DtaP and Health Outcomes

Citation	Methods	Participants	Outcomes
Griffin, M. R., Ray, W. A., Livengood, J. R., & Schaffner, W. (1988). Risk of sudden infant death syndrome after immunization with the diphtheria–tetanus–pertussis vaccine. New England Journal of Medicine, 319(10), 618-623. https://www.ncbi.nlm.nih.gov/pubmed/3261837	Retrospective review from 1974 and 1984. Computerized immunization records from these sources were linked with Tennessee birth and death certificates to establish the cohort, ascertain the timing of immunization, and identify cases of SIDS. 109 deaths were classified as SIDS.	129,834 children in 4 Tennessee counties who had received the DPT shot at least once.	A multivariate analysis which controlled for age, sex, race, year, birth weight, and Medicaid enrollment, produced similar results. Authors conclude that in this large population of children there was no increase in the risk of SIDS after immunization with the DTP vaccine.
Duszynski, K. M., Pratt, N. L., Lynch, J. W., Berry, J. G., Gold, M. S., & Vaccine Assessment Using Linked Data (VALiD) Working Group. (2019). Use of different combination diphtheria-tetanus-acellular pertussis vaccines does not increase risk of 30-day infant mortality. A population-based linkage cohort study using administrative data from the Australian Childhood Immunisation Register and the National Death Index. Vaccine, 37(2), 280-288. https://www.ncbi.nlm.nih.gov/pubmed/30503081	Observational nationwide cohort study of the linked population data from the Australian Childhood Immunization Register and National Death Index to determine whether differences in combination DTaP vaccine types at 2, 4 and 6 months of age were associated with mortality within 30 days of vaccination.	Australian infants administered a combination trivalent, quadrivalent or hexavalent DTaP vaccine (DTaP types) between January 1999 and December 2010 at 2, 4 and 6 months as part of the primary vaccination series. The study population included 2.9, 2.6, & 2.3 million children in the 2, 4- and 6-month vaccine cohorts, respectively.	The rate of 30-day all-cause mortality was low and declined from 127.4 to 59.3 deaths. When compared with trivalent DTaP vaccines, no elevated risk was seen with any quadrivalent or hexavalent DTaP vaccines, for any cohort. Use of routine DTaP combination vaccines with differing disease antigens administered during the first six months of life is not associated with infant mortality.

Citation	Methods	Participants	Outcomes
Moro, Pedro L., Perez-Vilar, Silvia, Lewis, Paige, Bryant-Genevier, Marthe, Kamiya, Hajime, Cano, Maria. Safety Surveillance of Diphtheria and Tetanus Toxoids and Acellular Pertussis (DTaP) Vaccines. Pediatrics. 2018;142(1): doi:10.1542/peds.2017-4171 https://www.ncbi.nlm.nih.gov/pubmed/29866795	Reviewed available medical records for all death reports and a random sample of reports classified as nondeath serious. We used Empirical Bayesian data mining to identify adverse events that were disproportionally reported after DTaP vaccination.	We searched VAERS for US reports of DTaP vaccinations occurring from January 1,1991, through December 31, 2016, and received by March 17, 2017. Median age at vaccination was 19 months (interquartile range 35 months).	Post licensure surveillance of adverse events after the 5 licensed diphtheria tetanus-acellular pertussis vaccines over a 19-year period did not find any new or unexpected safety concerns in the Vaccine Adverse Event Reporting System.
Müller-Nordhorn, J., Hettler-Chen, C. M., Keil, T., & Muckelbauer, R. (2015). Association between sudden infant death syndrome and diphtheria-tetanus-pertussis immunisation: an ecological study. BMC pediatrics, 15(1), 1. https://www.ncbi.nlm.nih.gov/pubmed/25626628	The CDC provided the number of cases of SIDS and live births per year (1968–2009), allowing the calculation of SIDS mortality rates. Immunization coverage was based on (1) the United States Immunization Survey (1968–1985), (2) the National Health Interview Survey (1991–1993), and (3) the National Immunization Survey (1994–2009). They used sleep position data from the National Infant Sleep Position Survey.	The entire infant populations of the USA from 1968-2009, including the cases of SIDS. Vaccine coverage of all U.S. infants from 1968-1985, based on two surveys: National Health Interview (1991-1993) and National Immunization Survey (1994-2009).	Increased DTP immunization coverage is associated with decreased SIDS mortality. Current recommendations on timely DTP immunization should be emphasized to prevent not only specific infectious diseases but also, potentially, SIDS.
Effectiveness of Vaccination During Pregnancy to Prevent Infant Pertussis Roger Baxter, Joan Bartlett, Bruce Fireman, Edwin Lewis, Nicola P. Klein Pediatrics May 2017, 139 (5) e20164091; DOI: 10.1542/peds.2016-4091 https://pediatrics.aappublications.org/content/139/5/e20164091	Retrospective study estimated the effectiveness of maternal pertussis vaccination for protecting newborns against pertussis in the first 2 months of life and in the first year of life accounting for each infant DTaP dose	148, 981 newborns born at Kaiser Permanente Northern California from 2010 to 2015	Maternal Tdap vaccination was highly protective against infant pertussis, especially in the first 2 months of life. Even after infant DTaP dosing, there was evidence of additional protection from maternal Tdap vaccination for the first year of life. This study strongly supports the United States' current recommendation to administer Tdap during each pregnancy.

Citation	Methods	Participants	Outcomes
Schmitt, H., Schuind, A., Knuf, M., Beutel, K., Schulte-Wissermann, H., & Gahr, M. et al. (1996). Clinical experience of a tricomponent acellular pertussis vaccine combined with diphtheria and tetanus toxoids for primary vaccination in 22,505 infants. The Journal Of Pediatrics, 129(5), 695-701. doi: 10.1016/s0022-3476(96)70152-x https://www.ncbi.nlm.nih.gov/pubmed/8917236	Prospective, double-blind, multicenter trial in Germany, to assess the safety and tolerability of 12 lots of SmithKline Beecham Biologicals' diphtheria-tetanus-tricomponent acellular pertussis vaccine (DTaP) in a large cohort of 22,000 vaccines, with detailed analyses of reactivity, immunogenicity , and immune response to pertussis toxin in subsets.	22,505 healthy infants received three vaccinations of DTaP at age 3, 4, and 5 months. Serious adverse events were followed for 1 month after each vaccination, and neurologic events for 1 year or longer.	In a large cohort of 22,505 infants vaccinated, SmithKline Beecham Biologicals' tricomponent DTaP vaccine was shown to be safe, well-tolerated, and immunogenic for all component antigens.
Hansen, Timbol, Lewis, Pool, Decker, Greenberg, Klein (2016). Safety of DTaP-IPV/Hib vaccine administered routinely to infants and toddlers. Vaccine, 4172-4179. https://www.ncbi.nlm.nih.gov/pubmed/27373595	This was an observational, retrospective study, that included all 2-month-old infants vaccinated with either DTaP-IPV/Hib or another DTaP-containing vaccine.	From October 1, 2008 through July 31, 2010, 14,042 subjects received a first dose of DTaP-IPV/Hib, 13,194 received 2 doses, 12,548 received 3 doses and 6702 received 4 doses.	This study did not detect any safety concerns following DTaP-IPV/Hib and provides reassurance that DTaP-IPV/Hib administered as part of routine care was not associated with unexpected safety risks.
Barlow, Reynolds , Cieslak, & Sullivan. (2014). Vaccinated children and adolescents with pertussis infections experience reduced illness severity and duration, Oregon, 2010-2012. Clinical Infectious Disease, 58(11), 1523-1529. https://www.ncbi.nlm.nih.gov/pubmed/24633685	To understand the effect of vaccination in the era of acellular pertussis vaccines (DTaP and Tdap), assessed if vaccination status is associated with disease severity and duration	The Multnomah County Health Department conducts enhanced pertussis surveillance for 1.7 million residents in the Portland, Oregon, metropolitan area. Surveillance activities include ascertaining demographics, clinical presentation, cough duration, vaccination history, and other health outcomes	Patients with pertussis vaccination had decreased morbidity characterized by less severe illness and significantly reduced illness duration. Therefore, vaccination is recommended among at-risk individuals, and research into the nature of the residual vaccine immunity is warranted.

Citation	Methods	Participants	Outcomes
Fleming, P. J., Blair, P. S., Platt, M. W., Tripp, J., Smith, I. J., Golding, J., & CESDI SUDI research group. (2001). The UK accelerated immunization program and sudden unexpected death in infancy: case-control study. BmJ, 322(7290), 822. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC30557/	Population based case-control study, February 1993 to March 1996. Parental interviews were conducted for each death and for four controls matched for age, locality, and time of sleep. Immunization status was taken from records held by the parents.	Five regions in England with a combined population of over 17 million. Immunization details were available for 93% (303/325) of infants whose deaths were attributed to the sudden infant death syndrome (SIDS); 90% of infants with explained sudden deaths; and 95% of controls.	After all potential confounding factors were controlled for, immunization uptake was strongly associated with a lower risk of SIDS. In fact, Immunization does not lead to sudden unexpected death in infancy, and the direction of the relation leans towards protection rather than risk.
Zhou, W., Pool, V., Iskander, J. K., English-Bullard, R., Ball, R., Wise, R. P., ... & Braun, M. M. (2003). Surveillance for safety after immunization: vaccine adverse event reporting system (VAERS)—United States, 1991–2001. MMWR Surveill Summ, 52(1), 1-24. https://www.cdc.gov/mmwr/preview/mmwrhtml/ss5201a1.htm	Population based study on retrospective data reported to the Vaccine Adverse Event Reporting System (VAERS) from January 1, 1991, through December 31, 2001.	307 SIDS cases and 971 controls	SIDS cases were vaccinated less frequently and far later than the controls; showing that vaccination actually protected against SIDS. The researchers also found that there was no increased risk for SIDS for 2 weeks after vaccination.
Institute of Medicine (US) Immunization Safety Review Committee. Immunization Safety Review: Vaccinations and Sudden Unexpected Death in Infancy. Washington, DC: National Academies Press, 2003. https://www.ncbi.nlm.nih.gov/books/NBK221465/	Retrospective study examining vaccination and SIDS for 15 years. Full literature review of all scholarly articles on vaccination and SIDS. Epidemiological studies.	USA National Health Data	The researchers looked at individual and combination doses of these vaccines: diphtheria, tetanus, both whole cell and acellular pertussis (DTP or DPT), the DTwP, the DTap, HepB, Hib, polio and SIDS. There was no evidence that any of these vaccines were the cause of the infant's death.

Citation	Methods	Participants	Outcomes
Schmitt, H., Schuind, A., Knuf, M., Beutel, K., Schulte-Wissermann, H., & Gahr, M. et al. (1996). Clinical experience of a tricomponent acellular pertussis vaccine combined with diphtheria and tetanus toxoids for primary vaccination in 22,505 infants. The Journal Of Pediatrics, 129(5), 695-701. doi: 10.1016/s0022-3476(96)70152-x https://www.ncbi.nlm.nih.gov/pubmed/16940831	Whole-cell pertussis (wP) and measles vaccines are effective in preventing disease but have also been suspected of increasing the risk of encephalopathy or encephalitis. A retrospective case–control study was performed at 4 health maintenance organizations.	Records from more than 2 million children from January 1, 1981, through December 31, 1995, were examined to identify children aged 0 to 6 years old hospitalized with encephalopathy or related conditions.	In this study of more than 2 million children, DTP and MMR va ccines were not associated with an increased risk of encephalopathy after vaccination.
Moore, D., Le Saux, N., Scheifele, D., & Halperin, S. (2004). Lack of Evidence of Encephalopathy Related to Pertussis Vaccine : Active Surveillance by IMPACT, Canada, 1993–2002. The Pediatric Infectious Disease Journal, 23(6), 568-571. doi: 10.1097/01.inf.0000130075.56368.02 https://www.ncbi.nlm.nih.gov/pubmed/15194842	To assess whether pertussis-containing vaccines cause encephalitis or encephalopathy	The IMPACT network of Canadian pediatric centers screened more than 12,000 admissions for neurologic disorders between 1993 and 2002.	Seven cases of encephalopathy began within 7 days after pertussis vaccination, but a more likely cause was found in each instance. No attributable case followed administration of >6.5 million doses of vaccine.
Kharbanda, E., Vazquez-Benitez, G., Lipkind, H., Klein, N., Cheetham, T., & Naleway, A. et al. (2016). Maternal Tdap vaccination: Coverage and acute safety outcomes in the vaccine safety datalink, 2007–2013. Vaccine, 34(7), 968-973. doi: 10.1016/j.vaccine.2015.12.046 https://www.ncbi.nlm.nih.gov/pubmed/26765288	Observational study using a retrospective matched cohort to evaluate Tdap during pregnancy among insured women with live births across seven health systems and adverse events occurring within 42 days of vaccination	Vaccine coverage cohort included 438,487 live births between January 1, 2007 and November 15, 2013.	Tdap coverage during pregnancy increased from 2007 through 2013, but was still below 50%. No acute maternal safety signals were detected in this large cohort.

Citation	Methods	Participants	Outcomes
Petousis-Harris, H., Walls, T., Watson, D., Paynter, J., Graham, P., & Turner, N. (2016). Safety of Tdap vaccine in pregnant women: an observational study. BMJ Open, 6(4), e010911. doi: 10.1136/bmjopen-2015-010911 https://bmjopen.bmj.com/content/6/4/e010911?int_source=trendmd&int_medium=trendmd&int_campaign=trendmd	A prospective observational study conducted in 2 New Zealand regions to Actively recruit and intensively follow pregnant women receiving a dose of acellular pertussis vaccine for 4 weeks after vaccination.	Women in their 28th–38th week of pregnancy, recruited from primary care and antenatal clinics at the time of Tdap administration. Telephone interviews were conducted at 48 h and 4 weeks postvaccination.	Vaccination with Tdap in pregnant women was well tolerated with no SAE likely to be caused by the vaccine.
McMillan, M., Clarke, M., Parrella, A., Fell, D., Amirthalingam, G., & Marshall, H. (2017). Safety of Tetanus, Diphtheria, and Pertussis Vaccination During Pregnancy. Obstetrics & Gynecology, 129(3), 560-573. doi: 10.1097/aog.0000000000001888 https://www.ncbi.nlm.nih.gov/pubmed/28178054	21 Studies from the following data sources were included in this review: PubMed, EMBASE, Literature in the Health Sciences in Latin America and the Caribbean, ClinicalTrials.gov, Cochrane Library, and World Health Organization (inception to May 5, 2016).	To assess antenatal, birth, and infant outcomes for pregnant women, fetuses, and infants after antenatal vaccination with any antigen present in combination pertussis vaccines	Evidence suggests that antenatal combined Tdap administered during the second or third trimester of pregnancy is not associated with clinically significant harms for the fetus or neonate. Medically attended events in pregnant women are similar between vaccinated and unvaccinated groups.
Thierry-Carstensen, B., Jordan, K., Uhlving, H., Dalby, T., Sørensen, C., Jensen, A., & Heilmann, C. (2012). A randomised, double-blind, non-inferiority clinical trial on the safety and immunogenicity of a tetanus, diphtheria and monocomponent acellular pertussis (TdaP) vaccine in comparison to a tetanus and diphtheria (Td) vaccine when given as booster vaccinations to healthy adults. Vaccine, 30(37), 5464-5471. doi:	Double-blind, controlled and randomized trial.	802 healthy adults, aged 18–55 years who had completed childhood vaccination with diphtheria, tetanus and whole cell pertussis vaccine (DTwP), were booster vaccinated with TdaP or Td	The frequencies of solicited local adverse reactions were low and comparable between TdaP and Td vaccines. In conclusion, TdaP Vaccine SSI was safe and immunogenic when given as a booster vaccination to adults.

Citation	Methods	Participants	Outcomes
10.1016/j.vaccine.2012.06.073 https://www.ncbi.nlm.nih.gov/pubmed/22776216			