# Supplemental materials:

### Table 1: Summary of rotavirus vaccine effectiveness studies – USA, 2006-2017

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference number** | **Setting** | **Seasons** | **Type of controls** | **Study outcomes** | **Ages** | **RV type** | **Dose** | **Cases** | **Controls** | **VE** | **LCL** | **UCL** |
| [1] | 1 Hospital in TX | 2008-2009 | RV neg | H, ED | <3yr | RV5 | Full | 98 | 153 | 83 | 66 | 91 |
| [2] | 1 Hospital in TX | 2008 | RV neg | H | <3yr | RV5 | Full | 72 | 75 | 89 | 70 | 96 |
| [3] | Retrospective study at 5 centers in 3 states (MN, GA, CT) | 2007-2009 | RV neg | H, ED | <5yr | RV5 | Full | 283 | 341 | 89 | 81 | 94 |
| H | <5yr | RV5 | Full | 140 | 280 | 92 | 86 | 96 |
| ED | <5yr | RV5 | Full | 41 | 280 | 81 | 53 | 92 |
| [4] | Active surveillance at 5 hospitals in 2 states (GA, CT) | 2010-2011 | RV neg | H, ED | <5yr | RV1 | Full | 95 | 140 | 91 | 80 | 95 |
| H | <5yr | RV1 | Full | 30 | 140 | 98 | 90 | 99.999 |
| ED | <5yr | RV1 | Full | 65 | 140 | 86 | 67 | 94 |
| H, ED | <5yr | RV5 | Full | 79 | 73 | 92 | 75 | 97 |
| H | <5yr | RV5 | Full | 30 | 73 | 97 | 77 | 99.999 |
| ED | <5yr | RV5 | Full | 49 | 73 | 91 | 67 | 98 |
| [5] | 1 Hospital in CT | 2006-2009 | Hospital controls | H | <5yr | Either | Full | 39 | 65 | 96.3 | 28.9 | 99.8 |
| [6] | Active surveillance (NVSN) at 3 sites in 3 states (NY, OH, TN) | 2006-2008 | RV neg | H, ED | <3yr | RV5 | Full | 68 | 132 | 92 | 21 | 99 |
| [7] | Retrospective study of 2 hospitals in CT | 2006-2008 | RV neg | H | <3yr | RV5 | Full | 54 | 270 | 92.2 | 48 | 99.999 |
| [8] | 3 metropolitan hospitals in GA | 2013 | RV neg | H, ED | >=8m | RV1 | Full | 51 | 69 | 83 | 58 | 93 |
| H, ED | >=8m | RV5 | Full | 57 | 55 | 83 | 51 | 94 |
| [9] | 3 metropolitan hospitals in GA | 2010-2013 | RV neg | H, ED | <5yr | Either | Full | 174 | 353 | 79 | 69 | 86 |
| [10] | Retrospective cohort study based on national insurance claims database | 2001-2010 | No RVGE | H | <2yr | Either | >=1 | NA | NA | 90 | 75 | 96 |
| [11] | Active surveillance at 7 centers in 7 states (CA, WA, KS, TX, OH, TN, NY) | 2009-2011 | RV neg | H, ED | <5yo | RV1 | Full | 56 | 140 | 70 | 39 | 86 |
| H, ED | <5yo | RV5 | Full | 307 | 1445 | 84 | 78 | 88 |
| [12] | Active surveillance (NVSN) in 7 centers | 2012-2013 | RV neg | H, ED | <8yo | RV1 | Full | 99 | 735 | 80 | 68 | 88 |
| H | <8yo | RV1 | Full | 27 | 148 | 84 | 53 | 94 |
| ED | <8yo | RV1 | Full | 72 | 587 | 79 | 63 | 87 |
| H, ED | <8yo | RV5 | Full | 354 | 2117 | 80 | 74 | 84 |
| H | <8yo | RV5 | Full | 96 | 433 | 83 | 71 | 90 |
| ED | <8yo | RV5 | Full | 258 | 1684 | 77 | 69 | 83 |
| [13] | Active surveillance (NVSN) in 6 centers | 2011-2013 | RV neg | H, ED | "children" | Mixed | Full | 212 | 578 | 80 | 51 | 92 |
| [14] | Retrospective study of 2 hospitals in GA | 2007-2015 | RV neg | H, ED | "children" | RV5 or RV1 | Full | 596 | Not provided | 67.6 | 57.8 | 75.2 |
| H | "children" | RV5 or RV1 | Full | Not provided | Not provided | 64.6 | 52.2 | 73.7 |
| ED | "children" | RV5 or RV1 | Full | Not provided | Not provided | 82.9 | 41.7 | 95 |
| [15] | Active surveillance at 3 centers in 3 states (OH, TN, NY) | 2006-2009 | RV neg | H, ED | <4yo | RV5 | Full | 143 | 238 | 87 | 71 | 94 |
| H | <4yo | RV5 | Full | 40 | 49 | 95 | 48 | 99 |
| ED | <4yo | RV5 | Full | 59 | 76 | 74 | 16 | 92 |
| [16] | Retrospective cohort study based on national insurance claims database | 2007-2008 | DTaP only | H, ED, OP | Infants | RV5 | Full | NA | NA | 100 | 87 | 100 |
| [17] | Retrospective cohort study based on national insurance claims database | 2007-2008 | DTaP only | H, ED, OP | Infants | RV5 | 2 dose | NA | NA | 94 | 61 | 100 |

Abbreviations H: Hospital; ED: Emergency Department; OP: Outpatient; NA: Not applicable; yo: year old; RV neg: rotavirus negative

### Table 2: Vaccine healthcare utilization impact studies of children < 5 years old – USA, 2006-2017

|  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Database | Prevax | Vax | Measure year | Age | RV Reduction | RVLCL | RVUCL | AGE Reduction | AGELCL | AGEUCL |
| Hospitalization-rate | | | | | | | | | | | |
| [18] | HCUP | 2000-2006 | 2008-2012 | 2012 | <5yo | 94 | 94 | 95 | 55 | 54 | 55 |
| 2011 | <5yo | 79 | 79 | 80 | 47 | 47 | 48 |
| 2010 | <5yo | 90 | 90 | 90 | 48 | 47 | 48 |
| 2009 | <5yo | 63 | 62 | 64 | 33 | 32 | 33 |
| 2008 | <5yo | 70 | 69 | 71 | 31 | 30 | 31 |
| [19] | MarketScan | 2000-1/2007 | 1/2007-2010 |  | <5yo | 67 |  |  |  |  |  |
| [20] | MarketScan | 2001-2006 | 2007-2011 | 2010 | <5yo | 80 | 78 | 81 | 47 | 46 | 49 |
| 2009 | <5yo | 94 | 93 | 95 | 54 | 52 | 55 |
| 2008 | <5yo | 60 | 58 | 63 | 25 | 23 | 27 |
| 2007 | <5yo | 75 | 72 | 77 | 33 | 31 | 35 |
| [21] | NIS | 2000-2006 | 2008-2010 |  | <5yo | 80 | 72 | 86 | 42 | 34 | 50 |
| [22] | Utah hospital and ED | 2003-2007 | 2008-2010 | 2009 | <5yo | 88 | 81 | 93 |  |  |  |
| 2008 | <5yo | 68 | 57 | 75 |  |  |  |
| 2007 | <5yo | 77 | 68 | 84 |  |  |  |
| [23] | Indian Health Service | 2001-2006 | 2008-2010 | 2010 | <5yo | 44 |  |  |  |  |  |
| 2009 | <5yo | 38 |  |  |  |  |  |
| 2008 | <5yo | 25 |  |  |  |  |  |
| [24] | HCUP | 2000-2006 | 2008-2009 | 2009 | <4yo |  |  |  | 33 |  |  |
| 2008 | <4yo |  |  |  | 31 |  |  |
| [25] | MarketScan | 2001-2006 | 2007-2009 | 2008 | <5yo | 60 | 58 | 63 | 34 | 32 | 36 |
| 2007 | <5yo | 75 | 72 | 77 | 47 | 45 | 49 |
| [26] | CHMPC | 2004-2005 | 2006-2009 | 2008 | <5yo |  |  |  | 60 | 35 | 63 |
| 2007 | <5yo |  |  |  | 50 | 34 | 62 |
| 2006 | <5yo |  |  |  | 28 | 7 | 44 |
| [27] | NY state hospitals | 2003-2006 | 2008 | 2008 | 1-23m | 83 |  |  | 35 |  |  |
| [28] | Military dependents | 2003-2006 | 2007-2009 | 2008 | <5yo | 55 | 49.6 | 60.3 |  |  |  |
| 2007 | <5yo | 70 | 65.1 | 73.9 |  |  |  |
|  | <5yo | 62 | 58.6 | 65.8 | 31.5 | 28.1 | 34.7 |
|  | Infant | 75 | 70.1 | 79.7 |  |  |  |
| [29] | HCUP | 2000-2006 | 2007-2008 | 2008 | <5yo |  |  |  | 45 |  |  |
| 2007 | <5yo |  |  |  | 16 |  |  |
| [30] | SDI Health | 2003-2006 | 2007-2008 | 2007 | Infant |  |  |  | 30 | 24 | 39 |
| <5yo | 81 | 77 | 84 |  |  |  |
| ED Visit Rate | | | | | | | | | | | |
| [31] | SED (10 states) | 2003-2006 | 2008-2013 |  | <5yo |  |  |  | 10.3 | 10 | 10.6 |
| [32] | 28 EDs | 2005 | 2010 |  | Infant |  |  |  | 41 | 37 | 45 |
| [19] | MarketScan | 2000-1/2007 | 1/2007-2010 |  | <5yo | 57 |  |  |  |  |  |
| [22] | Utah children's hospital | 2003-2007 | 2008-2010 | 2009 | <5yo | 91 | 79 | 97 |  |  |  |
| 2008 | <5yo | 77 | 60 | 88 |  |  |  |
| 2007 | <5yo | 57 | 35 | 73 |  |  |  |
| [26] | CHMPC | 2004-2006 | 2006-2009 | 2008 | <5yo |  |  |  |  |  |  |
| 2007 | <5yo |  |  |  |  |  |  |
| 2006 | <5yo | -17 | -79 | 24 |  |  |  |
| [30] | National claims | 2003-2006 | 2007-2008 |  | Infant |  |  |  | 19 | 11 | 25 |
| Outpatient visit rate | | | | | | | | | | | |
| [19] | MarketScan | 2000-1/2007 | 1/2007-2010 |  | <5yo | 57 |  |  |  |  |  |
| [23] | Indian Health Service | 2001-2006 | 2008-2010 | 2010 | <5yo |  |  |  | 36 |  |  |
| 2009 | <5yo |  |  |  | 21.2 |  |  |
| 2008 | <5yo |  |  |  | 15.6 |  |  |
| [30] | National claims | 2003-2006 | 2007-2008 |  | Infant |  |  |  | 12 | 5 | 20 |
| [26] | CHMPC (single center) | 2004-2006 | 2007-2008 | 2006 | <5yo |  |  |  | 6 | 1E-05 | 12 |

Abbreviations H: Hospital; ED: Emergency Department; OP: Outpatient; NA: Not applicable; yo: year old; RV neg: rotavirus negative

### **Table 3:** Vaccine healthcare utilization impact studies of unvaccinated children and adults – USA, 2006-2017

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study | Year | Study type | Database | Prevax | Vax | Vaccine type | Measure year | Strata | Age | RV Reduction | RVLCL | RVUCL | AGE Reduction | AGELCL | AGEUCL |
| **Hospitalization** | | | | | | | | | | | | | | | |
| [33] | 2015 | Ecologic | MarketSCan |  | 2008-2011 | RV5 |  | Child born 4/2006-7/2007 | >5 years (household members) |  |  |  | -21-50 |  |  |
| Child born 4/2006-7/2007 | 20-29 |  |  |  | 41 | 18 | 57 |
| Child born 4/2006-7/2007 | 20-29, female |  |  |  | 43 | 18 | 60 |
| Child born 8/2007-7/2008 | >5 yo (household members) |  |  |  | -28-27 |  |  |
| Child born 8/2007-7/2008 | 30-39, male |  |  |  | 32 | 1 | 53 |
| Child born 8/2008-7/2009 | >5 yo (household members) |  |  |  | -30-27 |  |  |
| [20] | 2014 | Ecologic | MarketScan Claims and commercially insured | 2001-2006 | 2007-2011 | RV5, RV1 | 2007 |  | <5 yo | 50 | 36 | 62 |  |  |  |
| 2008 | 2 | -17 | 18 |  |  |  |
| 2009 | 77 | 65 | 85 |  |  |  |
| 2010 | 25 | 4 | 41 |  |  |  |
| [34] | 2011 | Ecologic | HCUP's Nationwide Inpatient Sample | 2000-2006 | 2008 | RV5 |  |  | 5-14 | 71 | 55 | 81 | 29 | 22 | 35 |
| Hispanic | 5-14 | 84 | 63 | 93 | 42 | 31 | 51 |
|  | 15-24 | 65 | 18 | 85 | 8 | 2 | 14 |
| 25-64 | 26 | -16 | 53 | 1 | -3 | 5 |
| >=65 | 21 | -26 | 51 | -3 | -10 | 4 |
| [27] | 2010 | Ecologic | All NY state hospitals | 2003-2006 | 2007-2008 | RV5 |  |  |  | 70 |  |  | 12 |  |  |
| 10 sentinel hospitals |  | 70 |  |  | 9 |  |  |
| [28] | 2010 | Ecologic | Military dependents | 2003-2006 | 2007-2009 | RV5 |  |  | <4 yo | 57.2 | 52.7 | 61.3 |  |  |  |
| 2007 | <4 yo | 67.8 | 62.7 | 72.4 |  |  |  |
| 2008 | <4 yo | 45.6 | 38.5 | 52 |  |  |  |
|  | <1 yo | 60.3 | 51.4 | 67.9 |  |  |  |
| 1 yo | 54.5 | 46.4 | 61.5 |  |  |  |
| 2yo | 40.5 | 26 | 52.4 |  |  |  |
| 3yo | 18.2 | -13.1 | 41.4 |  |  |  |
| RV ED incidence | | | | | | | | | | | | | | | |
| [33] | 2015 | Ecologic | MarketSCan |  | 2008-2011 | RV5 |  | Child born 4/2006-7/2007 | >5 yo (household members) |  |  |  | -16-25 |  |  |
| Child born 8/2007-7/2008 | >5 yo (household members) |  |  |  | -14-16 |  |  |
| Child born 8/2007-7/2008 | 20-29, female |  |  |  | 16 | 1 | 29 |
| Child born 8/2008-7/2009 | >5 yo (household members) |  |  |  | -12-16 |  |  |
| Child born 8/2008-7/2009 | 5-19 |  |  |  | 16 | 0 | 29 |
| [25] | 2011 | Ecologic | MarketScan | 2001-2006 | 2007-2009 | RV5 | 1/2008-6/2008 |  | <2 yo | 45 | 37 | 54 | 27 | 21 | 32 |
| 1/2009-6/2009 | 6 | -6 | 17 | -5 | -12 | 2 |

# References

1. Boom JA, Tate JE, Sahni LC *et al.* Sustained protection from pentavalent rotavirus vaccination during the second year of life at a large, urban United States pediatric hospital. *Pediatr Infect Dis J*, 29(12), 1133-1135 (2010).

2. Boom JA, Tate JE, Sahni LC *et al.* Effectiveness of pentavalent rotavirus vaccine in a large urban population in the United States. *Pediatrics*, 125(2), e199-207 (2010).

3. Cortese MM, Leblanc J, White KE *et al.* Leveraging state immunization information systems to measure the effectiveness of rotavirus vaccine. *Pediatrics*, 128(6), e1474-1481 (2011).

4. Cortese MM, Immergluck LC, Held M *et al.* Effectiveness of monovalent and pentavalent rotavirus vaccine. *Pediatrics*, 132(1), e25-33 (2013).

5. Desai SN, Esposito DB, Shapiro ED, Dennehy PH, Vazquez M. Effectiveness of rotavirus vaccine in preventing hospitalization due to rotavirus gastroenteritis in young children in Connecticut, USA. *Vaccine*, 28(47), 7501-7506 (2010).

6. Donauer S, Payne DC, Edwards KM *et al.* Determining the effectiveness of the pentavalent rotavirus vaccine against rotavirus hospitalizations and emergency department visits using two study designs. *Vaccine*, 31(24), 2692-2697 (2013).

7. Guh AY, Hadler JL. Use of the state immunization information system to assess rotavirus vaccine effectiveness in Connecticut, 2006-2008. *Vaccine*, 29(37), 6155-6158 (2011).

8. Immergluck LC, Parker TC, Jain S *et al.* Sustained Effectiveness of Monovalent and Pentavalent Rotavirus Vaccines in Children. *J Pediatr*, 172, 116-120 e111 (2016).

9. Mohammed A, Immergluck L, Parker TC *et al.* Association between mixed rotavirus vaccination types of infants and rotavirus acute gastroenteritis. *Vaccine*, 33(42), 5670-5677 (2015).

10. Panozzo CA, Becker-Dreps S, Pate V *et al.* Direct, indirect, total, and overall effectiveness of the rotavirus vaccines for the prevention of gastroenteritis hospitalizations in privately insured US children, 2007-2010. *American journal of epidemiology*, 179(7), 895-909 (2014).

11. Payne DC, Boom JA, Staat MA *et al.* Effectiveness of pentavalent and monovalent rotavirus vaccines in concurrent use among US children <5 years of age, 2009-2011. *Clin Infect Dis*, 57(1), 13-20 (2013).

12. Payne DC, Selvarangan R, Azimi PH *et al.* Long-term Consistency in Rotavirus Vaccine Protection: RV5 and RV1 Vaccine Effectiveness in US Children, 2012-2013. *Clin Infect Dis*, 61(12), 1792-1799 (2015).

13. Payne DC, Sulemana I, Parashar UD. Evaluation of Effectiveness of Mixed Rotavirus Vaccine Course for Rotavirus Gastroenteritis. *JAMA pediatrics*, 170(7), 708-710 (2016).

14. Sederdahl BK, Yi J, Jerris R *et al.* The Residual Vaccine-preventable Burden of Rotavirus Disease. *Pediatr Infect Dis J*, 36(8), 780-781 (2017).

15. Staat MA, Payne DC, Donauer S *et al.* Effectiveness of pentavalent rotavirus vaccine against severe disease. *Pediatrics*, 128(2), e267-275 (2011).

16. Wang FT, Mast TC, Glass RJ, Loughlin J, Seeger JD. Effectiveness of the pentavalent rotavirus vaccine in preventing gastroenteritis in the United States. *Pediatrics*, 125(2), e208-213 (2010).

17. Wang FT, Mast TC, Glass RJ, Loughlin J, Seeger JD. Effectiveness of an incomplete RotaTeq (RV5) vaccination regimen in preventing rotavirus gastroenteritis in the United States. *Pediatr Infect Dis J*, 32(3), 278-283 (2013).

18. Leshem E, Tate JE, Steiner CA, Curns AT, Lopman BA, Parashar UD. Acute gastroenteritis hospitalizations among US children following implementation of the rotavirus vaccine. *Jama*, 313(22), 2282-2284 (2015).

19. Krishnarajah G, Demissie K, Lefebvre P, Gaur S, Sheng Duh M. Clinical and cost burden of rotavirus infection before and after introduction of rotavirus vaccines among commercially and Medicaid insured children in the United States. *Human vaccines & immunotherapeutics*, 10(8), 2255-2266 (2014).

20. Leshem E, Moritz RE, Curns AT *et al.* Rotavirus vaccines and health care utilization for diarrhea in the United States (2007-2011). *Pediatrics*, 134(1), 15-23 (2014).

21. Gastanaduy PA, Curns AT, Parashar UD, Lopman BA. Gastroenteritis hospitalizations in older children and adults in the United States before and after implementation of infant rotavirus vaccination. *Jama*, 310(8), 851-853 (2013).

22. Guerra AH, Stockmann C, Pavia AT *et al.* Laboratory-Confirmed Rotavirus Disease in Utah Children: Clinical and Economic Impact of Rotavirus Vaccination. *J Pediatric Infect Dis Soc*, 1(4), 268-277 (2012).

23. Desai R, Haberling D, Holman RC *et al.* Impact of rotavirus vaccine on diarrhea-associated disease burden among American Indian and Alaska Native children. *Pediatrics*, 129(4), e907-913 (2012).

24. Desai R, Curns AT, Steiner CA, Tate JE, Patel MM, Parashar UD. All-cause gastroenteritis and rotavirus-coded hospitalizations among US children, 2000-2009. *Clin Infect Dis*, 55(4), e28-34 (2012).

25. Cortes JE, Curns AT, Tate JE *et al.* Rotavirus vaccine and health care utilization for diarrhea in U.S. children. *The New England journal of medicine*, 365(12), 1108-1117 (2011).

26. Begue RE, Perrin K. Reduction in gastroenteritis with the use of pentavalent rotavirus vaccine in a primary practice. *Pediatrics*, 126(1), e40-45 (2010).

27. Chang HG, Smith PF, Tserenpuntsag B, Markey K, Parashar U, Morse DL. Reduction in hospitalizations for diarrhea and rotavirus infections in New York state following introduction of rotavirus vaccine. *Vaccine*, 28(3), 754-758 (2010).

28. Eberly MD, Gorman GH, Eide MB, Olsen CH, Rajnik M. The effect of rotavirus immunization on rotavirus gastroenteritis hospitalization rates in military dependents. *Vaccine*, 29(4), 650-659 (2011).

29. Curns AT, Steiner CA, Barrett M, Hunter K, Wilson E, Parashar UD. Reduction in acute gastroenteritis hospitalizations among US children after introduction of rotavirus vaccine: analysis of hospital discharge data from 18 US states. *J Infect Dis*, 201(11), 1617-1624 (2010).

30. Cortese MM, Tate JE, Simonsen L, Edelman L, Parashar UD. Reduction in gastroenteritis in United States children and correlation with early rotavirus vaccine uptake from national medical claims databases. *Pediatr Infect Dis J*, 29(6), 489-494 (2010).

31. Shah MP, Tate JE, Steiner CA, Parashar UD. Decline in Emergency Department Visits for Acute Gastroenteritis Among Children in 10 US States After Implementation of Rotavirus Vaccination, 2003 to 2013. *Pediatr Infect Dis J*, 35(7), 782-786 (2016).

32. Calello DP, Allegra SJ, Cochrane DG, Eskin B, Allegra JR. Emergency Department Visits for Gastroenteritis Before and After Rotavirus Vaccine Implementation in 2006. *Pediatric emergency care*, 31(10), 699-700 (2015).

33. Cortese MM, Dahl RM, Curns AT, Parashar UD. Protection against gastroenteritis in US households with children who received rotavirus vaccine. *J Infect Dis*, 211(4), 558-562 (2015).

34. Lopman BA, Curns AT, Yen C, Parashar UD. Infant rotavirus vaccination may provide indirect protection to older children and adults in the United States. *J Infect Dis*, 204(7), 980-986 (2011).