Evidence to Recommendations Framework for the use of Tdap for decennial Td booster, tetanus wound prophylaxis and the catch-up immunization schedule

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Lead, Pertussis Vaccines Work Group

Advisory Committee on Immunization Practices
June 26, 2019
Evidence to Recommendations (EtR) Framework

- Decennial Td booster and tetanus prophylaxis in wound management
  - Benefits and harms
    - Focus on programmatic issues
  - Values, preferences, acceptability and feasibility
  - Resource use
  - Work group interpretation
- Catch-up immunization schedule
Benefits and Harms
Are there programmatic benefits to allowing either Td or Tdap to be used?

- Provider ease and flexibility
  - Challenging to determine patient history and receipt of previous Tdap
  - Cumbersome to stock both Td and Tdap vaccines
Are there programmatic benefits to allowing either Td or Tdap to be used?

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  - Challenging to determine patient history and receipt of previous Tdap
  - Cumbersome to stock both Td and Tdap vaccines

Work group interpretation: There are benefits to giving providers flexibility to use either Td or Tdap
Are there benefits to repeat Tdap vaccination on pertussis prevention and control?

- Evidence that 2nd dose of Tdap is immunogenic
- Immunogenicity data on >2 doses of Tdap are lacking
- Uncertain duration of protection
  - Evidence of short duration of protection in persons given acellular pertussis vaccines for their childhood series
  - Lack of data on duration of protection among those primed with whole cell pertussis vaccines in childhood
- Uncertain role in the prevention of transmission and herd immunity
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- Uncertain role in the prevention of transmission and herd immunity

Work group interpretation: Insufficient evidence of benefit in pertussis control to recommend that Tdap replace Td for all decennial boosters
Are there benefits to repeat Tdap for healthcare personnel?

- Reviewed by previous ACIP work group
- Pertussis transmission occurs in healthcare settings
- Insufficient data that healthcare personnel at increased risk for pertussis infection
- Lack of strong evidence that additional Tdap doses for healthcare personnel would be beneficial for pertussis control in healthcare settings
Are there benefits to repeat Tdap for healthcare personnel?

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- Pertussis transmission occurs in healthcare settings
- Insufficient data that healthcare personnel at increased risk for pertussis infection
- Lack of strong evidence that additional Tdap doses for healthcare personnel would be beneficial for pertussis control in healthcare settings

Work group interpretation: Insufficient evidence to have recommendations for healthcare personnel that are different than those for the general population
Are there potential harms?

- Data lacking on safety of >2 Tdap doses
- Safety data of 2nd Tdap vaccination reviewed by previous Work Group with recent data presented at October 2018 ACIP meeting
Are there potential harms?

- Data lacking on safety of >2 Tdap doses
- Safety data of 2nd Tdap vaccination reviewed by previous Work Group with recent data presented at October 2018 ACIP meeting

Work group interpretation: No substantive safety concerns

Work group interpretation: Benefits outweigh harms
Values, Preferences, Acceptability and Feasibility
Do patients and providers value or have a preference for repeat Tdap vaccination?

- No studies about values and acceptability for stakeholders
  - Target population: general adult population
  - Providers
    - Immunization programs
- The proposed recommendation doesn’t require any additional vaccine doses
- Evidence indicating that repeat vaccination with Tdap is already a widespread practice
Provider dose ordering (public sector purchases): Adult Td and Tdap Doses, 2011-2017

<table>
<thead>
<tr>
<th>Year</th>
<th>Td</th>
<th>Tdap</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>33,243</td>
<td>530,175</td>
</tr>
<tr>
<td>2012</td>
<td>31,029</td>
<td>749,525</td>
</tr>
<tr>
<td>2013</td>
<td>32,508</td>
<td>670,615</td>
</tr>
<tr>
<td>2014</td>
<td>30,429</td>
<td>517,955</td>
</tr>
<tr>
<td>2015</td>
<td>30,526</td>
<td>484,775</td>
</tr>
<tr>
<td>2016</td>
<td>42,881</td>
<td>465,885</td>
</tr>
<tr>
<td>2017</td>
<td>41,881</td>
<td>441,075</td>
</tr>
</tbody>
</table>

Courtesy CDC Immunization Services Division, Vaccine Supply and Assurance Branch, Data Team
Tdap given more frequently than Td

- Vaccine Safety Datalink¹: 68,915 persons received Tdap and who received another Td-containing vaccine
  - Tdap: 89%
  - Td: 11%

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Commercial Insurance Claims:
Persons aged 19 to 64 years, 2017\(^2\)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
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</tr>
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<tbody>
<tr>
<td>Tdap</td>
<td>716,638</td>
</tr>
<tr>
<td>Td</td>
<td>61,468</td>
</tr>
</tbody>
</table>

Is repeat Tdap vaccination acceptable and feasible?

- Evidence that the practice of giving Tdap in place of Td is already widespread despite:
  - Not currently recommended by ACIP
  - Off-label use of Tdap vaccines in clinical practice
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Work group interpretation: Allowing either Tdap or Td to be used would be acceptable and feasible for stakeholders, and may be preferred by providers
Resource Use
# Tdap is more expensive than Td

<table>
<thead>
<tr>
<th>CDC Vaccine price list</th>
<th>CDC cost per dose</th>
<th>Incremental cost of Tdap over Td</th>
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<tbody>
<tr>
<td>Td (TDVAX™)</td>
<td>$13.96</td>
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<table>
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<tr>
<th>Commercial claims</th>
<th>Median cost</th>
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1. Source: https://www.cdc.gov/vaccines/programs/vfc/awardees/vaccine-management/price-list/index.html, updated April 1, 2019
2. Indicates cost for 10 pack – 1 dose vial. 3. Vaccine cost includes $1.50 per dose Federal Excise Tax. 4. Vaccine cost includes $2.25 per dose Federal Excise Tax. 5. Source: Truven MarketScan databases, Outpatient Services Table, DY 2016
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Is allowing either Tdap or Td to be used a reasonable and efficient allocation of resources?

- Work Group reviewed economic impact analyses, including internal CDC analysis
- Uncertainty on key parameters
  - All economic analyses sensitive to pertussis incidence estimates
  - Lack of reliable estimates of disease burden, particularly in adults
- Not accounted for:
  - Cost savings resulting from only carrying one vaccine
  - Repeat Tdap doses already given
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  - Repeat Tdap doses already given

Work group interpretation: Economic impact analyses did not drive the decision-making process for these programmatic questions
Should any Td-containing vaccine (Tdap or Td) be allowed for use for the decennial Td booster and tetanus prophylaxis in the setting of wound management?

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<th>Work Group Interpretation</th>
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<td>• Providers value flexibility</td>
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<tr>
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<tr>
<td>Resource Use</td>
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<tr>
<td></td>
<td>• Economic analyses limited by uncertainty in key parameters</td>
</tr>
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<td>Economic impact not a major consideration</td>
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Should any Td-containing vaccine (Tdap or Td) be allowed for additional catch-up doses for those with incomplete or unknown vaccine history?
Policy Options: Adolescent and adult series for those with incomplete or unknown vaccine history

1) No change

* Single dose of Tdap is preferred, followed by a dose of Td at least 4 weeks after Tdap and another dose of Td 6 to 12 months later. However, the single dose of Tdap can substitute for any of the Td doses in the 3-dose primary series.
Policy Options: Adolescent and adult series for those with incomplete or unknown vaccine history

1) No change

<table>
<thead>
<tr>
<th>Tdap*</th>
<th>Td</th>
<th>Td</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 month</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>6 to 12 months</td>
</tr>
</tbody>
</table>

2) 1 dose Tdap, 2 doses Td OR Tdap

<table>
<thead>
<tr>
<th>Tdap</th>
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### 2) 1 dose Tdap, 2 doses Td OR Tdap

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<td>3</td>
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### 3) Three doses Tdap

<table>
<thead>
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Policy Options: Adolescent and adult series for those with incomplete or unknown vaccine history

1) No change

- Tdap: 0
- Td: 1 month
- Tdap: 2
- Td: 3
- Tdap: 4
- Td: 5
- Tdap: 6 to 12 months

2) 1 dose Tdap, 2 doses Td OR Tdap

- Tdap: 0
- Td or Tdap: 1 month
- Tdap: 2
- Td or Tdap: 3
- Tdap: 4
- Td or Tdap: 5
- Td or Tdap: 6 to 12 months

3) Three doses Tdap

- Tdap: 0
- Tdap: 1 month
- Tdap: 2
- Tdap: 3
- Tdap: 4
- Tdap: 5
- Tdap: 6 to 12 months

* Single dose of Tdap is preferred, followed by a dose of Td at least 4 weeks after Tdap and another dose of Td 6 to 12 months later. However, the single dose of Tdap can substitute for any of the Td doses in the 3-dose primary series.
Should any Td-containing vaccine be allowed for additional **catch-up** doses in persons ≥7 years with incomplete or unknown vaccine history?

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<thead>
<tr>
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<th>Work Group Interpretation</th>
</tr>
</thead>
<tbody>
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<tr>
<td></td>
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<td>• Providers value flexibility</td>
</tr>
<tr>
<td></td>
<td>• Gives providers more options if Td availability decreases</td>
</tr>
<tr>
<td>Valued by stakeholders; change is acceptable and feasible</td>
<td></td>
</tr>
<tr>
<td>Resource Use</td>
<td><strong>Economic impact not a major consideration for this policy question</strong></td>
</tr>
</tbody>
</table>
Catch-up immunization in pregnant women

- Current catch-up schedule same for pregnant women and general population
- Previously unimmunized women may require two doses of a tetanus toxoid-containing vaccine to prevent obstetric and neonatal tetanus
- Data are lacking on safety of multiple doses of Tdap during a single pregnancy
  - Registry data: Patients who received >1 dose during a single pregnancy
  - No concerning safety signal for this or for women who receive closely-spaced Tdap vaccinations in different pregnancies
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- Data are lacking on safety of multiple doses of Tdap during a single pregnancy
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  - No concerning safety signal for this or for women who receive closely-spaced Tdap vaccinations in different pregnancies

Work group interpretation: Recommendations for catch up immunization in pregnancy should continue to be similar to those for the general population
## Potential off-label recommendations

<table>
<thead>
<tr>
<th>Licensed Tdap product</th>
<th>Current FDA indications, usage and administration</th>
<th>Possible off-label recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Decennial Td booster (adults only)</td>
<td>Tetanus prophylaxis for wound management</td>
</tr>
<tr>
<td></td>
<td>Catch-up immunization series&lt;sup&gt;1,2&lt;/sup&gt;</td>
<td></td>
</tr>
</tbody>
</table>
| **Adacel (Sanofi Pasteur)** | • Age: 10 through 64 years  
• Routine booster<sup>3</sup> with a 2<sup>nd</sup> dose ≥8 years after first (any) Tdap dose  
• Tetanus prophylaxis if ≥5 years since last tetanus containing vaccine<sup>4</sup> | • Age ≥65 years  
• Any dose beyond 2<sup>nd</sup> Adacel dose administered ≥8 years from first Tdap  
• Age <10 years or ≥65 years | • Age 7 to 9 years or ≥65 years  
• >1 Tdap dose |
| **Boostrix (GSK)**   | • Age: ≥10 years  
• Single dose<sup>3</sup>  
• Tetanus prophylaxis if no previous Tdap<sup>4</sup> | • Any dose if previously received Tdap  
• Age <10 years  
• Any dose if previously received Tdap | • Age 7 to 9 years  
• >1 Tdap dose |

<sup>1</sup> Current catch-up immunization recommendations: persons with incomplete or unknown vaccine history should receive a single dose of Tdap as one dose (preferably the first) of the three-dose catch-up series. If additional doses are needed, Td is recommended.  
<sup>2</sup> Note on pregnancy: Both Tdap vaccines may be administered during pregnancy with the same intervals and restrictions (vaccine specific) as would apply to a non-pregnant individual.  
<sup>3</sup> Five or more years after a dose of DTaP or Td vaccine.  
<sup>4</sup> Please see Td package insert for indications and intervals for wound management.
### Policy options for ACIP consideration

<table>
<thead>
<tr>
<th>Policy question</th>
<th>Work Group Interpretation</th>
</tr>
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<tbody>
<tr>
<td>Either Tdap or Td can be used for the decennial Td booster</td>
<td>We are in favor of the intervention</td>
</tr>
<tr>
<td>Either Tdap or Td can be used for tetanus prophylaxis in the setting of wound prophylaxis</td>
<td>We are in favor of the intervention</td>
</tr>
<tr>
<td>Either Tdap or Td can be used for additional doses of the catch-up immunization schedule for persons ≥7 years</td>
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Questions?

For more information, contact CDC
1-800-CDC-INFO (232-4636)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.