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| Supplemental Digital Content 4. Methodologic characteristics for studies included in the meta-analysis of strain-specific vaccine effective of RV1 and RV5 that may influence heterogeneity of results. | | | | | | |
| Author, Publication Year | Cases identifica-tion | Control Selection | Age | Vaccination comparison | Methods to control for confounding | Testing protocol |
| Braeckman, 2012 a | Hospital | Hospital | Median (range): cases=11 months (2-31), controls=12 months (2-31) | Full course (2 doses RV1) compared with unvaccinated | Controls matched by date of birth. Other factors assessed for possible confounding included sex, attendance at day care, attendance at preschool, medical history, history of breast feeding, maternal education level, and household size. | Rapid test then PCR of rapid-test positives |
| Matthijnssens, 2014 a | Hospital | Hospital | Median (range): cases=11 months (2-31), controls=12 months (2-31) | Full course (2 doses RV1) compared to unvaccinated | Controls matched by hospital and age | Rapid test then PCR of rapid-test positives |
| Boom, 2010 | Hospital or ED | Test-negativeb | Inclusion criteria: 15 days-23 months Median (range): cases=17 (1-23), controls=10 (0.5, 23), overall=13 (0.5, 23) | Full course (3 doses RV5) compared to unvaccinated | Models adjusted for age at presentation and month and year of birth | EIA then PCR of EIA-positives |
| Muhsen, 2018 | Hospital | Test-negative | Inclusion criteria: 2 to 59 months Cases=58.6% 2-12 months, controls=48.9% 2-12 months | More than 1 dose (>1) of RV5 compared to unvaccinated | Models adjusted for vaccination status, age, year and season of admission and socioeconomic status. | EIA then PCR of EIA-positives |
| Cortese, 2013 | Hospital or ED | Test-negativeb | Inclusion criteria: 8 to 23 months Distribution not reported | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for site, season and birth quarter in all models. Other factors assessed for possible confounding in each model were insurance status, and factors possibly associated with rotavirus disease. | EIA then PCR of EIA-positives |
| Payne, 2013 | Hospital or ED | Test-negative | Inclusion criteria: 8 months to 5 years Median (range): RV5: 26 (8-59) for cases, 20 (8-60) for controls RV1: 18 (9-30) for cases, 15 (8-33) for controls | Unclear if genotype specific VE compared full course or any dose. | Models adjusted for month/year of birth, month/year of symptom onset, and surveillance site. | EIA and PCR testing. Unclear if all samples PCR tested or just EIA positive. |
| Chang , 2014 | Hospital | Test-negativeb | Inclusion criteria: 8 to 35 months Average (SD): cases=20.5 (7.5), controls=18.2 (7.2) | Unclear if genotype specific VE compared full course or any dose. | Matched on age and hospital. | EIA then PCR of EIA-positives |
| Huang, 2020 | Hospital | Test-negativeb | Inclusion criteria: 8 months to <5 years Mean (SD), months: cases=29 (14), controls=27 (13) | Full course (2 doses RV1 or 3 doses RV5) compared to unvaccinated | Controls matched by gender, age, and enrolled date. | EIA then PCR of EIA-positives |
| Payne, 2015 | Hospital or ED | Test-negative | Inclusion criteria: Less than 8 years of age Median (range): RV5 Cases=35 (8–82), Controls= 26 (8–89) RV1 Cases= 24 (8–56) Controls= 18 (8–62) | Unclear if genotype specific VE compared full course or any dose (implies full-dose) | Models adjusted for month/year of birth, month/year of symptom onset, and surveillance site. | EIA then PCR of EIA-positives |
| Immergluck, 2016 | Hospital, short-stay, or ED | Test-negative | For RV1: median age in months (IQR; maximum) cases=32.4 (12.5; 47.1),controls=31.4 (10.8; 47.1) months. For RV5: cases=30.0 (13.0; 47.1), controls=32.2 (10.9; 46.2). | Full course (2 doses RV1 or 3 doses RV5) compared to unvaccinated | Models adjusted for birth quarter and year. Additional confounding assessed by univariate assessment and backward elimination (sex, insurance status, breastfed in the month before illness, attending childcare in the month before illness). | EIA then PCR of EIA-positives |
| Hoque, 2018 | Pediatric clinic | Test-negative | Inclusion criteria: 0-12 years Median, month (IQR) cases= 28 (20–55) controls= 25 (15–40) | Full course (2 doses RV1 or 3 doses RV5) compared to unvaccinated | Models adjusted for age. | PCR testing performed on all samples. |
| Araki, 2018 | Outpatient, inpatient hospital and ED | Test-negative | Inclusion criteria: 2 months to 3 years Median (IQR): cases=19 (2-35), controls=15 (2-35) | Full course (2 doses RV1 or 3 doses RV5) compared to unvaccinated | Models adjusted for age, use of day care, having siblings, current breastfeeding, facility, onset year, and severity score. | EIA then PCR of EIA-positives |
| Snelling, 2009 | Hospital | Neighborhood | Inclusion criteria: 10 weeks to 5 years | Full course (2 doses RV1) compared to unvaccinated | Matched on indigenous status and date of birth. Models adjusted for remote residence. | Unclear |
| Correia, 2010 | Hospital or ED, and IV hydration | Test-negativeb | Inclusion criteria: 6 months to 5 years. However, since only VE stratified by age (6-11 months and >11 months) weas reported, the VE for 6-11 months was abstracted. | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for month and year of birth. | EIA then PCR of EIA-positives |
| De Palma, 2010 | Hospital | Neighborhood | Inclusion criteria: Less than 2 years. Median (range), months: cases=10 (1-24), controls=10 (1-25) | Full course (2 doses RV1) compared to unvaccinated | Neighborhood controls matched by date of birth. Models adjusted for sex, history of breast feeding, daycare attendance, birth weight, and variables of socioeconomic status. | EIA then PCR of EIA-positives |
| Justino, 2011 | Hospital or emergency hydration | Neighborhood and Hospital | Median (range), months: cases=16 (3-36), controls=17 (3-36) | Full course (2 doses RV1) compared to unvaccinated | Matched by neighborhood. Unclear if strain-specific VE adjusted for confounders, but overall VE adjusted for sex, underlying medical conditions, breast feeding, DTP/Hib vaccination, age, year of birth was negligibly different than crude estimate (VE 75.4 vs 73.6). | EIA then PCR of EIA-positives |
| Snelling, 2011 | Hospital | Test-negativeb | Inclusion criteria: 6 weeks to 36 months Median (IQR): cases=10.5 (5.4-17.6), controls=13.8 (8.4-18.9) | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for age, sex, indigenous status, remoteness, breast feeding status, and date of birth. | EIA then PCR of EIA-positives |
| Yen, 2011 | Hospital | Neighborhood | Inclusion criteria: 15 days to 2 years Median (range), months: cases=12 (3-18), controls=13 (3-19) | Full course (2 doses RV1) compared to unvaccinated | Matched by date of birth and municipality. Assessed differences between cases and controls with regard to potential confounders, but no significant difference so crude results presented. | Gel electrophoresis; 10% random sample genotyped by RT-PCR |
| Patel, 2013 | Hospital | Test-negativeb | Median (range), months: cases=12 (1-35), controls= 12 (2-32) | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for hospital, age, and month/year of birth. Additional confounding assessed by univariate assessment and backward elimination. | EIA then PCR of EIA-positives |
| Groome, 2014 | Hospital | Test-negative | Inclusion criteria: 18 weeks to 23 months. Median (IQR), months: cases=9 (7-13), controls=10 (7-14) | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for hospital birth month/year, quarter/year of hospital admission and other covariates if inclusion changed the OR by more than 5%. | EIA then PCR of EIA-positives |
| Ichihara, 2014 | Hospital | Hospital | Inclusion criteria: 4 to 24 months. Mean age of cases and controls was 14 months. | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for age, sex, and year of birth. Assessed other potential confounders, but given of absence of apparent confounding no additional confounders included in the model. | EIA then PCR of EIA-positives and 25% of EIA-negatives |
| Gastanaduy, 2016 (Botswana) | Hospital | Test-negative | Inclusion criteria: 4 months to 5 years. Median (IQR), months: cases=9 (6-13), controls=8 (6-12) | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for age, birth month/year, and hospital. | EIA then PCR of EIA-positives |
| Pringle, 2016 | Hospital | Test-negative | Inclusion criteria: <5 years Median (IQR), months: cases= 13 (8-18), controls=14 (8-17) | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for hospital, age in months, and month/year of birth. Socioeconomic factors that reached statistically significance on bivariate analyses were included using backward elimination. | EIA then PCR of EIA-positives |
| Khagayi, 2019 | Hospital | Test-negative | Inclusion criteria: 0 to 59 months Median (range), months: cases=9.7 (1.4-29.5), controls=9.8 (1.4-32.0) | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for date of admission, age in weeks, and site. Variables assessed for confounding included any variable that changed the aOR by >10% was included in the final model. | EIA then PCR of EIA-positives |
| Leshem , 2016 | Hospital or ED | Test-negative | Inclusion criteria: less than 5 years Median (range), months: cases=11.4 (6.1-32.2), controls=11.5 (6.0-38.0) | Full course (3 doses RV5) compared to unvaccinated | Models adjusted for age and Clark score >16. | EIA then PCR of EIA-positives |
| Patel, 2009 | Hospital or ED w/IV hydration | Neighborhood and Hospital | Inclusion criteria: Less than 2 years Median, months: cases=10, controls=8 | Full course (3 doses RV5) compared to unvaccinated | Matching by date of birth. Variables assessed for confounding included age, sex, underlying chronic illness, history of breastfeeding, daycare attendance, birth weight, maternal education, ownership of a motorized vehicle, and access to electricity, telephone, or computer in the home. | EIA then PCR of EIA-positives |
| Patel, 2016 | Hospital or ED w/IV hydration | Test-negative | Children, but no clear age range specified.  Mean age, in months, over each study year: 11.9 in 2008, 17.0 in 2009, and 17.3 in 2010 | Full course (3 doses RV5) compared to unvaccinated | Potential confounders were defined as any variable that changed the odds ratio by >10%. The final model included age at hospitalization (in months), month/year of birth, and hospital, in addition to vaccination status. | EIA then PCR of EIA-positives |
| Ali, 2016 | Hospital | Test-negative | Inclusion criteria: less than 5 years 83.9% of cases and controls less than 24 months. | Full course (2 doses RV1 or 3 doses RV5) compared to unvaccinated | Models adjusted by geographic region and season. | EIA then PCR of EIA-positive and 5% of EIA-negatives |
| Gastanaduy, 2016 (Guatemala) | Hospital or ED | Test-negativeb | Median (range), months=12 (2-32), controls=11 (2-53) | Full course (2 doses RV1) compared to unvaccinated | Model adjusted for age, birth month/year, and hospital. | EIA then PCR of EIA-positives |
| Bar-Zeev, 2016 | Hospital or short-stay with oral rehydration | Test-negative | Inclusion criteria: less than 5 years Among cases 69.2% <12 months and controls 67.5% <12 months | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for year and month of presentation and for age. | EIA then PCR of EIA-positives |
| Platts-Mills, 2017 | Hospital | Test-negative | Inclusion criteria: 2 months to 5 years Mean (SD), months: cases=28.7 (13.7), controls=27.1 (13.3) | Full course (2 doses RV1) compared to unvaccinated | Models adjusted for sex, age in months, year of admission, and seasons. Other covariates were retained in the model if they changed vaccine effectiveness estimates by >5%. | EIA then PCR of EIA-positives |

ED=emergency department; EIA=enzyme immunoassay; IV=intravenous; OR=odds ratio; PCR=polymerase chain reaction; VE=vaccine effectiveness

a Braeckman and Matthijnssens are same studies, but present different strains

b Also enrolled secondary control groups, such as community or hospitalized controls, but given prioritization of test-negative design for consistency and homogeneity of methods being combined we only abstracted test-negative results if those were presented separately.