Cost-Effectiveness of Hepatitis A Vaccination in Children, Adolescents, and Adults

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Hepatitis A is a major public health problem in the United States and other developed countries, largely because decreased natural immunity allows for increased susceptibility. To evaluate the cost-effectiveness of routine vaccination of children, adolescents, and certain high-risk adults against hepatitis A, economic analyses of hepatitis A vaccination were identified through searches of MEDLINE, EMBASE, and BIOSIS (February, 1992, to December, 2001) for studies, reviews, editorials, and letters from peer-reviewed journals published in English, French, German, Italian, or Spanish. Experts were also contacted. Articles conforming to accepted standards of quality for health-economic studies were used to compile data on vaccination of children, and results were synthesized in a narrative review. This review of economic analyses of vaccine use in several developed countries shows cost-effectiveness comparable with that of other vaccines in children and within accepted boundaries for adolescents and high-risk adults. (HEPATOLOGY 2003;37:44-51.)

Hepatitis A infection is a major public health problem in developed countries.[1] With an annual incidence of up to 200,000 infections in the United States alone, it remains one of the most frequently reported vaccine-preventable diseases despite the availability of a vaccine since the middle 1990s and immune globulin for the past several decades.[2-4] Viral hepatitis A typically causes several weeks of symptomatic illness in 85% of infected adults, often involving hospitalization.[4-6] Mortality from fulminant disease exceeds 50%, despite liver transplantation.[5]

Transmitted primarily through the fecal-oral route by either person-to-person contact or ingestion of contaminated food or water,[7] hepatitis A infection may also be acquired, albeit rarely, through transfusion of blood or blood products, sexual contact, tattooing, and unhygienic dental practices.[4,8] Accordingly, high-risk groups include households with children,[5] daycare workers, persons who travel from developed to developing countries, men who have sex with men, intravenous drug users, and persons with clotting-factor disorders. The infection is by no means confined to these individuals, however.[5] Periodic outbreaks cross over to the general population,[3] and approximately half of the cases arise from unknown sources,[2,9] rendering effective control during large and sustained community-wide flare-ups extremely difficult.[5]

Paradoxically, improved sanitary standards in developed countries, which have reduced the likelihood of fecal contamination and thus the opportunity for environmental exposure, have simultaneously lowered the overall incidence of hepatitis A and increased susceptibility to the virus by decreasing natural immunity (anti–hepatitis A antibodies).[10] Therefore, a single lapse of appropriate hygiene during exposure to the virus is sufficient to cause infection.[10] Consequently, the decline in worldwide incidence rates over recent decades has facilitated the resurgence of hepatitis A in an expanding susceptible population.[10-16] In the United States and elsewhere, the burden has shifted largely to the elderly,[5,13-17] who are most likely to experience severe forms of the disease.[6,18]

The substantial morbidity caused by hepatitis A supports the case for prevention of community outbreaks through vaccination, especially of children, who have the highest infection rate and are the most important reservoir of infection in the community,[1] and adults during peak earning years, who may suffer the substantial economic impact of lost work days.[7] Because approximately half of hepatitis A infections occurs in patients with no

Abbreviations: ACIP, Advisory Committee on Immunization Practices; YOLS, years of life saved; QALY, quality-adjusted life years; HAV, hepatitis A virus.

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Table 1. Costs in Millions of U.S. Dollars (%) of Hepatitis A Among U.S. Adolescents and Adults in 1997

	Age at Infection, yr							
	15-19	20-29	30-39	40-49	50-59	60-69	≥70	Total
Treatment	10.9 (33)	30.8 (25)	34.1 (22)	22.1 (23)	14.9 (28)	5.6 (29)	6.9 (69)	125.3 (26)
Morbidity	5.1 (16)	43.4 (36)	67.5 (44)	39.5 (41)	16.1 (30)	4.4 (23)	1.1 (11)	177.1 (36)
Mortality	16.9 (51)	47.7 (39)	52.1 (34)	35.3 (36)	23.1 (43)	9.3 (48)	2.1 (20)	186.4 (38)
Total	32.9	121.9	153.7	96.9	54.1	19.2	10.1	488.8

NOTE. Data may not total exactly because of rounding. Adapted from Berge et al.[6] Reprinted with permission.

known risk factors, the current strategy of targeting high-risk groups is unlikely to achieve a sustained reduction of disease incidence.[2,3,5]

The trend toward support for universal immunization of the U.S. population is evident in the revised guidelines of the Advisory Committee on Immunization Practices (ACIP) of the Centers for Disease Control and Prevention. Vaccination against hepatitis A is recommended not only in certain high-risk groups but also for children in states where the average annual incidence of infection is double the national average.[2,19]

Although the public health benefits of universal vaccination are undeniable, the widespread use of hepatitis A vaccines requires consideration of their cost-benefit profiles.[5] This analysis examined the economic impact of routine vaccination of children, adolescents, and certain high-risk adults against hepatitis A.

Direct and Indirect Costs of Hepatitis A Infection

Because morbidity and mortality because of hepatitis A are much lower in children than in other age groups, most of the costs of this disease relate to the care of adolescents and adults.[2,6] A study that assessed the economic burden of hepatitis A in U.S. adolescents and adults during 1997 considered costs of symptomatic infection (including drugs, hospitalization, physician visits, diagnostic studies, therapy for fulminant disease, liver transplantation), morbidity (loss of income from missed work days and loss of ability to perform housekeeping activities), and mortality.[6] The annual cost of hepatitis A that resulted from this analysis was estimated at $488.8 million (Table 1).[6] Treatment costs represented 26% of this amount, whereas the bulk of the remaining expenditure was associated with morbidity (36%) and mortality (38%) (Table 1).[6] Another cost factor is the impact on quality of life, which recent studies have assumed to be virtually nil during symptomatic infection (approximately 1 month).[1,20]

Medical costs and productivity losses in individuals represent only a minor component of the total costs to society from periodic outbreaks, which include expenditures for disease control (intervention of state and local health department personnel, provision and administration of immune globulin, and extra serologic tests) and business losses.[21] During a 1992 food-borne outbreak at a caterer in Denver, Colorado, direct medical costs ($46,064) were far less onerous than disease-control costs ($689,314) (Table 2).[21] Although only 5,000 people were potentially exposed, more than 16,000 were treated with immune globulin.[21] Such inappropriate use of health care resources has occurred in many large food-borne outbreaks, which generate concern and anxiety among the general public and fear of litigation on the part of the responsible commercial entity.[21] Therefore, although the disease-control costs documented in that study are indisputably excessive, they reflect the pattern of health care utilization following food-borne hepatitis A outbreaks and are to be expected in similar future situations.[21]

Costs of Hepatitis A Vaccination

The introduction of an effective hepatitis A vaccine has given rise to 2 public health strategies: universal vaccination, in which patients are vaccinated without regard to serologic evidence of immunity, and serology-based vaccination, in which only individuals with serologically documented lack of immunity receive the vaccine.[22] Cost-decision analyses have revealed that universal vaccination is the less costly approach, except in subgroups with a very high prevalence of natural immunity.[22] Because of concerns about the ability of public and private insurers to

Table 2. Costs of a Food-Borne Hepatitis A Outbreak in Denver, Colorado, December, 1992

Cost Category	Cost in U.S. Dollars	Percentage of Total Cost of Outbreak
Disease-control costs	689,314	85
Health department personnel time	105,699	
Serologic studies and physician fees	133,218	
Immune globulin injections	450,397	
Business losses (discarded food)	45,000	6
Illness costs for cases	75,392	9
Direct medical	46,064	
Productivity losses	29,328	
Total cost to society	809,706	100

NOTE. Adapted from Dalton et al.[21] Reprinted with permission.

pay for a new vaccine program, the Vaccine for Children initiative, state legislatures, and private insurers will undoubtedly require evidence that mass immunization is cost-effective before agreeing to support it.[2]

Public health system expenses for implementing universal hepatitis A vaccination are restricted to reimbursed costs for drug and administration. Current U.S. federal contracts specify a price of approximately $11.15 per dose for patients covered under Vaccine for Children, whereas private costs for the vaccine vary nationally but have been estimated at $26 to $30 per dose.[23] Administration fees are about $11.92 per dose.[24]

Benefits of Hepatitis A Vaccination

Safe and effective vaccines against hepatitis A, which have demonstrated long-term protection in approximately 95% of patients following a complete series,[25-27] provide the opportunity to substantially prevent the morbidity and mortality of the disease and potentially eliminate the infection.[1,7]

Most hepatitis A outbreaks occur in children, adolescents, and young adults who live in intermediately endemic communities; these epidemics tend to move from community to community over time.[3] Therefore, widespread vaccination, rather than targeting of selected high-risk groups or short-term control measures, may be necessary to reduce the incidence of infection.[3]

Economic Analyses of Hepatitis A Vaccination

The following sections summarize economic data in subgroups proposed as potential targets for universal vaccination against hepatitis A. Analyses reviewed cost benefit and cost utility. Results are reported as ratios of cost per years of life saved (YOLS) or per quality-adjusted life years (QALY) and are adjusted to 1998 values using the consumer price index. A standard threshold maximum value of $50,000 per YOLS is generally accepted as a benchmark of cost-effectiveness in the medical literature, as is less than $20,000 per QALY.[28,29]

Pediatric Vaccination. Because of the high incidence of hepatitis A in children and their critical role in disease transmission, routine vaccination of this group is a potent way to prevent pediatric infection, to eliminate a major source of infection for other children and adults, and, eventually, to prevent infection in all older persons.[7] Moreover, because secondary infection may contribute to the maintenance of outbreaks, use of the vaccine in household contacts of persons with established hepatitis A is important in controlling spread in the wider community.[30] In fact, taking into account a 1:1 secondary attack rate would approximately double the benefits of vaccination.[31]

Current ACIP recommendations call for routine vaccination of children living in areas where hepatitis A rates are at least twice the national average.[7,19] These include 11 western states (Arizona, Alaska, Oregon, New Mexico, Utah, Washington, Oklahoma, South Dakota, Idaho, Nevada, and California) with annual rates of 20 to 48 per 100,000 between 1987 and 1997.[7]

Two studies have assessed the cost-effectiveness of mass immunization of 2-year-old children against hepatitis A. Both used a Markov model, which is often chosen to determine the economic impact of different health management strategies, particularly vaccination programs.[1,32] Table 3 presents the results in a league table that compares costs of vaccination against hepatitis A virus (HAV) with those of other immunizations. In a simulated cohort of 10,000 healthy children, the first study compared (1) universal vaccination of children, (2) vaccination of children with serologically documented susceptibility to hepatitis A, and (3) no vaccination.[1] Groups 1 and 2 received 2 recommended doses of hepatitis A vaccine given at 0 months and 6 to 12 months.[1] Both vaccination strategies

Table 3. League Table of Selected Cost-Utility Analyses for Immunizations (1998 U.S. Dollars)

Immunization	$/QALY	Reference
Haemophilus influenzae vaccination in Australian aboriginal children	Cost saving	33
Influenza vaccination of all healthy persons aged 15-65 yr	Cost saving	34
Hepatitis B virus-DTP combination vaccination vs. DTP vaccination alone in 1988 worldwide birth cohort in countries with very high, high, or medium under-5 mortality levels	30	35
H. influenzae vaccination among all Australian children	2,162	33
Hepatitis A vaccination following screening	7,268	1
Universal hepatitis A vaccination	12,833	1
Targeted vaccination against hepatitis A for patients with chronic hepatitis C	51,000	36
Hepatitis A vaccination of medical students	51,694	20
Vaccination against Lyme disease vs. no vaccination of residents in an endemic area	62,300	37
Diphtheria and tetanus toxoids with acellular pertussis vaccination vs. existing DTP vaccination in 1988 worldwide birth cohort in countries with very high, high, or moderate mortality levels	140,000	35

Table 4. Cost-Utility Analyses for Hepatitis A Immunization in Various Populations (in 1998 U.S. Dollars)

Hepatitis A Immunization	$/YOLS	Reference
Patient with chronic hepatitis C in highly endemic region	Cost saving	38
Men who have sex with men	Cost saving	39
Children in endemic regions	12,780	32
Adolescents	13,933	31
Food service workers	14,206	40
Patients with chronic hepatitis C in moderately endemic region	39,922 (age 50 yr)	41
Universal, children	40,923	32
Medical students	63,792	20

had cost-effectiveness ratios well within the currently accepted range for health care interventions, costing from $7,267 to $12,833 per QALY.[1] The second study compared universal vaccination with no vaccination in the 11-state region of high hepatitis A rates and in the United States as a whole (for a comparison of cost-utility studies of HAV vaccination, see Table 4).[32] Vaccination against hepatitis A had a cost-effectiveness comparable with that of other vaccines, *i.e.*, $12,780 per YOLS regionally and $40,923 per YOLS nationally.[32]

With nearly half the cost of vaccination offset by reduced treatment of symptomatic infections, the authors concluded that hepatitis A vaccination of young children is a cost-effective and beneficial intervention.[32] Taken together, these results show that hepatitis A vaccination is more cost-effective in susceptible children than in the general population but that universal childhood vaccination nevertheless offers cost-effectiveness comparable with that of many accepted medical interventions.[1,32]

A study in Germany assessed the economic influence of combined vaccination against hepatitis A and hepatitis B in all 1- to 15-year-old children and 11- to 15-year-old children over 3, 10-year cycles.[42] The study did not report economic values for hepatitis A alone but showed cost savings for the combined immunization strategies beginning in the second 10-year cycle for both age groups. Immunization of all 1- to 15-year-old children would result in a reduction of 57,596 new hepatitis A cases. The cost-effectiveness of vaccination in 1- to 15-year-old children reported was $12,601 per case averted.

Adolescent Vaccination. Because adolescents are entering the age group (20 to 39 years) with the highest risk of symptomatic hepatitis A infection,[43] ACIP recommendations for vaccination now include adolescents through age 18 years.[19] A recent study confirmed that vaccination in 15-year-old residents of the 10 states with the highest incidence of infection would be cost-effective by generally accepted standards.[31] A decision model that examined the risks and outcomes of hepatitis infection with and without routine vaccination of adolescents showed that the $30.9 million for vaccination would be more than offset by savings of $14.2 million in treatment costs and $23.8 million in indirect (work loss) costs resulting from reductions in the lifetime risk of symptomatic infection.[31] The cost-effectiveness ratio was calculated as $13,722 per YOLS.[31] From a societal perspective, vaccination would improve health outcomes and save $7.1 million.[31] Nationally, the cost-effectiveness ratio was $54,000 per YOLS, which is just at the acceptable level. The study results, however, support the cost-effectiveness of vaccinating adolescents in states with high disease burdens.[31]

Adult Vaccination. ACIP recommendations for hepatitis A vaccination include members of certain high-risk groups (travelers or workers in moderately or highly endemic countries, men who have sex with men, users of injectable and noninjectable drugs, and persons who work with nonhuman primates, have clotting factor disorders, or chronic liver disease).[19] Cost-effectiveness studies have been conducted in several of these and other high-risk groups.

Travelers to Endemic Regions. A formal decision analysis was conducted to compare the cost-effectiveness of no immunization, routine immunization, immunization only in serologically documented cases of susceptibility, or passive immunization with immunoglobulin in persons traveling from countries with low or moderate viral endemicity to countries with high endemicity (cost-benefit analyses of HAV immunization in various populations is summarized in Table 5).[48] Taking into account only direct treatment costs, active immunization was the most cost-effective strategy for frequent travelers ($\geq$3 trips/10 years) or for travelers whose visits exceed 6 months. For these travelers, the cost of active vaccination was $12,729 per case averted. Passive immunization was most cost-effective for less frequent travelers or those with shorter visits. Screening for susceptibility prior to vaccination was cost-effective only in older travelers or those leaving from moderately endemic areas. Vaccination

Table 5. Cost-Benefit Analyses for Hepatitis A Immunization in Various Populations (in 1998 U.S. Dollars)

Hepatitis A Immunization	Cost Per Case Averted (U.S. Dollars)	Cost: Benefit Ratio	Reference
Health care workers in Spain	Cost saving	<0	44
Universal, infants in Israel	Cost saving	0.52	45
United Nations peacekeeping troops	282	0.01	46
Dutch military personnel	Cost saving	0.65	47
Travelers	12,729	0.66	48
Selected Israeli day care workers	Cost saving	0.67	49
British military personnel	87,236	16.0	50
Health care workers in Ireland	123,229	126.8	51

would have had even greater cost-effectiveness if indirect costs of hepatitis infection had been part of the analysis.

Data from retrospective and cohort studies confirmed these results, concluding that safe and effective hepatitis A vaccines provide an opportunity to protect patients against the most frequently occurring vaccine-preventable infection in travelers.[52] Among destinations for which hepatitis A prophylaxis is indicated are all countries in Central and South America, the Caribbean (in areas of questionable sanitation), Africa, the Middle East, the Indian subcontinent, Asia and the Pacific Basin (excluding Japan, Australia, and New Zealand), and Eastern Europe, including the independent states of the former Soviet Union.[53]

Men Who Have Sex With Men. To estimate costs and benefits of immunizing men who have sex with men against hepatitis A, a decision-analytic model of vaccination from a societal perspective was used.[39] Effects of vaccination of homosexual men at age 20 were modeled for lifetime in a hypothetical cohort of 10,000. Hepatitis A-related hospitalizations declined from 366 to 76, representing a cost decrease from $2.57 million to $363,000. This savings would offset prevention costs in 10 years. Cost savings in productivity were $5.23 million, and vaccination would save 213 life-years and $2.84 million in mortality-related productivity losses. Each dollar spent on vaccination provided $10.73 in economic benefits; namely, $2.31 in treatment costs, $5.46 in reduced absenteeism, and $2.96 in losses because of premature death. Vaccination, therefore, is cost saving for patient, health insurer, and employer.

Military Personnel. Economic analyses of hepatitis A vaccination in Dutch, British, and Israeli military personnel have shown results similar to those for travelers. In the Dutch study, based on a Markov model, routine vaccination proved to be the most cost-effective strategy (vs. no vaccination, passive immunization with immunoglobulin, or immunization against hepatitis A only in serologically documented cases of susceptibility) for troops sent to an endemic area once every 3 years during a 10-year period.[47] The British study showed passive immunization to be less costly than routine vaccination only if one exposure to hepatitis A can be assumed; because of the uncertainty of deployment to widely dispersed geographical locations and the difficulty of achieving 100% coverage for a booster dose of immunoglobulin, routine vaccination was judged to be more desirable than passive immunization.[50] The Israeli study also noted that vaccination is more cost-effective than passive immunization for personnel serving long periods in endemic areas but not for those serving for short periods in low-endemic regions.[54]

Commercial Aircrews. A cost-effectiveness analysis based on a retrospective study of Swissair medical files over 5 years showed that vaccination against hepatitis A would become cost-beneficial within 10 years for pilots and flight attendants with destinations in developing countries.[55]

Health Care Workers. Among Irish doctors and nurses studied for 10 years, routine vaccination was the most cost-effective means of preventing hepatitis A infection, compared with no prevention, vaccination of susceptible individuals, routine passive immunization, and immunization of susceptible individuals.[51] A U.S. study in medical students identified routine vaccination as more cost-effective than vaccination only in susceptible individuals, although the cost per YOLS with routine vaccination ($63,792) was modestly higher than the accepted threshold.[20] Investigators did not adjust for underreporting, and, because the incidence of hepatitis A in health care workers is likely higher than that assumed for this study, vaccination would be more cost-effective than this analysis indicated.[20]

Patients With Hepatitis C. The ACIP recommends hepatitis A vaccination for persons with chronic liver disease, because these patients are at increased risk of hepatitis A-related complications and death.[7,56] Infection with hepatitis A poses a substantial risk of fulminant liver failure (41%) and death (35%) in patients with chronic hepatitis C infection.[43] Because nearly 50% of patients with hepatitis C are susceptible (seronegative) to hepatitis A, it has been proposed that they be screened for hepatitis A antibodies and that susceptible patients be immunized.[17]

In a 5-year, cost-effectiveness comparison of no vaccination, vaccination of susceptible patients, or routine vaccination regardless of immune status in a hypothetical cohort of North American patients with chronic hepatitis C, no vaccination was generally the least costly in terms of the incidence and seroprevalence of hepatitis A.[39] When incidence and seroprevalence estimates approached those of moderate to high endemicity, selective vaccination of susceptible patients was the most cost-effective approach. With assumptions of high annual infection rates and low innate immunity in the cohort (characteristics of an epidemic situation), universal immunization was the most cost-effective approach. Not unexpectedly, rates of symptomatic episodes, liver transplantation, and deaths related to hepatitis A infection were lowest with universal vaccination.[39]

Another study used a Markov model to examine the cost-effectiveness of hepatitis A vaccination in patients with chronic hepatitis C.[41] In this model, vaccination against HAV would substantially reduce morbidity and

mortality. Cost-effectiveness was greatest in younger patients. In the age 30 years cohort, societal cost per YOLS was $12,671, increasing to $39,922 in the age 45 years cohort. A similar study found targeted HAV immunization in patients with chronic hepatitis C also marginally cost-effective, with a ratio of $51,000 per QALY.[36]

Food Service Workers. The economics of vaccinating food service workers has been examined in 2 studies. Although food service workers are not necessarily at higher risk of contracting disease, they may potentially spread infection in common-source outbreaks. From a health service perspective, Jacobs et al.[40] found that vaccination of food service workers would be cost-effective, with a cost to the health care system of $14,206 per YOLS. Another study found that vaccination would not be cost-effective from the perspective of restaurant owners or society.[57]

Day Care Workers. A cost-benefit analysis of immunization strategies in Israeli daycare workers found that, compared with passive immunization, selective active vaccination saved $606,396, and universal active vaccination cost $2.36 million.[49] These data demonstrate that administration of hepatitis A vaccine to nonimmune individuals working in daycare centers is justified economically. These workers had an incidence of hepatitis A of 80 per 100,000 population.

Other Populations. Sensitivity analyses have shown that risk of HAV infection is often the pivotal variable in cost-effectiveness. Several populations with hepatitis attack rates comparable with those for which immunization is cost saving have been identified; however, economic data for these populations are lacking.

Vaccination is likely to be cost-effective in institutions. The prevalence of anti-HAV antibodies in institutionalized developmentally disabled individuals suggests that these persons are at a high risk of exposure.[58] At a special-needs school, the hepatitis A attack rate among pupils and staff was 42%.[59] Prison inmates also have high rates of HAV exposure compared with the general population.[60] Studies are needed to determine the cost-effectiveness of HAV immunization in prison populations.

Among children aged 1 to 18 years traveling with migrant workers, prevalence of anti-HAV antibodies rose from 35% in 2- to 5-year-old children to 81% in children aged 14 years and older.[61] The prevalence among children aged 6 to 11 years was 57%, compared with 10% in this age group in the general U.S. population. Potential benefits of vaccination of migrant farm workers include the prevention of common-source outbreaks. An outbreak associated with green onions was postulated to result from the lack of childcare in migrant field workers.[62]

Targeting Risk Groups for Vaccination: A Public Health Perspective. Most cases of hepatitis A in the United States occur not in high-risk individuals but among heterogeneous groups as epidemics spread from community to community.[3] Moreover, associated morbidity and mortality are highest in adults.[2] Therefore, reduction of both incidence and complications may require widespread vaccination of children and adults rather than restriction of vaccination to selected high-risk groups.[2,3]

Incorporation of the hepatitis A vaccine into the already loaded childhood immunization schedule will involve educating parents about the safety of vaccines, particularly in light of widespread and inappropriate consumer perceptions of a relationship between vaccination and various adverse outcomes. In this regard, a recent editorial in the *New England Journal of Medicine* focused on the importance of "negative" studies[63] (such as 2 recent reports demonstrating no association between the administration of several vaccines and certain serious outcomes).[64,65] Almost 30,000 children from a large community susceptible to recurrent epidemics received hepatitis A vaccination without experiencing serious adverse events.[66] Compelling evidence of the relative safety of hepatitis A vaccines also comes from a 2-year review by the Vaccine Adverse Event Reporting System, which affirmed that, since their licensure and administration of at least 6 million doses, these vaccines have been linked to rare unexpected serious events.[67]

Conclusions

Despite declining incidence in the United States, cyclic increases of hepatitis A have occurred approximately every decade. Largely as a result of continued community-wide outbreaks, hepatitis A remains a major public health problem and one of the most frequently reported vaccine-preventable diseases. The ACIP recommends universal vaccination of children who live in areas where the average annual hepatitis rate between 1987 and 1997 was 20 or more cases per 100,000 population (*i.e.*, approximately twice the national average)[7] and certain high-risk groups (travelers to moderately or highly endemic countries, men who have sex with men, users of injectable and noninjectable drugs, those who have clotting-factor disorders, persons working with nonhuman primates, and individuals with chronic liver disease).[19]

Economic analyses generally support these recommendations (Table 6), showing a degree of cost-effectiveness comparable with that of other vaccines in children living both in highly endemic areas of the United States and in the nation as a whole,[1,32,42] as well as cost-effectiveness well within accepted boundaries[28] for adolescents[31] and

Table 6. Summary of Cost-Effectiveness Studies of Hepatitis A in Various Populations

Population	Cost Saving	Acceptable Cost	Excessive Cost	Reference
Universal infant vaccination	●	●●		1,32,42
Children in endemic areas		●		32
Adolescents		●		31
Men who have sex with men	●			39
Food service workers		●		40
Military personnel	●●		●	46,47,50
Day care workers in Israel	●			49
Patient with chronic hepatitis C	●	●	●	36,38,41
Health care workers	●		●●	20,44,51
Travelers		●		48

NOTE. One bullet refers to 1 article from the references cited. Two bullets refers to 2 articles from the references cited.

adults in several high-risk categories.[20,36,38-40,46-50] Moreover, the combination vaccine for hepatitis A and hepatitis B may further improve the cost-effectiveness of vaccination programs.[42,69]

In summary, this review of universal immunization against hepatitis A in children, adolescents, and high-risk adults in developed countries supports the cost-effectiveness of implementing ACIP recommendations regarding the use of these vaccines in the United States.

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