Supplementary Data

Literature review strategies

A targeted analysis of time-motion studies published within the last 10 years (2002–June 2012) on resource use during pediatric vaccine administration (i.e. time and cost data for preparing, giving, documenting and disposal of waste associated with a single vaccine injection) was conducted.

The search strategy can be found in the Supplementary Table 1.

The purpose of obtaining this data is to delineate the economic impact of combination vaccines on provider practices by informing the vaccination efficiency analyzer model. The review on vaccination time yielded 11 publications that were finally included in the report (Supplementary Figure 2).[1–11] The literature on this topic was considerably lacking and the evidence in this area within the US needs to be investigated further with time-in-motion studies to understand if what is presented in the model is applicable and measurable. The publications included in the study were mainly observational studies that assessed the average cost and variable costs for a medical practice to deliver immunization events as well as the average time spent by personnel to conduct these immunization events. The studies chosen were conducted in various parts of the world including India, the US and New Zealand; however the standard of care with respect to vaccination was basic and could be applied transversally.[1–5] These publications were reviewed to identify the time required to complete each of the following vaccine-related activities: preparation (assembly of the vaccination syringe for administration), administration (physical dispensing of vaccination, including sterilization), clean-up (management and disposal of vaccination waste), charting (recording of vaccination in the patient chart) and registry (recording of vaccination in official vaccination registries).

Only five of the 11 publications included data on one or more of these activities,[1–5] the results of the time taken per task were heavily dependent on the method of recording used. The results are summarized in Supplementary Table 4. The results indicate that two methods dominate: (1) indirect data collection from time logs, diaries, and interviews; and (2) direct data collection using stopwatches. Supplementary Table 4 shows that time estimates from indirect data collection were generally higher than direct measures. Due to the limitations in published literature especially in the US, significant assumptions had to be made and some of the estimates used were not available for the US. To limit the impact of this, the authors ensured that the most conservative assumptions were adhered to when possible, that the inputs were evidence-based and reviewed by medical physicians including pediatricians.

A conservative evidence-based approach of using estimates based on direct observation was used when possible.[1–5] For those that had both alternative methods, stopwatch method was preferred.

Estimates and assumptions used in model

The following estimates and assumptions were used for the time required for each vaccination activity. Preparation, administration, and charting estimates from Wiedenmayer et al[3] (separated for fully liquid and lyophilized vaccines) were used for multi-dose vials and lyophilized vaccinations. Preparation, administration and charting estimates for prefilled syringes were calculated from the ratio of the single dose to unspecified from Turner et al[6] multiplied by the fully liquid time from Wiedenmayer et al.[3] This assumed that the unspecified vaccination time estimates from Turner et al[1] are representative of multi-dose vaccinations.

The cleaning time for all vaccination forms was estimated as the mean of the clean-up activities (disposal of the vial, syringe, and needle) times from Wiedenmayer et al[3] and Szilagyi et al.[2] The vaccination time for a true single-dose vial was assumed to be the same as for a multi-dose vial. The time required for vaccination registry was taken to be 0.33 minutes (based on expert opinion) for all vaccination dosage forms.

Ancillary items

Ancillary items included syringes, needles and medical waste disposal, alcohol wipes, cotton balls, and adhesive bandages, Epipens, Epipen Jr, diphenhydramine, tissues, medium sharps dispenser, dispensers for sanitizing hand cream

Physician practice patient population

This study examined the US population aged 0–6 years. The number of patients receiving injections each month was determined from the total number of patients appropriate for vaccination and age distribution. The injections received by each patient were determined by their birth month. For this analysis, the model used the most current population data: the 2010 Census data[12] (the total population aged 0–6 years and the distribution by age) and the 2010 National Vital Statistics Report[13] (to determine the age distribution by month) (Supplementary Tables 2 and 3).

Supplementary Table 1: MEDLINE literature search strategy.

ID	Topic	Search algorithm	Number of hits
1	Time and motion studies	"Time and Motion Studies"[Mesh] OR "time and motion studies" OR "time-motion"[tiab] OR "time and motion study" OR "time motion" Filters: published in the last 10 years; English	1,342
2	Vaccination	((("Vaccines"[Mesh]) OR ("Vaccination"[Mesh] OR "Immunization"[Mesh])) OR "Immunization Programs"[Mesh]) OR "Immunization Schedule"[Mesh] OR vaccin*[tiab] OR immuni*[tiab] Filters: published in the last 10 years; English	149,045
1 AND 2			**15**

Limits for search included articles published from 2002–June 2012 only concerning humans and in English.

Supplementary Table 2: Population data (2010)[12].

Age (years)	N	%
<1	3,944,153	4.74
1	3,978,070	4.78
2	4,096,929	4.92
3	4,119,040	4.95
4	4,063,170	4.88
5	4,056,858	4.87
6	4,066,381	4.88
7–9	12,225,418	14.68
10–14	20,677,194	24.83
15–19	22,040,343	26.47

Supplementary Table 3: Births by month (US 2010)[13].

Month	n	%
January	323,249	8.08
February	301,994	7.55
March	338,613	8.47
April	325,028	8.13
May	328,273	8.21
June	334,535	8.36
July	345,199	8.63
August	349,747	8.75
September	350,745	8.77
October	336,809	8.42
November	326,220	8.16
December	338,974	8.48

Supplementary Table 4: Targeted literature search results.

Vaccination activity	Time (minutes)				Method
	Single dose	Fully liquid	Lyophilized	Unspecified	
Preparation	1.90[1]			3.50[1]	Time logs
		0.69[3]	1.36[3]	1.00[2]	Stopwatch
Administration	2.70[1]			4.40[1]	Time logs
				3.40[4]	Interviews
		0.39[3]	0.39[3]	6.30[2]	Stopwatch
Clean-up		0.09[3]	0.09[3]	0.30[2]	Stopwatch
Charting	2.30[1]			3.90[1]	Time logs
		0.26[3]	0.34[3]	1.00[2]	Stopwatch
Total	6.90[1]			11.80[1]	Time logs
				8.60[5]	Time diary, interviews
				10.50[4]	Interviews
		1.42[3]	2.18[3]	2.60[2]	Stopwatch

Supplementary Table 5: Vaccination consumable costs.

Country	Amount	Cost year
New Zealand [1]	NZ $0.60	NR
US [4]	US $0.48	2002
US [5]	US $0.43	2007

NR = not reported; NZ = New Zealand dollars.

	Birth	1 m	2 m	4 m	6 m	9 m	12 m	15 m	18 m	19–23 m	2–3 y	4–6 y
DTaP			DTaP	DTaP	DTaP		[a]	DTaP				DTaP
Polio			IPV	IPV	IPV							IPV
Hep B	Hep B	Hep B			Hep B							
Pneu			PCV	PCV	PCV		PCV				PPSV	
Hib			Hib	Hib	(Hib)[b]		Hib					
MMR							MMR		[c]			MMR
Varicella							VAR		[c]			VAR
Hep A							Hep A[d]				Hep A series	
Rotavirus			RV	RV	(RV)[b]							
Influenza					Influenza (yearly)							
Men						MCV4						

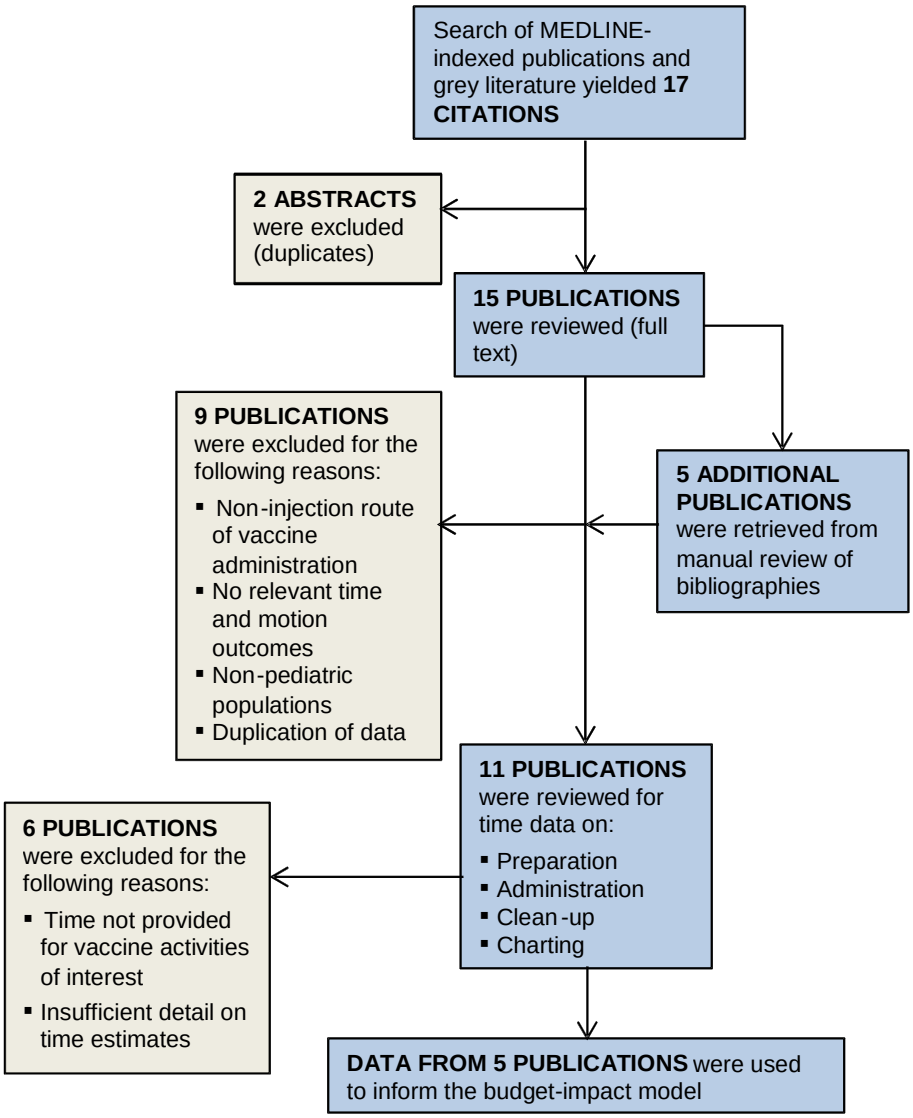
Supplementary Figure 1: Age 0–6 years vaccination schedule (2012)[14].

Range of recommended ages for all children.

Range of recommended ages for certain high-risk groups.

Range of recommended ages for all children and certain high-risk groups.

DTaP: diphtheria, tetanus, pertussis; Hep: hepatitis; Hib: *Haemophilus influenzae* type b; IPV: inactivated poliovirus; MCV4: meningococcal; MMR: measles, mumps, rubella; PCV: pneumococcal conjugate vaccine; Pneu: pneumococcal; PPSV: pneumococcal polysaccharide vaccine; RV: rotavirus; VAR: varicella. [a] The fourth dose can be administered from 12 months, provided ≥6 months have elapsed since the third dose. [b] Depending on which vaccine is used, and hence whether a third dose is required. [c] The second dose can be administered before age 4 years, provided ≥3 months have elapsed since the first dose. [d] First dose from 12 months; second dose 6–18 months later.



Supplementary Figure 2: An overview of the literature review process.

	Birth	1 m	2 m	4 m	6 m	9 m	12 m	15 m	18 m	19–23 m	2–3 y	4–6 y
DTaP			*Tripedia*™	*Tripedia*™	*Tripedia*™			*Tripedia*™				*Tripedia*™
Polio			IPOL	IPOL	IPOL							IPOL
Hep B	H	*RecombivaxHB*™			*RecombivaxHB*™							
Pneu			*Prevnar*™	*Prevnar*™	*Prevnar*™		*Prevnar*™					
Hib			*ActHIB*™	*ActHIB*™	*ActHIB*™		*ActHIB*™					
MMR							*M-M-R-II*™					*M-M-R-II*™
Varicella							*Varivax*™					*Varivax*™
Hep A							*Havrix*™/*VAQTA*™[a]		*Havrix*™/*VAQTA*™[a]			
Rotavirus			*RotaTeq*™	*RotaTeq*™	*RotaTeq*™							
Influenza					INFLUENZA (1 dose/flu season)							

Supplementary Figure 3: Least efficient currently available vaccination schedule.

DTaP: diphtheria, tetanus, pertussis; H: in hospital dose; Hep: hepatitis; Hib: *Haemophilus influenzae* type b; IPOL: inactivated poliovirus; m, months; MMR: measles, mumps, rubella; Pneu: pneumococcal; y: years. [a] *VAQTA*™ and *Havrix*™ are both pre-filled syringes so should be equally efficient.

Note: A total of 10 vaccinations with 30 injections would be required.

<table>
<tr><td></td><td>Birth</td><td>1 m</td><td>2 m</td><td>4 m</td><td>6 m</td><td>9 m</td><td>12 m</td><td>15 m</td><td>18 m</td><td>19–23 m</td><td>2–3 y</td><td>4–6 y</td></tr>
<tr><td>DTaP</td><td></td><td></td><td rowspan="3">Pediarix™</td><td rowspan="3">Pediarix™</td><td rowspan="3">Pediarix™</td><td></td><td></td><td colspan="2">Infanrix™</td><td></td><td></td><td rowspan="3">Kinrix™</td></tr>
<tr><td>Polio</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Hep B</td><td>H</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Pneu</td><td></td><td></td><td>Prevnar™</td><td>Prevnar™</td><td>Prevnar™</td><td></td><td colspan="2">Prevnar™</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Hib</td><td></td><td></td><td>PedvaxHIB™</td><td>PedvaxHIB™</td><td></td><td></td><td colspan="2">PedvaxHIB™</td><td></td><td></td><td></td><td></td></tr>
<tr><td>MMR</td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="2" rowspan="2">ProQuad™</td><td></td><td></td><td></td><td rowspan="2">ProQuad™</td></tr>
<tr><td>Varicella</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Hep A</td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="2">Havrix™/VAQTA™[a]</td><td colspan="2">Havrix™/VAQTA™[a]</td><td></td><td></td></tr>
<tr><td>Rotavirus</td><td></td><td></td><td>Rotarix™</td><td>Rotarix™</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Influenza</td><td></td><td></td><td></td><td></td><td colspan="8">INFLUENZA (1 dose/flu season)</td></tr>
</table>

Supplementary Figure 4: Most efficient currently available vaccination schedule.

DTaP: diphtheria, tetanus, pertussis; H: in hospital dose; Hep: hepatitis; Hib: *Haemophilus influenzae* type b; IPOL: inactivated poliovirus; m, months; MMR: measles, mumps, rubella; Pneu: pneumococcal; y: years. [a] *VAQTA*™ and *Havrix*™ are both pre-filled syringes so should be equally efficient.

Note: A total of 10 vaccinations with 20 injections would be required.

	Birth	1 m	2 m	4 m	6 m	9 m	12 m	15 m	18 m	19–23 m	2–3 y	4–6 y
DTaP			6-V	6-V	6-V			*Infanrix*™				*Kinrix*™
Polio												
Hep B	H											
Pneu							*Prevnar*™					
Hib			*PedvaxHIB*™	*PedvaxHIB*™			*PedvaxHIB*™					
MMR							*ProQuad*™					*ProQuad*™
Varicella												
Hep A							*Havrix*™*/VAQTA*™[a]		*Havrix*™*/VAQTA*™[a]			
Rotavirus			*Rotarix*™	*Rotarix*™								
Influenza					INFLUENZA (1 dose/flu season)							

Supplementary Figure 5: Hypothetical 6-valent vaccination schedule.

6-V: a hypothetical 6-valent vaccine; DTaP: diphtheria, tetanus, pertussis; H: in hospital dose; Hep: hepatitis; Hib: *Haemophilus influenzae* type b; IPOL: inactivated poliovirus; m, months; MMR: measles, mumps, rubella; Pneu: pneumococcal; y: years. [a] *VAQTA*™ and *Havrix*™ are both pre-filled syringes so should be equally efficient.

<table>
<tr><th></th><th>Birth</th><th>1 m</th><th>2 m</th><th>4 m</th><th>6 m</th><th>9 m</th><th>12 m</th><th>15 m</th><th>18 m</th><th>19–23 m</th><th>2–3 y</th><th>4–6 y</th></tr>
<tr><td>DTaP</td><td></td><td></td><td rowspan="6">7-V</td><td rowspan="6">7-V</td><td rowspan="6">7-V</td><td></td><td></td><td colspan="2">Infanrix™</td><td></td><td></td><td rowspan="2">Kinrix™</td></tr>
<tr><td>Polio</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Hep B</td><td>H</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Pneu</td><td></td><td></td><td></td><td></td><td></td><td colspan="2">Prevnar™</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Hib</td><td></td><td></td><td></td><td></td><td></td><td colspan="2">PedvaxHIB™</td><td></td><td></td><td></td><td></td><td></td></tr>
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<tr><td>Varicella</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Hep A</td><td></td><td></td><td></td><td></td><td></td><td></td><td colspan="2">Havrix™/VAQTA™[a]</td><td colspan="2">Havrix™/VAQTA™[a]</td><td></td><td></td></tr>
<tr><td>Rotavirus</td><td></td><td></td><td>Rotarix™</td><td>Rotarix™</td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>Influenza</td><td></td><td></td><td></td><td></td><td colspan="8">INFLUENZA (1 dose/flu season)</td></tr>
</table>

Supplementary Figure 6: Hypothetical 7-valent vaccination schedule.

7-V: a hypothetical 7-valent vaccine; DTaP: diphtheria, tetanus, pertussis; H: in hospital dose; Hep: hepatitis; Hib: *Haemophilus influenzae* type b; IPOL: inactivated poliovirus; m, months; MMR: measles, mumps, rubella; Pneu: pneumococcal; y: years. [a] *VAQTA*™ and *Havrix*™ are both pre-filled syringes so should be equally efficient.

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