**Supplementary Digital Content**

**Equation 1**

Where

and represent the fixed intercept and the random intercept for the *jth* surveillance site, respectively

*RVVi,j* represents the vaccination status for the *ith* child at the *jth* surveillance site (referent = unvaccinated)

*T2i,j* to *T6i,j* represent indicator variables for study years 2012, 2013, 2014, 2016, and 2017 (referent = study year 2015)

**Equation 2**

and represent the fixed intercept and the random intercept for the *jth* surveillance site, respectively

*RVVi,j* represents the vaccination status for the *ith* child at the *jth* surveillance site (referent = unvaccinated)

*Posi,j* represents the percent-positive metric (same value for all children across all surveillance sites in each study year)

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| Graphical user interface, chart, histogram  Description automatically generated |
| **eFigure 1.** Number of cases of acute gastroenteritis and rotavirus gastroenteritis by outcome severity. Rotavirus gastroenteritis cases were defined as cases of acute gastroenteritis that tested positive by site enzyme immunoassay only. |

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| **eTable 1.** Rotavirus vaccine effectiveness (VE) estimates against any-severity rotavirus gastroenteritis (RVGE), moderate-to-severe RVGE, and RVGE hospitalization using site enzyme immunoassay (EIA) only or site EIA and CDC testing to define cases and controls. For each combination of rotavirus outcome and case definition, the standard approach (mixed effect regression models including vaccination status, year, and a vaccination-year interaction term) and the force of infection approach (mixed-effect regression models including vaccination status, annual percent of rotavirus-positive tests, and a vaccination-percent positive interaction term) were used to estimate VE.  |
| Outcome | Case Definition | Regression Approach | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
| VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) |
| Any-Severity RVGE | Site EIA | Standard | 80% | (60-90%) | 77% | (70-82%) | 58% | (35-72%) | 70% | (60-77%) | 62% | (32-79%) | 67% | (51-78%) |
| FOI | 66% | (55-74%) | 73% | (67-77%) | 68% | (61-74%) | 73% | (67-77%) | 65% | (51-75%) | 69% | (63-74%) |
| Site EIA + CDC testing | Standard | 79% | (58-90%) | 77% | (70-83%) | 74% | (57-84%) | 73% | (64-79%) | 71% | (43-85%) | 69% | (55-79%) |
| FOI | 74% | (64-81%) | 75% | (70-79%) | 74% | (68-79%) | 75% | (70-79%) | 74% | (62-82%) | 74% | (69-79%) |
| Moderate-to-Severe RVGE | Site EIA | Standard | 77% | (42-91%) | 81% | (72-87%) | 70% | (45-84%) | 75% | (63-83%) | 80% | (52-92%) | 75% | (56-85%) |
| FOI | 76% | (63-84%) | 77% | (70-82%) | 76% | (68-82%) | 77% | (70-82%) | 75% | (61-85%) | 76% | (69-82%) |
| Site EIA + CDC testing | Standard | 77% | (40-91%) | 81% | (72-87%) | 75% | (54-87%) | 75% | (63-83%) | 86% | (64-95%) | 77% | (60-87%) |
| FOI | 79% | (68-86%) | 78% | (71-83%) | 79% | (71-84%) | 78% | (71-83%) | 79% | (66-87%) | 79% | (72-83%) |
| RVGE Hospitalization | Site EIA | Standard | 92% | (69-98%) | 84% | (71-91%) | 72% | (37-87%) | 78% | (63-86%) | 85% | (53-95%) | 72% | (49-84%) |
| FOI | 79% | (65-87%) | 78% | (68-84%) | 78% | (69-85%) | 78% | (69-84%) | 79% | (62-88%) | 78% | (70-84%) |
| Site EIA + CDC testing | Standard | 94% | (73-99%) | 85% | (72-91%) | 76% | (41-90%) | 79% | (65-87%) | 82% | (33-95%) | 73% | (51-85%) |
| FOI | 80% | (65-88%) | 80% | (71-86%) | 80% | (70-86%) | 80% | (71-86%) | 80% | (62-89%) | 80% | (72-85%) |
| *RVGE:* rotavirus gastroenteritis; *EIA:* enzyme immunoassay; *FOI:* force of infection; *VE:* vaccine effectiveness; *CI:* confidence interval |

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| **eTable 2.** Rotavirus vaccine effectiveness (VE) estimates against any-severity rotavirus gastroenteritis (RVGE), moderate-to-severe RVGE, and RVGE hospitalization using site enzyme immunoassay (EIA) only or site EIA and CDC testing to define cases and controls and when age is included in regression models. For each combination of rotavirus outcome and case definition, the standard approach (mixed effect regression models including vaccination status, year, age, and a vaccination-year interaction term) and the force of infection approach (mixed-effect regression models including vaccination status, annual percent of rotavirus-positive tests, age, and a vaccination-percent positive interaction term) were used to estimate VE. Age was dichotomous (8-23 months versus 24-59 months). No estimates changed more than 10% relative to the VE estimate from the respective model without a term for age included. |
| Outcome | Case Definition | Regression Approach | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
| VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) |
| Any-Severity RVGE | Site EIA | Standard | 78% | (57-89%) | 76% | (68-81%) | 56% | (33-72%) | 69% | (60-76%) | 61% | (30-78%) | 66% | (50-77%) |
| FOI | 65% | (53-74%) | 72% | (66-77%) | 67% | (59-73%) | 72% | (66-76%) | 64% | (49-74%) | 68% | (62-73%) |
| Site EIA + CDC testing | Standard | 78% | (55-89%) | 76% | (69-82%) | 73% | (56-84%) | 72% | (64-79%) | 70% | (41-85%) | 69% | (54-79%) |
| FOI | 73% | (63-80%) | 74% | (69-79%) | 73% | (66-79%) | 74% | (69-78%) | 73% | (61-81%) | 73% | (68-78%) |
| Moderate-to-Severe RVGE | Site EIA | Standard | 72% | (30-89%) | 80% | (70-86%) | 68% | (42-83%) | 74% | (62-83%) | 80% | (50-92%) | 75% | (56-85%) |
| FOI | 74% | (60-83%) | 76% | (69-82%) | 75% | (66-81%) | 76% | (69-82%) | 73% | (57-83%) | 75% | (68-81%) |
| Site EIA + CDC testing | Standard | 72% | (26-89%) | 80% | (70-86%) | 74% | (50-86%) | 75% | (63-83%) | 86% | (63-95%) | 77% | (60-87%) |
| FOI | 78% | (65-86%) | 77% | (70-82%) | 77% | (69-83%) | 77% | (70-82%) | 78% | (64-86%) | 77% | (71-83%) |
| RVGE Hospitalization | Site EIA | Standard | 91% | (64-98%) | 83% | (69-90%) | 71% | (35-87%) | 77% | (63-86%) | 85% | (51-95%) | 72% | (49-84%) |
| FOI | 78% | (63-87%) | 77% | (67-84%) | 78% | (68-84%) | 77% | (67-84%) | 78% | (60-88%) | 77% | (69-83%) |
| Site EIA + CDC testing | Standard | 94% | (68-99%) | 83% | (70-91%) | 75% | (39-90%) | 79% | (65-87%) | 81% | (30-95%) | 73% | (51-85%) |
| FOI | 79% | (63-88%) | 79% | (69-85%) | 79% | (69-85%) | 79% | (70-85%) | 79% | (60-88%) | 79% | (70-85%) |
| *RVGE:* rotavirus gastroenteritis; *EIA:* enzyme immunoassay; *FOI:* force of infection; *VE:* vaccine effectiveness; *CI:* confidence interval |

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| **eTable 3.** Rotavirus vaccine effectiveness (VE) estimates against any-severity rotavirus gastroenteritis (RVGE), moderate-to-severe RVGE, and RVGE hospitalization using site enzyme immunoassay (EIA) only or site EIA and CDC testing to define cases and controls and when data are stratified by year. For each combination of rotavirus outcome and case definition, we used a mixed effect regression model including vaccination status and a random intercept for surveillance site to estimate VE. The same model was applied to each subset of data after stratifying the main dataset by study year.  |
| Outcome | Case Definition | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
| VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) |
| Any-Severity RVGE | Site EIA | 79% | (59-90%) | 78% | (71-83%) | 57% | (35-72%) | 69% | (60-76%) | 65% | (36-80%) | 67% | (51-78%) |
| Site EIA + CDC testing | 79% | (56-90%) | 79% | (72-84%) | 73% | (56-84%) | 73% | (64-79%) | 72% | (45-86%) | 70% | (55-80%) |
| Moderate-to-Severe RVGE | Site EIA | 77% | (42-91%) | 82% | (73-88%) | 70% | (45-84%) | 75% | (62-83%) | 80% | (50-92%) | 75% | (56-85%) |
| Site EIA + CDC testing | 77% | (38-91%) | 82% | (73-88%) | 75% | (53-87%) | 75% | (63-83%) | 85% | (61-94%) | 77% | (60-87%) |
| RVGE Hospitalization | Site EIA | 91% | (91-91%) | 84% | (71-91%) | 72% | (37-87%) | 78% | (64-87%) | 88% | (58-97%) | 72% | (49-84%) |
| Site EIA + CDC testing | 94% | (94-94%) | 85% | (73-91%) | 77% | (42-90%) | 79% | (65-88%) | 82% | (34-95%) | 74% | (52-85%) |

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| **eFigure 2.** Misclassification-corrected vaccine effectiveness (VE) estimates against any-severity rotavirus gastroenteritis (RVGE), moderate-to-severe RVGE, and RVGE hospitalization. The red line represents the VE obtained using original EIA test results to define cases and controls. Each shade of blue represents the VE estimated under a different specificity assumption (ranging from 0.97 to 1), with darker blues indicating higher specificity. Translucent fill represents the range of VE estimates as assumed sensitivity varied from 0.75 to 0.95 and assumed specificity was fixed. |

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| **eTable 4.** Rotavirus vaccine effectiveness (VE) estimates against any-severity rotavirus gastroenteritis after multiple over-imputation to address misclassification by enzyme immunoassay. For each combination of sensitivity and specificity, we used a multiple over-imputation approach (100 iterations) to probabilistically reclassify the enzyme immunoassay results. Cases were defined based on these reclassified results. The force of infection approach (mixed-effect regression models including vaccination status, annual percent of rotavirus-positive tests, and a vaccination-percent positive interaction term) was used to estimate VE. |
| Specificity | Sensitivity | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
| VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) |
| 0.97 | 0.75 | 81% | (72-87%) | 80% | (76-84%) | 81% | (75-85%) | 80% | (76-84%) | 81% | (71-87%) | 81% | (76-84%) |
| 0.80 | 80% | (72-86%) | 80% | (75-83%) | 80% | (74-85%) | 80% | (75-83%) | 80% | (70-87%) | 80% | (75-84%) |
| 0.85 | 80% | (71-86%) | 79% | (74-83%) | 80% | (74-84%) | 79% | (74-83%) | 80% | (70-87%) | 80% | (75-84%) |
| 0.90 | 80% | (71-86%) | 78% | (73-82%) | 79% | (73-84%) | 78% | (73-82%) | 80% | (70-87%) | 79% | (74-83%) |
| 0.95 | 80% | (71-86%) | 77% | (72-81%) | 79% | (73-84%) | 77% | (72-81%) | 80% | (70-87%) | 79% | (74-83%) |
| 0.98 | 0.75 | 75% | (65-82%) | 79% | (74-83%) | 77% | (70-82%) | 79% | (74-83%) | 75% | (63-83%) | 77% | (72-81%) |
| 0.80 | 75% | (65-82%) | 78% | (73-82%) | 76% | (70-81%) | 78% | (73-82%) | 75% | (63-83%) | 77% | (71-81%) |
| 0.85 | 75% | (65-82%) | 77% | (72-82%) | 76% | (69-81%) | 77% | (72-81%) | 75% | (63-83%) | 76% | (71-81%) |
| 0.90 | 75% | (64-82%) | 77% | (72-81%) | 75% | (68-81%) | 77% | (72-81%) | 75% | (62-83%) | 76% | (70-80%) |
| 0.95 | 75% | (64-82%) | 76% | (71-80%) | 75% | (68-81%) | 76% | (71-80%) | 75% | (62-83%) | 75% | (70-80%) |
| 0.99 | 0.75 | 71% | (60-79%) | 78% | (73-82%) | 73% | (66-79%) | 78% | (73-82%) | 70% | (56-79%) | 74% | (68-79%) |
| 0.80 | 70% | (59-78%) | 77% | (72-81%) | 72% | (65-78%) | 77% | (72-81%) | 69% | (56-79%) | 73% | (67-78%) |
| 0.85 | 71% | (60-79%) | 76% | (71-80%) | 72% | (66-78%) | 76% | (71-80%) | 70% | (57-79%) | 73% | (67-78%) |
| 0.90 | 70% | (60-78%) | 75% | (70-80%) | 72% | (65-78%) | 75% | (70-80%) | 70% | (57-79%) | 73% | (67-77%) |
| 0.95 | 70% | (59-78%) | 75% | (69-79%) | 71% | (64-77%) | 75% | (69-79%) | 69% | (56-78%) | 72% | (66-77%) |
| 1.00 | 0.75 | 67% | (56-75%) | 77% | (72-81%) | 70% | (63-76%) | 77% | (72-81%) | 65% | (52-75%) | 71% | (66-76%) |
| 0.80 | 66% | (55-75%) | 76% | (70-80%) | 69% | (62-75%) | 76% | (70-80%) | 65% | (51-75%) | 71% | (65-75%) |
| 0.85 | 67% | (55-75%) | 75% | (70-79%) | 69% | (62-75%) | 75% | (70-79%) | 66% | (52-75%) | 70% | (65-75%) |
| 0.90 | 66% | (55-75%) | 74% | (69-78%) | 69% | (62-75%) | 74% | (69-78%) | 65% | (51-75%) | 70% | (64-75%) |
| 0.95 | 66% | (55-75%) | 73% | (68-78%) | 69% | (61-74%) | 73% | (68-78%) | 65% | (52-75%) | 69% | (64-75%) |

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| **eTable 5.** Rotavirus vaccine effectiveness (VE) estimates against moderate-to-severe rotavirus gastroenteritis after multiple over-imputation to address misclassification by enzyme immunoassay. For each combination of sensitivity and specificity, we used a multiple over-imputation approach (100 iterations) to probabilistically reclassify the enzyme immunoassay results. Cases were defined based on these reclassified results. The force of infection approach (mixed-effect regression models including vaccination status, annual percent of rotavirus-positive tests, and a vaccination-percent positive interaction term) was used to estimate VE. |
| Specificity | Sensitivity | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
| VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) |
| 0.97 | 0.75 | 84% | (74-90%) | 86% | (80-90%) | 85% | (78-89%) | 86% | (81-90%) | 84% | (72-91%) | 85% | (80-89%) |
| 0.80 | 83% | (72-90%) | 84% | (78-88%) | 84% | (76-89%) | 84% | (78-88%) | 83% | (70-91%) | 84% | (78-88%) |
| 0.85 | 83% | (72-89%) | 83% | (76-87%) | 83% | (76-88%) | 83% | (77-87%) | 83% | (70-90%) | 83% | (77-87%) |
| 0.90 | 83% | (72-90%) | 81% | (75-86%) | 83% | (75-88%) | 81% | (75-86%) | 83% | (70-91%) | 82% | (76-87%) |
| 0.95 | 83% | (72-89%) | 80% | (74-85%) | 82% | (75-87%) | 81% | (74-85%) | 83% | (70-90%) | 82% | (76-86%) |
| 0.98 | 0.75 | 81% | (70-88%) | 85% | (80-89%) | 82% | (76-87%) | 85% | (80-89%) | 80% | (67-88%) | 83% | (77-87%) |
| 0.80 | 81% | (69-88%) | 84% | (78-88%) | 82% | (75-87%) | 84% | (78-88%) | 80% | (67-88%) | 82% | (76-86%) |
| 0.85 | 81% | (70-88%) | 82% | (75-87%) | 81% | (74-86%) | 82% | (76-87%) | 81% | (67-89%) | 81% | (75-86%) |
| 0.90 | 80% | (69-88%) | 81% | (74-86%) | 80% | (73-86%) | 81% | (74-86%) | 80% | (66-88%) | 80% | (74-85%) |
| 0.95 | 80% | (68-88%) | 80% | (73-85%) | 80% | (72-86%) | 80% | (73-85%) | 80% | (66-88%) | 80% | (73-85%) |
| 0.99 | 0.75 | 79% | (67-87%) | 85% | (79-89%) | 81% | (74-86%) | 85% | (79-89%) | 78% | (63-87%) | 82% | (76-86%) |
| 0.80 | 79% | (66-87%) | 83% | (77-87%) | 80% | (72-86%) | 83% | (77-87%) | 78% | (62-87%) | 80% | (74-85%) |
| 0.85 | 79% | (67-87%) | 82% | (75-86%) | 80% | (72-85%) | 82% | (75-86%) | 78% | (64-87%) | 80% | (74-85%) |
| 0.90 | 78% | (66-86%) | 80% | (73-85%) | 79% | (71-84%) | 80% | (73-85%) | 78% | (63-87%) | 79% | (72-84%) |
| 0.95 | 78% | (66-86%) | 79% | (72-84%) | 78% | (70-84%) | 79% | (72-84%) | 78% | (63-87%) | 78% | (72-83%) |
| 1.00 | 0.75 | 77% | (64-85%) | 84% | (78-89%) | 79% | (72-85%) | 84% | (78-89%) | 76% | (60-85%) | 80% | (74-85%) |
| 0.80 | 77% | (64-85%) | 82% | (76-87%) | 79% | (71-84%) | 82% | (76-87%) | 76% | (60-86%) | 79% | (73-84%) |
| 0.85 | 76% | (64-84%) | 81% | (74-86%) | 78% | (70-84%) | 81% | (74-86%) | 76% | (61-85%) | 78% | (72-83%) |
| 0.90 | 76% | (63-84%) | 79% | (72-85%) | 77% | (69-83%) | 79% | (72-84%) | 76% | (60-85%) | 78% | (71-83%) |
| 0.95 | 76% | (63-84%) | 78% | (71-84%) | 76% | (68-82%) | 78% | (71-83%) | 75% | (60-85%) | 77% | (70-82%) |

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| **eTable 6.** Rotavirus vaccine effectiveness (VE) estimates against rotavirus gastroenteritis hospitalization after multiple overimputation to address misclassification by enzyme immunoassay. For each combination of sensitivity and specificity, we used a multiple overimputation approach (100 iterations) to probabilistically reclassify the enzyme immunoassay results. Cases were defined based on these reclassified results. The force of infection approach (mixed-effect regression models including vaccination status, annual percent of rotavirus-positive tests, and a vaccination-percent positive interaction term) was used to estimate VE. |
| Specificity | Sensitivity | 2012 | 2013 | 2014 | 2015 | 2016 | 2017 |
| VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) | VE | (95% CI) |
| 0.97 | 0.75 | 87% | (75-93%) | 85% | (78-90%) | 86% | (79-91%) | 85% | (78-90%) | 87% | (73-94%) | 86% | (80-91%) |
| 0.80 | 86% | (74-93%) | 84% | (76-90%) | 86% | (78-91%) | 84% | (76-90%) | 86% | (73-93%) | 85% | (79-90%) |
| 0.85 | 86% | (74-92%) | 83% | (75-89%) | 85% | (77-90%) | 84% | (75-89%) | 86% | (72-93%) | 85% | (78-90%) |
| 0.90 | 86% | (74-92%) | 82% | (74-88%) | 85% | (77-90%) | 82% | (74-88%) | 86% | (72-93%) | 84% | (77-89%) |
| 0.95 | 85% | (72-92%) | 82% | (73-88%) | 84% | (75-90%) | 82% | (73-88%) | 85% | (70-93%) | 84% | (76-89%) |
| 0.98 | 0.75 | 84% | (72-91%) | 85% | (77-90%) | 84% | (77-90%) | 85% | (77-90%) | 84% | (69-92%) | 84% | (78-89%) |
| 0.80 | 84% | (70-91%) | 83% | (75-89%) | 84% | (75-89%) | 83% | (75-89%) | 84% | (68-92%) | 84% | (76-89%) |
| 0.85 | 84% | (72-91%) | 82% | (73-88%) | 83% | (75-89%) | 82% | (74-88%) | 84% | (70-92%) | 83% | (76-88%) |
| 0.90 | 84% | (71-91%) | 81% | (72-88%) | 83% | (74-89%) | 81% | (72-87%) | 84% | (69-92%) | 83% | (75-88%) |
| 0.95 | 83% | (70-91%) | 80% | (71-87%) | 82% | (73-88%) | 80% | (71-87%) | 83% | (68-92%) | 82% | (74-87%) |
| 0.99 | 0.75 | 83% | (69-90%) | 84% | (75-89%) | 83% | (75-89%) | 84% | (76-89%) | 82% | (66-91%) | 83% | (76-88%) |
| 0.80 | 82% | (68-90%) | 82% | (74-88%) | 82% | (73-88%) | 82% | (74-88%) | 82% | (65-90%) | 82% | (75-87%) |
| 0.85 | 82% | (69-89%) | 81% | (73-88%) | 82% | (73-88%) | 81% | (73-87%) | 82% | (66-90%) | 82% | (74-87%) |
| 0.90 | 81% | (68-89%) | 80% | (71-86%) | 81% | (72-87%) | 80% | (71-86%) | 81% | (66-90%) | 81% | (73-86%) |
| 0.95 | 81% | (67-89%) | 79% | (70-86%) | 80% | (71-87%) | 79% | (70-86%) | 81% | (65-90%) | 80% | (72-86%) |
| 1.00 | 0.75 | 81% | (67-89%) | 83% | (74-89%) | 81% | (73-87%) | 83% | (74-89%) | 81% | (64-89%) | 82% | (74-87%) |
| 0.80 | 81% | (67-89%) | 82% | (73-88%) | 81% | (72-87%) | 82% | (73-88%) | 80% | (64-89%) | 81% | (74-86%) |
| 0.85 | 79% | (65-88%) | 80% | (71-87%) | 80% | (71-86%) | 80% | (71-87%) | 79% | (62-89%) | 80% | (72-85%) |
| 0.90 | 80% | (66-88%) | 79% | (70-86%) | 80% | (71-86%) | 79% | (70-86%) | 80% | (63-89%) | 80% | (72-85%) |
| 0.95 | 79% | (65-88%) | 79% | (69-85%) | 79% | (70-85%) | 79% | (69-85%) | 79% | (63-89%) | 79% | (71-85%) |