



Human Vaccines & Immunotherapeutics

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/khvi20

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To cite this article: Linda M. Niccolai & Caitlin E. Hansen (2020): Suboptimal uptake of meningococcal vaccines among older adolescents: Barriers, solutions, and future research directions, Human Vaccines & Immunotherapeutics, DOI: <u>10.1080/21645515.2020.1754052</u>

To link to this article: https://doi.org/10.1080/21645515.2020.1754052

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Published online: 02 Jul 2020.

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#### COMMENTARY

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# Suboptimal uptake of meningococcal vaccines among older adolescents: Barriers, solutions, and future research directions

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#### ABSTRACT

Over the past 15 y, several vaccines have been added to the recommended immunization schedule for adolescents in the United States. In addition to annual influenza vaccination, the Advisory Committee on Immunization Practices recommends tetanus, diphtheria, and pertussis (Tdap), meningococcal conjugate (MenACWY), and human papillomavirus (HPV) vaccine for routine administration at ages 11–12 y, and a second dose of MenACWY at age 16. A vaccine against meningococcal disease caused by serogroup B (MenB) is also available and recommended for shared clinical decision-making. Though notable gains in uptake have been achieved for some adolescent vaccines, coverage varies considerably with lower rates for HPV vaccine and second dose of MenACWY. Coverage for MenB is especially low. While extensive research has focused on barriers to and solutions for higher uptake of HPV vaccine, limited attention has been given to the reasons for lower uptake of meningococcal vaccines among older adolescents. This purpose of this commentary is to discuss barriers to and solutions for higher uptake of meningococcal vaccines among older adolescents, and to identify gaps in knowledge that can inform research efforts going forward.

#### **ARTICLE HISTORY**

Received 17 March 2020 Accepted 4 April 2020

#### **KEYWORDS**

Adolescents; meningococcal; vaccine; vaccination; coverage

# Background

Since 2005, several vaccines have been added to the recommended immunization schedule for adolescents in the United States, resulting in the establishment of two vaccination platforms for adolescents. In 2005, the Advisory Committee on Immunization Practices (ACIP) recommended routine vaccination with a meningococcal conjugate vaccine for protection against four serogroups (A, C, W, and Y) of *Neisseria meningitidis* (MenACWY) for adolescents at ages 11–12 y, which was followed in 2006 by updated recommendations for prevention of tetanus, diphtheria, and pertussis with Tdap vaccination at the same visit.<sup>1,2</sup> Human papillomavirus (HPV) vaccine became the third vaccine to be added to the 11–12y-old-platform, with a routine recommendation for vaccination issued in 2007 for females and 2011 for males.<sup>3</sup>

In 2010, ACIP added a recommendation for a second dose of MenACWY at age 16 y based on evidence of waning immunity of a single dose given at ages 11-12 y.<sup>4</sup> In 2015, ACIP recommended that shared clinical decision-making (formerly referred to as permissive, Category B, or individual clinical decision-making recommendation) be used for a meningococcal serogroup B vaccine (MenB) for healthy adolescents ages 16–18 y.<sup>5</sup> This recommendation was based on recognition of the severity of meningococcal disease balanced against its relatively low prevalence in the population and insufficient evidence about vaccine effectiveness (e.g., duration of protection) to inform a recommendation for routine vaccination. In addition to the vaccination visits at 11–12 and 16 y of age, adolescents require additional vaccination visits for completion of the multi-dose HPV and MenB vaccine series and for annual seasonal influenza vaccine.

Adolescent vaccination coverage varies considerably. According to the 2018 National Immunization Survey – Teen (NIS–Teen), coverage was highest for Tdap (89%) and at least 1 dose of MenACWY (87%) among adolescents age 13–17 y.<sup>6</sup> Coverage for HPV vaccination has slowly but steadily increased to moderate levels of 68% for at least 1 dose and 51% for up-todate coverage for the multi-dose series. Among adolescents aged 17 y, coverage for a second dose of MenACWY was 51% and coverage for at least one dose of MenB was 17%. Approximately half of adolescents (52%) received seasonal influenza vaccine during the most recent 2018–19 season.<sup>7</sup>

While extensive research has focused on challenges to higher uptake of HPV vaccine,<sup>8-11</sup> limited attention has been given to the reasons for lower uptake of meningococcal vaccines among older adolescents. This is a critical age period to target for vaccination because a peak in the rate of invasive meningococcal disease is seen between the ages of 16–23 y.<sup>12</sup> Though invasive meningococcal disease has declined in the US since the 1990 s, it remains an important concern because each case is life-threatening. The onset of disease is rapid, the case-fatality rate is high, and severe consequences among survivors include limb amputations, neurologic complications, and hearing and vision loss.<sup>12,13</sup> Occurrence of disease is also unpredictable: most cases are sporadic, yet notable outbreaks, often in college settings, also occur.<sup>14,15</sup>

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The purpose of this paper is to discuss the reasons for suboptimal uptake of meningococcal vaccines among older adolescents (16–18 y of age), and to propose approaches to increasing uptake that are likely to be impactful at the patient, provider, practice, and/or policy levels.

#### MenACWY at age 16 y

#### **Patient factors**

One factor that is often cited for low coverage of recommended vaccines among older adolescents is that they have fewer preventive health-care visits than younger children. Despite recommendations for an annual well-child visit throughout adolescence, analyzes of health-care utilization patterns have shown that a wide range of adolescents (43– 81%) had a preventive health-care visit in the past 12 months.<sup>16,17</sup> Furthermore, it has been shown that preventive visits decline among adolescents after age 16 y.<sup>18,19</sup> A recent analysis suggested that the lower rates of MenACWY uptake between younger (72%) and older adolescents (49%) is partially driven by fewer preventive health-care visits among older adolescents.<sup>20</sup> Another analysis found that recent health-care visits were associated with receipt of the second dose at age 17 y.<sup>21</sup>

While health-care utilization is clearly essential for vaccination, the lack of visits by older adolescents does not fully explain low coverage. Among younger adolescents, studies have shown that substantial missed opportunities for vaccination exist, indicating that health-care visits occurred at which vaccines could have been given but were not.<sup>22,23</sup> The same is true for older adolescents. Research among older adolescents has revealed missed opportunities for MenACWY booster dose. In one study, an analysis of NIS-Teen data revealed a gap between actual (51%) and achievable (64%) coverage if MenACWY had been administered at visits where adolescents age  $\geq 16$  y received other recommended vaccines.<sup>21</sup> In another study, a greater proportion of older adolescents (32%) had missed opportunities for MenACWY vaccination than did younger adolescents (22%).<sup>20</sup> These missed opportunities may be related to provider and practice factors, discussed below.

Another possible factor is the extent to which older adolescents may decline vaccination for themselves, though less is known about this potential barrier. One study of HPV vaccine found little influence of adolescents in making the decision to decline vaccination, but this study was predominantly among younger adolescents (range 9–17, mean 11 y).<sup>24</sup> Older adolescents may have at least some role in decision-making but the extent to which this results in increased coverage is an important area for future research.<sup>25</sup> This is a critical area to understand more deeply because adolescence is a developmental stage during which some initiated behaviors may continue into adulthood, thus it could be a formative time to develop healthy patterns of vaccine acceptance across the lifespan.<sup>26</sup>

#### Provider and practice-related factors

Extensive research on HPV vaccination among adolescents has demonstrated that a strong recommendation from

a clinician is one of the most important facilitators of uptake.<sup>8,10,27</sup> Thus, clinician recommendations for the MenACWY are also likely to be important, though this has not been extensively studied. In one study of parents of high school teens, 34% reported the reason for their child not being vaccinated against MenACWY was that it was not recommended by a health-care provider.<sup>28</sup>

Given competing demands to address numerous important topics at older adolescents' clinic visits including sexual behaviors, alcohol and illicit drug use, and mental health, clinicians may find it challenging to make strong recommendations for vaccination, particularly if parents are hesitant. These pressures may increase for older adolescents as health-care visits become less frequent. For HPV vaccination, training in efficient communication styles (e.g., announcement vs. conversation) have resulted in increases in uptake.<sup>29,30</sup> Such approaches could also be impactful for the MenACWY booster dose by streamlining the conversation and reducing the need for prolonged conversations, but this has not been empirically studied yet to the best of our knowledge.

There is evidence that clinicians can be supported in best clinical practices to ensure that every visit is used for vaccination with proven strategies such as the use of electronic medical record prompts, standing orders for vaccination, and reminder/recall systems, and these approaches are recommended by medical organizations.<sup>31–33</sup> For HPV vaccination among adolescents in particular, there is a robust body of evidence about the effectiveness of provider and practice-based interventions.<sup>34</sup> These systems-based approaches can have broader reach than individual-targeted efforts, though they may not work in all settings.<sup>35</sup> Innovative eHealth approaches may hold promise for older adolescents as well, such as the use of mobile technologies including applications ("apps"), social media, wearable devices, and internet-based gaming.<sup>26</sup>

#### Policy

Adolescents' ability to receive vaccinations without parent consent is another important consideration for increasing coverage.<sup>36</sup> Local (not federal) laws govern health-care delivery processes and procedures for adolescents, and all states in the US have laws that adolescents can consent for certain services in some circumstances, though the extent to which these laws apply to vaccines is not always clear. Legal options that enhance adolescents' ability to consent could help to increase coverage, and there has been recent movement in this direction in some jurisdictions.<sup>37</sup> In fact, it has also been argued that there is legal and ethical precedence for adolescents to self-consent because in some cases not doing so could result in substantial harm by leaving them vulnerable to serious infectious diseases.<sup>38</sup> However, barriers will exist for adolescent self-consent even when permissible including clinicians' lack of understanding of legal status and a desire to maintain parents' roles in this decision-making process.<sup>39</sup>

The lack of school entry requirements for vaccinations for older adolescents also likely contributes to lower coverage of MenACWY booster dose. At the end of 2019, 32 states had a school entry requirement for MenACWY vaccine, but 14 of these states did not require the booster dose.<sup>40</sup> Middle school entry requirements that do exist for Tdap and MenACWY have been effective at increasing coverage for the 11–12-year-old platform, and have also achieved more equitable coverage for hepatitis B vaccine.<sup>41–44</sup> One study of MenACWY booster found that coverage with two doses at age 17 was significantly associated with school entry requirements.<sup>21</sup>

Lack of school entry requirements can reinforce the barriers at other levels. Parents may not sense the importance of vaccines that are not required for school entry. Furthermore, providers may discuss vaccines differently when they are not required for school. One study reported that lack of school entry requirements for HPV vaccination was an important reason for framing vaccination as optional and not urgent.<sup>45</sup>

Twenty-five states currently have MenACWY vaccine requirements for colleges and universities, although the types of institutions covered by these requirements and whether requirements apply to all students or only those residing on-campus varies by state.<sup>40</sup> In one survey of colleges conducted in 2016, approximately half (52%) had requirements for at least one dose of MenACWY and <1% had a requirement for MenB.<sup>46</sup> In some cases, university requirements exceed those of state of local laws.<sup>47</sup> However, little is known about the effect of college and university prematriculation requirements on adolescent meningococcal vaccination coverage, so the impact of these policies is an important area for future investigation.

As school entry requirements remain an underused tool for meningococcal vaccination at present, state legislatures and health departments may consider whether school entry requirements could be implemented to increase vaccination rates to more optimal levels. Any public health policy involving use of mandates must be carefully considered for its public health utility and potential negative consequences.48 The Association of Immunization Managers recommends that new school requirements are evaluated to address any concerns and ensure that adequate time has passed to integrate the vaccine into funding and delivery mechanisms, establish safety, and gain clinician and public acceptance of the vaccine, because requirements that are enacted poorly or unnecessarily may jeopardize the legitimacy and effectiveness of requirements for that vaccine and other vaccines.<sup>49</sup> If states consider enacting requirements as a next step for increasing both coverage and equity, it will be important for legislators and policy makers to engage with key stakeholder groups including clinicians who have the primary responsibility for immunizing children and adolescents, as they will play an important role in this effort, both through their support of enacting legislation and their subsequent efforts to increase compliance with the new regulations.<sup>50</sup>

#### MenB

For MenB, the ACIP recommendation for shared clinical decision-making (formerly referred to as individual clinical decision-making) is likely the driving factor in keeping coverage low at 17% in 2018. ACIP determined that there was insufficient evidence for effectiveness against clinical outcomes and duration of protection to make a routine recommendation that all adolescents be vaccinated with the MenB vaccine.<sup>5</sup> However, given the seriousness of meningococcal disease and the availability of licensed vaccines, ACIP noted that sufficient evidence does exist to encourage individual clinical decision-making. In this way, it is available to patients and importantly health insurance including private and public plans will cover the cost.<sup>51</sup>

The shared clinical decision-making recommendation likely affects uptake by influencing parents, providers, and policies. For parents, knowledge of MenB vaccine is low: in 2017-2018, 2 y post-MenB recommendation in 2015, over 80% of parents had not heard of MenB vaccination, yet most (90%) were at least somewhat willing to accept vaccination for their children.<sup>28</sup> For providers, poor understanding of the recommendation for shared clinical decision-making (SCDM) exists for this vaccine. In a national survey of pediatricians and family practitioners, a majority (76%) did not correctly define a category B recommendation, and approximately half did not know that private insurance and the Vaccines for Children (VFC) program would pay for vaccines with a category B recommendation.<sup>52</sup> Other studies have shown a very low proportion (7%) who correctly interpret and follow the SCDM recommendation for Men B.<sup>53</sup> Yet another study found that 51% of pediatricians reported always or often discussing Men B with their patients.<sup>54</sup> The lack of specific and clear guidance for how to conduct SCDM with patients is thus a notable challenge for at least some clinicians and therefore a barrier for uptake among patients.<sup>55,56</sup>

Novel communication strategies may be needed for the MenB vaccine, given the non-routine ACIP recommendation. Currently, the limited guidance on how to discuss vaccines with a SCDM recommendation can make the implementation of such recommendations into practice challenging. Communication tools may be helpful in this regard. Given the target age for MenB, and the heightened risk of meningococcal disease among college students, shared decisionmaking should seek to engage not only parents, but also the older adolescents themselves who are the ones who will be directly affected by vaccination decisions.

In the absence of SCDM implementation guidance from ACIP, clinicians may turn to professional societies for direction; for example, the AAP's Committee on Infectious Diseases has encouraged pediatricians to discuss the availability of MenB vaccines with patients and families, in order to permit necessary information to be shared regarded vaccine benefits, risks, and costs that can ultimately permit a decision that is in the patient's best interest to be made.<sup>57</sup>

Regarding policies, no state currently requires MenB vaccine for school entry and with a permissive recommendation this is an unlikely way forward at present time. However, even in the absence of MenB requirements at the state level, colleges and universities may either recommend or require MenB vaccination for their students.<sup>46</sup>

### Conclusions

Invasive meningococcal disease is preventable through vaccination, however current low coverage estimates indicate that many adolescents and young adults remain inadequately protected through the period of greatest disease risk. Though a complete understanding of the barriers to greater uptake of meningococcal vaccines may not be fully known at this time, several promising approaches that have proven successful for other vaccines to increase coverage are available, and empirical testing for MenACWY and MenB among older adolescents is an important research priority. Furthermore, adolescence is a formative time during which a pattern can be established for healthy immunization practices across the lifespan.<sup>26</sup> While at ages 11–12 y, parents are likely to be the primary decision-makers, this may change through age 18 y. Encouraging annual preventive visits throughout older adolescence could also help to achieve higher coverage for the second adolescent vaccination platform at ages 16-18 y and promote the utilization of preventive health care more broadly. Finally, efforts toward strengthening general vaccine attitudes during adolescence could have broad effects on multiple vaccines. Collectively, these efforts can have significant public health impact for adolescents and throughout the lifespan.

# **Disclosure of potential conflicts of interest**

Dr. Niccolai has served as Scientific Advisor for Merck.

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