Childhood Immunization

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Prepared by

Michael V. Maciosek, PhD[1]

Amy B. LaFrance, MPH[1]

[1]HealthPartners Institute
8170 33rd Avenue South
PO Box 1524, MS 23301A
Minneapolis MN 55440-1524

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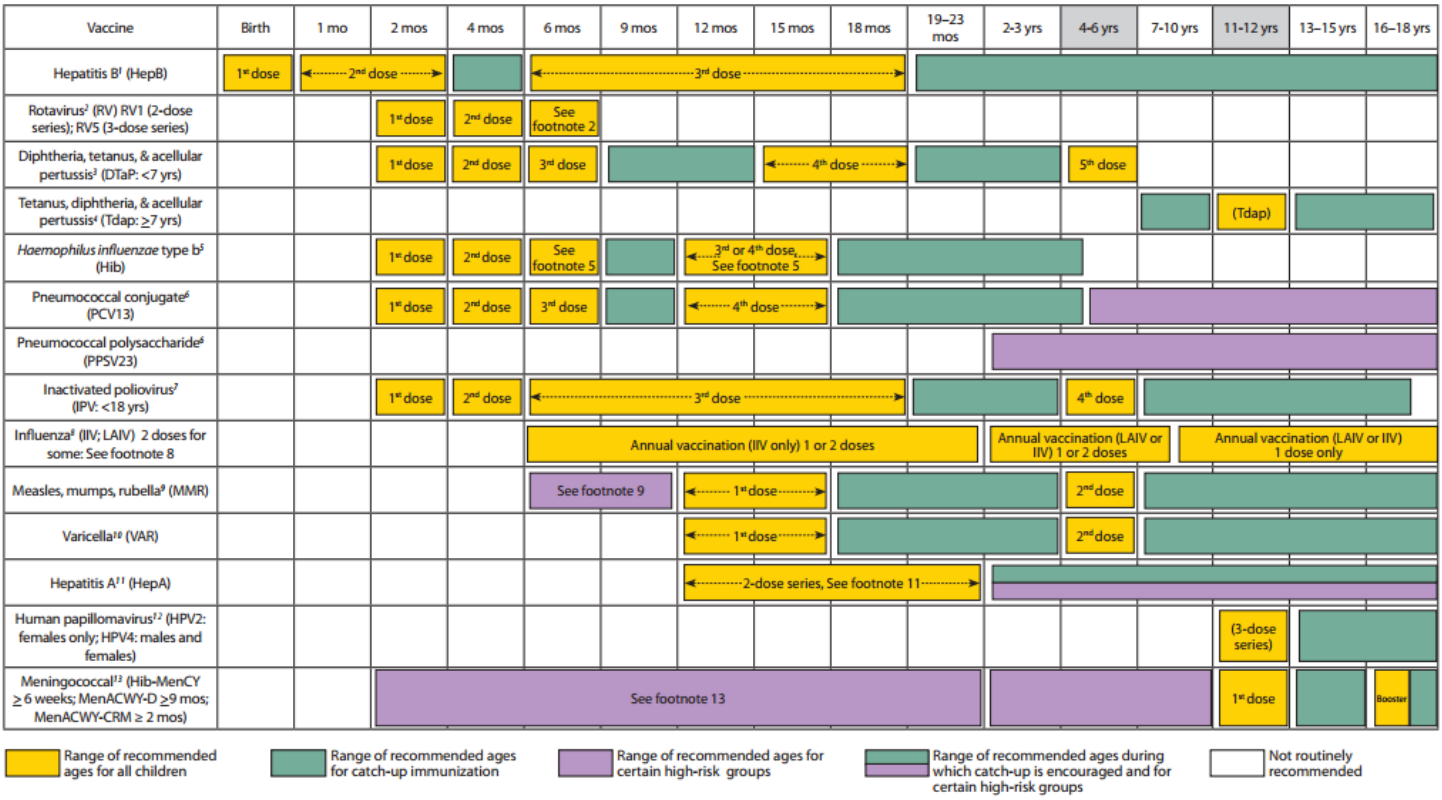
This report summarizes estimates of health impact and cost-effectiveness that were created to assess the relative value of most of the clinical preventive services recommended by the United States Preventive Services Task Force (USPSTF) and the Advisory Committee on Immunization Practices (ACIP). This ranking of clinical prevention priorities is guided by the National Commission on Prevention Priorities (NCPP).

Introduction

Preventing disease, disability and death in children reaps great benefits. Routine childhood immunizations in the United States are "one of the most cost-effective prevention programs in public health."[1] The most recent comprehensive assessment shows that because of vaccination, American children born in 2009 will contract 20 million fewer cases of vaccine-preventable diseases and avoid 42,000 early deaths due to those same diseases during their lifetimes.[1]

This report on childhood immunization includes all vaccines recommended for children from birth to 10 years, as well as influenza, which is recommended annually to age 18. The current Advisory Committee on Immunization Practices (ACIP) recommendation for childhood immunizations is shown in Table 1 below.[2] All children are recommended to have the following vaccinations prior to reaching adulthood: Hepatitis B; Rotavirus; diphtheria, tetanus, and acellular pertussis (Dtap); Haemophilus influenzae type b (Hib); Pneumoccocal conjugate (PCV 13); inactivated poliovirus (IPV); influenza; measles, mumps, and rubella (MMR); varicella; Hepatitis A (HPV); and meningococcal.

Table 1. Recommended Immunization Schedule for Persons Aged 0 Through 18 Years, United States, 2015



This schedule includes recommendations in effect as of January 1, 2015. Any dose not administered at the recommended age should be administered at a subsequent visit, when indicated and feasible. The use of a combination vaccine generally is preferred over separate injections of its equivalent component vaccines. Vaccination providers should consult the relevant Advisory Committee on Immunization Practices (ACIP) statement for detailed recommendations, available online at http://www.cdc.gov/vaccines/hcp/acip-recs/index.html. Clinically significant adverse events that follow vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS) online (http://www.vaers.hhs.gov) or by telephone (800-822-7967). Suspected cases of vaccine-preventable diseases should be reported to the state or local health department. Additional information, including precautions and contraindications for vaccination, is available from CDC online (http://www.cdc.gov/vaccines/recs/vac-admin/contraindications.htm) or by telephone (800-CDC-INFO [800-232-4636]).

This schedule is approved by the Advisory Committee on Immunization Practices (http://www.cdc.gov/vaccines/acip), the American Academy of Pediatrics (http://www.aap.org), the American Academy of Family Physicians (http://www.aafp.org), and the American College of Obstetricians and Gynecologists (http://www.acog.org).

NOTE: The above recommendations must be read along with the footnotes of this schedule.

Extensive footnotes should be consulted for a full understanding of this schedule. They can be found on the CDC website (http://www.cdc.gov/vaccines/schedules/hcp/imz/child-adolescent.html).[2] The scope of this report is the general population of children; analyses exclude children at high risk and those undergoing catch-up vaccinations.

Methods

For this analysis, we employed published estimates of the health benefits and medical cost savings from childhood immunizations, scaled to a birth cohort of 4,000,000. Medical cost savings are adjusted to 2012 dollars. To maintain consistency with costing methods across preventive services in the Prevention Priorities ranking, we calculated our estimate of the cost of delivering the childhood vaccination series using the same approach (see "Vaccination costs" under "Cost Effectiveness," below).

Clinically Preventable Burden

The clinically preventable burden (CPB) estimate is summarized in Table 2. For most infectious diseases, the event counts in Table 2 refer to events prevented that are directly attributable to the infectious disease. Events related to sequelae and long-term complications are shown in Table 3 for pertussis, Hib, polio, measles, mumps, rubella and congenital rubella syndrome. The QALYs associated with those events are included in Table 2 as "QALYs saved from prevented complications." Complications of tetanus, diphtheria, influenza, hepatitis A, hepatitis B, and pneumococcal are reflected in the event counts and the duration of events (sick days) in Table 3.

Whitney et al. was our primary source for health benefits of the childhood immunization series, specifically the illnesses, hospitalizations and deaths prevented for Hepatitis B, diptheria, tetanus, pertusis, Hib, polio, measles, mumps, rubella, congenital rubella syndrome, varicella, pneumococcal disease, and rotavirus.[3] They reported estimates over multiple birth cohorts, varying according to the number of years a vaccine for the infectious disease has been in use. We scaled their results to be representative of a single birth cohort. Events prevented by influenza vaccination are based on rates reported by Prosser et al.[4] To estimate influenza events prevented over the lifetime of a birth cohort, we applied their rates to estimates of the portion of children at increased risk, the portion receiving live attenuated vaccine, and the number of years of life lived at each age group by a birth cohort. Prevented events for hepatitis A vaccination are those modeled by Rein et al. [5]

Estimates for duration of episodes are updated primarily from a series of reports prepared by Hatziandreu et al. for the Centers for Disease Control and Prevention.[6-9] Where needed, we based duration estimates on clinical features described in the "Pinkbook," CDC's *Epidemiology and Prevention of Vaccine-Preventable Diseases*.[10] We also drew from estimates for the duration of hepatitis events used by Rein et al.[5] For congenital rubella syndrome, quality of life decrements are reflected in lifelong duration of complications (see Table 3).

Life years saved per death prevented are estimated as the average life expectancy at the median age of death, where our estimates of the median age of death are based on data from the same sources detailed above, in addition to Bloom[11] for deaths from Hepatitis B and its complications. When discounted life-years saved per death were the basis for the estimate, non-discounted LYs were approximated based on the discount rate used, the presumed year to which present value was calculated and the approximate years lived after the present value year. For Hepatitis A, Hepatitis B, and pneumococcal disease, the health impact of complications are reflected in the counts and durations for illnesses, hospitalizations and deaths prevented in Table 2. The quality of life weights applied to the number of events and associated duration in Table 2 is 0.30, the standard health utility decrement of acute conditions applied to most conditions in the Prevention Priorities ranking.

Table 2. Clinically preventable burden of the childhood immunization series

Infectious disease	Illnesses prevented[1]	Sick days[2] per non-hospitalized case	Hospitalization[1] without complications	Sick days[2] per hospitalization	Deaths prevented[1]	Life years saved per death prevented[3]	QALYs saved from prevented complications[4]	Total QALYS[5]
HepB	203,919	31	31,705	68	3,038	43		136,611
Diptheria	258,168	N/A	258,168	19	25,817	76		1,971,189
Tetanus	153	N/A	153	42	25	72		1,844
Pertussis	2,768,753	35	56,533	41	1,033	77	1,421	159,864
HIB	18,372	2	-		697	78	22,887	77,372
Polio	63,308	26	26,972	40	753	56	373,656	417,227
Measles	3,600,407	5	206,904	6	2,916	75	805	233,428
Mumps	2,173,232	8	59,184	3	10	73	3,065	16,785
Rubella	1,859,542	6	6,113	3	15	72	6	9,954
Congenital Rubella Syndrome	611	See footnote 2	865	See footnote 2	66	79	14,411	14,411
Varicella	3,483,206	3	8,957	8	61	60	-	10,908
PCV13	1,932,243	10	65,649	24	2,799	78		235,900
Influenza	4,607,972	7	42,700	14	38	75		29,835
Rotavirus	1,740,167	5	47,546	10	5	78		7,933
Hep A	172,334	31	2,699	68	20	41		5,363
							Total QALYs Saved = CPB:	**3,328,623**

1. Unless noted, illnesses, hospitalizations and deaths prevented are based on Whitney et al.[3] Events prevented by influenza vaccination are based on rates reported by Prosser et al.[4] Prevented events for hepatitis A vaccination are as modeled by Rein et al.[5]
2. Estimates for duration of episodes are updated primarily from a series of reports prepared by Hatziandreu et al. for the Centers for Disease Control and Prevention.[6-9] Estimates for the duration of hepatitis events used by Rein et al 2007.[5] For congenital rubella syndrome, quality of life decrements are reflected in life-long complications (see Table 3).
3. See table 3. For Hepatitis A, Hepatitis B, and pneumococcal disease, the health impact of complications is reflected in the counts and durations for illnesses, hospitalizations and deaths prevented in Table 2.
4 and 5. As described in the text.

Table 3 details the sequelae and manifestations that contribute to the burden described in Table 2. The frequency of hospitalizations, duration of hospitalizations and number of cases of chronic manifestations in Table 3 are sourced from reports by Hatziandreu et al. produced for the Centers for Disease Control and Prevention.[6-9] The average years of chronic manifestations are assumed to continue from average age of onset until average life-expectancy (general population). Quality of life decrements are informed by a review of health utility and disability scales, including Gold,[12] Mathers, [13] Sullivan,[14] and Sullivan.[15]

Table 3. Sequelae and chronic manifestations prevented by the childhood vaccination series							
	Pertussis	HIB	Polio	Measles	Mumps	Rubella	Congenital Rubella Syndrome
Sequelae 1:	Seizure	Meningitis & related complications		Otitis	Aseptic Meningitis	Arthritis	
Hosptializations prevented[1]	5,431	10,903		44,554	162,992	460	
Days per hospitalization[1]	42.5	18.5		6.5	11.0	9.6	
Sequelae 2:	Pneumonia	Epiglottitis & other complications		Pneumonia		Thrombo-cytopenia or Encephalitis	
Hosptializations prevented	36,116	6,095		103,086		246	
Days per hospitalization	40.5	6.2		6.5		10.6	
Sequelae 3:	Cephalothopy			Encephalitis			
Hosptializations prevented	703			2,869			
Days per hospitalization	50.0			6.5			
Chronic Manifestations:		Mental retardation	Permanent paralysis		Partial Deafness		All
Cases[1]		588	13,486		109		611
Average years of chronic manifestations[2]		77.2	69.3		73.2		78.7
Quality of life reduction per year[3]		0.50	0.40		0.20		0.30
Total QALYs saved from prevented complications	1,421	22,887	373,656	805	3,065	6	14,411

1. Frequency of hospitalizations, duration of hospitalizations and number of cases of chronic manifestations from Hatziandreu et al.[6-9]
2. Average years of chronic manifestations assumed to continue from average age of onset until average life-expectancy of the general population.
3. Quality of life decrements informed by a review of published health utility and disability scales including Gold 1998,[12] Mathers 1999, [13] Sullivan 2005,[14] and Sullivan 2012.[15]

When the recommended childhood immunization series is viewed as one preventive intervention, the clinically preventable burden is 3,328,623 QALYs.

Cost-Effectiveness

Vaccination costs

We estimated the cost of the childhood vaccination series on a visit-by-visit basis. This approach accounts for the availability of combination vaccines such as DTaP, Hep B and IPV that reduce the number of shots and vaccine administration costs. It also allows us to account for lower vaccine administration cost for second and subsequent costs in the same visit.

Vaccine administration costs represent the average of 75% of median private sector charges and average Medicare payment. First immunization for a visit is determined using CPT4 code 94701; subsequent immunizations in the same visit use CPT4 94702 for intramuscular vaccination and CPT4 94704 for oral (such as Rotavirus vaccine), though intramuscular and oral administration have the same private sector and Medicare costs for subsequent vaccines. The assignment of first vaccine for the purpose of assigning vaccine administration costs is arbitrary.

Our estimate of the health sector cost of vaccination was developed by adding vaccine costs from the CDC Vaccine Price List of December 2012 to the cost of vaccine administration.[16] We allocated 53% of doses to the CDC cost and 47% to private sector cost, based on analyses by Zhou et al.[1] We added 5% for wastage. In calculating net costs, we use Zhou et al.'s estimates of medical costs savings, which are net of the cost of adverse events.[1] Therefore, to avoid double

counting, we exclude from vaccine prices the federal excise tax that supports the vaccine injury compensation program. Vaccine-specific cost assumptions are detailed in Table 4.

We used our standard method for valuing patient time for an office visit: two hours travel and visit time, valued by average hourly earnings in 2012. For our model of childhood immunizations, we assumed parents accompanied the children to the visit and valued the parent time. We did not value the children's time. We used average hourly earnings plus benefits in 2005[17] to estimate the value of parent time at $31 per hour in 2012 dollars. Parental time for vaccinations assumes that 2 minutes is spent on the first vaccine during a visit and one minute on each subsequent vaccine. Parental time and travel costs are distributed according to the portion of a 15-minute visit devoted to that vaccine.

Total vaccination costs per person were $2,435. Vaccination costs were $2,246 after discounting to the first year the service was offered.

Table 4. Cost of Childhood Immunization Series

Well child visit	Vaccine	Vaccine cost[1]	Vaccine administration cost[2]	Time cost[3]	Total visit vaccination cost
Birth	Hep B	$16.19	$25.16	NA	$41.34
2 months	DTaP, Hep B, IPV combined vaccine	$59.96	$25.16	$8.27	
	Hib	$17.01	$12.47	$4.13	
	PCV13	$113.32	$12.47	$4.13	
	Rotavirus[4]	$85.81	$12.47	$4.13	$359.32
4 months	DTaP, Hib, IPV combined vaccine	$66.08	$25.16	$8.27	
	PCV13	$113.32	$12.47	$4.13	
	Rotavirus[4]	$85.81	$12.47	$4.13	$331.84
6 months	DTaP, Hep B, IPV combined vaccine	$59.96	$25.16	$8.27	
	PCV13	$113.32	$12.47	$4.13	
	Hib[5]	$17.01	$12.47	$4.13	
	Rotavirus[4]	$51.23	$6.24	$2.07	$316.44
12 months	MMR, Varicella combined vaccine	$118.20	$25.16	$8.27	
	Hep A	$21.63	$12.47	$4.13	
	Hib	$17.01	$12.47	$4.13	
	PCV	$116.47	$12.47	$4.13	$356.54
15-18 months	DTaP	$17.49	$25.16	$8.27	$50.92
2 years	Hep A	$21.63	$25.16	$4.13	$50.92
4 years	DTaP, IPV combined vaccine	$40.29	$25.16	$8.27	
	Varicella, MMR combined vaccine	$118.20	$12.47	$4.13	$208.52
Influenza x 17	Influenza[6]	$11.82	$22.92	$7.54	$42.28
Undiscounted total cost, per person		$1,471	$734	$229	$2,435
Discounted total cost, per person		$1,406	$641	$199	$2,246

Hep B = Hepatitis B; DTaP = diphtheria, tetanus, acellular pertussis; IPV = inactivated poliovirus; Hib = Haemophilus influenzae type b; PCV13 pneumococcal conjugate vaccine; MMR = measles, mumps, rubella; Hep A = Hepatitis A.
1. Following Zhou et al. 2014,[1] we assume 53% of vaccines are purchased at CDC-listed public cost and 47% are purchased ad CDC-listed private cost and we added 5% for wastage. In calculating net costs, we use Zhou et al.'s

estimates of medical costs savings, which are net of the cost of adverse events.[1] Therefore, to avoid double counting, we exclude from vaccine prices the federal excise tax that supports the vaccine injury compensation program.
2. Represents average of 75% of median private sector charges and average Medicare payment. First immunization for a visit is costed using CPT4 code 94701; subsequent immunization same visit are costed using CPT4 94702 for intramuscular vaccination and CPT4 94704 for oral (Rotavirus vaccine), though intramuscular and oral administration have same private sector and Medicare costs for subsequent vaccines. See footnotes for influenza for additional detail on administrative costs for that vaccine.
3. Parental time for vaccinations is valued by assuming 2 minutes is spent on the first vaccine during a visit and one minute on each subsequent visit. Parental time and travel costs are distributed according to the portion of a 15-minute visit devoted to that vaccine.
4. Rotavirus immunization can be provided as either a 3-dose series (RotaTeq®) or 2-dose series (Rotarix®) at a higher per-dose price. Vaccine cost estimates reflect an average that presume 50% of children get each series and 50% of children have the third dose of RotaTeq®, and related vaccine administration and parent-time costs.
5. Hib can be provided as a 2-dose series if the same vaccine is used each time or a 3-dose series if a different vaccine is used for the second dose than was used in the 1st dose. For consistency with our simplifying assumption that all children receive the combined DTaP, Hib, IPV combined vaccine as their second dose (4-month visit), we assume all children will receive a third Hib dose.
6. Based on approximately 6% market share across all ages for FluMist®, which is contraindicated for adults 50+, we assume that 25% of children receive FluMist® in deriving and average cost per vaccination. In estimating vaccine administration and parent-time costs, we assume 17 vaccinations are received before age 18, 14 of which are the only immunization received during a visit.

Medical cost savings:

We used Zhou et al.'s recent estimate of the cost-savings of the childhood vaccination series in a U.S. birth cohort, with adjustment to 2012 dollars using the medical care price index for all urban consumers.[1] The comparison of vaccination costs to medical cost-savings is shown in Table 4. Because net costs are negative, we did compute discounted QALYs or a cost-effectiveness ratio. For services with cost-savings, we express results as the savings per-person targeted by the service. The savings per person of the childhood immunization series is $3,576.

Table 5. Cost Effectiveness Summary	
Discounted vaccination costs, per person[1]	$2,246
Average adherence to immunizations in schedule[2]	90%
Discounted vaccination costs for a U.S. birth cohort	$8,085,810,401
Discounted medical savings for a U.S. birth cohort[3]	$22,388,108,793
Discounted net costs for a U.S. birth cohort	-$14,302,298,391
Discounted savings per person	**-$3,576**

1. See Table 3
2. Approximated from Zhou 2014[1]
3. Zhou 2014,[1] inflation-adjusted to $2012 using the MCPI

Sensitivity analysis

Because the childhood immunization series falls so clearly in the top-scoring categories for both clinically preventable burden and cost-effectiveness, we did not conduct formal sensitivity analysis. Vaccination costs would need to be nearly 200% higher or medical cost savings to be 64% lower than estimated for the childhood vaccination series to have positive net costs. Clinically preventable burden would need to be more than 80% lower for the CPB score to be reduced from a 5 to a 4 in the prevention priorities ranking. That large a reduction in CPB would not be realized even if we eliminated all non-fatal prevented events and decreases deaths prevented for all infectious diseases by two-thirds.

Limitations

Although the CPB and CE scores are not in doubt, significant limitations remain that may cause the point-estimates of CPB and CE to be biased. Most notably, the estimates of prevented events from most of the infectious diseases in the childhood immunizations series are based on comparisons of current event rates to pre-vaccination rates. If not for the

advent of vaccinations, innovations may have been developed that would lead to more rapid identification and control of some of these infectious diseases and to more effective treatments that might reduce case-fatality rates. While such innovations would lead to lower clinically preventable burden, their net impact on cost-effectiveness of vaccines would depend on the expense and effectiveness of the new treatments.

It has been noted that combining childhood vaccinations into a series can hinder a prioritization process because less cost-effective vaccinations benefit when their value is averaged in with more cost-effective vaccines.[18] We concur with Zhou et al., who note that vaccines have been added to the immunization program with consideration given to health impact and price.[19] As a result, variation in value of the vaccines within the childhood vaccination schedule may be less than other among other medical services. In addition, the vaccination schedule is delivered as an integrated service, with multiple vaccines being administered in a single visit and combination vaccines, such as DTaP, Hep B and IPV and MMR with varicella, having been developed that more efficiently use the timing of integrated vaccine visits. Therefore, assessment of the value of individual series or the marginal value of a single toxoid (say of tetanus with the Dtap series) would require separation of vaccine administration costs that would result in artificial inflation of the costs of delivering each vaccine.

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