



Cost-effectiveness of adult pertussis vaccination in Germany

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ABSTRACT

Background: The incidence of pertussis in adults is high despite good childhood vaccination coverage. An adult formulation of an acellular pertussis vaccine is licensed and available for use in Germany.

Objective: To evaluate the potential health benefits, risks, costs and cost-effectiveness of routine pertussis vaccination programs for German adults.

Methods: A Markov model was used to simulate health states and immunity levels associated with pertussis disease and vaccination. The following strategies were evaluated: (1) no adult pertussis vaccination, (2) one-time adult vaccination at 20–64 years, and (3) adult vaccination with decennial boosters. Our main outcome measures were costs (2006 Euros), cases prevented, incremental cost per case prevented and incremental cost per quality-adjusted life year (QALY) saved. We performed sensitivity analyses for key assumptions in the model including disease incidence, vaccine cost, vaccine efficacy, disease costs and frequency of adverse events. Future costs and benefits were discounted at 3%.

Results: At a disease incidence of 165 per 100,000, the one-time adult vaccination strategy would prevent 498,000 cases, and the decennial adult vaccination strategy would prevent 1 million cases. Approximately 31 million adults (~62% of the cohort) would be vaccinated with a one-time adult vaccination strategy for a total program cost of 366 million Euros, while a decennial vaccination strategy would cost 687 million Euros. The one-time adult vaccination strategy resulted in CE ratios of 5800 Euros per QALY saved, or 160 Euros per pertussis case prevented. The decennial booster strategy cost 7200 Euros per QALY saved, or 200 Euros per case prevented. The results were most sensitive to assumptions about disease incidence and vaccine cost.

Conclusions: Routine vaccination of German adults aged 20–64 years with Tdap is cost-effective.

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1. Background

Pertussis remains an endemic disease in Germany despite the availability of vaccination. Children and adolescents are still hospitalized with complications due to pertussis, particularly infants under 6 months of age [1]. Although pertussis has traditionally been thought of as a disease of childhood, recent reports indicate a rising disease burden among adolescents and adults [2,3]. The morbidity associated with pertussis in adults can be substantial, with prolonged illnesses lasting nearly 100 days and complications such as urinary incontinence, rib fractures, and loss of consciousness [4–6]. In addition, adults are often implicated as the source of infection

for young infants, who suffer the most severe complications due to pertussis including apnea, encephalopathy, and death.

The high rate of pertussis among adults is thought to be due, in part, to waning immunity after vaccination [7,8]. The availability of a combination vaccine with an acellular pertussis component (Tdap) for adults in Germany may not only reduce the incidence of pertussis among adults, it may also potentially reduce transmission of pertussis to young infants in the population. The objective of our study was to estimate the cost-effectiveness of vaccinating German adults 20–64 years of age with a single dose of Tdap or with decennial Tdap boosters, instead of Td vaccination.

2. Methods

2.1. Model

We used a previously constructed Markov model with a cycle length of 1-year to calculate the health benefits, risks, costs, and

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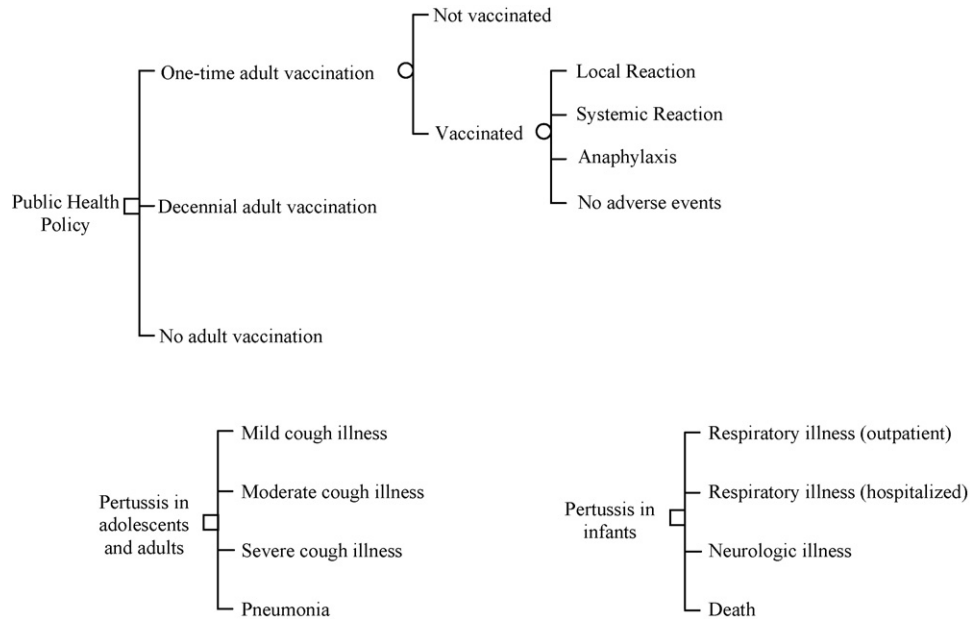


Fig. 1. Model structure for adult, adolescent, and infant disease. Strategies included one-time adult vaccination, decennial adult vaccination, and no adult vaccination. If a vaccination program were implemented, adults may or may not receive vaccine. Among vaccine recipients, adverse events such as local reaction, systemic reaction, and anaphylaxis may occur. Each year, adults and adolescents have an age-specific risk of pertussis infection resulting in mild cough illness, moderate cough illness, severe cough illness, or pneumonia. Pertussis disease in infants could result in respiratory illness, neurologic illness, or death.

cost-effectiveness of alternative vaccination strategies for healthy German adults using an analytic horizon of a lifetime (Fig. 1) [9]. The model allowed for waning immunity due to vaccination or disease over time, repeat vaccination for the decennial booster strategy, recurrent cases of pertussis, and age-specific death rates due to other causes. In this analysis, we evaluated the following strategies: (1) no adult pertussis vaccination, (2) one-time adult pertussis vaccination at 20–64 years, where Tdap is administered instead of Td, and (3) adult pertussis vaccination with decennial boosters. In this computer simulation model, we analyzed the health outcomes and costs of a hypothetical cohort of 50 million adults in Germany aged 20–64 years over their lifetime [10]. The age distribution of the initial cohort was based on the German population as follows: 20–29-year olds (19%), 30–39-year olds (24%), 40–49-year olds (26%), 50–59-year olds (20%), and 60–64-year olds (10%) [11]. The base case analysis assumed that childhood and adolescent pertussis vaccination programs were already established and that the adult vaccination strategies had reached steady state in their implementation.

Probabilities, costs, and utilities used in the model are described in Table 1. Disease probabilities were based on estimates from recent epidemiologic data available from Germany [12,13]. Vaccine delivery rates in adults were estimated to be 40–82% based on reported estimates of decennial Td vaccination [14,15]. Disease and vaccine-mediated immunity were assumed to wane over a period of 15 years and individuals could develop pertussis more than once in their lifetime [16–24]. Medical costs were based on diagnosis-related group (DRG) costs and data available from physicians in Germany and included ambulatory visits, hospitalizations, laboratory tests, use of chest radiography, and antibiotics [12,25]. Non-medical costs included time missed from work and over-the-counter medications. The median wage rate of parents was used to estimate the cost of missed work [11]. The incremental vaccine cost of Tdap over Td was estimated at 12 Euros [26]. We assumed there was no incremental cost for vaccine administration or for vaccine visits because Tdap would be given to adults in place of Td vaccine and vaccine delivery rates are expected to remain stable

in the adult population. Utilities refer to preferences for different health outcomes that are associated with disease or vaccine adverse events [27]. We used utilities obtained using the time trade-off method from the only published study on preferences in adults with pertussis illness [16]. We assumed that the mean durations of vaccination health states were 4 days for anaphylaxis and 7 days for local or systemic reactions. Estimates for the mean durations of infant disease (80 days) and adult disease (68 days) were derived from available data and assumed to be independent of disease severity [5,12,28–30].

In order to assess the impact of herd immunity on outcomes, we incorporated estimates derived from a published model of the transmission dynamics of pertussis and from published studies of the sources of infection of young infants [31–34]. Estimates from the literature were used, as our model did not incorporate transmission dynamics, which is needed to estimate disease reduction from herd immunity. We assumed children and adolescents were already receiving pertussis vaccination via established programs, so that herd immunity primarily affected unvaccinated infants, adolescents and adults. Disease reduction from herd immunity was assumed to depend on vaccination rates in the adult population and time since last vaccination of the cohort. One-time adult vaccination was assumed to result in lower levels of herd immunity over the lifetime of a cohort due to waning immunity after vaccination compared with a strategy of adult vaccination with decennial boosters.

Results from a dynamic model for the US suggested that the addition of an adult decennial vaccination program (assuming vaccine delivery rates of 60%) to already existing childhood and adolescent vaccination programs would reduce symptomatic pertussis by 15% in infants, 3% in adolescents, and 64% in adults ≥ 65 years [31]. Reductions in adult disease were also significant at 37% for 18–24 years, 42% for 25–34 years, and 54% for 35–64 years; however, the majority of disease reduction in adults may be attributed to the direct effects of vaccination. Since we were unable to derive estimates of the indirect effects of vaccination, we chose to conservatively assume that approximately one quarter of the disease

Table 1
Probabilities, costs (in 2006 Euros), and utilities used in the model

Variable	Base case estimate	Range	Source
Disease probabilities			
Disease incidence per 100,000 population			
Adults	165	50–500	[12]
Adolescents	95	–	[52]
Infants	22	–	[13]
Adult and adolescent disease outcomes			
Mild cough illness	1%		
Moderate cough illness	72%	[12]	
Severe cough illness	26%		
Pneumonia (hospitalized)	1%		
Infant disease outcomes			
Respiratory (outpatient)	38.8%	[1]	
Respiratory (inpatient)	59%	[1]	
Neurologic	1.2%	[1]	
Death	0.7%	[51,53]	
Vaccine probabilities			
Vaccine efficacy			
Year 1	87%	50–100%	[17–23,54]
Year 2	80%		
Year 3	78%		
Year 4	77%		
Year 5	76%		
Year 6	65%		
Year 7	55%		
Year 8	44%		
Year 9	34%		
Year 10	23%		
Year 11	19%		
Year 12	14%		
Year 13	10%		
Year 14	4%		
Year 15	0%		
Vaccine adverse events			
Local reaction (Tdap vs. Td)	2%	0–10%	[27,54–60]
Systemic reaction (Tdap vs. Td)	1%	0–10%	[27,54–60]
Anaphylaxis	0.0001%	–	[61]
Vaccine delivery in adults			
20 years	82%	–	[14,15]
30 years	58%		
40 years	40%		
50 years	75%		
60 years	62%		
Disease costs			
Medical costs for adults			
Mild cough illness	10	0.2–5X BC	[12,25,62]
Moderate cough illness	97		
Severe cough illness	165		
Pneumonia	2435		
Non-medical costs for adults			
Mild cough illness	58	0.2–5X BC	[12,25]
Moderate cough illness	442		
Severe cough illness	442		
Pneumonia	789		
Medical costs for adolescents			
Mild cough illness	7	0.2–5X BC	[5,12,25,62]
Moderate cough illness	72		
Severe cough illness	122		
Pneumonia	1802		
Non-medical costs for adolescents			
Mild cough illness	20	0.2–5X BC	[5,12,25]
Moderate cough illness	155		
Severe cough illness	155		
Pneumonia	276		

Table 1 (Continued)

Variable	Base case estimate	Range	Source
Medical costs for infants			
Respiratory (outpatient)	43	–	[63]
Respiratory (inpatient)	4771		[25]
Neurologic	2539		[25]
Death	4771		Assumed
Non-medical costs for infants			
Respiratory (outpatient)	119	–	[11]
Respiratory (inpatient)	1132		[11]
Neurologic	1115		[11]
Death	1132		Assumed
Vaccine costs			
Vaccine price (incremental Tdap vs. Td)	12	5–25	[26]
Vaccine visit	0		Assumed
Vaccine administration	0		Assumed
Vaccine adverse events			
Local reaction	1		[9]
Systemic reaction	1		[9]
Anaphylaxis	1162		[25]
Utilities			
Mild cough illness	0.90	0.65–1.1X BC	Assumed
Moderate cough illness	0.85	0.65–1.1X BC	[16]
Severe cough illness	0.81	0.65–1.1X BC	[16]
Pneumonia	0.82	0.65–1.1X BC	[16]
Local reaction	0.95	0.8–1.05X BC	[16]
Systemic reaction	0.93	0.8–1.05X BC	[16]
Anaphylaxis	0.60	0.8–1.05X BC	Assumed
Infant respiratory (outpatient)	0.85	–	Assumed
Infant respiratory (hospitalized)	0.58	–	[16]
Infant neurologic	0.51	–	[16]

BC = base case assumptions.

reduction among adults was due to herd immunity (10% for 20–29, 12% for 30–39 years, and 14% for 40–64 years).

In order to assess the impact of herd immunity on infants and adolescents, we created separate decision analytic models to determine costs and outcomes in these cohorts (Fig. 1B). For infants, we assumed that medical and non-medical costs associated with pertussis deaths was similar to the cost of respiratory complications resulting in hospitalization. We did not include productivity costs due to infant mortality in the calculation of the cost-effectiveness ratio as recommended by the Panel on Cost-Effectiveness in Health and Medicine [27]. In order to fairly estimate the population benefit of herd immunity to infants, we included benefits to consecutive infant cohorts over the time period that the adult population was followed in the model, rather than following a single cohort of infants over their lifetime. Because adolescent vaccination rates for Td are low in Germany (16% for 11–13-year olds and 39% for 14–17-year olds) and Tdap rates are expected to be similar to Td rates, we considered the potential for impact of herd immunity in the adolescent population [35]. For adolescents, we assumed that pertussis infection could result in mild cough, moderate cough, severe cough, and pneumonia, similar to adults. Medical and non-medical costs associated with pertussis in adolescents were estimated to be a fraction of the cost of adult pertussis cases [5,12,25]. Similar to adults, we followed a single cohort of adolescents over time to estimate the costs and health benefits of a vaccination program. Total costs, health outcomes, and cost-effectiveness ratios for infant, adolescent and adult cohorts were calculated using an Excel spreadsheet.

We also performed sensitivity analyses to examine the impact of disease incidence, vaccine cost, vaccine efficacy, disease costs, vaccine adverse events, health state utilities, herd immunity and discount rate on model outcomes. We varied disease incidence

Table 2
Costs (2006 Euros) and benefits of adult pertussis vaccination over the lifetime of a hypothetical German population of 79 million from the societal perspective

Incidence (cases per 100,000)	No vaccination program		One-time adult vaccination program			Decennial adult vaccination program		
	Pertussis cases	Cost of pertussis cases, in millions	Cases prevented ^a	Net costs ^b , in millions	QALYs saved	Cases prevented ^a	Net costs ^b , in millions	QALYs saved
50	1,611,000	828	154,000	277	3,600	327,000	626	7,500
100	2,839,000	1539	304,000	190	8,100	641,000	444	16,800
150	4,060,000	2245	454,000	103	12,500	952,000	264	26,100
165	4,425,000	2576	498,000	78	13,400	1,046,000	207	28,700
200	5,274,000	2948	603,000	17	17,000	1,261,000	85	35,300
250	6,480,000	3646	751,000	(68)	21,400	1,568,000	(92)	44,400
300	7,680,000	4340	897,000	(153)	25,700	1,872,000	(268)	53,500
400	10,057,000	5717	1,188,000	(322)	34,400	2,472,000	(616)	71,300
500	12,407,000	7077	1,475,000	(488)	42,900	3,063,000	(958)	88,900

^a Total number of cases over the lifetime of the cohort discounted at a future rate of 3%.

^b Net costs (societal) = Cost of implementing a vaccination program – costs averted by preventing pertussis cases.

from 50 to 500 per 100,000 population based on the range of plausible estimates from published studies in Europe and the US [12,19,36–40]. The range of incidence estimates is wide due to the timing of these studies given the cyclical nature of pertussis, sampling uncertainty, and variability among different populations. Disease costs for German adults were varied from 0.2 to 5 times baseline estimates. The incremental vaccine cost of Tdap (vs. Td) was varied from 5 to 25 Euros [41] and initial vaccine efficacy was varied from 50 to 100%. Vaccine efficacy was assumed to wane over a 15 year period in a pattern similar to base case analyses. For incremental vaccine adverse events due to Tdap relative to Td, we varied the rate of local and systemic reactions from 0 to 10%. Health state utilities for disease and vaccination were varied from 0.65–1.1X to 0.8–1.05X base case estimates, respectively. These ranges were chosen to preserve the rank order of disease or vaccination health states as a group (e.g., utility of anaphylaxis always lower than utility of local reaction). We varied herd immunity estimates from 0%, i.e., no herd immunity, to two times baseline estimates.

Outcomes included cases of pertussis prevented, costs, and incremental cost-effectiveness (CE) ratios expressed as Euros per case prevented and Euros per quality-adjusted life year (QALY) saved. Net costs were calculated as the cost of implementing a vaccination program minus the costs averted by preventing pertussis cases. All costs were converted to 2006 Euros [42]. The societal perspective was adopted and future costs and health benefits were discounted at an annual rate of 3% [27]. We also calculated CE ratios from the health care payer perspective. Vaccination was considered to be cost-effective if the cost-effectiveness ratio was less than three times the gross domestic product per capita, which was 28,000 Euros for Germany in 2006 [43,44]. Modeling was performed using TreeAge Pro 2005 Suite and Microsoft Excel 2000 [45].

3. Results

3.1. Health benefits and risks

Health outcomes were projected over the lifetime of a hypothetical cohort of 79 million German children and adults, of whom 50 million were adults 20–64 years of age. At a disease incidence of 165 per 100,000 population for adults, similar to that observed in a recent epidemiologic study in Germany, approximately 4.4 million cases would occur over the lifetime of the cohort. The one-time adult vaccination strategy would potentially prevent 498,000 cases (Table 2), while the adult vaccination strategy with decennial boosters would potentially prevent 1 million cases. Because herd immunity was incorporated into the base case analysis, the one-time adult vaccination strategy prevented infant pertussis

by averting 178 cases, 109 hospitalizations, 2 cases with neurologic sequelae, and 1 death in successive infant cohorts. For the decennial booster strategy, 1505 infant cases, 891 hospitalizations, 18 cases with neurologic sequelae and 11 deaths could be prevented.

Mild adverse events due to vaccination would be expected to occur such as local and systemic reactions. Assuming an incremental risk of 2% for local reactions and 1% for systemic reactions, approximately 620,000 adults would have mild local reactions and 310,000 adults would have systemic reactions after one-time adult vaccination. A decennial booster vaccination strategy would result in 1.9 million local reactions and 1 million systemic reactions. Rare adverse events, such as anaphylaxis, would be expected to occur in 31 adults with a one-time vaccination program and 97 adults for a decennial booster vaccination program.

Health benefits and risks of an adult pertussis vaccination program in Germany were also expressed in terms of QALYs. At a low disease incidence of 50 per 100,000 population, one-time and decennial adult vaccination programs could save 3600 and 7500 QALYs, respectively.

3.2. Cost of disease and vaccination

The societal cost of adult pertussis without a vaccination program over the lifetime of the cohort ranged from 828 million to 7.1 billion Euros, depending on assumptions about disease incidence (Table 2). A one-time vaccination strategy for adults 20–64 years of age would result in 31 million people vaccinated, or approximately 62% of the adult cohort, for a vaccination program cost of 366 million Euros in this cohort. A decennial booster vaccination strategy would result in 97 million immunizations in the adult population for a total discounted program cost of 687,000 Euros for this cohort. Adult vaccination strategies could prevent significant medical and non-medical costs due to pertussis at high incidence rates of pertussis. The net costs of a one-time adult vaccination and decennial booster strategies were 78 million Euros and 207 million Euros, respectively, at a disease incidence of 165 per 100,000 (Table 2).

3.3. Cost-effectiveness of one-time and decennial adult vaccination programs

At an incidence rate of 165 per 100,000 population, the cost-effectiveness of a one-time adult vaccination program was 160 Euros per case prevented or 5800 Euros per QALY saved from the societal perspective. The decennial booster strategy results in cost-effectiveness ratios of 200 Euros per case prevented or 7200 per QALY saved (Table 3). If disease incidence were greater than 200 per 100,000 population, adult vaccination programs become cost-

Table 3
Cost-effectiveness of adult pertussis vaccination by disease incidence

Incidence (cases per 100,000)	One-time adult vaccination program		Decennial adult vaccination program	
	€ per QALY saved	€ per case prevented	€ per QALY saved	€ per case prevented
50	77,000	1800	83,000	1900
100	23,500	620	26,200	700
150	8,200	230	10,000	280
165	5,800	160	7,200	200
200	1,000	30	2,300	70
250	Cost saving	Cost saving	Cost saving	Cost saving
300	Cost saving	Cost saving	Cost saving	Cost saving
400	Cost saving	Cost saving	Cost saving	Cost saving
500	Cost saving	Cost saving	Cost saving	Cost saving

Cost and benefits are discounted at a future rate of 3%.

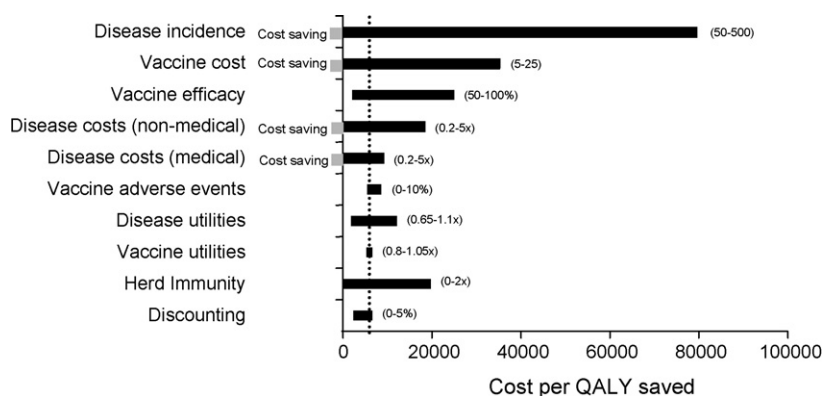


Fig. 2. Tornado diagram summarizing one-way sensitivity analyses for the one-time adult vaccination strategy. Bars represent range of cost-effectiveness ratios of a vaccination strategy as base case estimates are varied. The dotted line represents the cost-effectiveness of using base case assumptions. Ranges for sensitivity analyses are described in parentheses.

saving. When analyses were conducted from the healthcare payer perspective, the one-time vaccination and decennial booster strategies cost 21,000 and 27,000 Euros per QALY saved, respectively. The cost per case prevented and cost per QALY saved were slightly higher for the decennial adult vaccination strategy because of the incrementally higher cost of preventing each additional case of pertussis due to the persistence of low-level immunity after 10 years.

3.4. Sensitivity analyses

In order to understand the impact of our assumptions for disease incidence, vaccine efficacy, vaccine adverse events, costs, and utilities on the cost-effectiveness of adult vaccination programs, we performed one-way sensitivity analyses (Fig. 2). Disease incidence (50–500 per 100,000), vaccine cost (5–25 Euros), and initial vaccine efficacy (50–100%) all had significant impacts on our CE ratios. At a high vaccine cost of 25 Euros or low vaccine efficacy of 50%, the cost per QALY exceeded 25,000 Euros. Results were less sensitive to estimates used for disease costs, frequency of adverse events, utilities, and discount rate. We also examined the potential impact of herd immunity on the cost-effectiveness of adult vaccination (Fig. 2). If herd immunity estimates were 0%, the CE ratios for the one-time and decennial adult vaccination strategies were 21,000 and 23,000 Euros per QALY saved, respectively. If herd immunity estimates were two times base case estimates, the CE ratio fell to 1 Euro per QALY saved.

4. Discussion

We found that a one-time and decennial booster Tdap vaccination for adults aged 20–64 years cost approximately 5800

and 7200 Euros per QALY, respectively. Our results are in accord with earlier analyses of adult Tdap vaccination programs in the US which also found adult vaccination to be cost-effective from the societal perspective [9,41]. Our results were most sensitive to assumptions about disease incidence. If disease incidence were greater than 200 per 100,000 population in Germany or if the incremental cost of a vaccine was only 5 Euros, adult vaccination programs would be cost saving. In contrast, low disease incidence resulted in cost-effectiveness ratios that exceeded 50,000 Euros per QALY.

The current vaccination schedule in Germany recommends pertussis-containing vaccines to be given at 3–5, and 12–15 months of age with an additional booster dose between 9 and 17 years [46]. Recently, a pre-school booster at age 5–6 was also recommended in order to prevent disease in this age group [46]. Despite achieving high rates of childhood vaccination (>90%) for the primary childhood series [35], however, pertussis has remained endemic in Germany [12]. Several countries have noted an epidemiological shift in the average age of pertussis infection, with a rising number of cases now reported in adolescents and adults [8,47]. Waning immunity is thought to contribute to this growing pool of susceptible adolescents and adults.

There has been increased recognition by both clinicians and policymakers regarding the frequency and morbidity of pertussis in adults. In Germany, studies about the disease burden and symptoms in adults have found similar incidences as in other countries, and 25% of adults in one study developed complications, such as rib fractures, herniae, otitis media, pneumonia and others [4]. This is similar to the findings of a Canadian study, where older adults suffer from complications of pertussis in more than 50% [6]. Additionally, adults have often been cited as the source of pertussis in the household [34,48]. Transmission to young infants poses a par-

ticularly concerning problem as these infants are likely to suffer severe complications such as apnea, encephalopathy, and death due to pertussis [33,49–51]. The addition of an adult booster to the German vaccination schedule would not only protect adults from the morbidity of pertussis, but also potentially prevent transmission to vulnerable infants.

While our model incorporated the potential impact of herd immunity on vaccine cost-effectiveness, we are unable to directly estimate the degree of benefit conferred by herd immunity to the German population in our model. Our model was also dependent on baseline estimates used for parameters that may be uncertain, such as disease incidence in Germany. A national surveillance program for pertussis may be useful to monitor disease trends, particularly if a Tdap vaccination program is adopted for adults. Finally, the duration of immunity after Tdap vaccination is unknown at this time. As information becomes available about the duration of immunity, it is possible that a vaccination program that includes decennial boosters, rather than one-time adult vaccination, may be the optimal approach to reducing disease burden due to pertussis.

We conclude that a Tdap vaccination program in adults aged 20–64 years to prevent pertussis is cost-effective, and may even be cost saving if disease incidence among adults is higher than 200 per 100,000 population.

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References

- Juretzko P, Fabian-Marx T, Haastert B, Giani G, von Kries R, Wirsing von Konig CH. Pertussis in Germany: regional differences in management and vaccination status of hospitalized cases. *Epidemiol Infect* 2001;127(August (1)):63–71.
- Halperin SA. The control of pertussis—2007 and beyond. *N Engl J Med* 2007;356(January 11 (2)):110–3.
- von Konig CH, Halperin S, Riffelmann M, Guiso N. Pertussis of adults and infants. *Lancet Infect Dis* 2002;2(December (12)):744–50.
- Postels-Multani S, Schmitt HJ, Wirsing von Konig CH, Bock HL, Bogaerts H. Symptoms and complications of pertussis in adults. *Infection* 1995; 23(May–June (3)):139–42.
- Lee GM, Lett S, Schauer S, LeBaron C, Murphy TV, Rusinak D, et al. Societal costs and morbidity of pertussis in adolescents and adults. *Clin Infect Dis* 2004;39(December 1 (11)):1572–80.
- De Serres G, Shadmani R, Duval B, Boulianne N, Dery P, Douville Fradet M, et al. Morbidity of pertussis in adolescents and adults. *J Infect Dis* 2000;182(July 1):174–9.
- Nelson JD. The changing epidemiology of pertussis in young infants. The role of adults as reservoirs of infection. *Am J Dis Child* 1978;132(April (4)):371–3.
- Skowronski DM, De Serres G, MacDonald D, Wu W, Shaw C, Macnabb J, et al. The changing age and seasonal profile of pertussis in Canada. *J Infect Dis* 2002;185(May 15 (10)):1448–53.
- Lee GM, Murphy TV, Lett S, Cortese MM, Kretsinger K, Schauer S, et al. Cost effectiveness of pertussis vaccination in adults. *Am J Prev Med* 2007;32(March 3):186–93.
- Human Mortality Database. <http://www.mortality.org/> [accessed February 12, 2007].
- Statistisches Bundesamt. www.destatis.de/ [accessed September 7, 2007].
- Riffelmann M, Littmann M, Hulse C, O'Brien J, Wirsing von Konig CH. Pertussis: incidence, symptoms and costs. *Dtsch Med Wochenschr* 2006;131(December 15 (50)):2829–34.
- Anon. Pertussis in den neuen Bundesländern *Epid Bulletin* 23/2005. http://www.rki.de/cln_049nn.196322/DE/Content/Infekt/EpidBull/Archiv/ [accessed September 7, 2007].
- Anon. Adults vaccination coverage, *Epidem. Bulletin*, 1/1999. September 7; http://www.rki.de/cln_049nn.196322/DE/Content/Infekt/EpidBull/Archiv/.
- Hellenbrand W. Adults vaccination coverage *Rovert-Koch-Institut*, personal communication.
- Lee GM, Salomon JA, LeBaron CW, Lieu TA. Health-state valuations for pertussis: methods for valuing short-term health states. *Health Qual Life Outcomes* 2005;(March 21 (3)):17.
- Ward J. The APERT Study. Paper presented at National Consensus Conference on Pertussis; May 25–28, 2002; Toronto.
- Ward JI, APERT Study Group. Pertussis epidemiology and acellular pertussis vaccine efficacy in older children: NIH APERT Multicenter Pertussis Trial. Paper presented at Pediatric Academic Societies Annual Meeting, 2001; Baltimore, MD.
- Ward JI, Cherry JD, Change SJ, Partridge S, Lee H, Treanor J, et al. Efficacy of an acellular pertussis vaccine among adolescents and adults. *N Engl J Med* 2005;353(October 13 (15)):1555–63.
- Jenkinson D. Duration of effectiveness of pertussis vaccine: evidence from a 10 year community study. *Br Med J Clin Res Ed* 1988;296(February 27 (6622)):612–4.
- Lambert HJ. Epidemiology of a small pertussis outbreak in Kent County. *Michigan Public Health Report* 1965;80(4):365–7.
- Cattaneo LA, Reed GW, Haase DH, Wills MJ, Edwards KM. The seroepidemiology of Bordetella pertussis infections: a study of persons ages 1–65 years. *J Infect Dis* 1996;173(May (5)):1256–9.
- Ramsay ME, Farrington CP, Miller E. Age-specific efficacy of pertussis vaccine during epidemic and non-epidemic periods. *Epidemiol Infect* 1993;111(August (1)):41–8.
- Wendelboe AM, Van Rie A, Salmaso S, Englund JA. Duration of immunity against pertussis after natural infection or vaccination. *Pediatr Infect Dis J* 2005;24(May (5 Suppl)):S58–61.
- German DRGs: Institut für das Entgeltsystem im Krankenhaus (InEK gGmbH). <http://www.g-drg.de> [accessed September 7, 2007].
- Rote Liste: official list of German pharmaceutical products, 2006 edition: Rote Liste Service GmbH, Frankfurt/Main, Germany.
- Gold MR, Siegel JE, Russell LB, Weinstein MC. Cost-effectiveness in health and medicine. New York: Oxford University Press; 1996.
- Tozzi AE, Rava L, Ciofi degli Atti ML, Salmaso S. Clinical presentation of pertussis in unvaccinated and vaccinated children in the first six years of life. *Pediatrics* 2003;112(November (5)):1069–75.
- Yih WK, Lett SM, des Vignes FN, Garrison KM, Sipe PL, Marchant CD. The increasing incidence of pertussis in Massachusetts adolescents and adults, 1989–1998. *J Infect Dis* 2000;182(November (5)):1409–16.
- Birkebaek NH, Kristiansen M, Seefeldt T, Degn J, Moller A, Heron I, et al. Bordetella pertussis and chronic cough in adults. *Clin Infect Dis* 1999;29(November 5):1239–42.
- Van Rie A, Hethcote HW. Adolescent and adult pertussis vaccination: computer simulations of five new strategies. *Vaccine* 2004;22(August 13 (23–24)):3154–65.
- Deen JL, Mink CA, Cherry JD, Christenson PD, Pineda EF, Lewis K, et al. Household contact study of Bordetella pertussis infections. *Clin Infect Dis* 1995;21(November 5):1211–9.
- Crowcroft NS, Booy R, Harrison T, Spicer L, Britto J, Mok Q, et al. Severe and unrecognized: pertussis in UK infants. *Arch Dis Child* 2003;88(September 9):802–6.
- Bisgard KM, Pascual FB, Ehresmann KR, Miller CA, Cianfrini C, Jennings CE, et al. Infant pertussis: who was the source? *Pediatr Infect Dis J* 2004;23(November 11):985–9.
- Poethko-Muller C, Kuhnert R, Schlaud M. Vaccination coverage and predictors for vaccination level. Results of the German health interview and examination survey for children and adolescents (KiGGS). *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 2007;50(May–June (5–6)):851–62.
- Nennig ME, Shinefield HR, Edwards KM, Black SB, Fireman BH. Prevalence and incidence of adult pertussis in an urban population. *JAMA* 1996;275(June 5 (21)):1672–4.
- Strelbel P, Nordin J, Edwards K, Hunt J, Besser J, Burns, et al. Population-based incidence of pertussis among adolescents and adults, Minnesota, 1995–1996 *J Infect Dis* 2001;183(May 1 (9)):1353–9.
- Gilberg S, Njamkepo E, Du Chatelet IP, Partouche H, Gueirard P, Ghasarossian C, et al. Evidence of Bordetella pertussis infection in adults presenting with persistent cough in a French area with very high whole-cell vaccine coverage. *J Infect Dis* 2002;186(August 1 (3)):415–8.
- Miller E, Fleming DM, Ashworth LA, Mabbett DA, Vurdien JE, Elliott TS. Serological evidence of pertussis in patients presenting with cough in general practice in Birmingham. *Commun Dis Public Health* 2000;3(June (2)):132–4.
- Schmitt-Grohe S, Cherry JD, Heininger U, Uberall MA, Pineda E, Stehr K. Pertussis in German adults. *Clin Infect Dis* 1995;21(October (4)):860–6.
- Purdy KW, Hay JW, Botteman MF, Ward JI. Evaluation of strategies for use of acellular pertussis vaccine in adolescents and adults: a cost-benefit analysis. *Clin Infect Dis* 2004;39(July 1 (1)):20–8.
- Harmonisierter Verbraucherpreisindex. <http://www.destatis.de/indicators/d/vpi120ad.htm> [accessed February 21, 2007].
- World Health Organization. The World Health Report 2002. Geneva, Switzerland: World Health Organization; 2002.
- International Monetary Fund. World Economic Outlook Database. April 2007; <http://www.imf.org/external/pubs/ft/weo/2007/01/data/index.aspx> [accessed July 31, 2007].
- TreeAge Pro 2005 Suite [computer program]. Version 0.4. Williamstown, MA: TreeAge Software, Inc.; 2005.

- [46] Impfpfehlungen der Ständigen Impfkommission beim Robert-Koch-Institut (STIKO), actual version and archived versions Available at: http://www.rki.de/cln_049/nn_199596/DE/Content/Infekt/Impfen/STIKO.Empfehlungen/stiko_empfehlungen_node.html?_nnn=true [accessed September 9, 2007].
- [47] Guris D, Strebel PM, Bardenheier B, Brennan M, Tachdjian R, Finch E, et al. Changing epidemiology of pertussis in the United States: increasing reported incidence among adolescents and adults. 1990–1996 *Clin Infect Dis* 1999;28(June 6):1230–7.
- [48] Wirsing von König CH, Postels-Multani S, Bock HL, Schmitt HJ. Pertussis in adults: frequency of transmission after household exposure. *Lancet* 1995;346(November 18 (8986)):1326–9.
- [49] Kowalzik F, Barbosa AP, Fernandes VR, Carvalho PR, Avila-Aguero ML, Goh DY, et al. Prospective multinational study of pertussis infection in hospitalized infants and their household contacts *Pediatr Infect Dis J* 2007;26(March 3):238–42.
- [50] Wendelboe AM, Njamkepo E, Bourillon A, Floret DD, Gaudelus J, Gerber M, et al. Transmission of Bordetella pertussis to young infants *Pediatr Infect Dis J* 2007;26(April 4):293–9.
- [51] Pertussis—United States, 1997–2000. *MMWR* 2002;51(February 1 (4)):73–6.
- [52] *Epidemiologisches Bulletin* Nr. 50. Berlin: Robert Koch Institut; December 14, 2007.
- [53] Pertussis—United States, 2001–2003. *MMWR* 2005;54(December 23 (50)):1283–6.
- [54] Lee GM, Lebaron C, Murphy TV, Lett S, Schauer S, Lieu TA. Pertussis in adolescents and adults: should we vaccinate? *Pediatrics* 2005;115(June (6)):1675–84.
- [55] Van der Wielen M, Van Damme P, Joossens E, Francois G, Meurice F, Ramalho A. A randomised controlled trial with a diphtheria-tetanus-acellular pertussis (dTpa) vaccine in adults. *Vaccine* 2000;18(April 14 (20)):2075–82.
- [56] Halperin SA, Smith B, Russell M, Hasselback P, Guasparini R, Skowronski D, et al. An adult formulation of five-component acellular pertussis vaccine combined with diphtheria and tetanus toxoids is safe and immunogenic in adolescents and adults. *Vaccine* 2000;18(January 31 (14)):1312–9.
- [57] Halperin SA, Smith B, Russell M, Scheifele D, Mills E, Hasselback P, et al. Adult formulation of a five components acellular pertussis vaccine combined with diphtheria and tetanus toxoids and inactivated poliovirus vaccine is safe and immunogenic in adolescents and adults *Pediatr Infect Dis J* 2000;19(April 4):276–83.
- [58] Rennels MB. Extensive swelling reactions occurring after booster doses of diphtheria-tetanus-acellular pertussis vaccines. *Semin Pediatr Infect Dis* 2003;14(July (3)):196–8.
- [59] Rennels MB, Deloria MA, Pichichero ME, Losonsky GA, Englund JA, Meade BD, et al. Extensive swelling after booster doses of acellular pertussis-tetanus-diphtheria vaccines. *Pediatrics* 2000;105(January 1):e12.
- [60] Jackson LA, Carste BA, Malais D, Froeschle J. Retrospective population-based assessment of medically attended injection site reactions, seizures, allergic responses and febrile episodes after acellular pertussis vaccine combined with diphtheria and tetanus toxoids. *Pediatr Infect Dis J* 2002;21(August (8)):781–6.
- [61] Bohlke K, Davis RL, Marcy SM, Braun MM, DeStefano F, Black SB, et al. Risk of anaphylaxis after vaccination of children and adolescents. *Pediatrics* 2003;112(October 4):815–20.
- [62] Szucs T, Behrens M, Volmer T. Public health costs of influenza in Germany 1996—a cost-of-illness analysis. *Med Klin (Munich)* 2001;96(February 15 (2)):63–70.
- [63] German tariff for outpatient care: Einheitlicher Bewertungsmaßstab (EBM 2000 plus). www.kbv.de/ebm2000plus/EBMGesamt.htm [accessed September 9, 2007].