**Question:** Should hepatitis A catch-up vaccination be recommended for children age 2–18 years?

**Population:** Children aged 2–18 years

**Intervention:** Hepatitis A vaccination (2-dose schedule)

**Comparison(s):** Hepatitis A catch-up vaccination based on individual clinical decision-making

**Outcome:**
- Hepatitis A infection

**Background:** Despite successful implementation of the United States’ routine hepatitis A vaccination recommendation for children aged 12–23 months, there remains a small gap to close among adolescents who have not received hepatitis A vaccine and are thus missing long-term and potential lifetime protection from hepatitis A.

Decreased hepatitis A incidence in the United States and reduced exposure to hepatitis A virus (HAV) have resulted in decreased anti-HAV seroprevalence among adults, and an increased proportion of susceptible adults, including younger adults (i.e., aged 20–29 years). Vaccinating adolescents will lead to increased protection among adults—particularly young adults—more quickly than waiting for the routinely vaccinated cohort of children to reach adulthood. It also will protect those with undisclosed risk factors (e.g., drug use, men who have sex with men [MSM]) more consistently and earlier in life.

In 2006, the Advisory Committee on Immunization Practices (ACIP) recommended routine hepatitis A vaccination for all children aged 12–23 months. Children who are not vaccinated by age 2 years can be vaccinated at subsequent health care visits, and catch-up vaccination of unvaccinated children aged 2–18 years can be considered based on shared clinical decision-making. Catch-up vaccination ensures that the percentage of children/adolescents who miss vaccination as scheduled or who were born outside of the routinely vaccinated cohort (i.e., born prior to 2006) are protected and is a way to increase herd immunity.

In 2017, national hepatitis A vaccination coverage among adolescents aged 13–17 years was 77.2% for 1 dose and 68.4% for ≥2 doses, compared to 36.2% and 25.3% for 1 and ≥2 doses, respectively, in 2008. This indicates substantial catch-up implementation and acceptance despite a recommendation based on clinical decision-making (1, 2).

The vaccines containing HAV antigen that are currently licensed in the United States for children are the inactivated, single-antigen vaccines HAVRIX® (manufactured by GlaxoSmithKline, Rixensart, Belgium) and VAQTA® (manufactured by Merck & Co., Inc., Whitehouse Station, New Jersey).

*Additional background information supporting the ACIP recommendations on the use of hepatitis A vaccines can be found in the relevant publication of the recommendations referenced on the ACIP website. [https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hepa.html](https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/hepa.html)*
<table>
<thead>
<tr>
<th>CRITERIA</th>
<th>WORK GROUP JUDGMENTS</th>
<th>EVIDENCE</th>
<th>ADDITIONAL INFORMATION</th>
</tr>
</thead>
</table>
| Is the problem of public health importance? | □ □ □ □ □ □ □ no probably uncertain probably yes varys | Incidence: The rate of reported acute hepatitis A cases in 2017 was 1.0 cases/100,000 population (3).  
- However, the rate of reported acute hepatitis A cases for young adults aged 20–30 years was 1.45 cases/100,000 population (0.87 in 2016); and 2.07 cases/100,000 population for persons aged 30–39 (3).  
- The 30–39 years age group has the highest incidence, which is more than double the 2016 rate for this age group (0.92 cases per 100,000 in 2016) (4).  

HAV outbreaks: Since widespread person-to-person outbreaks of hepatitis A across the United States were first identified in 2016, 23 states have publicly reported the following as of June 14, 2019 (5):  
- Cases: 20,133  
- Hospitalizations: 11,595 (58%)  
- Deaths: 191  
- Among states with publicly available case information by age group, the median age of HAV cases is in the 30s, with a substantial percentage of cases among individuals in their 20s and 40s.  

Hepatitis A vaccination coverage: In 2017, national hepatitis A vaccination coverage was 77.2% for 1 dose among adolescents aged 13–17 years and 68.4% for ≥2 doses (1). | Vaccinating teens protects those who may be at risk for HAV infection (e.g., persons who use drugs, persons experiencing homelessness, travelers) at present and in the future. |
### ACIP Evidence to Recommendations Framework

<table>
<thead>
<tr>
<th>Benefits &amp; Harms</th>
<th>Minimal</th>
<th>Small</th>
<th>Moderate</th>
<th>Large</th>
<th>Don’t know</th>
<th>Varies</th>
</tr>
</thead>
</table>
| **How substantial are the desirable anticipated effects?** | ☐ ☐ ☐ ☑ ☑ ☑ | HAVRIX and VAQTA are highly immunogenic when administered to children and adolescents according to multiple schedules.  
- 97%–100% of persons aged 2–18 years had protective levels of antibody 1 month after receiving the first dose, and 100% had protective levels 1 month after the second dose, with high geometric mean concentrations (6–14).  

Due to demonstrated long-term protection from the vaccines, there is little concern that childhood vaccination will result in risk later in life due to waning immunity.  
- Antibody to HAV (anti-HAV) has been shown to persist for at least 22 years in adults administered inactivated vaccine as children (aged 3–6 years) (15, 16).  
- Mathematical modelling based on persons vaccinated as adults predicted that seropositive anti-HAV levels would persist in ≥95% of vaccinees at year 30 and ≥90% at year 40 (17).  
- Vaccine-induced cellular immunity has been shown to promote HAV-specific |
| | | Catch-up vaccination ensures children and adolescents who miss vaccination as scheduled or who were born outside of the routinely vaccinated cohort are protected and increases herd immunity.  
In addition, since implementation of risk-based vaccination in adults has been poor, catch-up vaccination will more rapidly increase the proportion of adults with risk factors who are protected. |
cellular immunity similar to that induced by natural infection \((18)\).

### ACIP Evidence to Recommendations Framework

<table>
<thead>
<tr>
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<th>RESEARCH EVIDENCE</th>
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</tr>
</thead>
<tbody>
<tr>
<td>How substantial are the undesirable anticipated effects?</td>
<td>Minimal</td>
<td>Small</td>
<td>Moderate</td>
</tr>
<tr>
<td>Do the desirable effects outweigh the undesirable effects?</td>
<td>Favors intervention</td>
<td>Favors comparison</td>
<td>Favors both</td>
</tr>
<tr>
<td>What is the overall certainty of this evidence for the critical outcomes?</td>
<td>Effectiveness of the intervention</td>
<td>Safety of the intervention</td>
<td>GRADE was not used to evaluate the evidence.</td>
</tr>
<tr>
<td></td>
<td>No included studies</td>
<td>4</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>Safety of the intervention</td>
<td>No included studies</td>
<td>4</td>
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</tbody>
</table>
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</tr>
</thead>
<tbody>
<tr>
<td>Is there important uncertainty about or variability in how much people value the main outcomes?</td>
<td>Important uncertainty or variability □</td>
<td>The high coverage rate, despite this recommendation being based on clinical decision-making, provides strong and consistent evidence that most parents believe that it is important.</td>
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<td></td>
<td>Possibly important uncertainty or variability □</td>
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<tr>
<td></td>
<td>Probably no important uncertainty or variability □</td>
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<tr>
<td></td>
<td>No important uncertainty or variability □</td>
<td></td>
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</tr>
<tr>
<td></td>
<td>No known undesirable outcomes □</td>
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</table>

- There are no known safety concerns with hepatitis A vaccines.

In 2017, national hepatitis A vaccination coverage among adolescents aged 13–17 years was 77.2% for 1 dose and 68.4% for ≥2 doses compared to 36.2% and 25.3% for 1 and ≥2 doses, respectively, in 2008 (1, 2).

- This indicates substantial catch-up vaccination implementation and acceptance despite a recommendation based on clinical decision-making.

- Specific studies of demand among older children for hepatitis A vaccine have not been done. However, almost 70% of teens have already initiated the vaccine series even though catch-up vaccination is not routinely recommended, suggesting parental acceptance or demand for hepatitis A vaccination.

Compared to other vaccines with a routine catch-up schedule, hepatitis A adolescent 2-dose coverage is comparable (e.g., quadrivalent meningococcal conjugate vaccine) or greater (e.g., human papillomavirus vaccine), providing evidence of acceptability by the target population (1).

<table>
<thead>
<tr>
<th>Does the target population feel that the desirable effects are large relative to undesirable effects?</th>
<th>No</th>
<th>Probably</th>
<th>Uncertain</th>
<th>Probably</th>
<th>Yes</th>
<th>Varies</th>
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<tbody>
<tr>
<td>[ ] no</td>
<td>[ ] yes</td>
<td>[ ] Varies</td>
<td>[ ] yes</td>
<td>[ ] no</td>
<td>[ ] yes</td>
<td>[ ] no</td>
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</table>
### ACIP Evidence to Recommendations Framework

<table>
<thead>
<tr>
<th>ACCEPTABILITY</th>
<th>Is the intervention acceptable to key stakeholders?</th>
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<tbody>
<tr>
<td></td>
<td>CDC currently does not have a routine catch-up recommendation for children aged 2–18 years, yet 21 states have introduced mandates for daycare, daycare plus school, or school alone. This represents an increase in states with mandates from 28% in 2011 to 40% in 2018 (20).</td>
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<td><strong>As of October 2018, 12 states have a daycare and school mandate; 8 states plus part of Arizona have a daycare-only mandate; 1 state has a school-only mandate (Indiana).</strong></td>
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</table>

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<thead>
<tr>
<th>RESOURCE USE</th>
<th>Is the intervention a reasonable and efficient allocation of resources?</th>
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<tr>
<td></td>
<td><strong>Cost analysis:</strong> After universal childhood recommendation implementation, a cost-effectiveness model used to assess nationwide routine hepatitis A vaccination was adapted to assess the cost-effectiveness of catch-up hepatitis A vaccination among unvaccinated and partially vaccinated children compared with unvaccinated children (21).</td>
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<td><strong>Over the cohort's lifetime, catch-up vaccination would reduce the total number of infections relative to baseline by 741.</strong></td>
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<td></td>
<td><strong>Catch-up vaccination would increase net cost by $2.38 per person.</strong></td>
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</table>

Children who were 1 year of age when the routine recommendation was first published in 2006 were ~12–13 years old in 2017 when these data were collected; nearly all of the cohort of children 13–17 assessed in 2017 were not subject to the routine recommendation for children 12–23 months of age. High overall coverage in this age group demonstrates that catch-up vaccination is occurring.

As noted above, the hepatitis A adolescent 2-dose coverage is comparable or greater than other vaccines with a routine catch-up schedule, which provides evidence of acceptability by key stakeholder populations.

**Other studies:** To assess the population-level impact and cost-effectiveness of US hepatitis vaccination programs, an age-structured population model of hepatitis A transmission dynamics was developed to evaluate two policies of administering a 2-dose hepatitis A vaccine to children aged 12 to 18 months (22).

- The model predicted universal childhood vaccination...
### ACIP Evidence to Recommendations Framework

- Incremental cost of hepatitis A vaccine catch-up intervention at age 10 years, the midpoint of the ages modeled, was $452,239 per QALY gained.
- Across age cohorts, cost effectiveness of catch-up vaccination is most favorable at age 12 years, resulting in an incremental cost-effectiveness ratio (ICER) of $189,000 per QALY gained.
  - The impact of vaccination on the ICER was most sensitive to the discount rate, followed by the rate of adult vaccination.
- The model assumed administration costs of hepatitis A vaccination were split with other vaccines routinely administered at age 12 years, thus lowering the cost of vaccination.
- Catch-up vaccination in adolescence is more effective when it is assumed to replace later vaccination as an adult.
  - Catch-up became more cost effective when targeting children in late adolescence, due to higher probability of symptomatic disease among older children, less discounting of future costs of disease, and less delay in averting adult vaccination costs.
- Limitations: model output is based on hepatitis A incidence from 2008 to 2012 and the cost-effectiveness conclusions are strongly tied to factors such as vaccine uptake and disease transmission patterns which may change over time, altering future cost.
- Universal vaccination was cost saving compared with a regional vaccination policy.
- The model predicts US incidence will fall to 27/100,000 by 2020, compared to a CDC-reported incidence (adjusted for underreporting) of just 1.71/100,000.
  - This model overestimates incidence which limits applicability of inferences from these findings to catch-up policies.
  - While this model provides a favorable cost-effectiveness estimate, limitations exist.

### Incremental costs of catch up now, given current rates of coverage among 13–17-year-olds:

Hepatitis A vaccination would lead to significant reduction in hepatitis A mortality and morbidity.

### Additional Considerations:

- Cost of outbreak response and hospitalization is substantial and would offset some of additional costs of catch-up vaccination.

Based on 2017 hepatitis A vaccination coverage rates:
olds, would be more favorable, because hepatitis A vaccination coverage rates are higher among vaccinated children who are aging into the adolescent cohort:

- 2008, 1 dose: 36.2%, ≥2-dose: 25.3%, versus 2017, 1 dose: 77.2%, 2-dose 68.5%. (1,2).

Achieving 80%–90% coverage among teens would require a much smaller number of additional vaccines given. In addition, HAV incidence overall is higher due to the ongoing multistate outbreaks (0.5 cases/100,000 population in 2012 versus 1.0 case/100,000 population in 2017) (1, 22).

- To achieve 80% hepatitis A vaccine series completion among adolescents, 2,205,491 additional persons would need to be vaccinated with one dose and 701,747 persons would need to be vaccinated with 2 doses, at a cost of $59.3M (private) or $37M (CDC).

- To achieve 90% hepatitis A vaccine series initiation among adolescents, 3,207,987 persons would need to be vaccinated with 1 dose, at a cost of $52.8M (private), $32.9M (CDC).

Assumptions:
1) 2017 coverage rates apply to all children; however, in actuality, younger adolescents have higher coverage.
2) 100% of 1-dose recipients complete series when calculating cost of 80% completion.
3) Private sector covers 50% of these adolescents and CDC covers 50%.
**ACIP Evidence to Recommendations Framework**

<table>
<thead>
<tr>
<th>Is the intervention feasible to implement?</th>
<th>No</th>
<th>Probably No</th>
<th>Uncertain</th>
<th>Probably Yes</th>
<th>Yes</th>
<th>Varies</th>
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Of the 30 registries American Immunization Registry Association (AIRA) were able to query to test forecasting algorithms, 27 already routinely forecast hepatitis A vaccine for an 18-year-old who has never been vaccinated. All 30 algorithms forecast the second dose in any 18-year-old who has had one dose. Essentially, these algorithms are implemented as routine catch-up. Therefore, 27 of 30 registries would not have to change to implement routine catch-up.

Findings from a 2014 survey indicate:
- If ACIP made a recommendation for catch-up hepatitis A vaccination at health maintenance visits for all children 2 to 18 years of age, 96% of pediatricians and 79% of family physicians reported it would be very feasible to routinely assess hepatitis A vaccination status and vaccinate children and adolescents who were not fully vaccinated.
  - An additional 4% and 19%, respectively, indicated it would be moderately feasible.
- The most common barriers to implementing a hepatitis A vaccine catchup recommendation included infrequent visits by adolescent patients (65%); parents’ lack of knowledge on the seriousness of HAV disease (39%); hepatitis A vaccination not being required for childcare or school entry (39%); difficulty obtaining immunization records to determine a patient’s hepatitis A vaccination status (35%); and parental concerns about giving too many vaccines at 1 visit (33%).

Routine hepatitis A catch-up already exists in states that have school mandates (21 states have introduced mandates for daycare, daycare plus school, or school alone.). In New York City, all children and adolescents not previously vaccinated should receive the two-dose hepatitis A vaccine series by their 19th birthday for long-term protection.

There are opportunities to administer hepatitis A vaccine to adolescents concurrently with vaccines protecting against other infections, such as human papillomavirus and meningococcal disease.
**ACIP Evidence to Recommendations Framework**

- This study was performed 6 years ago and there is currently more education and awareness among providers and the public due to ongoing outbreaks, likely decreasing barriers to vaccination.

<table>
<thead>
<tr>
<th>Balance of consequences</th>
<th>Undesirable consequences clearly outweigh desirable consequences in most settings</th>
<th>Undesirable consequences probably outweigh desirable consequences in most settings</th>
<th>The balance between desirable and undesirable consequences is closely balanced or uncertain</th>
<th>Desirable consequences probably outweigh undesirable consequences in most settings</th>
<th>Desirable consequences clearly outweigh undesirable consequences in most settings</th>
<th>There is insufficient evidence to determine the balance of consequences</th>
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Is there sufficient information to move forward with a recommendation?

Yes ☑

No ☐

**Policy Options for ACIP Consideration**

- ACIP does not recommend the intervention
- ACIP recommends the intervention for individuals based on clinical decision-making
- ACIP recommends the intervention

**Recommendation (text)**

Recommended for all unvaccinated children and adolescents aged 2–18 years. Children and adolescents who have not previously received hepatitis A vaccine should be vaccinated routinely at any age (i.e., children and adolescents are recommended for catch-up vaccination).

**Additional considerations (optional)**

Final deliberation and decision by the ACIP
**ACIP Evidence to Recommendations Framework**

<table>
<thead>
<tr>
<th>Final ACIP recommendation</th>
<th>ACIP does not recommend the intervention</th>
<th>ACIP recommends the intervention for individuals based on shared clinical decision-making</th>
<th>ACIP recommends the intervention</th>
</tr>
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<tbody>
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<td>X</td>
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</table>

**ACIP considerations**

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This Evidence to Recommendation table is based on the GRADE Evidence to Decision framework developed through the *DECIDE* project. Further information is available at [http://www.decide-collaboration.eu/evidence-decision-etd-framework](http://www.decide-collaboration.eu/evidence-decision-etd-framework)

**References:**


