An Economic Assessment of Pre-Vaccination Screening for Hepatitis A and B

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SYNOPSIS

Objective. The availability of a single vaccine active against hepatitis A and B may facilitate prevention of both infections, but complicates the question of whether to conduct pre-vaccination screening. The authors examined the cost-effectiveness of pre-vaccination screening for several populations: first-year college students, military recruits, travelers to hepatitis A–endemic areas, patients at sexually transmitted disease clinics, and prison inmates.

Methods. Three prevention protocols were examined: (*1*) *screen and defer* vaccination until serology results are known; (*2*) *screen and begin* vaccination immediately to avoid a missed vaccination opportunity; and (*3*) *vaccinate without screening*. Data describing pre-vaccination immunity, vaccine effectiveness, and prevention costs borne by the health system (i.e., serology, vaccine acquisition, and administration) were derived from published literature and U.S. government websites. Using spreadsheet models, the authors calculated the ratio of prevention costs to the number of vaccine protections conferred.

Results. The *vaccinate without screening* protocol was most cost-effective in nine of 10 analyses conducted under baseline assumptions, and in 69 of 80 sensitivity analyses. In each population considered, *vaccinate without screening* was less costly than and at least equally as effective as *screen and begin vaccination*. The *screen and defer vaccination* protocol would reduce costs in seven populations, but effectiveness would also be lower.

Conclusions. Unless directed at vaccination candidates with the highest probability of immunity, pre-vaccination screening for hepatitis A and B immunity is not cost-effective. Balancing cost reduction with reduced effectiveness, *screen and defer* may be preferred for older travelers and prison inmates.

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In the U.S., most symptomatic hepatitis A and B infections occur in adults.[1] Vaccination against hepatitis A and B is recommended for several adult populations,[2,3] yet many U.S. adults are immune as a result of prior infection.[4,5] Because vaccination of immune individuals is not harmful,[6] pre-vaccination screening to prevent unneeded vaccinations is essentially an economic issue. Both vaccination of immune individuals and pre-vaccination screening of susceptible individuals represent a waste of resources. The key question is, "What strategy minimizes waste?"

The cost-effectiveness of pre-vaccination screening is determined by vaccine prices, serology costs, and seroprevalence. When serology costs less than vaccination, there is always a break-even seroprevalence rate above or below which pre-vaccination screening reduces or increases costs.[7] One assessment of adult travelers found that screening reduced costs.[8] Another study showed that when vaccine was purchased at a lower public sector price and vaccination candidates were younger, screening increased costs.[9] Pre-vaccination screening also has been shown to increase costs when serology expenses are higher.[10] For adult hepatitis B immunization, screening reduces costs only when seroprevalence exceeds 17%,[7] a rate several times the U.S. population norm.[4]

The availability of a bivalent vaccine provides an opportunity to reduce hepatitis A and B infections among adults but complicates the question of whether to conduct pre-vaccination screening. Rather than classifying patients as those who do vs. those who do not require vaccination, serology allows assignment to four strata based on the presence or absence of hepatitis A and B immunity (i.e., susceptible to hepatitis A and B, susceptible to hepatitis A only, susceptible to hepatitis B only, or immune to both hepatitis A and B). These groups require different vaccine regimens, with different costs and vaccination schedules. Prior examinations of pre-vaccination screening assumed that all patients would complete the vaccination series.[7–11] In fact, some patients do not return when vaccination is deferred pending serology results,[6] thereby incurring screening costs but no benefits. Further, populations differ with respect to compliance with subsequent doses, and the probability of protection with an incomplete series differs between recipients of hepatitis A and B vaccines. For these reasons, we investigated the cost-effectiveness of screening in populations that may present for consideration of hepatitis A and B vaccination.

METHODS

We considered the cost-effectiveness of pre-vaccination screening from the health system's perspective by relating screening and vaccination costs to the numbers of individuals conferred hepatitis A and/or B protection. We used data obtained from the published literature and U.S. government websites to estimate, for hypothetical cohorts of 1,000 adult vaccination candidates: (*1*) hepatitis A and B prevention costs; (*2*) the number of vaccine protections conferred; and (*3*) cost-effectiveness, defined as the ratio of prevention costs to vaccine protections conferred.

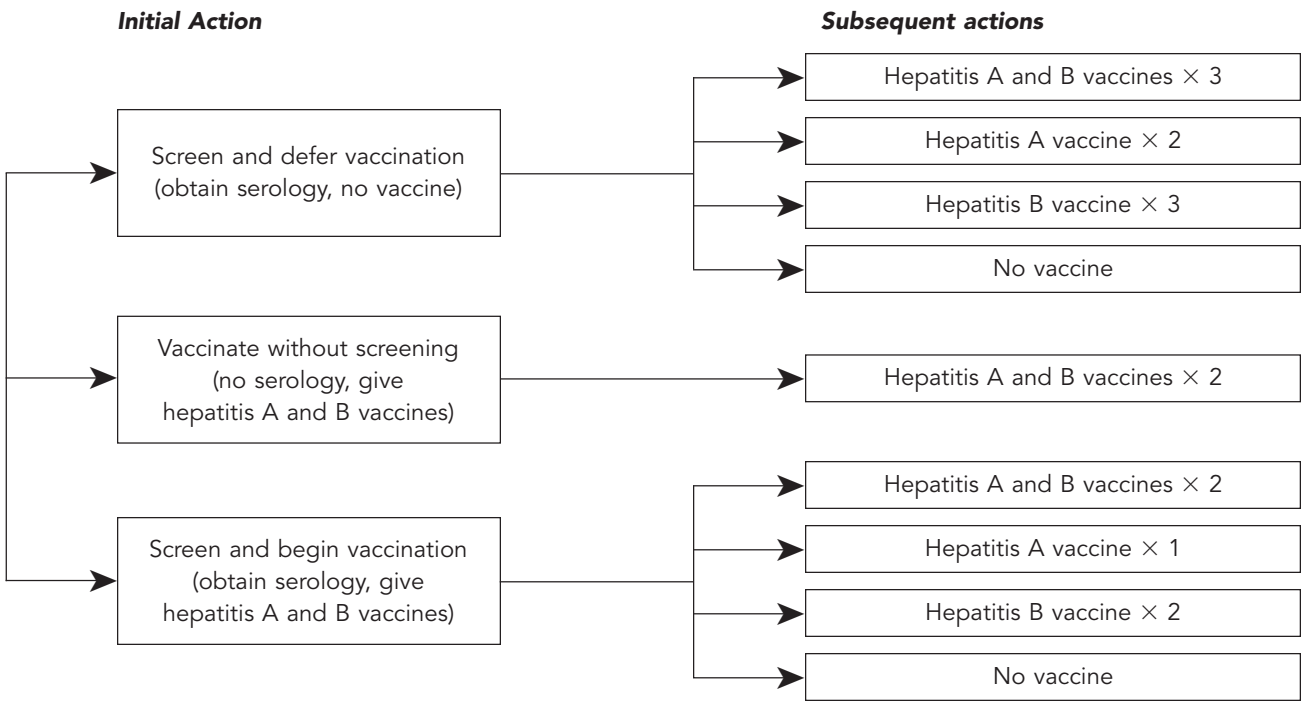
Vaccination strategies

We considered three prevention protocols: (*1*) *screen and defer* vaccination; (*2*) *screen and begin* vaccination; and (*3*) *vaccinate without screening*. (See Figure.) Under *screen and defer*, sera would be obtained at baseline to determine the presence of hepatitis A antibody (anti-HAV) and hepatitis B core antibody (anti-HBc). Patients found susceptible to both hepatitis A and B would be asked to return for three doses of the bivalent vaccine (720 El U inactivated hepatitis A antigen and 20 μg recombinant HbsAg protein) on a 0-month, 1-month, and 6-month schedule. Those susceptible to either hepatitis A or B would be asked to return for hepatitis A vaccine (1,440 El U) at 0 and 6 months or hepatitis B vaccine (20 μg) at 0, 1, and 6 months. The *screen and begin* protocol is similar in that sera would be obtained at baseline to determine the presence of anti-HAV and anti-HBc, but patients would be given bivalent vaccine before leaving the center to avoid a missed vaccination opportunity. Patients initially susceptible to hepatitis A and B would be asked to return at months 1 and 6 for bivalent vaccine. Those susceptible to just hepatitis A would be asked to return at month 6 for a dose of 1,440 El U hepatitis A vaccine, while those susceptible to just hepatitis B would be asked to return at months 1 and 6 for hepatitis B vaccine. Under *vaccinate without screening*, sera would not be obtained. All patients would be immediately given the bivalent vaccine and asked to return at months 1 and 6 for bivalent vaccine doses.

Settings

We considered several patient populations expected to vary in terms of hepatitis A and B immunity, vaccine series completion, and vaccination costs: first-year college students aged 18 years; military recruits aged 18 years; travelers to hepatitis A–endemic countries ages 25, 45, and 65 years; patients seen in public sexually transmitted disease (STD) clinics ages 25 and 35 years;

Figure. Vaccination strategies



and prison inmates ages 25 and 35 years. All vaccination candidates were presumed to deny a history of prior hepatitis infection or vaccination.

Pre-vaccination immunity

We assumed that college students, military recruits, and travelers are at normal age-specific risk of prior hepatitis A or B infection[4,5] and that their risks of prior hepatitis A and B infection are independent (Table 1). For patients seen in STD clinics, we assumed that hepatitis B seroprevalence is 10% among those who are 25 years of age and 15% among those who are 35 years of age.[11–14] For prisoners, we assumed that hepatitis B seroprevalence is 25% among those who are 25 years of age and 35% among those who are 35 years of age.[15–19] Hepatitis A immunity is not well studied in STD clinic and prison settings, although prisoners appear to have elevated hepatitis A seroprevalence compared to the general population.[20,21] Unfortunately, the coexistence of hepatitis A and B immunity among STD clinic patients and prisoners has not been described. Because hepatitis A and B share several risk factors (e.g., homosexual activity, injection drug use),[1–3] we assumed that anti-HBc-negative prisoners and STD clinic patients are at normal age-specific risk of hepatitis A immunity and that those who are anti-HBc-positive are at twice normal risk.

Vaccine series compliance

Since the analysis was limited to patients who would agree to a hepatitis prevention protocol (i.e., vaccination and/or pre-vaccination screening), we assumed 100% compliance with first vaccine doses offered at initial presentation (Table 1). For military recruits, we assumed 100% compliance with subsequent vaccine doses, and for prisoners, we assumed 95% compliance with subsequent doses. For college students, we accepted estimates of vaccine series completion from cost-effectiveness studies of adult vaccination.[22–24] We assumed that completion rates for patients seen in STD clinics are 67% as great as those for adults generally.[22] Lacking empirical data, we assumed that compliance rates for travelers fall midway between those for college students and STD clinic patients.

Vaccine protection

Vaccination success rates were based on the results of clinical trials of the bivalent vaccine.[25,26] These data indicate that hepatitis A protection is conferred to 93.6% of vaccinees after one dose, 99.0% after two

Table 1. Population-specific model parameter values

	Setting and age								
			Travel clinic			STD clinic		Prison	
Variable	College 18 years Percent	Military 18 years Percent	25 years Percent	45 years Percent	65 years Percent	25 years Percent	35 years Percent	25 years Percent	35 years Percent
Hepatitis immunity[8,9,11–21]									
A and B susceptible	87.3	87.3	78.5	62.7	38.9	72.7	63.8	60.6	48.8
B susceptible only	11.5	11.5	18.6	30.9	53.3	17.3	21.2	14.4	16.2
A susceptible only	1.1	1.1	2.3	4.3	3.3	6.2	7.5	15.4	17.6
A and B immune	0.1	0.1	0.6	2.1	4.5	3.8	7.5	9.6	17.4
Vaccine compliance[22–24]									
First vaccine dose (if immediate)	100	100	100	100	100	100	100	100	100
First vaccine dose (if deferred)	85	100	71	71	71	57	57	95	95
Vaccine dose given at month 1[a]	83	100	69	69	69	56	56	95	95
Vaccine dose given at month 6[a]	80	100	67	67	67	54	54	95	95

[a]Assuming prior dose was given.

STD = sexually transmitted disease

doses, and 99.9% after three doses. The data also show that hepatitis B protection is conferred to 29.7% of vaccinees after one dose, 77.4% after two doses, and 98.2% after three doses. We assumed equivalent protection against hepatitis B with the monovalent vaccine.[27] For the 1,440 El U hepatitis A vaccine, we assumed that 98.1% of recipients are protected after one dose and 99.3% after two doses.[26] Hepatitis A seroprotection with a 720 El U dose at month 0 and a 1,440 El U dose at month 6 has not been studied. We assumed that the second dose increases the proportion protected from 93.6% to 99.0%.

Screening and vaccination costs

The base year of the analysis is 2002, and costs from earlier years were adjusted to 2002 levels using the Consumer Price Index for Medical Care.[28] We based costs of anti-HAV ($17.12) and anti-HBc ($16.66) serology on national Medicare fees.[29] We based vaccine acquisition costs on private sector ($59.45) and public sector ($17.75) prices of hepatitis A vaccine, private sector ($51.73) and public sector ($24.25) prices of hepatitis B vaccine, and private sector ($77.67) and public sector ($36.16) prices of the bivalent vaccine.[30] We assumed that military recruits, prisoners, and patients at STD clinics receive publicly purchased vaccine. Because college students may be subject to public or private sector prices, we assessed each cost structure for the college student population. We assumed that travelers receive vaccine purchased in the private sector. For college, STD, and travel medicine settings, we assumed vaccine administration costs of $11.13 per dose.[31] Lacking empirical data, we assumed that costs would be 50% less in military and prison settings owing to large volumes and the ease of contacting vaccinees for their next dose.

Analytical methods

We added serology and vaccination costs to derive a total prevention cost for each population for each vaccination protocol. Our primary measure of cost-effectiveness is the ratio of prevention costs to the number of vaccine protections conferred, with each individual conferred protection against 0, 1, or 2 viruses. We compared the *screen and defer* vaccination, *screen and begin* vaccination, and *vaccinate without screening* protocols on the basis of their average cost-effectiveness (total prevention cost divided by number of vaccine protections conferred). In sensitivity analysis, we varied each of serology and vaccine administration costs ±33% and ±67%. While arbitrary, these percentages likely cover the range of costs incurred by individual centers. In base case and sensitivity analyses, we determined which prevention protocol had the lowest average cost-effectiveness ratio. We did not conduct further sensitivity analyses because the populations considered already differ with respect to seroprevalence and vaccine compliance.

In some populations, one protocol was dominant (i.e., it conferred the greatest number of vaccine protections at the lowest cost). In others, the most effective protocol was also the most costly. In these cases, we calculated the most costly protocol's incremental cost-effectiveness,[32] defined as its additional costs divided by the number of additional vaccine protections conferred. In this context, incremental cost-effectiveness represents the amount spent for each additional vaccine protection.

RESULTS

Prevention costs per 1,000 individuals vary dramatically between populations (Table 2). In addition to choice of prevention protocol, costs are largely affected by compliance with subsequent doses and whether vaccines are purchased in the public vs. private sector. Thus, the lowest per-capita costs are seen at public STD clinics, which have access to public sector vaccines and which have clients who are assumed to be the least compliant of the populations considered. The *screen and defer* protocol is least costly in seven populations, while *vaccinate without screening* is least costly in three. The *vaccinate without screening* and *screen and begin* protocols are equally (or near equally) effective in each population. Both are more effective than *screen and defer* except among military recruits, who are assumed to always complete their vaccination series. Average cost-effectiveness (the ratio of prevention costs to the number of vaccine protections conferred) is lowest for the *vaccinate without screening* protocol in nine of the 10 populations examined. The exception is prisoners 35 years of age, for whom *screen and defer* provides the most favorable average cost-effectiveness ratio.

The ranking of average cost-effectiveness ratios seldom varies in sensitivity analyses (Table 3). For college students, military recruits, travelers 25 years of age, and STD clinic patients, the *vaccinate without screening* protocol remains most cost-effective through the range of screening and vaccine administration costs considered. For travelers 65 years of age and prisoners 25 years of age, *screen and defer* becomes most cost-effective when serology costs are reduced 33%. For travelers 45 years of age, *screen and defer* becomes most cost-effective when serology costs are reduced 67% (i.e., to $11.15 for both anti-HAV and anti-HBc). For prisoners 35 years of age, *screen and defer* is most cost-effective under baseline assumptions, but *vaccinate without screening* is most cost-effective when serology costs are increased 33%. No change in vaccine administration costs results in a different ranking of the prevention protocols. In no sensitivity analysis is the *screen and begin* vaccination protocol most cost-effective.

In each population, *vaccinate without screening* dominates the *screen and begin* protocol. That is, it provides at least an equal number of vaccine protections at lesser cost. In three populations—college students with access to publicly purchased vaccine, military recruits, and prisoners 25 years of age—*vaccinate without screening* also dominates *screen and defer*. In the remaining seven populations, the choice between *vaccinate without screening* and *screen and defer* is less clear, as the former provides greater seroprotection, but at greater cost. In these seven settings, the incremental cost-effectiveness of *vaccinate without screening* ranged from $17 to $162 per vaccine protection conferred (Table 4). By comparison, the cost of a successful vaccination series for an individual initially susceptible to both hepatitis A and B (i.e., three doses of bivalent vaccine) is $71 per vaccine protection conferred in the public sector and $133 per vaccine protection conferred in the private sector. On this basis, the added cost of *vaccinate without screening* is warranted for all groups except 65-year-old travelers and 35-year-old prisoners.

DISCUSSION

Because many hepatitis vaccination candidates have immunity from prior infection, appropriate screening protocols may improve the cost-effectiveness of immunization programs. Yet, considering 10 populations that may present for hepatitis A and B vaccination, we found that routine screening would seldom prevent enough unneeded vaccine doses to justify serology costs. The *vaccinate without screening* protocol was found to have the most favorable average cost-effectiveness ratio in nine of 10 populations analyzed under base case assumptions, and in 69 of 80 sensitivity analyses. In each population considered, the *screen and begin* protocol would increase costs without improving effectiveness. In three populations, this is also true of the *screen and defer* protocol. In the other seven populations, *screen and defer* reduces both costs and effectiveness. A comparison of incremental cost-effectiveness ratios with the cost of a successful vaccine series shows that the *screen and defer* protocol may be preferred for older travelers and inmates.

Our study considered the limited time horizon surrounding hepatitis prevention activities. It did not address whether prevention costs are justified in the populations considered. Hepatitis A and B vaccinations have been well studied on economic grounds,[33,34] and the evidence suggests that their cost-effectiveness is largely determined by vaccine costs, infection risks, and the

Table 2. Average cost-effectiveness of prevention protocols under base case assumptions

	Prevention protocol		
Setting, patient age, and vaccine source	*Screen and defer vaccination*	*Screen and begin vaccination*	*Vaccinate without screening*
College, 18 years, public sector			
Screening and vaccination costs	$130,410	$149,081	$117,941
Number of vaccine protections conferred	1,439	1,693	1,693
Average cost-effectiveness	$91	$88	$70
College, 18 years, private sector			
Screening and vaccination costs	$214,632	$249,820	$221,467
Number of vaccine protections conferred	1,439	1,693	1,693
Average cost-effectiveness	$149	$148	$131
Military, 18 years, public sector			
Screening and vaccination costs	$153,857	$155,471	$125,175
Number of vaccine protections conferred	1,853	1,853	1,853
Average cost-effectiveness	$83	$84	$68
Travel clinic, 25 years, private sector			
Screening and vaccination costs	$160,095	$217,465	$191,124
Number of vaccine protections conferred	1,059	1,491	1,491
Average cost-effectiveness	$151	$146	$128
Travel clinic, 45 years, private sector			
Screening and vaccination costs	$152,143	$211,153	$191,124
Number of vaccine protections conferred	945	1,331	1,331
Average cost-effectiveness	$161	$159	$144
Travel clinic, 65 years, private sector			
Screening and vaccination costs	$140,527	$202,552	$191,124
Number of vaccine protections conferred	766	1,078	1,078
Average cost-effectiveness	$183	$188	$177
STD clinic, 25 years, public sector			
Screening and vaccination costs	$78,346	$116,965	$88,073
Number of vaccine protections conferred	758	1,329	1,329
Average cost-effectiveness	$103	$88	$66
STD clinic, 35 years, public sector			
Screening and vaccination costs	$75,672	$114,728	$88,073
Number of vaccine protections conferred	698	1,224	1,224
Average cost-effectiveness	$108	$94	$72
Prison, 25 years, public sector			
Screening and vaccination costs	$120,586	$133,711	$119,021
Number of vaccine protections conferred	1,386	1,459	1,460
Average cost-effectiveness	$87	$92	$82
Prison, 35 years, public sector			
Screening and vaccination costs	$109,648	$126,071	$119,021
Number of vaccine protections conferred	1,207	1,269	1,271
Average cost-effectiveness	$91	$99	$94

NOTE: Average cost-effectiveness is the ratio of the total prevention cost (cost of screening plus cost of vaccination) to the number of vaccine protections conferred.

STD = sexually transmitted disease

Table 3. Most cost-effective prevention protocol under base case and sensitivity analysis assumptions

	Setting, patient age, and vaccine source									
				Travel clinic			*STD clinic*		*Prison*	
	College, 18 years, public sector	*College 18 years, private sector*	*Military 18 years, publice sector*	*25 years, private sector*	*45 years, private sector*	*65 years, private sector*	*25 years, public sector*	*35 years, public sector*	*25 years, public sector*	*35 years, public sector*
Base case assumptions	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	S/D
Serology costs										
Increased 67%	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX
Increased 33%	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX
Reduced 33%	VAX	VAX	VAX	VAX	VAX	S/D	VAX	VAX	S/D	S/D
Reduced 67%	VAX	VAX	VAX	VAX	S/D	S/D	VAX	VAX	S/D	S/D
Administration costs										
Increased 67%	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	S/D
Increased 33%	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	S/D
Reduced 33%	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	S/D
Reduced 67%	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	VAX	S/D

NOTE: The most cost-effective protocol has the lowest ratio of prevention costs to number of vaccine protections conferred.

VAX = vaccinate without screening

S/D = screen and defer vaccination

probability of poor clinical outcomes. Because infection risks decline with age,[4,35] vaccination of the general population meets accepted standards of cost-effectiveness for children,[36–38] adolescents,[36,39] and young adults,[40] but not for those older than 40 years.[22,41] Among adults, favorable cost-effectiveness has been reported for individuals at high risk of infection due to lifestyle factors[42–44] and those at elevated risk of poor outcomes due to pre-existing liver disease.[24,45] Whether vaccination costs are warranted in the popu-

Table 4. Incremental cost-effectiveness of *vaccinate without screening* protocol compared to *screen and defer* protocol

Setting and patient age (vaccine source)	*Additional cost*[a]	*Number of additional vaccine protections conferred*	*Incremental cost-effectiveness*[b]
College, 18 years (public)	−$12,469	254	<$0
College, 18 years (private)	$6,835	254	$27
Military, 18 years	−$28,682	0	<$0
Travel clinic, 25 years	$31,029	432	$72
Travel clinic, 45 years	$38,981	386	$101
Travel clinic, 65 years	$50,597	312	$162
STD clinic, 25 years	$9,727	571	$17
STD clinic, 35 years	$12,401	526	$24
Prison, 25 years	−$1,565	74	<$0
Prison, 35 years	$9,372	64	$146

[a]Per 1,000 vaccination candidates; negative numbers represent savings.

[b]Additional costs divided by additional vaccine protections conferred

lations we considered will depend on population-specific risks and consequences of hepatitis A and B.

Even within the time horizon considered, our analysis has several limitations. First, we did not quantify work loss or travel costs associated with screening and vaccination visits. Had these costs been considered, our results would have been more favorable to the *screen and begin* protocol—which requires the fewest visits—and less favorable to *screen and defer*—which requires the most. Second, because the coexistence of hepatitis A and B immunity has not been extensively studied, we assumed that these risks are independent in several populations. If hepatitis A and B immunity more frequently coexist than assumed here, screening would identify more individuals requiring no vaccine, and thus be more cost-effective. Third, we considered only screening protocols that would be applied to all vaccination candidates. In some settings, screening may be more cost-effective if limited to clients with selected characteristics.[8,12] Fourth, our analysis was limited to adults with a reliable history of never having been vaccinated against hepatitis A or B. Most American children now complete hepatitis B immunization as infants.[46] As the proportion of previously vaccinated adults increases with time, our model will be applicable to fewer individuals. It is hoped that continued expansion of immunization registries will allow determination of vaccination histories without reliance on patient recall.[47] Otherwise, it may be prudent to consider screening for both natural and vaccine-induced immunity.

Because serology and vaccination costs, seroprevalence rates, and vaccine compliance vary, no series of parameter estimates will accurately reflect the experience of any individual center. In settings with clients more likely to have hepatitis A and B immunity, pre-vaccination screening may be considerably more cost-effective than our analysis indicates. In most settings, however, screening of vaccination candidates would increase costs or provide cost reduction that is insufficient to justify the smaller number of clients conveyed vaccine protection. In these settings, the cost-effective use of pre-vaccination screening will require selection of vaccine candidates with the highest probabilities of hepatitis A and B immunity.

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