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Background: Pediatric hematopoietic cell transplant (HCT) recipients often fail to have robust responses to influenza (flu) vaccine. We conducted a blinded phase II trial comparing high-dose (HD) trivalent inactivated vaccine (TIV) vs. standard dose (SD) quadrivalent inactivated vaccine (QIV).

Methods: Children 3–17 years old and 3–35 months post-allogeneic HCT were enrolled at 9 centers and randomized to either 2 doses of HD-TIV or SD-QIV during the 2016–2017 flu season. We compared immune responses by hemagglutination inhibition (HAI) from children 3–11 (early) vs. 12–35 (late) months (m) post-HCT to 3 common flu vaccine antigens, irrespective of vaccine type. HAI responses were evaluated at baseline (visit 1), 1 m post dose 1 (visit 2) and dose 2 (visit 3), and 7 m post dose 2 (visit 4). Geometric mean titers (GMT) were adjusted for baseline log-titer values.

Results: Thirty-one children, median age 11 (7–15) years, were enrolled; 17 (55%) were immunized early and 14 (45%) late. Over 50% of patients had a potentially seroprotective (≥1:40) HAI titer at baseline, with no significant difference post-vaccination between early and late subjects. Table 1 compares early vs late subjects with HAI seroconversion (4-fold HAI titer rise). Post dose 1, late subjects, compared with early, had higher rates of seroconversion to all influenza strains. Post dose 2, early subjects, compared with late, had increased seroconversion. Late subjects had higher GMTs for H1N1 post dose 1 and 2, H3N2 after dose 1, and strain B/VIC post dose 1 and 2 (Figure 1). Although immunogenicity waned throughout flu season, higher seroconversion rates and GMT to H3N2 and strain B/VIC were retained in late subjects.

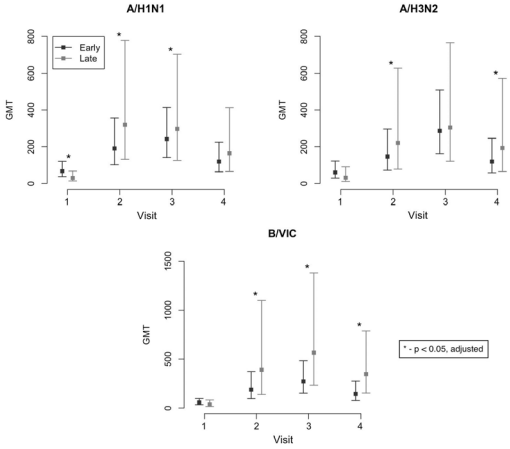
Conclusion: Compared with subjects in early post-HCT group, late post-HCT subjects had better flu vaccine immune responses as noted by higher GMT and HAI seroconversion. However, 2 doses seemed more beneficial in the early post-HCT group. Future analyses are underway, including comparing immunogenicity of HD vs. SD flu vaccine.

Table 1. Percent of early (E) vs late (L) subjects with HAI seroconversion[d]

Visit	Strain								
	A/H1N1			A/H3N2			B/VIC		
	E	L	P Value	E	L	P Value	E	L	P Value
2[b]	6	71	<0.001	0	57	0.002	19	71	0.01
3[c]	24	71	0.02	29	64	0.11	35	79	0.04
4[c]	8	46	0.08	15	62	0.04	15	77	0.006

[a]Early (n=17) & Late (n=14)
[b]Early (n=16) & Late (n=14)
[c]Early (n=13) & Late (n=13)
[d]From baseline

Figure 1. Geometric Mean Titers Pre- and Post-Vaccination in Subjects Receiving Early vs Late Flu Vaccine



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2760. Accounting for Vaccination History in Estimates of Current Season Vaccine Effectiveness in the US Flu VE Network, 2012–2013 Through 2017–2018

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Background: Current season vaccine effectiveness (VE) and influenza risk may vary in persons based on vaccination history. United States Influenza Vaccine Effectiveness (US Flu VE) Network studies have explored prior vaccination effects using a single referent group of patients unvaccinated in both the prior and current seasons. We investigated vaccine benefit among those with and without prior season vaccination.

Methods: Our analysis included data from the US Flu VE Network among patients aged ≥9 years old with acute respiratory illness during 6 influenza seasons, 2012–2013 through 2017–2018. We determined current and prior season vaccination status from documented immunizations. Current season VE against laboratory confirmed influenza was estimated using multivariate logistic regression with an interaction term for prior and current season vaccination. Models were adjusted for age, calendar time, high-risk status, and site.

Results: Of 31,819 patients included in the analysis over 6 seasons, 9188 were influenza positive by RT–PCR. Percent flu positivity was greatest among those unvaccinated (34%), followed by those vaccinated in the prior season only (29%), those vaccinated in both seasons (25%), and those vaccinated in the current season only (23%). Among patients with prior season vaccination, current season VE against any influenza was 14% (95% CL: 5, 22) and against A(H3N2), A(H1N1)pdm09, and B was 10% (95% CL: 3, 17), 36% (95%CL: 25, 46), and 40% (95% CL: 33, 46), respectively. Among patients unvaccinated in the prior season, VE was 42% (95% CL: 37, 46) against any influenza in the current season and was 31% (95%CL: 22, 39), 57% (95% CL: 47, 65), and 55% (95% CL: 48, 61) against A(H3N2), A(H1N1)pdm09, and B, respectively. We observed significant interaction of prior season vaccination on current season VE in 4 of 6 seasons ($P < 0.20$).

Conclusion: Current season vaccination was overall protective regardless of vaccination history. Among those vaccinated in the prior season, current season vaccination may provide some benefit in addition to residual protection from previous vaccination.

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2761. Interventions to Improve Influenza Vaccination Coverage in Children with Medical Comorbidities: A Meta-Analysis

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Background: Influenza vaccination is the most effective influenza prevention tool for children with medical comorbidities. Despite this, coverage remains inadequate. Numerous interventions to improve vaccination coverage have been assessed, yet there remains a paucity of data comparing the relative efficacy and effectiveness of different interventions.

Methods: We searched MEDLINE, PubMed, Scopus, Embase, CINAHL, CENTRAL, and Web of Science (1980 to March 2019) for studies evaluating interventions which sought to improve influenza vaccine coverage in children with medical comorbidities. Interventions were divided into those targeting parents, targeting vaccination providers, and targeting the hospital, clinic or ward. Screening and data extraction from publications meeting inclusion criteria was performed by two reviewers. Results were pooled and meta-analyses were performed using Mantel–Haenszel random-effects models in Review Manager 5.

Results: 35 articles met inclusion criteria; 14 cross-sectional, 12 randomized trials, and 9 cohort studies, 25 articles had sufficient data for pooled analysis. Of the included interventions, 17 were based within primary care or community-based settings, 17 were based in hospitals or tertiary clinics, and 1 intervention was conducted across both primary and tertiary settings. Interventions overall increased influenza vaccination likelihood by 33% (RR = 1.33: 95% CI 1.31, 1.35). Interventions targeting providers' influenza vaccine knowledge increased vaccine coverage (RR = 1.42: 95% CI

1.36, 1.49) greater than those targeting parental knowledge (RR = 1.23: 95% CI 1.21, 1.26). Conversely, vaccination reminders targeting parents increased vaccine coverage (RR = 1.53: 95% CI 1.49, 1.58) greater than reminders targeting providers (RR = 1.23: 95% CI 1.20, 1.27). Interventions targeting hospitals, clinics or ward processes had the weakest impact on coverage (RR = 1.15: 95% CI 1.13, 1.17).

Conclusion: Interventions targeting parents, providers, and places individually have all shown to improve influenza vaccination in children with medical comorbidities. However, specifically targeting providers' vaccine knowledge and parental reminders appear to have the greatest impact on vaccine uptake.

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2762. A Cohort Analysis of Completion of the Pediatric Measles-Mumps-Rubella-Varicella Series in the United States

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Background: Since 2006, the recommended US vaccination schedule has included combination Measles-Mumps-Rubella (MMR) vaccine and separate Varicella (V) vaccine administered as first dose between 12–15 months, and second dose between 4–6 years, administered either separately or as a combination MMRV vaccine. Vaccine coverage alone does not provide information on the timeliness of vaccine receipt, a critical step in ensuring optimal protection, thus, we sought to evaluate overall series completion rates and identify factors related to under-vaccination.

Methods: A cohort of children born between 2006 and 2010, with continuous enrollment from birth to age 7 in the MarketScan® Commercial Claims and Encounters Database was studied. The administration of first and second doses of MMR- and V-containing vaccines was evaluated. Administration timeliness was categorized as recommended, acceptably early (prior to age 4 for the second dose), late (after the recommended time period), invalid, or missing at least one vaccine. A logistic regression analysis evaluated factors associated with under-vaccination.

Results: Among the 104,999 children included, 55.9% were vaccinated within the recommended time periods for both first and second doses, with timeliness higher for the second dose (80.1%) than the first dose (63.5%). By age 4, 20.1% of children were missing the first dose of either MMR or V (or both) and by age 7, 26.6% of children were missing at least one dose, with 9.4% missing all required vaccines. Factors associated with missed or delayed vaccination included geographic region, vaccination by a provider other than a pediatrician, and, for the second dose, having missed or delayed the first dose. Having additional children in the family was associated with a higher likelihood of missed or delayed vaccination for the first dose, but with a lower likelihood of missed or delayed vaccination for the second dose.

Conclusion: About one in four children were missing at least one dose of MMR or V by age 7, indicating vaccine coverage is below Healthy People 2020 95% target. Additionally, delays in administration of the first dose indicate a potential for the development of cohorts of susceptible children large enough to sustain outbreaks. Strategies for addressing timeliness of vaccine receipt should incorporate factors associated with under-vaccination.

Figure 1. First dose of MMR or V (or both) by age 4

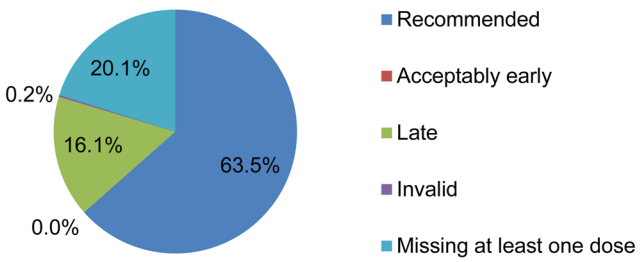


Figure 2. Second dose of MMR or V (or both) by age 7

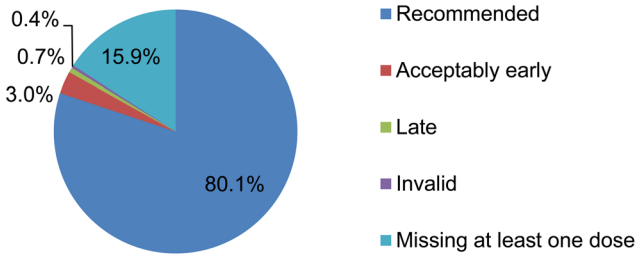
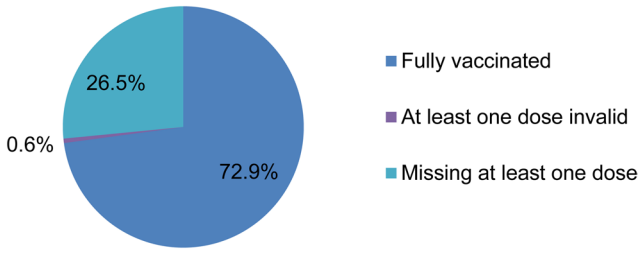


Figure 3. Two doses of MMR or V (or both) by age 7



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2763. Uptake and Safety of Measles-Mumps-Rubella (MMR) Vaccine in Adolescents and Adults in the Vaccine Safety Datalink

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Background: MMR vaccine is given routinely to young children but may be given at other ages. We described MMR use in adolescent and adult populations in the Vaccine Safety Datalink (VSD) and estimated the incidence of medically-attended outcomes after MMR to inform future studies estimating vaccine-associated risk.

Methods: The study population included adolescents (9–17 years) and adults (≥18 years) in VSD who received at least one MMR vaccine from 2010 through 2016. Outcomes were pre-specified based on previous vaccine safety studies and categorized as clinically serious (anaphylaxis, encephalitis/myelitis, GBS, meningitis, seizure) or non-serious (allergic reaction, arthropathy, fever, injection site reaction, lymphadenopathy, nonspecific reaction, parotitis, rash, syncope). Outcomes were identified by searching for ICD-9 and ICD-10 diagnosis codes in post-vaccination exposure windows. Medical records were reviewed for all serious outcomes to verify incident diagnoses. Incidence and 95% confidence intervals were calculated for validated serious and all non-serious outcomes.

Results: 146,503 adolescents and adults received 162,992 MMR vaccines during the study period. The mean age at vaccination was 33.7 years, 65% were female, and 53% received at least one other vaccine simultaneously. Demographic and vaccination characteristics varied across age groups (Table 1). The analysis of post-vaccination outcomes included 162,053 MMR vaccinations. The incidence of validated serious outcomes was low, ranging from 0 to 6.8 per 100,000 vaccinations. Only one serious outcome (anaphylaxis) was noted to be vaccine-associated in the medical record. Incidence of clinically non-serious outcomes varied from 0.4 to 56.0 per 10,000 vaccinations. Injection site reactions were more common among adolescents (118.1 per 10,000 vaccinations), who also had a higher frequency of simultaneous vaccination (80%).

Conclusion: Clinically serious outcomes were rare following MMR vaccination. Rates of clinically non-serious outcomes varied but were similar to or lower than previous reports in children. This descriptive analysis did not evaluate the association between MMR and adverse events. Future analysis with an appropriate comparison group is needed for risk estimation.

Table 1. Descriptive Characteristics of Adolescent and Adult MMR Vaccine Recipients in the VSD, 2010-2016

Characteristic	Overall (N=162,992)		Age Group							
			9-17 Years (N=26,060)		18-25 Years (N=26,559)		26-64 Years (N=71,034)		≥45 Years (N=39,339)	
	No.	%	No.	%	No.	%	No.	%	No.	%
Sex										
Female	106,135	65.1	13,002	49.9	18,763	70.7	50,267	70.8	24,103	61.3
Male	56,857	34.9	13,058	50.1	7,796	29.4	20,767	29.2	15,236	38.7
Race/Ethnicity										
White, Non-Hispanic	64,715	39.7	9,203	35.3	9,065	34.1	26,257	37.0	20,190	51.3
Black, Non-Hispanic	10,352	6.4	2,236	8.6	1,394	5.3	3,966	5.6	2,756	7.0
Asian, Non-Hispanic	29,832	18.3	3,283	12.6	4,747	17.9	15,015	21.1	6,787	17.3
Multiple Races, Non-Hispanic	13,972	8.6	3,233	12.4	2,456	9.3	5,305	7.5	2,978	7.6
Hispanic, Any Race	41,174	25.3	7,490	28.7	8,371	31.5	19,252	27.1	6,061	15.4
Other, Non-Hispanic	2,947	1.8	615	2.4	526	2.0	1,239	1.7	567	1.4
Received ≥1 Simultaneous Vaccine										
Yes	85,855	52.7	20,743	79.6	12,809	48.2	32,355	45.6	19,948	50.7
No	77,137	47.3	5,317	20.4	13,750	51.8	38,679	54.5	19,391	49.3
Postpartum[1]										
Yes	20,025	18.9	269	2.1	5,104	27.2	14,620	29.1	32	0.1
No	86,109	81.1	12,733	97.9	13,659	72.8	35,646	70.9	24,071	99.9
Vaccination Year										
2010	16,727	10.3	4,177	16.0	2,710	10.2	6,957	9.8	2,883	7.3
2011	20,162	12.4	5,401	20.7	3,278	12.3	7,850	11.1	3,633	9.2
2012	19,152	11.8	4,292	16.5	3,383	12.7	8,005	11.3	3,472	8.8
2013	17,956	11.0	2,850	10.9	3,516	13.2	7,932	11.2	3,658	9.3
2014	20,940	12.9	2,859	11.0	3,905	14.7	9,506	13.4	4,670	11.9
2015	38,344	23.5	3,910	15.0	5,252	19.8	16,784	23.6	12,398	31.5
2016	29,711	18.2	2,571	9.9	4,515	17.0	14,000	19.7	8,625	21.9
Documented Dose Number[2]										
1	104,140	63.9	7,914	30.4	10,293	38.8	54,480	76.7	31,453	80.0
2	42,351	26.0	13,944	53.5	6,596	24.8	14,120	19.9	7,691	19.6
3	14,647	9.0	3,972	15.2	8,404	31.6	2,094	3.0	177	0.5
≥4	1,854	1.1	230	0.9	1,266	4.8	340	0.5	18	0.1

Abbreviations: N=sample size; No.=number; %=percentage; MMR=measles-mumps-rubella.
Percentages may not add to 100% due to rounding.
[1]Postpartum status is based on VSD automated data and only applies to female vaccine recipients.
[2]Dose number is based on all available VSD automated data on MMR-containing vaccines; full vaccination history may not be captured for all members.

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