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Highlights

- Pertussis remains endemic globally, with peaks occurring every three to five years
- Uptake of maternal pertussis immunisation has declined in several countries
- As severe pertussis cases rise in infants globally, clear messaging is vital
- Open discussions should address concerns of vaccine-hesitant pregnant women
- Pregnant women access immunisation through primary care and/or maternity services

Perspective

Recent increase in infant pertussis cases in Europe and the critical importance of antenatal immunisations: we must do better...now

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Abstract

Recent months have seen an increase in pertussis cases in several countries across

the Northern and Southern hemispheres. The lack of immune stimulation during the

COVID-19 pandemic due to the reduced circulation of Bordetella pertussis, the

pathogen responsible for pertussis, is likely to have led to increased population

susceptibility which has been magnified the typical 3-5 yearly cyclical peaks in

Maternal immunization for pertussis proves highly effective in protecting activity.

infants under three months of age. It's also critical for immunisers and parents to

maintain high and timely immunisation uptake to ensure infants receive maximum

early protection when they are most at risk of severe disease.

Keywords: pertussis, whooping cough, antenatal immunization, pregnancy, vaccine

hesitancy

Introduction

Pertussis is a highly contagious respiratory infection that is easily spread through droplets via coughing or sneezing [1]. It poses a significant risk to neonates and young infants, and, in the absence of vaccination, may lead to severe illness and even death.

Symptoms onset is 7 to 10 days after infection but may manifest up to 21 days later. The illness can initially resemble a common cold, with symptoms of sneezing, runny nose, low-grade fever and a mild cough. This may then progress to persistent cough with a characteristic whooping sound that gave perfussis its common name, whooping cough, as the patient breathes through a swollen glottis. During coughing episodes, the patient may turn blue and vomit, with several coughing fits occurring in quick succession and causing exhaustion. These coughing fits can be triggered by eating, laughing, or crying and are usually worse at night. Pertussis is feared for its potential to cause permanent disability or death due to complications, including neurological and pulmonary. Infants under six weeks with pulmonary hypertension are at the highest risk of death.

Infected individuals are most contagious during the first three weeks of coughing, although coughing spells can last for several months ('100-day cough'). Treatment involves antibiotics to manage the infection and prevent further spread of the bacteria which, to be most effective, must begin early in the course of disease, ideally during the first one to two weeks before the episodes of rapid coughing occur [2].

There are no pertussis vaccines licensed or recommended for newborns at birth. To protect young infants, maternal pertussis antibodies are transferred transplacentally [3-4]. The best prevention methods include vaccinating mothers during pregnancy, ensuring people around the infant are up to date with their pertussis vaccines, and administering the childhood pertussis vaccine series on time [3-4].

Pertussis resurgence after COVID-19

Measures implemented to control the spread of COVID-19 between March 2020 and July 2021 also affected the transmission of other infectious diseases, including *Bordetella pertussis*, the pathogen responsible for pertussis. The increase in population susceptibility as a result of reduced transmission of *B. pertussis*, commonly termed immunity debt, has been proposed as a potential reason for the current resurgence of pertussis after the removal of all COVID-19 mitigation measures [5].

In 2019, the World Health Organization (WHO) reported a pre-pandemic pertussis incidence rate of 29.8 per million [6]. These rates significantly dropped during the pandemic, falling to 9.2 in 2020 and 4.6 in 2021, before rising to 10 in 2022 and 22.8 in 2023 [6]. In Europe, pertussis cases surged, with over 25,000 cases reported in 2023 and already more than 32,000 between January and March 2024 [7]. Such high annual numbers were reported in the previous peak years of 2016 (41,026) and 2019, highlighting the typical cyclical nature of pertussis (34,468) [7]. (**Figure**)

Between 2011 and 2022, a total of 103 deaths were reported, with 69 (67%) fatalities in infants and 25 (24%) in adults aged 60 and older, in the EU/EEA. Notably, 64

infant deaths occurred in <6 month-olds, with most deaths occurring in one-month-old infants [7]. From January 2023 to April 2024, there have already been 19 deaths: 11 (58%) in infants and eight (42%) in older adults.

In Europe, **Denmark** initially reported a resurgence of pertussis cases in May and June 2023, sadly with the death of a prematurely born infant at two months of age [8]. In **England**, on a background of a small and gradual decline in childhood vaccine uptake over the past decade alongside falls in maternal vaccine uptake and additional short-term declines in vaccination rates during the COVID-19 pandemic [9], the UK Health Security Agency (UKHSA) reported that there were 4,793 new pertussis cases diagnosed in England during January and April 2024 [10]. (**Figure**) This is notably higher than 858 total cases reported in the entirety of 2023 and marks the re-emergence of pertussis after a prolonged period which included historically low levels instigated by COVID-19 control measures [10].

According to the UKHSA, eight infants in England died after developing whooping cough during the first four months of 2024 [10-11]. The first infant death since 2019 was reported in the last quarter of 2023 in England. Additionally, the **Netherlands** has also reported 4 infant deaths within a 6-week period in 2024 [12]. In **Northern Ireland**, there were 72 confirmed cases of pertussis by March 11, 2024, 527 cases by April 21, 2024 and 1,425 cases by May 26, 2024, compared with only two cases between 2021 and 2023, with the Public Health Agency urging pregnant women and parents of young children to get vaccinated to help curb the current outbreak [13]. In **Wales**, pertussis cases also rose rapidly during the first few weeks of 2024, reaching 135 cases compared with about 200 in the whole of 2023 [14].

In **Spain**, between October 4, 2023 (week 41) and April 11, 2024 (week 15), 11,175 cases of whooping cough and 4 deaths have been reported [15]. Among the deaths were a 3-month-old premature infant whose mother had not been vaccinated during pregnancy, and a 2-month-old premature infant whose mother was vaccinated 5 days before delivery [15]. In **Czechia**, which has about one-fifth of Spain's population, a total of 9,370 pertussis cases were reported to the State Health Institute from the beginning of the year till April 21, 2024, and 3 deaths, which included a neonate [16]. The number of cases reported in Czechia is the largest in the country's past sixty years. According to Dr Milan Jovanovic Batut Public Health Institute, **in Serbia**, two unvaccinated children aged two and a half months and three months have already died in 2024, increasing the total to 4 deaths since January 2023 [17-18]. An infant too young to have been vaccinated also died of pertussis in **Belgium** in October 2023 [19]. Croatia has also reported 6,443 cases of pertussis from January 1 till April 19, 2024 [20].

Pertussis remains endemic worldwide, with peaks in disease occurring every three to five years, even in countries with high vaccination coverage against pertussis. With 15,275 cases reported in January 2024, a 15-fold increase over the same period in 2023, pertussis remains a pressing public health issue in **China** [21]. **Australia** is also facing a pertussis outbreak, with more than 4,400 cases reported by the end of April 2024, versus less than 2445 annual cases reported in 2023 [22]. In the **US**, elevated pertussis activity has been observed across multiple areas, according to the National Notifiable Diseases Surveillance System (NNDSS), with a total of 4,864 cases reported from January 1 to May 25, 2024. This is 2.8 times higher than the

1,746 cases reported during the same period in 2023 [23], although currently cases remain below pre-pandemic levels (**Figure**).

Neonates and young infants, particularly those too young to have completed their primary vaccination as part of the national childhood immunisation programme, account for the majority of pertussis-related deaths in the EU/EEA [24]. This emphasizes the importance of maternal vaccination during each pregnancy to protect newborn infants from severe illness and death until they can complete their routine primary immunisations. The UK recommendation states that the optimal window for maternal vaccination is between 20 and 32 weeks of pregnancy. However, receiving the vaccine later (ideally at least two weeks before delivery) will still be beneficial.

Decline in maternal pertussis vaccination rates

Where recommended, antenatal immunisation uptake has been suboptimal overall and particularly in the post-pandemic period. Several factors likely contribute to this. Lack of awareness among parents about the risks of pertussis in newborns and the protection from maternal vaccination, and challenges in accessing vaccination, especially following a period of exceptionally low pertussis activity, are crucial issues. Vaccine hesitancy in some countries alongside has also increased questioning of vaccines offered in pregnancy following the pandemic and COVID vaccine programs.

In England, reported uptake of antenatal immunisation in England has declined in recent years, with considerable geographical variation in uptake across the country from 74.7% in December 2017 to 59.5% in December 2023, though this marks an

improvement from around 58% in September 2023 [25]. The calculated vaccine effectiveness against infant death for those who received the vaccine at least seven days before delivery is 92%, highlighting the critical importance of antenatal pertussis immunisation in protecting infants against such a severe and fatal disease are birth (UKHSA unpublished data) [25] In England, there have been changes in the delivery model, with a shift of antenatal vaccination from primary care to maternity service providers, with the aim of improving access and opportunities for pregnant women to be vaccinated. This, however, has posed challenges in data capture, raising questions about the reliability of data transfer of vaccines administered outside of general practice back to the GP record, which is used to monitor national coverage of the program.

A decline in antenatal and infant immunisation uptake is not unique to England. The current state of antenatal immunization against pertussis in Europe is focused on protecting neonates and young infants through transfer of vaccine-induced antibodies from the mother to the fetus during pregnancy. The <u>ECDC</u> reports that 24 EU/EEA countries recommend pertussis vaccination for pregnant women to provide immunity to newborns [7]. All EU/EEA countries, apart from Bulgaria, Estonia, Finland, Malta, and Slovakia have a recommendation in place for a booster dose of an acellular pertussis-containing vaccine with reduced antigen content during pregnancy. The recommendation is government-funded in all countries and was also introduced temporarily in Croatia and Hungary, respectively, in areas and during periods of high incidence.

In Finland, the diphtheria-tetanus-pertussis vaccine is also recommended, preferably in late pregnancy [26]. In Norway, new policy changes have been recently implemented, such as offering the pertussis vaccine to pregnant women during the 24-week prenatal check-up starting in May 2024 [27]. Similarly, in Bulgaria, free immunization of pregnant women against pertussis between the 27th and 36th gestational week of pregnancy has been recently approved [28], and the Slovak Republic has also recommended pertussis vaccination for pregnant women [29]. However, data on maternal immunization uptake are limited, with only nine countries reporting antenatal immunisation uptake rates for 2023, which vary widely from 1.6% to 88.5%. According to national data, maternal vaccination coverage in Belgium varies greatly among regions (85% in Flanders, 49% in Wallonia, 37% in Brussels) [30]. This significant variability highlights the need for better data collection and efforts to increase vaccine uptake among pregnant women to effectively prevent pertussis in the most vulnerable age groups.

Conclusion

As cases of pertussis and, in particular, severe disease and death due to pertussis in young infants continue to increase in many countries across Europe and elsewhere, clinicians, immunisers, maternity care providers, public health bodies and policymakers need to work together to improve messaging of the life-saving potential of antenatal vaccinations. They should encourage open and clear discussions to allay any fears and provide reassurance to vaccine-hesitant pregnant women and facilitate access to antenatal vaccines for pregnant women through primary care and maternity services. These measures would ensure women can receive the vaccination at the optimal time to maximise protection for their newborn infants. The

effectiveness of maternal immunisation against pertussis against infant disease in babies under 3 months of age is estimated to be around 90% against laboratory-confirmed disease and 97% against death [31].

Parents must continue their vaccination efforts postpartum, ensuring their infants receive timely protection according to their national childhood vaccination schedules, which typically begin at two to three months of age.

Author contributions

AK and AS conceived the article. All authors reviewed the first draft and contributed to the final draft.

Declaration of Competing Interests

AK is the Vice President for academia and strategy of the RCOG. All authors declare no competing interests.

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Ethical Approval Statement

Not applicable

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Figure. Laboratory confirmed cases of pertussis in England, US and EU/EEA:

January 2018 to March 2024 (2023, 2024 provisional data). Sources: Pertussis

epidemiology in England 2024 - GOV.UK (www.gov.uk) and ECDC Surveillance

Atlas of infectious diseases EU/EEA (ECDC) and Pertussis cases by year-CDC

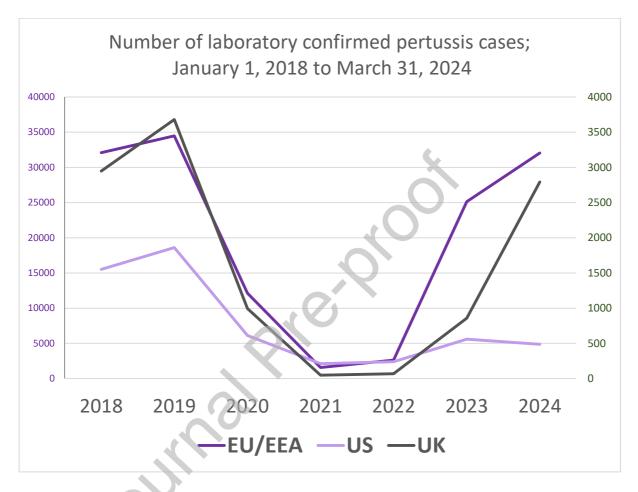


Table: DTP vaccination coverage (%) in EU/EEA countries, Serbia and the UK, from 2018 to 2023 (source WHO), showing the percentage in the target population who have received one dose (DTP1) or 3 doses (DTP3) of the combined diphtheria, tetanus toxoid and pertussis-containing vaccine in a given year. Countries are instructed to report routine immunization coverage using the administrative method (ADMIN), based on registry data of administered doses; only doses incorporated in the national immunization schedule are included. Immunization coverage figures from the administrative system can be biased or inaccurate. OFFICIAL estimates may be based on administrative data, surveys, or other sources. WHO/UNICEF Estimates of National Immunization Coverage (WUENIC).

	Data Source		2023	2022	2021	2020	2019	2018		2023	2022	2021	2020	2019	2018
	ADMIN						V 1	4							
Austria	OFFICIAL			90.84	95.83	95		90.3			83.5	86.36	84.61		84
	WUENIC			91	96	95	93	90			84	86	85	85	
	ADMIN					-									
Belgium	OFFICIAL		98.4	98.4	98.4	98.5	98.5	99.1		97.5	97.5	97.5	97.3	97.3	9
•	WUENIC			98	98	98	98	99			98	98	97	97	
	ADMIN		95.02	93.93	92.37	94.26	95.6	94.5		92.39	91.37	89.48	91.24	92.8	91
Bulgaria			95.02	93.93	92.37	94.26	95.6	94.5		92.39	91.37	89.48	91.24	92.8	9
Duigaria	OFFICIAL		95.02							92.39					9
	WUENIC			94	92	94	96	94		00.05	91	89	91	93	
	ADMIN									92.65	92.04	92.13	93.72	94.41	9
Croatia	OFFICIAL									92.65	92.04	92.13	93.72		9
	WUENIC			98	98	98	98	98			92	92	94	94	
	ADMIN		100	00.15	00 =		00 =	00.5		95	70.00	05.5	05.5	05.5	
Cyprus	OFFICIAL		100	98.43	99.7	99.7	99.7	99.8		95	78.39	95.9	95.9	95.9	9
	WUENIC	4		98	98	98	98	99			96	96	96	96	
	ADMIN		96.26	~							93.74	93.74	96.78	96.69	
Czechia	OFFICIAL		96.26								93.7	93.7		96.69	
	WUENIC (98	98	99	99	99			94	94	97	97	
	ADMIN		97.12	96.8	97.22	96.52	97	97		96.34	95.76	95.83	96.04	96	
Denmark	OFFICIAL		97.72	97.6	97.8	97.1	97	97.2		97.44	97.1	96.9	97.1	97	9
	WUENIC			98	98	97	97	97			97	97	97	97	
	ADMIN		73.04	85.52	91.18	92.26	92.5	93.3		74.59	84.96	89.51	91	91,4	91
F-4!-			73.04	85.5	91.18	92.26	92.5	93.3		74.59	85	89.51	91	91.4	9
Estonia	OFFICIAL		73.4	86	91.16	92.26	92.5	93.3		12	85	90	91	91.4	9
	WUENIC		98	00	91	92	92	93		92	00	90	91	91	
			98	07			00	00.0			04			04	
Finland	OFFICIAL		97	97	98		98	98.6		91	91	89	00	91	
	WUENIC		00.0	97	98	98	98	99		00.0	91	89	90	91	_
_	ADMIN		98.8	98.8	99.2					96.3	96.4	96.4			9
France	OFFICIAL		98.8	98.8	99.2		001	99 99		96.3	96.4	96.4	00	00	9
	WUENIC ADMIN			99	99 98.05	99 98.49	99 98.5	98.5			96	96	96	96	
Germany	OFFICIAL				98.05	98.49	98.5	98.5							
sermany	WUENIC			98	98	98	98	98			91	91	91	91	
	ADMIN	-		- 50	- 50	- 50	- 30	- 50			01	01	٥.	01	
Greece	OFFICIAL		100	100	100	100	100	100				99.5	99.5	99.5	9
dieece	WUENIC		.00	99	99	99	99	99			99	99	99	99	
	ADMIN	-	99.95	99.96	99.97	99.96	99.9	99.9		99.89	99.86	99.85	99.88	99.9	9
Lungary	OFFICIAL		99.95	99.96	33.31	33.30	33.3	33.3		99.89	99.86	33.00	33.00	33.3	3
Hungary	WUENIC		99.90	99.90	99	99	99	99		99.09	99.00	99	99	99	
	ADMIN	-	95.45	95.4	96.66	95.64	94.8	97		92.43	92.16	91.99	93.36	92.55	
Iceland	OFFICIAL		95.45	95.4	96.66	95.64	94.8	97		92.43	92.16	91.99	93.36	92.5	
iceianu	WUENIC		33.43	95	97	96	95	97		32.43	92.10	92	93	92.5	
		_		95	91	90	93	31		90.49	92.69	93.5	94.16	93.46	0.4
tooler 1	ADMIN									89.48					94
Ireland	OFFICIAL	D			00		00		D	89.48	92.69	93.5	94.16	93.5	94
	WUENIC	-1		97	98	98	98	98			93	94	94	94	
	ADMIN	Т				93.65	94.99	95	Т		95.15	93.9	93.65	96	95.
Italy	OFFICIAL	Р				93.65			Р		95.15	93.9	93.65		
	WUENIC			98	94	94	98	95			95	94	94	96	
	ADMIN	1	97.88	99.83	95.93	99.36	98.81	97	3	98.14	95.2	94.41	100.24	99.99	
Latvia	OFFICIAL		97.88	99.83	95.93	99	99	97		98.14	95.2	94.41	100	100	

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