant well-being. Vaccine-induced maternal antibodies were transferred efficiently, with enhanced transfer (1.29 to 1.92-fold, depending on the antibody specificity measured) when the interval from immunization to delivery was 30 days. Efficacy against severe LRTI through 90 days of life in infants was as follows:

Table 1. HMPV added few severe cases, but including these did not dilute efficacy possibly due to cross-reactive F protein immunity between RSV and HMPV. With decay of maternal antibodies, efficacy estimates declined from day 90 through day 180 of life. Persistence of protective effects from 90 to 180 days remains to be better defined with larger case numbers.

CONCLUSION: RSV F vaccine was safe in the 3rd trimester and was associated with reduced rates of severe infant LRTI. Our data suggest that this strategy could reduce infant all-cause LRTI with severe hypoxemia by 13 cases, and all-cause LRTI hospitalization by 28.5 cases, per 1000 infants over the first 180 days of life.

LEARNING OBJECTIVES: To recognize the impact of the timing of maternal immunization on the efficiency of transplacental transfer of vaccine-induced antibodies. To recognize the potential impact of RSV prophylaxis in early infancy on pneumovirus and all-cause respiratory morbidity beyond the RSV season.

12 Randomized trial to prevent congenital cytomegalovirus

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OBJECTIVES: Primary CMV infection during pregnancy carries a high risk of transmission to the fetus with the potential for severe sequelae including fetal death, premature birth, hearing loss and developmental delay. There is no universally accepted method of preventing congenital CMV. Our objective was to evaluate whether CMV hyperimmune globulin (HIG) administered to women with primary CMV during pregnancy reduces congenital infection.

METHODS: Multicenter randomized double-masked trial of women with a singleton gestation < 24 weeks with primary CMV infection defined by the presence of either CMV IgM and IgG with low avidity or IgG seroconversion, as assessed at a central reference laboratory. Those with presumptive or confirmed evidence of fetal CMV were not eligible. Monthly infusions of HIG (100 units/kilogram) or placebo were given until delivery. The primary outcome was fetal loss or neonatal CMV infection defined as CMV by PCR or culture in urine or saliva within 3 weeks of birth, in amniotic fluid prior to delivery or in postmortem tissue. A sample size of 800 was planned to detect at least 30% reduction in the primary outcome with 90% power and type I error 5%.

RESULTS: From 2012 to 2018, 206,111 pregnant women were screened; 712 (0.35%) had primary CMV infection, of whom 399 (56%) were enrolled at 17 centers. The trial was stopped for futility at the recommendation of the Data and Safety Monitoring Committee due to a planned interim analysis that revealed complete enrollment was statistically very unlikely to demonstrate a significant difference between the groups. The mean gestational age at randomization was 16.2 and 15.6 weeks in the HIG and placebo groups, respectively. Primary outcome data were available for 394 participants (98.7%). The primary outcome rate was 22.7% in the HIG group and 19.4% in the placebo group (relative risk [RR], 1.17; 95% confidence interval [CI], 0.80 to 1.72; p=0.42). Overall there was no significant difference in the proportion of women with a side effect; however, those receiving HIG had a higher rate of headache (P=0.05) and shaking chills (P=0.03). The rate of preterm birth was 12.2% in the HIG group and 8.3% in the placebo group (RR, 1.47; CI 0.81 to 2.67; P=0.2). No statistical interactions were found in pre-specified subgroup analyses.

CONCLUSION: CMV HIG was not effective at decreasing the risk of congenital CMV infection or fetal death among women with primary CMV infection in early pregnancy.

LEARNING OBJECTIVES: Learners will be able to characterize the effectiveness of CMV HIG at prevention of congenital CMV infection among women with primary CMV in early pregnancy

13 Real-world outcomes associated with nucleic acid amplified versus direct DNA probe testing for vaginitis

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OBJECTIVES: To address the ongoing discussion related to the costs of diagnosing vaginitis the study compared the impact of diagnoses using nucleic acid amplified testing (NAAT) with direct DNA probe (DP). Real-world outcomes using commercial medical claims data compared the diagnostic and therapeutic costs among vaginitis patients between a general population of women and women with diabetes.

METHODS: The IBM Watson Health MarketScan® Commercial database was used to identify women aged 18 to 64 years with evidence of a new diagnosis of vaginitis that occurred between 2012 and 2017. Patients were stratified by type of testing used to determine the vaginitis diagnosis. All-cause healthcare expenditures were measured during 6-month and 12-month follow-up periods. Outcomes were described by testing cohort (NAAT, DP) and patient type: general and diabetic (Type I, II).

RESULTS: In total, 207,113 women with commercial insurance met the inclusion and exclusion criteria (NAAT cohort, N=108,559; DP cohort, N = 98,554) a sub-cohort of 12,522 women with diabetes (NAAT cohort, N=6,463; DP cohort, N = 6,059) was analyzed separately. Overall healthcare costs among all patients were higher in the DP cohort in the 6-month follow-up period ($5,042 DP vs $4,872 NAAT, p=.0025) and 12-month follow-up period ($9,366 DP vs $8,938 NAAT, p<.0001). In the cohort of women with diabetes, the NAAT group trended lower in both the 6 months ($9,344 DP vs $8,972 NAAT) and in the 12 months following the diagnosis ($17,715 vs $17,083 NAAT) although not statistically significant.

CONCLUSION: NAAT testing for vaginitis reduces healthcare costs compared to DP in the general population. While managing vaginitis among women with diabetes presents challenges for the clinician, more information will be helpful to understand how a NAAT test may provide improved outcomes and impact patient management decisions.

LEARNING OBJECTIVES: Learners will be able to describe the healthcare resource utilization and costs of vaginitis diagnosis associated with use of NAAT and DP tests.

14 Characterizing the vaginal microbiome in women with recurrent bacterial vaginosis and treatment implications

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OBJECTIVES: We aimed to characterize the vaginal microbiome in women with recurrent bacterial vaginosis (BV) compared to women without infection, and to describe the effect of oral metronidazole treatment on the microbiome of recurrent BV.

METHODS: Women aged 18-40 years, with recurrent BV, were prospectively enrolled. Vaginal samples (lavage) were collected at baseline (D0), at 7-10 days (D7) and 30-40 days (D30) after initiation of oral metronidazole treatment (500mg BID, 7 days). DNA was extracted, amplified using primers targeting the V3-V4 region of the 16srRNA, and then sequenced and processed through a hybrid Qiime MICCA bioinformatics pipeline.

RESULTS: Sixty-three participants, 17 recurrent BV patients and 46 controls, were enrolled. Beta diversity (p=0.045), but not alpha diversity (p=0.076) differed significantly between recurrent BV and control groups. The genera Gardnerella and Prevotella were relatively more abundant, while Lactobacillus was relatively less abundant in recurrent BV vs. control groups. Alpha diversity decreased (p=0.0049) after treatment with oral metronidazole, but increased (p=0.0062) to near baseline by D30. Metronidazole treatment resulted in an increase in Lactobacillus and decrease in Gardnerella that was not maintained after 30 days. Of the 10 recurrent BV patients with data for all three time points, 4 relapsed by D30. Beta diversity (p=0.044), but not alpha-diversity (p=0.07), differed significantly between patients that relapsed and those that did not.

CONCLUSION: Recurrent BV patients have significantly different beta diversity, less Lactobacillus and more Gardnerella and Prevotella, when compared to control patients. Oral metronidazole is associated with a decrease in alpha diversity, increased levels of Lactobacillus and decreased amounts of Gardnerella.

LEARNING OBJECTIVES: Learners will be able to describe (1) the composition of the vaginal microbiome in women with recurrent BV and how it differs from that of controls (2) how the vaginal microbiome of women with recurrent BV changes with metronidazole treatment.

15 Diagnostic accuracy of clinical criteria for bacterial vaginosis, vulvovaginal candidiasis and BV/VVC co-infections

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OBJECTIVES: Approximately 8-18% of women having vaginal symptoms have been reported to have concurrent BV and VVC. The objective of this study was to assess the agreement between laboratory and clinical diagnosis of BV alone, VVC alone and BV/VVC co-infections when standardized criteria were employed in the context of a clinical treatment trial.

METHODS: Between 6/5/15 and 5/31/18, 1315 women were screened for a clinical trial evaluating treatment of vaginal infections at 51 sites in the US. Clinical diagnosis of BV was based on four Amsel criteria (discharge, vaginal pH >4.5, positive whiff test, ≥ 20% clue cells). Diagnosis of VVC was based on composite signs and symptoms score ≥2 (itching, burning, irritation, edema, erythema, excoriation) plus hyphae/pseudohyphae or yeast buds in vaginal fluid. Women having clinically documented co-BV/VVC had to meet the criteria for both conditions. Vaginal smears for diagnosis of BV using the Nugent criteria and vaginal swab samples were shipped overnight to a centralized laboratory for cultivation of yeast on Sabouraud's agar. A total of 891 women were randomized to treatment; Gram stains, vaginal yeast cultures or both were missing for 19 women leaving an evaluable population of 872 women..

RESULTS: The study population had a median age of 29 (range 17-66) and was 33.7% white, 62.7% black and 3.6% other self-reported race. Of the 194 women diagnosed with BV alone, 156 (80%) had a Nugent score ≥7, but 42 (22%) also had yeast detected by culture, with 33 (20%) women having both BV and yeast based on lab testing. Among 207 women diagnosed with VVC alone, only 147 (71%) had a positive yeast culture and 34 (16%) had a Nugent score ≥7. Based on lab testing, both BV and yeast were present in 29