

## Public health management of pertussis in adults: Practical challenges and future strategies

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### ABSTRACT

A panel of 24 international experts met in July 2022 to discuss challenges associated with pertussis detection, monitoring, and vaccination in adults; conclusions from this meeting are presented. There has been a shift in the epidemiology of pertussis toward older children and adults. This shift has been attributed to the waning of infection- or vaccine-induced immunity, newer detection techniques causing detection bias, and possibly the replacement of whole-cell pertussis with acellular vaccines in high-income countries, which may lead to immunity waning more quickly. The burden of adult pertussis is still likely under-ascertained due to widespread under-recognition by healthcare professionals (HCPs), under-diagnosis, and under-reporting in this age group. Non-standardized testing guidance and varied case definitions have contributed to under-reporting. Key barriers to HCP engagement with the tetanus, diphtheria, and pertussis (Tdap) vaccine include low awareness, lack of time/funding, and lack of motivation due to low prioritization of Tdap.

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## Introduction

Pertussis, an acute, highly infectious respiratory disease caused by *Bordetella pertussis* (*B. pertussis*) is a global problem, with large epidemics occurring irregularly every few years.<sup>1,2</sup> Over 62,000 cases of pertussis were reported worldwide in 2022, although the true estimate is expected to be much higher as many cases go undiagnosed or unreported.<sup>3</sup> Infants younger than 12 months demonstrate the highest incidence (32.7–72.3/100,000) and greatest disease burden (intensive care unit admission incidence 2.1–18.6/100,000),<sup>4–6</sup> but in the past two decades, there has been a shift in the age distribution of pertussis toward older children and adults.<sup>7,8</sup> In the USA, a significant increase in pertussis notification and hospitalization was observed among children aged 7–10 years between 2000 and 2016.<sup>9</sup> In Asia and Europe, a trend of increased pertussis in adolescents/adults has been seen over time; among European countries with the highest pertussis notification incidences, ~50% of cases were reported in adults.<sup>4,10,11</sup>

Several factors have been hypothesized to contribute to this trend (Supplementary Table S1). Although pediatric vaccinations are widely implemented, there are marked national variations in adolescent and adult booster recommendations.<sup>7,12,13</sup> Other proposed explanations for the apparent pertussis resurgence include an aging population, and mutated strains of circulating *B. pertussis*, driven by selection pressure.<sup>14,15</sup> Notably, due to widespread under-recognition, under-diagnosis, and under-reporting, the epidemiology and burden of adult pertussis is not as well described as that in children.<sup>16–18</sup>

## Methods

A panel of 24 international academic experts convened in July 2022 to discuss the challenges associated with pertussis detection, monitoring, and vaccination in adults. The objective was to consolidate existing information and explore gaps in knowledge. Global and regional immunization policies were

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reviewed to identify opportunities for improved vaccine uptake in adults.

The panel's views described herein are informed by peer-reviewed publications, surveillance data, and health authority assessments, as well as the experts' real-world experiences. The panel acknowledges a previously published position paper examining methods to improve pertussis vaccination rates in older adults and at-risk groups.<sup>19</sup> This paper aims to provide up-to-date perspectives on the practical challenges of adult pertussis surveillance, diagnosis, and vaccination, while exploring strategies to overcome these barriers.

## Barriers to optimal assessment of disease burden and surveillance

### Under-recognition

The panel acknowledged that understanding the true epidemiology of adult pertussis is critical to raise awareness, improve care quality, and drive changes in vaccination policy. Low awareness of adult pertussis among the public and health-care professionals (HCPs) is a barrier to prompt diagnosis. In adolescents and adults, early symptoms can be like those of a common cold. Typical signs like paroxysms of cough, post-tussive vomiting, and the distinctive inspiratory whoop are often absent.<sup>1,20</sup> While pertussis is typically associated with a subacute cough of 3–8 weeks' duration, ~20% of adolescents and adults with ≥1–2 weeks' cough have been found to have confirmed (e.g., positive culture or polymerase chain reaction [PCR] for *B. pertussis*) or probable (e.g., rise in antibody titers against pertussis toxin) pertussis.<sup>21,22</sup> HCPs often do not consider pertussis in their differential diagnosis of persistent cough in adults.<sup>23</sup> In those with respiratory comorbidities such as asthma and chronic obstructive pulmonary disease (COPD), diagnosis is further complicated by a presentation similar to an acute exacerbation, particularly in older adults (≥50 years).<sup>24,25</sup>

### Under-diagnosis

Even with heightened clinical suspicion, successful diagnosis hinges on HCPs making appropriate testing choices, given the time-sensitivity of diagnostic modalities.<sup>26,27</sup> Nasopharyngeal culture is the gold standard due to its excellent specificity,<sup>28</sup> but PCR is a more sensitive and rapid test.<sup>29,30</sup> Regardless, both culture and PCR demonstrate a decrease in sensitivity after the second week of cough onset.<sup>30</sup> As most adults are not considered for diagnosis until they have had a prolonged cough (mean duration 36–48 days),<sup>29</sup> a serological assay measuring IgG antibodies against pertussis toxin is often the only viable diagnostic option.<sup>28,30</sup>

The panel discussed limitations of current testing methodologies, including impact of swabbing techniques on test accuracy; different PCR testing cycle thresholds – criteria used to determine positive, negative, and inconclusive results – among some countries, and how this influences clinical/public health decision-making;<sup>31</sup> plus the complex relationship between PCR test-signal intensity and degree of infectiousness. Disease awareness remains low despite

*B. pertussis* infection being reported in ~20% of adults with persistent (7–31 days) cough,<sup>32,33</sup> and this may have been impacted further by the COVID-19 pandemic. Testing is an important tool for epidemiological studies and for diagnosis in index cases (to prevent community spreading), highlighting the relevance of timely diagnosis for individual patients.

Diagnosis of pertussis relies on a thorough clinical history of signs and symptoms, a high degree of suspicion, and reflex appropriate testing (culture or PCR testing).<sup>20</sup> Antibiotics may be administered if pertussis diagnosis is confirmed, or with high clinical suspicion during local outbreaks, but should be started during the first one to two weeks of cough, before paroxysms begin.<sup>34,35</sup> After 2–3 weeks, *B. pertussis* is no longer detectable in airway samples, although serologic diagnosis is possible.<sup>36</sup> Paroxysms of cough are a consequence of epithelial damage, not persistent infection, hence antibiotic treatment is unlikely to be beneficial.<sup>37</sup> The window of opportunity for antibiotic treatment is limited if PCR or serologic diagnosis is required.<sup>36</sup> For additional information see <https://www.cdc.gov/pertussis/index.html>.

The atypical presentation of pertussis symptoms in adults contributes to under-diagnosis and therefore an increased prescription of antibiotics for respiratory conditions, which could be avoided.<sup>38</sup> Although not discussed by the panel experts, a recent survey has highlighted that pertussis vaccination could play a role in limiting antimicrobial resistance.<sup>39</sup>

### Under-reporting

Although the World Health Organization (WHO) recommends pertussis surveillance,<sup>1,40</sup> effective systems are often absent, particularly in low-income countries, even though pertussis is notifiable in just under half of all countries worldwide.<sup>3,41–43</sup> The panel highlighted that testing guidance and case definitions are not standardized (Supplementary Table S2). The processes of reporting and diagnosing pertussis can be complex and time-consuming for HCPs, requiring input from multiple personnel.<sup>41,44</sup> In countries where pertussis is a notifiable disease, evidence of significant under-reporting in adults exists.<sup>16,17</sup> Comparing reported cases of pertussis infections among the Italian population in 2019–2020 with collected seroprevalence data, based on antibody levels indicative of infection within the last 12 months, the estimated infection rate was ~141- to 3464-fold higher than the notification rate.<sup>16</sup> This may partly be due to the fact that most countries utilize passive surveillance, where health authorities do not stipulate reporting from HCPs.<sup>41,45</sup>

The panel was unanimous in their assessment that as long as HCPs remain unaware of the signs and symptoms of adult pertussis, and do not take steps to perform appropriate diagnostic tests, the issues of under-recognition, under-diagnosis, and under-reporting will persist. Data on the incidence of pertussis from surveillance and serodiagnosis are key to generating evidence that supports vaccination guidelines and policies.

## Barriers to adult Tdap immunization

Considering pertussis is among the least well controlled of the vaccine-preventable diseases, regular boosting of immunity in the population with the tetanus, diphtheria, and acellular pertussis (Tdap) vaccine is a sound strategy.<sup>46</sup> A key barrier to adult Tdap immunization is cost,<sup>47</sup> with acellular pertussis vaccines having significantly higher development and production costs compared to previously used whole-cell vaccines.<sup>48</sup> In some countries, however, Tdap will be fully reimbursed.<sup>49</sup> Cost could partially explain why, despite existing recommendations, the Tdap vaccination coverage rate among US adults aged  $\geq 19$  years was only  $\sim 30\%$  in 2019–2020.<sup>50</sup> Further, the vaccine coverage in pregnant women in England in 2022–2023 was 61%.<sup>51</sup> Whilst Tdap has reduced reactogenicity in comparison to previously used whole-cell vaccines, waning immunity is a global concern for ongoing pertussis outbreaks among adults.<sup>52,53</sup>

The panel discussed challenges that must be addressed to improve adult uptake of Tdap in countries where booster recommendations are in place. Barriers were characterized according to the ‘COM-B’ framework, which illustrates how ‘Capability,’ ‘Opportunity,’ and ‘Motivation’ interplay to generate ‘Behaviors’.<sup>54</sup>

### Capability-related barriers to vaccine uptake

Capability-related barriers to vaccine uptake identified by the panel were low awareness of pertussis and of the possibility of vaccination, and low perception of pertussis as an adult disease among HCPs and the public (Figure 1).<sup>55–57</sup> Unsurprisingly, the perceived low risk of contracting pertussis is the most commonly cited reason for declining pertussis vaccination in adults.<sup>56</sup>

### Motivation-related barriers to vaccine uptake

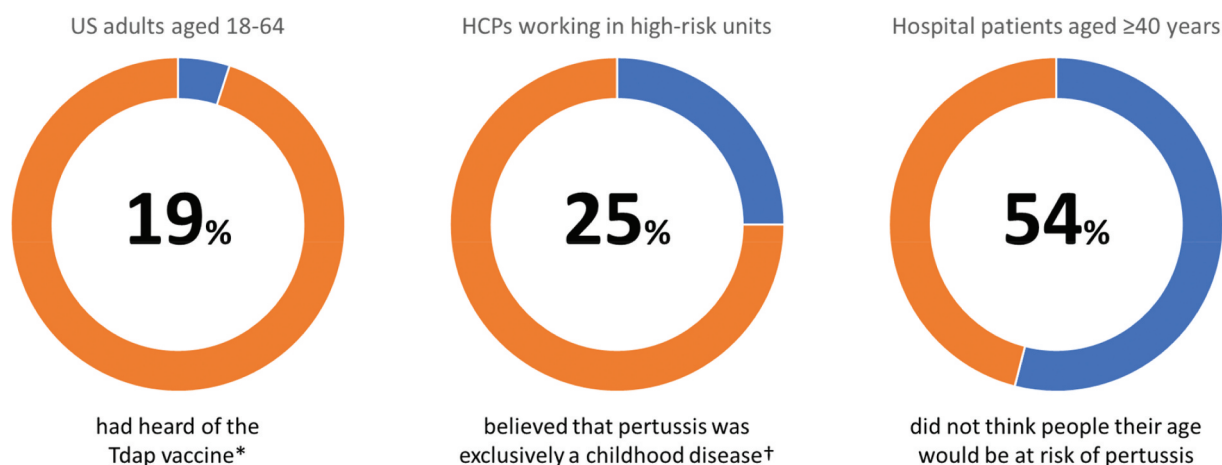
Limited awareness is linked to a lack of desire to implement change. The panel explored motivation-related barriers to adult immunization, including the perception that

pertussis in adults is not associated with significant morbidity or mortality,<sup>58</sup> pertussis is seen as low priority versus other vaccine-preventable infectious diseases (e.g., hepatitis B),<sup>58,59</sup> and the widespread misconception that prior infection or pediatric vaccination confer lifelong immunity. Although most severe cases occur in infants, pertussis-related complications, including sinusitis, otitis media, pneumonia, weight loss, rib fracture, and syncope have been reported among adults.<sup>60–62</sup> In both hospital and primary healthcare settings, adult pertussis is also associated with substantial medical expenditures.<sup>63–65</sup> Despite the evidence, pertussis is considered less serious and less prevalent than many other infectious diseases,<sup>58</sup> likely due to the low awareness of disease burden in adults.

### Opportunity-related barriers to vaccine uptake

As well as motivation, there are external factors that hinder behavioral changes. These can be broadly grouped into lack of or missed opportunities,<sup>54</sup> e.g., limited time of HCPs to routinely discuss the benefits and safety of adult vaccinations with patients, the low likelihood of healthy patients visiting an HCP solely for vaccinations, and lack of social opportunities afforded by the wider community – funding, existence of health inequities, and low patient demand or acceptance. The panel noted the lack of strong pertussis vaccination recommendations from national and international health authorities for the adult population except during pregnancy, compounded by low collective awareness of the adult vaccine.<sup>55,56,66</sup> Pertussis vaccine uptake is also influenced by socioeconomic status, ethnicity, and geographical location.<sup>67,68</sup> Moreover, there are logistical and ethical challenges associated with delivering vaccination to certain vulnerable populations, e.g., care-home residents.<sup>69</sup>

The COVID-19 pandemic has impacted immunization programs globally, leading to public health priorities being modified.<sup>70</sup> Lockdown measures have reduced access to routine pediatric immunization in both high- and low-income



**Figure 1.** Findings from previous studies highlight low awareness of the pertussis vaccine, and low perception of pertussis as an adult disease among HCPs and the public. **Note:** \*Data from a US survey conducted shortly after Tdap replaced Td.<sup>56</sup> †Data from a 2022 survey.<sup>57</sup> HCP, healthcare professional; Td, tetanus-reduced-dose diphtheria vaccine; Tdap, tetanus, reduced-dose diphtheria, and acellular pertussis vaccine.

countries, causing vaccine coverage to decline at all milestone ages.<sup>71,72</sup> Conversely, for Tdap vaccination in pregnancy, coverage has been maintained or showed no pronounced decline in developed countries.<sup>73,74</sup> Importantly, the COVID-19 pandemic enabled the first mass vaccination programs for all adults since the eradication of smallpox, so ultimately may result in better systems and infrastructure for adult vaccination. Innovations adapted during the pandemic to continue delivering routine immunizations can also be used to streamline future vaccination programs.<sup>75</sup>

### **Which adult populations are at greatest risk from pertussis and its complications?**

Understanding which groups within the adult population are at an increased risk of pertussis infection and associated morbidity/mortality is essential to the design and implementation of effective immunization strategies.

#### **Older adults**

Although data on incidence and burden of pertussis disease in adults are limited, studies have shown that rates of pertussis-related hospitalization increase progressively with advancing age.<sup>76,77</sup> Adults aged  $\geq 45$  years are at an increased risk of complications, more severe disease, and hospitalization due to pertussis.<sup>76,78</sup> For older adults ( $\geq 65$  years) with chronic comorbidities, it is likely that these are documented as the cause of hospitalization or death even when pertussis is present.<sup>60,76,79</sup> Uncommon complications such as intracranial hemorrhage, stroke, encephalopathy, carotid artery dissection, pneumomediastinum, and herniated lumbar discs have also been reported in older adults.<sup>32,78,80</sup> Multiple factors are linked to older adults' susceptibility to severe pertussis sequelae, including an increased risk of multimorbidity, immunosenescence, and loss of vaccine- and/or infection-induced immunity.<sup>81–83</sup> Aged care facility outbreaks may also occur and are associated with substantial morbidity.<sup>84,85</sup> Pertussis outbreaks in aged care may be under-recognized. In one study, 3/7 respiratory outbreaks in aged care were negative on multiplex viral respiratory PCR, suggesting a bacterial cause.<sup>86</sup>

#### **Adults with chronic respiratory comorbidities**

Adults with chronic respiratory conditions, such as asthma and COPD, have a higher risk of pertussis infection, with an up to ~four-fold increased incidence compared with those without either condition.<sup>76,87</sup> Evidence suggests that COVID-19 has increased susceptibility to other infections;<sup>88</sup> more research is now required to assess how this may have affected the incidence of pertussis. Further effects and consequences of chronic respiratory conditions in relation to pertussis are summarized in Supplementary Table S3.

#### **Cigarette smoking**

Current and past smoking status is associated with increased pertussis severity, such as prolonged paroxysmal cough, a greater number of nights disturbed by pertussis, and a higher risk of hospitalization.<sup>61,78</sup> Further effects and consequences of smoking in relation to pertussis are presented in Supplementary Table S3.

#### **Adults with obesity**

A review of 2011–2015 data from the US Enhanced Pertussis Surveillance program found that among patients with pertussis who were hospitalized, 48% were obese;<sup>78</sup> in comparison, the prevalence of obesity in the general public at that time was ~39%.<sup>89</sup> Similarly, in a small nested case-control study of adults  $\geq 45$  years who had a record of pertussis notification, compared with individuals whose body mass index (BMI) was  $< 25$  kg/m<sup>2</sup>, higher BMI was linked to an increased likelihood of pertussis notification.<sup>76</sup> A follow-up analysis did not, however, detect a statistically significant association between obesity and pertussis-related hospitalization,<sup>77</sup> suggesting that either obesity itself or related comorbidities could be possible risk factors for pertussis.

#### **Adults with immunocompromising conditions**

A higher prevalence of immunosuppression was observed among adult pertussis patients ( $\geq 21$  years) who were hospitalized versus the general population (20% vs 3%).<sup>78,90</sup> Although data remain sparse for this population, long-term survivors of autologous peripheral blood stem cell transplantation may be highly susceptible to pertussis, as demonstrated by their low levels of antibodies against pertussis toxin.<sup>91</sup>

#### **Healthcare workers and people working closely with children and young people**

Pertussis among HCPs is of concern due to the potential for transmission of nosocomial infection to their households, vulnerable patients, and other HCPs.<sup>92</sup> Serological studies have shown that HCPs across various specialties have a relatively high annual rate of unrecognized *B. pertussis* infection.<sup>92,93</sup> Furthermore, pertussis outbreaks have been reported from a range of healthcare settings including maternity wards, neonatal wards, surgical units, and residential care homes for older adults.<sup>85,94,95</sup> Outbreaks can lead to considerable disruption to the function of the medical units, staff shortages, and resource expenditure. The risk of pertussis infection may also be greater for teachers and childcare workers than that for the general population.<sup>61,96</sup> Therefore, through vaccination, teachers and childcare workers would not only protect themselves from contracting pertussis but also reduce the risk of spreading the disease to children.

**Table 1.** Pertussis immunization recommendations for children differ between territories and global health agencies.

Agency/territory	Recommendation
WHO <sup>7</sup>	A 3-dose primary series – the first dose being administered as early as 6 weeks of age and subsequent doses given 4–8 weeks apart
CDC <sup>97</sup>	A series of the diphtheria-tetanus-pertussis (DTaP) vaccine in 5 doses from the age of 2 months to 6 years
ECDC <sup>98</sup>	A similar schedule to the CDC, with some variations in timing of administration across the region <sup>a</sup>
Asia-Pacific <sup>99</sup>	Established vaccination programs that include a minimum number of routine vaccines against pertussis
Latin America and the Caribbean <sup>100</sup>	A 3-dose series of the DTaP vaccine (either wp or ap) within the first year of life, with two additional tetanus-containing boosters given during childhood and adolescence

<sup>a</sup>In several European countries, the primary series comprises a so-called “2 + 1” schedule with two doses in the first few months of life (e.g., at 2 and 4 months) and a third dose between 11 and 13 months of age.<sup>98</sup>

ap, acellular pertussis; CDC, Centers for Disease Control and Prevention; ECDC, European Centre for Disease Prevention and Control; WHO, World Health Organization; wp, whole-cell pertussis.

## Global and regional recommendations for vaccination

### Current childhood vaccination policies

The key objective of pertussis vaccination remains the protection of infants and young children. Despite this, recommendations for vaccination vary between regions and global health agencies (Table 1).<sup>7,97–100</sup>

### Adult vaccination recommendations

Generally, adult recommendations for pertussis vaccination focus primarily on pregnant women and close contacts of newborns, the so-called ‘cocooning’ strategy.<sup>7,97,98,101</sup> Beyond these groups, recommendations vary widely with no universal strategies. The WHO makes no recommendation for booster vaccination against pertussis in adolescents and/or adults, stating that these should only be introduced after assessment of local epidemiology and cost-effectiveness, once high infant coverage has been achieved.<sup>7</sup> The Centers for Disease Control and Prevention (CDC) recommend that all adults over the age

of 19 years should be vaccinated with Tdap or tetanus-diphtheria toxoid-containing (Td) vaccine every 10 years; whenever feasible, Tdap should be given to adults over the age of 65 years.<sup>97</sup> Across Europe, there are national variations in recommendations for adult pertussis vaccination; countries that have adult recommendations are listed in Table 2.<sup>98,102–112</sup> There are no routine adult vaccination recommendations in Asian or Latin-American countries.<sup>100,113,114</sup>

For at-risk populations, an adult pertussis booster recommendation was issued by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) in their 2023 report, where they support the CDC’s recommendation for people with COPD to receive Tdap vaccination if they were not vaccinated in adolescence,<sup>115</sup> a recommendation that had not been included in the preceding 2010 report.<sup>116</sup>

The WHO has recommended that HCPs should be prioritized in countries with an adult pertussis immunization program, as a strategy to prevent nosocomial transmission to vulnerable patients.<sup>7,117</sup> Some countries, e.g., Germany, have issued a universal Tdap recommendation for HCPs every 10 years,<sup>2,118</sup> while others, such as the UK, recommend pertussis

**Table 2.** National recommendations on adult pertussis vaccination in Europe vary between age groups and countries.

Country	Age (years)	Recommended	Funded
Austria <sup>102</sup>	≥16	Tdap-IPV every 10 years	No
	≥61	Tdap-IPV every 5 years	No
Belgium <sup>112</sup>	>16	Tdap every 10 years	No
	≥65	Tdap every 10 years	No <sup>a</sup>
Czech Republic <sup>104</sup>	18–64	At least 1 dose during lifetime (vaccine not specified)	No
	65+	Recommended in case of risk factors (vaccine not specified)	No
Finland <sup>105</sup>	14–15	1 Tdap booster	Yes
	25 <sup>b</sup>	1 Tdap booster	Yes
	>25	No	No
France <sup>110,111</sup>	25	1 Tdap-IPV booster	Yes
	45	1 Tdap-IPV booster	Yes
	≥65	1 Tdap-IPV booster every 10 years	Yes
Germany <sup>109</sup>	≥18	Td booster every 10 years, next due Td requires one dose as Tdap	Yes
Greece <sup>106</sup>	18–25	1 booster dose with Tdap or Tdap-IPV	Yes
	≥25	Td or Tdap every 10 years	Yes
Italy <sup>98,108</sup>	≥19	Tdap every 10 years	Yes
Liechtenstein <sup>98</sup>	25	1 Tdap booster	Yes
	45	1 Td booster	Yes
	65	1 Td booster	Yes
	≥65	1 Td booster every 10 years	Yes
Luxembourg <sup>98</sup>	15–20	1 booster of MenC and Tdap-IPV	Yes
	21–65	Tdap-IPV every 10 years	Yes
	≥65	No	No
Norway <sup>107</sup>	–	Tdap booster if 10 years or more since the last dose	No
Switzerland <sup>103</sup>	25	1 Tdap booster	Yes

<sup>a</sup>One region (Flanders) is funding 10-year adult Tdap vaccinations; <sup>b</sup>If born in 1993 or later.

IPV, inactivated polio vaccine; MenC, meningococcal vaccine; Td, tetanus-reduced-dose diphtheria vaccine; Tdap, tetanus, reduced-dose diphtheria, and acellular pertussis vaccine.

vaccination for certain HCP groups, for instance, those working in neonatal, maternal, or pediatric intensive care settings.<sup>119</sup>

### Future considerations for adult booster recommendations

The panel agreed that since most recommendations are determined by risk factors, an initial Tdap recommendation targeting at-risk groups would more likely achieve widespread adoption than a universal adult booster recommendation. It was nonetheless highlighted that universal recommendations are easier to implement and ultimately will lead to higher uptake, rather than attempting to qualify which patient groups are most at risk.

Adult booster vaccination is currently recommended by select countries at 10-year intervals, primarily to align with tetanus protection. Some panel members agreed that this schedule does not provide adequate protection against pertussis, while others put forward the counter argument that this is better than no booster, although the biggest problem is poor implementation and uptake. It has been suggested that the alternative may be a standalone, i.e., not combined with diphtheria and tetanus toxoids, pertussis vaccine<sup>120</sup> that could be administered at more regular intervals, to be utilized alongside currently available options. In the case of patients vaccinated with Td in the past 3 years, a single pertussis vaccine would likely be recommended in place of Tdap. The panel agreed that a modeling study to determine the optimal time frame for a pertussis booster would generate decisive data to drive policy change for more frequent vaccination, perhaps at different intervals for the general population versus at-risk groups. However, to change and/or standardize policy recommendations for pertussis adult vaccination across the world and convince all stakeholders, further studies are necessary to establish the true epidemiology and burden of disease.

### Opportunities and recommendations for overcoming obstacles to effective adult diagnosis and vaccination

The panel discussed several potential strategies to address the challenges of adult pertussis diagnosis, surveillance, and vaccination. Furthermore, they explored the potential of next-generation pertussis vaccines.

#### Optimizing assessment of adult disease burden

To improve recognition of pertussis and achieve timely diagnosis in the adult population, including in aged care, the first step is to increase awareness of the often-atypical presentation of pertussis among both the public and HCPs. Methods

proposed to achieve this are summarized in Table 3.<sup>121</sup> Pertussis recognition would be improved in adults if there were targeted pertussis awareness campaigns to prompt identification of patients with probable pertussis. The accuracy of pertussis surveillance could be improved if HCPs have increased awareness of when to perform which type of test.<sup>122</sup> Additionally, systemic changes in the pertussis diagnostic workflow, to incorporate testing for pertussis within combined multiplex immunoassay panels, could increase the frequency of pertussis testing.<sup>121</sup> Administrative and logistical issues related to notification shown in past studies can be minimized by standardizing case definition and test interpretation, and using automated, digital systems for reporting.<sup>122</sup>

#### Optimizing uptake of Tdap vaccination

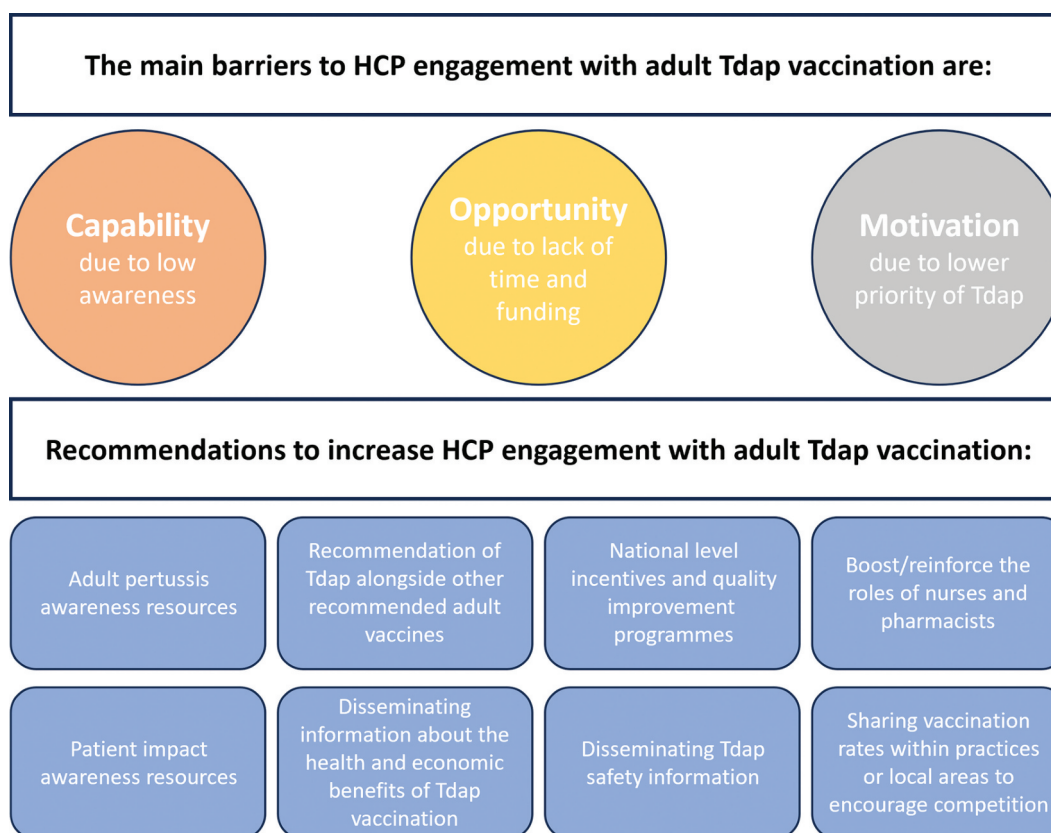
A lifelong approach to pertussis booster vaccination is fundamental to prevent infection and curb transmission to those at the highest risk, e.g., newborns and infants. Revisiting the COM-B framework as a guidance, the panel identified strategies to increase adult pertussis vaccine uptake in countries where recommendations exist (Figure 2).

Methods to overcome barriers faced by HCPs in relation to pertussis were discussed:

- (1) Capability- and motivation-related barriers could be addressed through education and training, whereas opportunity-related barriers could be overcome by implementing more extensive changes involving guidelines, workflow structures, and national-level incentives.<sup>54</sup>
- (2) Through awareness-raising campaigns and resources, HCPs are more likely to have a better knowledge of adult pertussis. Increased awareness of disease risk may encourage members of the public to agree to vaccination when it is suggested or recommended by an HCP.
- (3) Capability-related barriers faced by HCPs could be overcome by continued education on topics such as national recommendations, and the health and economic benefits of Tdap vaccination.
- (4) Incentivizing HCPs to engage with devised and delivered educational resources should lead to an enhancement in their understanding of the impact of pertussis, particularly in at-risk groups. Knowing patients with asthma or COPD are more prone to pertussis infection and its complications should motivate HCPs to vaccinate this population.

**Table 3.** Methods to improve the recognition of pertussis and achieve timely diagnosis in the adult population rely on educating the public and HCPs.

Proposal	Intended outcome
Targeted pertussis awareness campaigns and supporting HCPs via specialized diagnostic resources	Prompt identification of patients with probable pertussis, or even another viral infection
Proactive testing of in-hospital, high-risk patients, and testing of adult contacts of children diagnosed with pertussis	To optimize testing procedures
Systemic changes in diagnostic workflow to facilitate rapid testing	To incorporate testing for pertussis within combined multiplex immunoassay panels (multiplex PCR tests have been increasingly utilized in outpatient settings in the wake of the COVID-19 pandemic) <sup>121</sup>



**Figure 2.** Barriers to pertussis vaccine uptake in adults and strategies to overcome them. **Note:** HCP, healthcare professional; Tdap, tetanus, reduced-dose diphtheria, and acellular pertussis vaccine.

The panel advised implementing systemic changes in HCPs' workflows to firstly incorporate a pertussis vaccination needs assessment into routine care for adults and secondly incorporate the recommendation for Tdap alongside other routine adult vaccines, such as influenza. Empowering the wider HCP team (nurses, pharmacists, etc.) to discuss the benefits of pertussis vaccination will alleviate one of the most common challenges physicians face – limited time allocated to each patient. However, these discussions may only be beneficial to physicians and come at the expense of the wider HCP team in terms of workload and time management. Additionally, although there is no universal recommendation and its implementation is challenging,<sup>101</sup> cocooning, the strategy of household vaccination to protect infants against pertussis, may offer additional safeguarding from transmission via close-contact persons.<sup>117,123</sup> Grandparents who provide care to infants should be included. Ideally, this would be discussed during the process of family planning. The panel suggested introducing national-level incentives for adult pertussis vaccination and quality-improvement programs for vaccination coverage among primary care practices. Lastly, the panel identified ways to address health inequalities as potential barriers to vaccine uptake, including promotional campaigns in areas of greater deprivation, reducing financial barriers such as out-of-pocket costs.

National medical societies tend to follow the lead of National Immunization Technical Advisory Groups and reflect their recommendations. In many countries, medical

societies also play a key role in information dissemination and defining recommendations and their implementation. It is crucial for information and recommendations to come from a central source and be harmonized across national medical societies to minimize uncertainty.

The panel agreed that confidence and uptake in existing pertussis vaccines could be boosted with more comprehensive data on their effectiveness, especially in at-risk populations. Meanwhile, the development of new and more effective vaccines may be another promising solution. There is increasing recognition that optimal protection against *B. pertussis* likely requires mucosal immunity; currently, available pertussis vaccines do not achieve protection locally at respiratory mucosa.<sup>124,125</sup> Live-attenuated vaccines mimic natural infection when delivered by the mucosal route; they therefore have the potential to induce mucosal immunity and long-term protection.<sup>124</sup> This has led to the investigation of several vaccine candidates (Supplementary Table S4); one (BPZE1) has advanced into clinical development.

## Conclusion

Despite decades of worldwide immunization programs, pertussis remains one of the most common vaccine-preventable infectious diseases. The true epidemiology and burden of adult pertussis is hampered by under-recognition, under-diagnosis, and under-reporting due to a combination of factors,

including atypical presentation, low awareness, and technological and administrative barriers within healthcare systems. Effective pertussis control could be achieved by optimizing surveillance and vaccine uptake in adults. This will require a multidisciplinary approach of education, training, and policy changes. This experts' panel meeting concluded by highlighting the need for a lifelong approach to pertussis vaccination. Increased standardization for pertussis diagnosis and vaccine recommendations across nations would also be highly advisable.

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## Author contributions

A panel of 24 international academic experts convened in July 2022 to discuss the challenges associated with pertussis detection, monitoring, and vaccination in adults. The authors listed wished to develop two publications associated with the discussions. Given the nature of discussions, all authors contributed equally to the paper. It was agreed that Professor C Raina MacIntyre would take overall responsibility and serve as lead and corresponding author; all other authors are listed alphabetically. The second publication, submitted to *Human Vaccines & Immunotherapeutics* is as follows: Understanding the impact of adult pertussis and current approaches to vaccination: A narrative review and expert panel recommendations. Dr Peter Kardos, Dr Jaime Correia de Sousa, Professor Ulrich Heininger, Professor Andreas Konstantopoulos, Professor C Raina MacIntyre, Dr Donald Middleton, Professor Terry Nolan, Professor Alberto Papi, Dr Adrian Rendon, Dr Albert Rizzo, Mr Kim Sampson, Dr Alessandro Sette, Ms Elizabeth Sobczyk, Dr Tina Tan, Professor Catherine Weil-Olivier, Dr Birgit Weinberger, Professor Tom Wilkinson, Dr Carl Heinz Wirsing von König.

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