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Background: Varicella (VAR) and measles-mumps-rubella (MMR) vaccines are recommended for children at ages 12–15 months and 4–6 years. These are administered as separate MMR and VAR vaccines (MMR+VAR) or as combined measles-mumps-rubella-varicella (MMRV) vaccine. Herpes zoster (HZ), caused by wild-type or vaccine-strain varicella-zoster virus, can occur in children after varicella vaccination. It is unknown whether HZ incidence after varicella vaccination varies by vaccine formulation or simultaneous receipt of MMR.

Methods: Using data from six integrated health systems, we examined HZ incidence among children who turned 12 months old during 2003–2008 and received varicella and MMR vaccines according to routine recommendations. All HZ cases ≥ 21 days after first varicella vaccination were identified using ICD-9 codes from inpatient, outpatient, emergency room encounters, and claims data, through 2014. HZ incidence was examined by vaccine formulation (MMR+VAR, MMRV, or VAR without same-day MMR) and doses received and compared using incidence rate ratios (IRR).

Results: Among 199,797 children, we identified 601 HZ cases. Crude HZ incidence after first-dose MMR+VAR (18.6 [95% CI 11.1–29.2] cases/100,000 person-years) was similar to the rate after first-dose MMRV (17.9 [95% CI 10.6–28.3] cases/100,000 person-years), but approximately double the rate among those with first-dose VAR without same-day MMR (7.5 [95% CI 3.1–15.0] cases/100,000 person-years); see Table 1. The IRR for HZ after first-dose MMR+VAR or MMRV, compared with VAR, was 2.5 (95% CI 1.4–4.4; $P = 0.002$). When examining any first or second dose formulation, crude HZ incidence was lower after the second varicella vaccine dose (13.9 cases/100,000 person-years), than in the period before the second dose (i.e., between first and second doses or after the first dose in children with only one dose; 21.8 cases/100,000 person-years, $P < 0.0001$). HZ incidence was also lower after two varicella vaccine doses in each of the three first-dose formulation groups.

Conclusion: HZ incidence among children varied by first-dose varicella vaccine formulation and number of varicella vaccine doses. Regardless of the first-dose varicella vaccine formulation, children who received two vaccine doses had lower HZ incidence after the second dose.

Table 1. Herpes zoster crude incidence rates by varicella vaccine formulation and number of doses, 2003-2014

Formulation of first varicella vaccine dose, age 12-18 months (N)	Number of HZ cases following one dose / two doses of varicella vaccine	Overall incidence rate (CI) [1]	Incidence rate after one dose of varicella vaccine (CI) [2]	Incidence rate after two doses of varicella vaccine, by first dose vaccine formulation (CI)	P value [3]
VAR alone [4] (9,386)	8 / 4	7.5 (3.1-15.0)	9.8 (4.7-18.1)	5.0 (1.6-11.7)	0.26
MMR+VAR [5] (126,349)	245 / 176	18.6 (11.1-29.2)	21.5 (13.4-32.6)	15.7 (8.9-25.6)	0.001
MMRV (64,062)	116 / 52	17.9 (10.6-28.3)	24.5 (15.8-36.3)	11.2 (5.6-19.9)	<0.0001
Overall (199,797)	369 / 232	17.9 (10.6-28.3)	21.8 (13.6-33.0)	13.9 (7.6-23.4)	<0.0001

NOTE: HZ = herpes zoster, CI = confidence interval, VAR = single-antigen varicella vaccine, MMR = combination measles, mumps, rubella vaccine, MMRV = combination measles, mumps, rubella, varicella vaccine; incidence rates displayed per 100,000 person-years

[1] Includes all HZ cases following receipt of one or two doses of varicella vaccine

[2] Limited to cases in children following one dose of varicella vaccine, either occurring before the receipt of a second varicella vaccine or in those that received only one dose of varicella vaccine

[3] Comparing HZ incidence after one varicella vaccine dose vs. two varicella vaccine doses, by first dose varicella formulation group; any second dose varicella formulation

[4] Children also received MMR between 12-18 months of age, but at least 30 days before or after VAR

[5] Received both vaccines on the same day

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2768. Does Social Media Contribute to Knowledge About Vaccine Safety?

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Background: Social media is frequently used to share medical information. Current European regulatory guidance for the pharmaceutical industry calls for reporting valid adverse events (AE) derived from social media as well as consideration of non-valid AEs. This guidance is followed when our company utilizes social media related to any company products and interests. Here we evaluate its application to vaccines.

Methods: Posts collected from all screened social media sources (company owned, or company reviewed) were examined (August 1, 2017–February 28, 2019) to identify safety-related information pertaining to any of its 14 licensed vaccines. Posts were classified as valid cases (i.e., containing information about company product, AE, and identifiable reporter), non-valid cases (i.e., company product, AE, but missing an identifiable reporter), or not relevant (no safety-related information; not further analyzed). Valid cases were added to the company's safety database; non-valid cases were reviewed for trends requiring further analysis. Both, valid and non-valid cases, were analyzed as part of routine safety surveillance

Results: Among 69,682 vaccine-related posts reviewed, 285 (0.4%) were valid; 11,464 (16.5%) were non-valid; 47,966 (83.1%) were not relevant. Most non-valid cases concerned the company's 4-valent (8,934 [78%]) or 9-valent (1,420 [12%]) human papillomavirus vaccines, followed by its measles-mumps-rubella (336 [2.9%]), pneumococcal (282 [2.5%]), and herpes zoster (246 [2.1%]) vaccines. Review of data from selected temporal spikes in posts demonstrated that they were usually attributable to increased reposts of an original post or to personal views, rather than containing incremental factual new safety data.

Conclusion: Fewer than 1% of posts from relevant social media sources contained sufficient information to be considered valid cases. No new safety signals were identified for any of the vaccines from social media cases (valid or non-valid). Among posts containing safety information, the nature of this information tends to be redundant or sentimental, precluding meaningful safety analyses.

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2769. The Clinical and Economic Impact of MMR Vaccinations to Prevent Measles Importations from US Pediatric Travelers Returning from Abroad

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Background: Although pediatric travelers comprise < 10% of US international travelers, they account for almost half of all measles importations among returning travelers. For travelers 1–18 years with no other evidence of measles immunity, the Advisory Committee on Immunization Practices (ACIP) recommends 2 MMR vaccine doses before departure; 1 dose is recommended for infant travelers (6 to <12 months) and does not count toward their primary immunization series. All US travelers (6 months to < 6 years) are at risk for being undervaccinated for measles because MMR is routinely given at 1 years and 4–6 years.

Methods: We developed a decision tree model to evaluate the clinical impact and cost per case averted of pretravel health encounters (*PHE*) that vaccinate MMR-eligible pediatric international travelers. We compared 2 strategies for infant (6 to < 12 months) and preschool-aged (1 to <6 years) travelers: (1) *no PHE*: travelers departed with baseline MMR vaccination status vs. (2) *PHE*: MMR-eligible travelers were offered vaccination. All simulated travelers experienced a destination-specific risk of measles exposure during travel (mean, 237exposures/10M travelers; range, 19–6,750 exposures/10M travelers); if exposed to measles, travelers were at risk of illness stratified by age and MMR vaccination status (range, 0.03–0.90). Costs include direct medical costs and lost work wages for guardians. Model outcomes included measles cases, costs, and cost per case averted. We varied inputs in sensitivity analyses.

Results: Compared with *no PHE*, *PHE* averted 451 measles cases at $985,000/case averted for infant travelers and 54 measles cases at $1.5 million/case averted for preschool-aged travelers (table, bottom). *PHE* can be cost-saving for travelers to regions with higher risk of measles exposure and if more MMR-eligible travelers are vaccinated at PHE (Figure 1). At a risk of exposure associated with European travel, PHE had better value when a measles importation led to a higher number of contacts or more US-acquired cases per importation (Figure 2).

Conclusion: *PHE* for pediatric travelers (6 months to <6 years) decreased the number of imported measles cases and saved costs, especially if targeted to travelers with higher-risk destinations, if more MMR-eligible travelers are vaccinated at PHE, or if outbreaks are larger.

Table: Input parameters and base case results in a model of clinical and economic impact of MMR vaccinations to prevent measles importations from US pediatric travelers

	Infant (age 6-<12m)			Preschool-aged (age 1-<6y)			Reference
Model Input Parameters							
Number of past MMR vaccinations	0	1	2	0	1	2	
% of cohort with past MMR vaccination	92%	8%	N/A	8%	52%	40%	[1]
Risk of measles infection, if exposed	90%	16%	N/A	90%	7%	3%	[2,3,4]
US-acquired cases per importation (n)	4	4	N/A	4	4	0	[5,6]
Contacts per importation (n)	1,500	1,500	1,500	1,500	1,500	1,500	[7]
Vaccination of MMR-eligible at PHE		44%			56%		[1]
Cost of vaccination		$90			N/A*		[8]
Cost per PHE			$7				[9]
Cost per measles importation			$13,200				[9]
Cost per US-acquired case			$4,800				[9]
Cost per contact			$550				[7,9]
Model Results							
Measles importations/10M travelers							
No PHE		199			29		
PHE		109			19		
US-acquired cases/importation							
No PHE		797			103		
PHE		436			59		
Cases averted		451			54		
Costs per 10M travelers (USD)							
No PHE		$170.6M			$24.4M		
PHE		$616.5M			$104.4M		
Cost/case averted		$985,000			$1.5M		

*Because MMR-eligible pre-school aged travelers receive a routine dose of MMR early at the PHE, there is no added cost of vaccination.
Abbreviations: MMR: Measles-mumps-rubella; PHE: pretravel health encounter
References: [1] Global TravEpiNet (GTEN) data (2009-18) [2] McLean HQ et al. *MMWR* 2013 [3] Moss WJ *JID* 2011 [4] CDC Yellow Book 2018 [5] Fiebelkorn AP et al. *JPIDS* 2017 [6] Rota et al. *JID* 2011 [7] Ortega-Sanchez IR et al. *Vaccine* 2014 [8] CDC vaccine price list 2019 [9] Hyle EP et al. *Ann Int Med* 2017

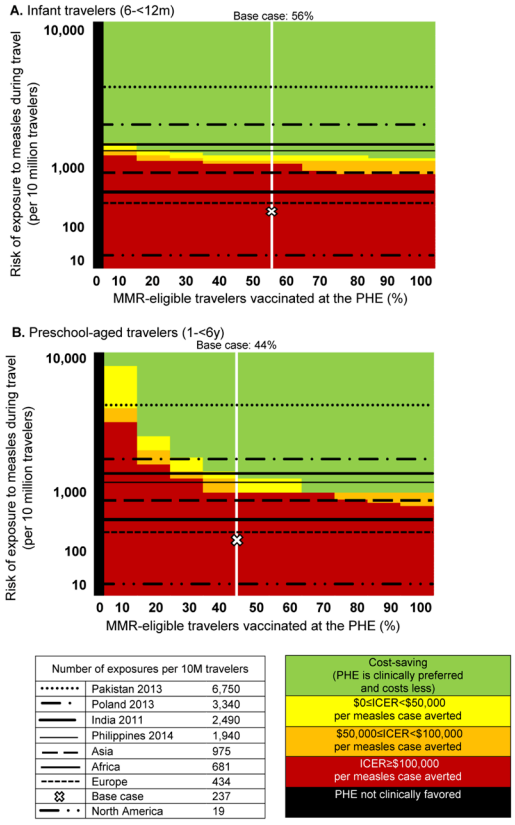

Figure 1. Two-way sensitivity analyses examining the value of MMR vaccination at the PHE across a range of possible risk of exposure to measles during travel and the percentage of MMR-eligible travelers vaccinated. Abbreviations: MMR: measles-mumps-rubella; PHE: pretravel health encounter; ICER: incremental cost-effectiveness ratio.

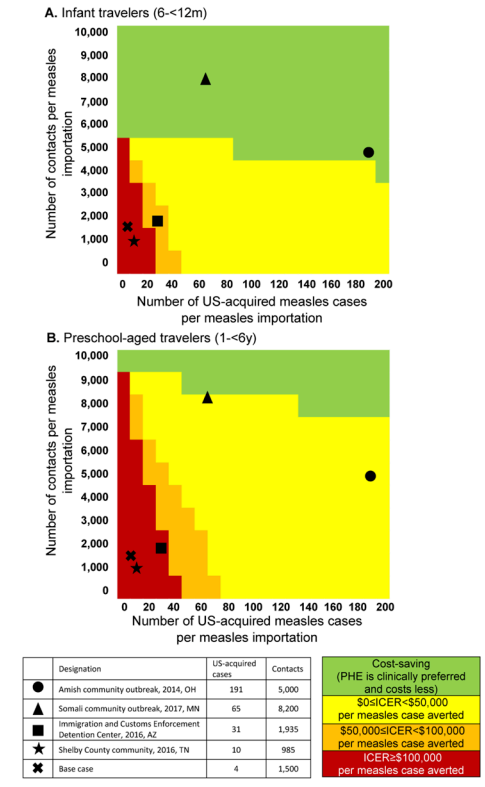

Figure 2. Two-way sensitivity analyses of the value of MMR vaccination at the PHE varying the number of contacts traced per measles importation and the number of US-acquired measles cases per measles importation at a risk of measles exposure associated with travel to Europe (434 exposures/10M travelers). Abbreviations: PHE: pretravel health encounter; ICER: incremental cost-effectiveness ratio.

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2770. Intrapulmonary Vaccination with an M Protein-Deficient Respiratory Syncytial Virus (RSV) Vaccine Protects Infant Baboons Against an RSV Challenge

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Background: RSV infection is a major cause of lung disease in infants, yet there is no licensed vaccine. We are developing a live RSV vaccine with a deletion of the M protein ("Mnull RSV"). The RSV M protein is responsible for assembling newly synthesized RSV proteins into intact virus. Mnull RSV infects cells, replicates all proteins except M, and incites antibody and T-cell responses but, in the absence of the M protein, cannot replicate and infect other cells. We wished to show that vaccination with Mnull RSV directly into the lung in early infancy induces persistent neutralizing antibody (NA) responses that protect infant baboons against an RSV challenge.

Methods: Two-week-old infants were vaccinated with a single dose of Mnull RSV (8×10^7 vaccine units) or a sham preparation instilled into an endotracheal tube. Infants were observed continuously for signs of rapid breathing using infrared cameras. Four to six months later, serum RSV NA titers were determined, and infants were challenged intratracheally with the human RSV A2 strain. Respiratory rates were calculated daily. On days 0, 5, 7, and 12 after infection, arterial blood was drawn for blood gas analysis, lung function was assessed using a pneumotachometer, and bronchoalveolar lavage was performed for virus titrations.

Results: At 4–6 months following vaccination, RSV NA was present at a mean titer of 192 in sera of Mull RSV recipients, but was undetectable in sera of sham vaccinated animals. Animals were then challenged with RSV, and sham vaccinated animals developed increased respiratory rates, increased alveolar-arterial (A-a) oxygen gradients, and BAL viral titers on day 5 were 3,500 pfu/mL. In contrast, Mnull RSV vaccinated animals had lower respiratory ratios throughout the length of the study ($P = 0.038$), lesser A-a gradients (improved oxygenation) vs. controls, and no virus was recovered from BAL fluids ($P < 0.0001$).

Conclusion: Intrapulmonary vaccination of infantswith Mnull RSV at 2 weeks of age results in strong RSV NA responses that persist beyond the length of an average RSV season. Mnull RSV recipients were protected against tachypnea, reduced oxygenation and viral replication for at least 4–6 months following vaccination. We will next study intrapulmonary vaccination administering Mnull RSV via a nebulizer.

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2771. Seroprotection against Measles, Rubella, Tetanus, and Diphtheria Among Children in Haiti—2017

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Background: Measles, rubella, and maternal and neonatal tetanus have been verified to be eliminated in Haiti, but a diphtheria outbreak has been ongoing since 2014. To evaluate progress toward maintaining vaccine preventable disease (VPD) elimination and control, we conducted the first survey to estimate immunity to these VPDs among children in Haiti.

Methods: We conducted a nationally representative, two-stage cluster survey in 2017, stratifying Haiti into 2 regions: (1) West Region, the highly urban West department that includes one-third of Haiti's population; (2) Non-West Region (all other departments). We sampled 4,286 households to recruit at least 910 children aged 5–7 years. We obtained vaccination history and dried blood spots from one eligible child per household. Antibody concentrations to VPDs were measured on a multiplex bead assay. We compared seroprotection and vaccination coverage estimates.

Results: Among 1146 enrolled children, tetanus (83%, 95% CI: 80%–86%) and diphtheria (83%, 95% CI: 81%–85%) seroprotection were higher than coverage with ≥3 doses of tetanus and diphtheria containing vaccine (DTP3) (68%, 95% CI: 61%–74%). No participants had antibody concentrations consistent with long-term immunity to tetanus or diphtheria. Measles (87%, 95% CI: 85%–89%) and rubella (84%, 95% CI: 81%–87%) seroprotection were higher than or similar to coverage with at least one dose of measles-rubella (MR) vaccine (84%, 95% CI: 80%–87%) (Figure 1). MR second-dose coverage was 20% (95% CI: 16%–24%). Seroprotection in the West Region was lower than in the non-West region for all VPDs.