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ORIGINAL RESEARCH

Assessing the Underestimation of Adult Pertussis Disease in Five Latin American Countries

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ABSTRACT

Introduction: Pertussis, a contagious respiratory disease, is underreported in adults. The study objective was to quantify underestimation of pertussis cases in adults aged ≥ 50 years in five Latin American countries (Argentina, Brazil, Chile, Mexico, Peru).

Methods: A previously published probabilistic model was adapted to adjust the number of pertussis cases reported to national surveillance systems by successive multiplication steps (proportion of pertussis cases seeking healthcare; proportion with a specimen collected; proportion sent for confirmatory testing; proportion positive for pertussis; proportion reported to passive surveillance). The proportions at each step were added in a random effects model to produce a pooled overall proportion, and a final multiplier was calculated as the simple inverse of this proportion. This multiplier was applied to the number of cases reported to surveillance to estimate the number of pertussis cases. Monte Carlo simulation with 10,000 iterations estimated median as well as upper and lower 90% values. Input data were obtained from surveillance systems and published sources.

Results: The estimated median underestimation factor for pertussis cases in adults ranged from 104 (90% limits 40, 451) in Chile to 114 (90% limits 39, 419) in Argentina. In all five countries, the largest estimated number of cases was in the group aged 50–59 years. The highest number per 100,000 population was in the group aged ≥ 90 years in most countries. The estimated median underestimation factor for pertussis hospitalizations was 2.3 (90% limits 1.8, 3.3) in Brazil and 2.4 (90% limits 1.8, 3.2) in Chile (data not available for other countries).

Conclusion: This analysis indicates that the number of pertussis cases in adults aged ≥ 50 years in five Latin American countries is approximately 100 times higher than the number captured in surveillance data. These

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results could support decision-making in the diagnosis, management, and prevention of pertussis disease in adults.

PLAIN LANGUAGE SUMMARY

Pertussis, also called whooping cough, is an infectious respiratory disease that can be severe in infants and older adults, and can cause complications in people with other conditions such as chronic obstructive pulmonary disease and asthma. Although it is compulsory to report cases of pertussis infection in many countries, it is known that many pertussis cases in adults are not captured (underreported). The aim of this study was to measure pertussis underestimation in adults aged 50 years or over in five Latin American countries (Argentina, Brazil, Chile, Mexico, Peru). There are several steps to identify a pertussis case (seeking medical care; specimen collected for testing; specimen sent for testing; pertussis confirmed by testing; case reported), and at each step there is potential for underestimation. These steps were combined in a model to calculate a multiplication factor to estimate the real burden of pertussis. The results showed that the estimated number of pertussis cases in adults aged 50 years or over in five Latin American countries is approximately 100 times higher than the number reported. These results show that pertussis is common in older adults, and should help to support health authorities and doctors making decisions about the management of pertussis disease.

Keywords: Adults; Argentina; Brazil; Epidemiology; Latin America; Mexico; Pertussis; Underascertainment; Underestimation; Underreporting

Key Summary Points

Why carry out this study?

Pertussis is a highly contagious respiratory illness. Current disease surveillance systems underreport the potential number of cases, especially in adolescents and adults.

What was learned from the study?

The aims of this study were to quantify the underestimation of pertussis in adults aged 50 years or over in Latin American countries (Argentina, Brazil, Chile, Mexico, Peru), and to estimate a multiplier factor to assess the potential burden of pertussis disease in this age group.

The estimated number of pertussis cases in adults aged 50 years or over was a median of 104 (90% limits 40–451) to 114 (90% limits 39–419) times the number of cases reported to surveillance systems in five Latin American countries.

These results highlight the substantial disease burden of pertussis in older adults, and should help to support decision-making in the management of pertussis disease.

INTRODUCTION

Pertussis, also known as whooping cough, is an acute respiratory illness characterized by a distinctive cough. Most cases (86–95%) are caused by infection with the Gram-negative bacterium *Bordetella pertussis*, with some cases, usually milder, caused by *Bordetella parapertussis* [1]. Pertussis is highly contagious, and in an immune-naïve population one primary case has been estimated to cause a mean of 17 secondary cases [2], similar to measles and higher than mumps, rubella, poliomyelitis, smallpox, or influenza [3]. In newborns and young infants, pertussis can be a severe illness requiring hospitalization and intensive care, and the case

fatality rate of pertussis in newborns has been estimated at 1–3% [1]. While most current vaccination programs focus on preventing pertussis in infants, the epidemiology of pertussis has shifted towards older age groups such as adolescents and adults [4]. Approximately 20% of pertussis cases are estimated to occur in adolescents aged 10–19 years and 25% in adults aged 20 years or over in the USA [1]. A study in five European countries (Finland, Germany, Italy, the Netherlands, and UK) estimated pertussis incidence at 1–6% per year, with a peak in adolescents and a second peak in young adults [4].

The clinical presentation of pertussis changes with age, with data suggesting that adults are at increased risk of complications and severe disease requiring hospitalization from pertussis, compared with adolescents [5, 6]. Pertussis can lead to complications linked directly to bacterial infection or as a consequence of the cough associated with pertussis. After children, adults aged ≥ 50 years are most at risk of complications from pertussis; in a study in Canada, 6% of patients aged ≥ 50 years were hospitalized [6]. In this study of pertussis morbidity in Canada ($N = 664$), the proportion of cases with at least one complication was higher in adults (aged ≥ 18 years) than in adolescents (aged 12–17 years) (28% vs 16%, respectively; $P < 0.001$), with reported complications including pneumonia, sinusitis, otitis media, urinary incontinence, weight loss, rib fracture, and fainting [6]. In a review of 18 publications, adults and adolescents with conditions such as chronic obstructive pulmonary disease (COPD), asthma, and obesity were found to be at potentially increased risk of being diagnosed with pertussis [7]. Asthma, COPD, immune deficiency, and smoking were associated with worse pertussis symptoms and increased risk of hospitalization for pertussis-related complications [7].

The incidence of pertussis in adults and older adults, based on serological studies and estimates of the fraction of medically attended cough illness attributable to pertussis, is estimated to be substantially higher than reported in surveillance data, meaning the true burden of disease among older adults is underestimated [8, 9]. Several successive steps are required to identify a pertussis case, as illustrated schematically in Fig. 1. Starting with the total number of cases at the bottom of the pyramid, a fraction are symptomatic, a further fraction of symptomatic cases attend healthcare, a further fraction of those attending healthcare receive a confirmed pertussis diagnosis, and finally a fraction of those with confirmed pertussis diagnosis are reported to surveillance systems. At each step, there is potential for underestimation and many factors can affect the fraction retained at each level, such as perceived severity of symptoms, limited access to healthcare, lack of awareness of pertussis disease, limitations in routine diagnostic capability and limitations in reporting systems [10]. The clinical features of pertussis may be mild or atypical in adults, often without the characteristic whoop [11]. Limitations in timing and specificity of diagnostic tests make laboratory confirmation challenging, and late presentation to healthcare professionals among adults may also contribute to underdiagnosis [12, 13]. The underestimation of pertussis disease in adults can occur at two levels: underascertainment and underreporting. Underascertainment is used to cover cases that do not seek healthcare, and underreporting to cover cases that have sought healthcare but not been reported to surveillance (Fig. 1), although definitions vary [10]. In this study, underestimation is used to describe the fraction of pertussis cases not captured by

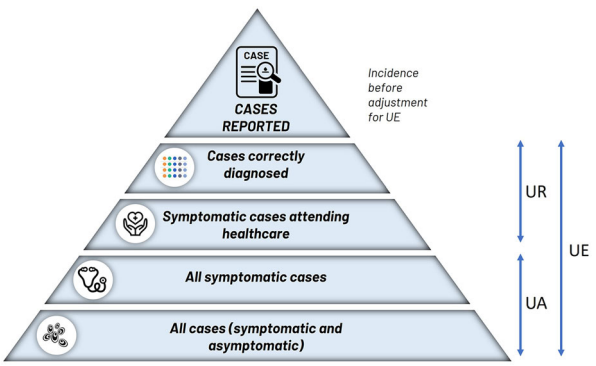

Fig. 1 Schematic illustration of underreporting and underestimation of infectious disease burden. Adapted from Gibbons et al. [10]. *UA* underascertainment, *UE* underestimation, *UR* underreporting

surveillance systems, and includes both underascertainment and underreporting.

It is important to understand the burden of pertussis in adolescents and adults. Many countries have surveillance systems in place that rely on statutory clinical notification of cases and laboratory reports [14]. However, underestimation of disease burden is a recognized problem in surveillance systems, particularly for infectious diseases [10]. A systematic literature review assessing the burden of pertussis in Latin American countries (Argentina, Brazil, Chile, Colombia, Mexico, Panama, and Uruguay) highlighted the limited epidemiological data available in adolescents, adults, and older adults as well as the need for standardized diagnostic tools and improvement of surveillance systems [15].

The objective of this study was to quantify the underestimation of pertussis in adults aged 50 years and over in five Latin American countries (Argentina, Brazil, Chile, Mexico, Peru), by quantifying an underestimation multiplier factor that can be applied to surveillance results to estimate the potential number of pertussis cases in older adults in these countries.

METHODS

Model

We adapted a published model used previously to estimate the number of people infected with pandemic H1N1 influenza in 2009 [16] and acute viral hepatitis in 2011 [17] in the USA. This model was considered applicable to pertussis because viral hepatitis and influenza share some similar surveillance challenges with pertussis. These similarities include many infections being atypical and/or asymptomatic; not all sick people seek healthcare; specimens sometimes produce false results; and not all cases are reported to health departments.

The model was a simple probabilistic multiplier model that aimed to estimate the fraction of adult patients aged 50 years or over with pertussis who would have been diagnosed and reported to surveillance systems in five countries in Latin America (Argentina, Brazil, Chile, Mexico and Peru). Briefly, the model adjusted the number of pertussis cases reported to surveillance systems in each country by successive multiplication steps, as outlined in Fig. 2. These steps described the proportion of pertussis cases who would seek medical care, the proportion of those who had a specimen collected, the proportion of collected specimens sent for confirmatory testing, the proportion of tests positive for pertussis, and the proportion of positive tests reported to passive surveillance systems.

The proportions at each step were added in a random effects model to produce a pooled overall proportion, and a final multiplier was calculated as the simple inverse of this proportion. This multiplier was then applied to the number of cases reported to each national surveillance system to derive an estimate of the potential number and incidence of pertussis cases in each country.

To account for variability and uncertainty in the model parameters, a probabilistic approach using Monte Carlo simulation was applied. For each parameter, the model randomly sampled a value using a uniform probability distribution covering a range of minimum to maximum

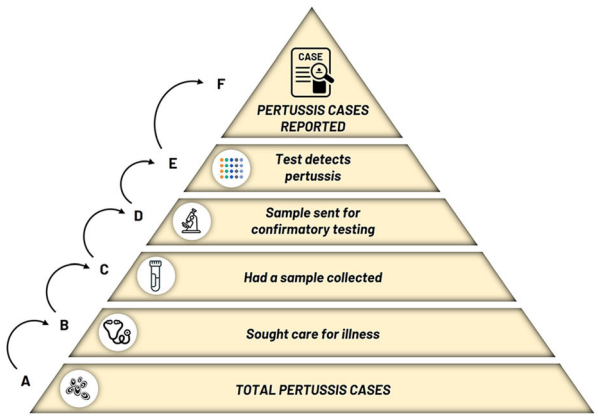

Fig. 2 Steps in the estimation of total pertussis cases in adults aged 50 years or over in Latin America. Step A, proportion of patients with pertussis attending healthcare; step B, proportion of patients seeking care with a sample collected; step C, proportion of samples collected that are sent for testing; step D, proportion of tests that detect pertussis; step E, proportion of cases confirmed by positive test reported to surveillance

Table 1 Population data for each country in 2020 [18]

Age group	Argentina	Brazil	Chile	Mexico	Peru
Total aged 50 years or over	11,445,858	54,278,642	5,674,905	27,030,922	7,438,231
50–59 years	4,424,940	24,421,202	2,352,271	12,757,971	3,313,879
60–69 years	3,528,742	16,896,862	1,791,787	8,264,953	2,276,639
70–79 years	2,300,637	8,801,551	993,126	4,188,713	1,255,409
80–89 years	999,369	3,492,448	436,406	1,668,488	519,922
90 years or over	192,170	666,579	101,315	150,797	72,382

values. Results from 10,000 iterations were used to estimate median as well as upper and lower 90% values for the estimated number of cases.

To produce estimated case numbers for five age groups (50–59, 60–69, 70–79, 80–89, and 90 years or over), the estimated total case numbers were divided according to published data on the age distribution of pertussis in older adults.

Input Data

The size of the population aged 50 years or over, stratified into five age groups (50–59, 60–69, 70–79, 80–89, and 90 years or over), in each country in 2020 was obtained from United Nations estimates [18] (Table 1).

Data on the number of pertussis cases in adults aged 50 years or over reported to national surveillance systems during the period from 1 January 2017 to 31 December 2021 were obtained from the national health ministries in Argentina [19], Brazil [20], Chile [21], Mexico [22], and Peru [23] (Table 2). Data on the number of pertussis hospitalizations reported over the same period for this age group were available only for Brazil [24] and Chile. The hospitalization data for Chile were obtained directly from the Ministry of Health (Ministerio de Salud [MINSAL], Chile. Unidad de Transparencia. Solicitud de Acceso a la Información Pública—Ley de Transparencia. Folio N AO001T0019380. Received 17 May 2023). The final surveillance data for Argentina were obtained through a request to the Ministry of

Table 2 Number of pertussis cases in patients aged 50 years or over reported to national surveillance systems in each country, from 1 January 2017 to 31 December 2021 [19–24]

	Argentina[a]	Brazil	Chile	Mexico	Peru
Number of cases	2[b]	243	408	36	12
Number of hospitalizations	NA	44	247[c]	NA	NA

NA not available

[a]Source: Request to Ministry of Health through Public Data Transparency Laws. Reference number EX2023-28921934-APN-DNPAIP#AAIP

[b]The final surveillance data from Argentina comprised 2 hospitalizations (one from 2017 and one from 2018) and 0 cases reported for the total study period. It is not feasible to run the model with a data input of 0, so the model for Argentina was run using the 2 hospitalized cases as a minimum proxy for ambulatory cases. It was not possible to run the hospitalization model for Argentina because of the limited data

[c]Source: Ministerio de Salud (MINSAL), Chile. Unidad de Transparencia. Solicitud de Acceso a la Informacion Publica—Ley de Transparencia. Folio N AO001T0019380. Received 17 May 2023

Health through Public Data Transparency Laws (Reference number EX2023-28921934-APN-DNPAIP#AAIP), and comprised two hospitalizations (one from 2017 and one from 2018) and zero cases reported for the total study period. It is not feasible to run the model with a data input of zero, so the model for Argentina was run using the two hospitalized cases as a minimum proxy for ambulatory cases. It was not possible to run the hospitalization model for Argentina because of the limited data.

The model was capable of producing results for two distinct periods, 1 January 2017 to 31 December 2019 and 1 January 2020 to 31 December 2021, to allow the option of analyzing the coronavirus disease 2019 (COVID-19) pandemic period separately. However, as the available surveillance data were limited, the model was run for the total time period.

The age distribution of pertussis in adults aged 50 years or over was adapted from a study in England [25] (Table 3). The age distribution for pertussis hospitalizations was adapted from a separate published study in Australia [26] (Table 3). The same age distributions for cases and hospitalizations were applied for all countries in the study.

Table 3 Age distribution of pertussis cases and hospitalizations in adults aged 50 years or over

Age group (years)	Number in publication	Calculated percentage
Cases (adapted from [25])		
50–59	855	52%
60–69	483	29%
70–79	231	14%
80–89	42	3%
90 or over	27	2%
Total	1638	100%
Hospitalizations (adapted from [26])		
50–59	11 (age 45–54 years)	11%
60–69	21 (age 55–64 years)	21%
70–79	28 (age 65–74 years)	27%
80–89	21 (age 75 years or over)	21%
90 or over	21 (age 75 years or over)	21%
Total	102	100%

Minimum and maximum values for the input data for parameters of pertussis disease at each of the steps in Fig. 2, for non-hospitalized and hospitalized pertussis cases, were obtained from published literature [9, 27, 28] and a Delphi panel consensus with experts in Brazil [29] (Table 4). The same parameter ranges were used in all countries in the study.

Statement of Ethics Compliance

Ethics approval was not required as this study was based on published data and therefore did not involve human participants. Data for Chile and Argentina were obtained via Public Data Transparency Laws. All the disease data were extracted from publicly accessible surveillance system databases which report aggregated anonymized data.

RESULTS

Estimated Multipliers

Table 5 shows the estimated median multiplier factors, together with upper and lower 90% limits, for pertussis cases in all five countries and for pertussis hospitalizations in Brazil and Chile. The estimated median multiplier for pertussis cases ranged from 104 (90% limits 40, 451) in Chile to 114 (90% limits 39, 419) in Argentina. The multiplier values were similar across all countries studied, because the same pertussis input data were used across all countries. The variability in the multiplier was derived from the probabilistic model. The multiplier values indicate that every pertussis case reported to national surveillance systems in adults aged 50 years or over represents approximately 100 cases that are not captured by surveillance. For hospitalizations in Brazil and Chile, the estimated multipliers were much

Table 4 Pertussis parameter estimates

Parameter	Non-hospitalized cases			Hospitalized cases		
	Minimum	Maximum	Source	Minimum	Maximum	Source
Proportion of patients with pertussis attending healthcare (step A)	9%	50%	8.89% [27] 25–50% [9, 28]	95%	100%	Assumption. Patients with severe symptoms typically present to hospital or transfer from outpatient to inpatient
Proportion of patients seeking care with a sample collected (step B)	1%	10%	Delphi panel in Brazil	40%	75%	[16]
Proportion of samples collected that are sent for testing (step C)	70%	100%	Assumption. Based on Delphi panel and expert opinion	90%	100%	Assumption. Based on Delphi panel and expert opinion
Proportion of tests that detect pertussis (step D)	80%	90%	Assumption. Tests would include culture or polymerase chain reaction	80%	90%	Assumption. Tests would include culture or polymerase chain reaction [9]
Proportion of cases confirmed by positive test reported to surveillance (step E)	90%	95%	Assumption. Pertussis is a mandatory notifiable disease in all countries studied, so this should approach 100%	90%	95%	Assumption. Pertussis is a mandatory notifiable disease in all countries studied, so this should approach 100%

Steps A–E refer to Fig. 2

smaller (in Brazil, median 2.3, lower and upper 90% limits 1.8, 3.3; in Chile, median 2.4, lower and upper 90% limits 1.8, 3.2).

Estimated Pertussis Case and Hospitalization Numbers

The estimated median and 90% limits of pertussis cases by age in each country are shown in Table 6, and the estimated median numbers of

Table 5 Multiplier estimates by country

Country	Multiplier[a]		
	Median	90% limits	
		Lower	Upper
Cases			
Argentina	114	39	419
Brazil	107	40	475
Chile	104	40	451
Mexico	111	39	482
Peru	113	41	475
Hospitalizations[b]			
Brazil	2.3	1.8	3.3
Chile	2.4	1.8	3.2

[a]Based on reported cases for all countries for the time period from 1 January 2017 to 31 December 2021
[b]Hospitalization surveillance data were available only for Brazil and Chile

pertussis cases per 100,000 population are shown in Table 6 and Fig. 3. The highest estimated number of cases per 100,000 population was in Chile (Fig. 3). In all the countries, the largest estimated number of cases was in the group aged 50–59 years (Table 6). In all countries except Chile and Argentina, the highest number per 100,000 population was in the oldest age group, aged 90 years or over (Fig. 3, Table 6).

The estimated median number and 90% limits for pertussis hospitalizations in Brazil and Chile are shown in Table 6. Hospitalization data were not available for the other countries. The age group with the highest number of hospitalizations was the group aged 70–79 years. The highest number of hospitalizations per 100,000 population occurred in the group aged 90 years or over (Table 6), which would be consistent with declining immunity to infection resulting from immunosenescence, frailty, and presence of comorbidities.

DISCUSSION

Although pertussis is a mandatory notifiable disease regardless of age in all countries in this study [30–34], many cases in adults are not captured by surveillance systems. This issue of underestimation is also recognized in other countries. For example, a community cohort study in healthy people in South Africa estimated the incidence of pertussis at 0.21 per 100 person-weeks, higher than the previously reported mean annual incidence of 17 per 100,000 population in patients hospitalized for pneumonia [35]. To our knowledge, this is the first study in Latin America to estimate the underestimation rate for pertussis in adults aged 50 years or over based on a probabilistic model using data from literature and national surveillance systems. Our results indicated that the number of pertussis cases in these countries is approximately 104–114 times higher than the number reported to national surveillance systems. The 90% limits around the estimated median values were broad, with a lower limit of 39 to 41 and an upper limit of 419 to 482, reflecting some uncertainty in some of the input values for the pertussis parameters in the model. For pertussis hospitalizations, the median estimated multipliers were smaller and had narrower 90% limits (in Brazil, median 2.3, lower and upper 90% limits 1.8, 3.3; in Chile, median 2.4, lower and upper 90% limits 1.8, 3.2). This is because the data inputs used for the proportion seeking healthcare and the proportions with a specimen collected and sent for testing were higher and less variable in patients hospitalized for pertussis disease, compared with non-hospitalized cases. The median multiplier estimates were similar for all five countries, because the same pertussis input data were used across all countries, and the variability in the multipliers was derived from the probabilistic model. If the study had used different input data values for each country, it is likely that the multipliers would also have differed between the countries. We were not able to use country-specific input data because of a lack of available information. The limited real-world surveillance data available for pertussis cases in

Table 6 Estimated pertussis cases and hospitalizations (median and 90% limits) by age group and country, total number, and per 100,000 population for the period from 1 January 2017 to 31 December 2021

	Total number			Per 100,000 population		
	Median	Lower 90% limit	Upper 90% limit	Median	Lower 90% limit	Upper 90% limit
Cases						
Argentina						
Total	227	79	838	2	1	7
50–59 years	118	41	436	3	1	10
60–69 years	66	23	243	2	1	7
70–79 years	32	11	117	1	0	5
80–89 years	7	2	25	1	0	3
90 years or over	5	2	17	2	1	9
Brazil						
Total	21,457	8171	94,692	40	15	174
50–59 years	11,157	4249	49,240	46	17	202
60–69 years	6222	2370	27,461	37	14	163
70–79 years	3004	1144	13,257	34	13	151
80–89 years	644	245	2841	18	7	81
90 years or over	429	163	1894	64	25	284
Chile						
Total	17,487	6965	73,234	308	123	1290
50–59 years	9093	3622	38,082	387	154	1619
60–69 years	5071	2020	21,238	283	113	1185
70–79 years	2448	975	10,253	247	98	1032
80–89 years	525	209	2197	120	48	503
90 years or over	350	139	1465	345	138	1446
Mexico						
Total	3970	1407	17,350	15	5	64
50–59 years	2064	732	9022	16	6	71
60–69 years	1151	408	5032	14	5	61
70–79 years	556	197	2429	13	5	58
80–89 years	119	42	521	7	3	31
90 years or over	79	28	347	53	19	230
Peru						

Table 6 continued

	Total number			Per 100,000 population		
	Median	Lower 90% limit	Upper 90% limit	Median	Lower 90% limit	Upper 90% limit
Total	1359	486	5699	18	7	77
50–59 years	707	253	2963	21	8	89
60–69 years	394	141	1653	17	6	73
70–79 years	190	68	798	15	5	64
80–89 years	41	15	171	8	3	33
90 years or over	27	10	114	38	13	157
Hospitalizations						
Brazil						
Total	102	78	143	0.2	0.1	0.3
50–59 years	11	8	15	0	0	0.1
60–69 years	21	16	29	0.1	0.1	0.2
70–79 years	28	21	39	0.3	0.2	0.4
80–89 years	21	16	29	0.6	0.5	0.8
90 years or over	21	16	29	3.2	2.4	4.4
Chile						
Total	573	442	801	10.1	7.8	14.1
50–59 years	62	48	86	2.6	2.0	3.7
60–69 years	118	91	165	6.6	5.1	9.2
70–79 years	157	121	220	15.8	12.2	22.1
80–89 years	118	91	165	27.1	20.8	37.8
90 years or over	118	91	165	116.5	89.7	162.8

adults in the selected countries might suggest differences in the multipliers between the countries. However, considering the scarcity of parameter data for pertussis in adults, we standardized the input data in the present simplistic model, resulting in little difference between the resulting country multipliers. The results aim to serve as baseline data that can be used in sensitivity analyses in further modelling studies. Even with the small multiplier range, our results provide a baseline estimate for specific country pertussis incidence, adjusted to country-specific population and surveillance data stratified by age group.

Our results are broadly consistent with previous studies in Europe and Israel that have also estimated pertussis reporting rates to be hundreds of times lower than the number of infections estimated from serological data. In Israel, the incidence of pertussis infection in 2000, estimated from serology, was 2448 per 100,000 population aged 3 years or over, compared with 5.6 per 100,000 for reported pertussis cases in the same year, indicating an incidence of infection approximately 400 times higher than

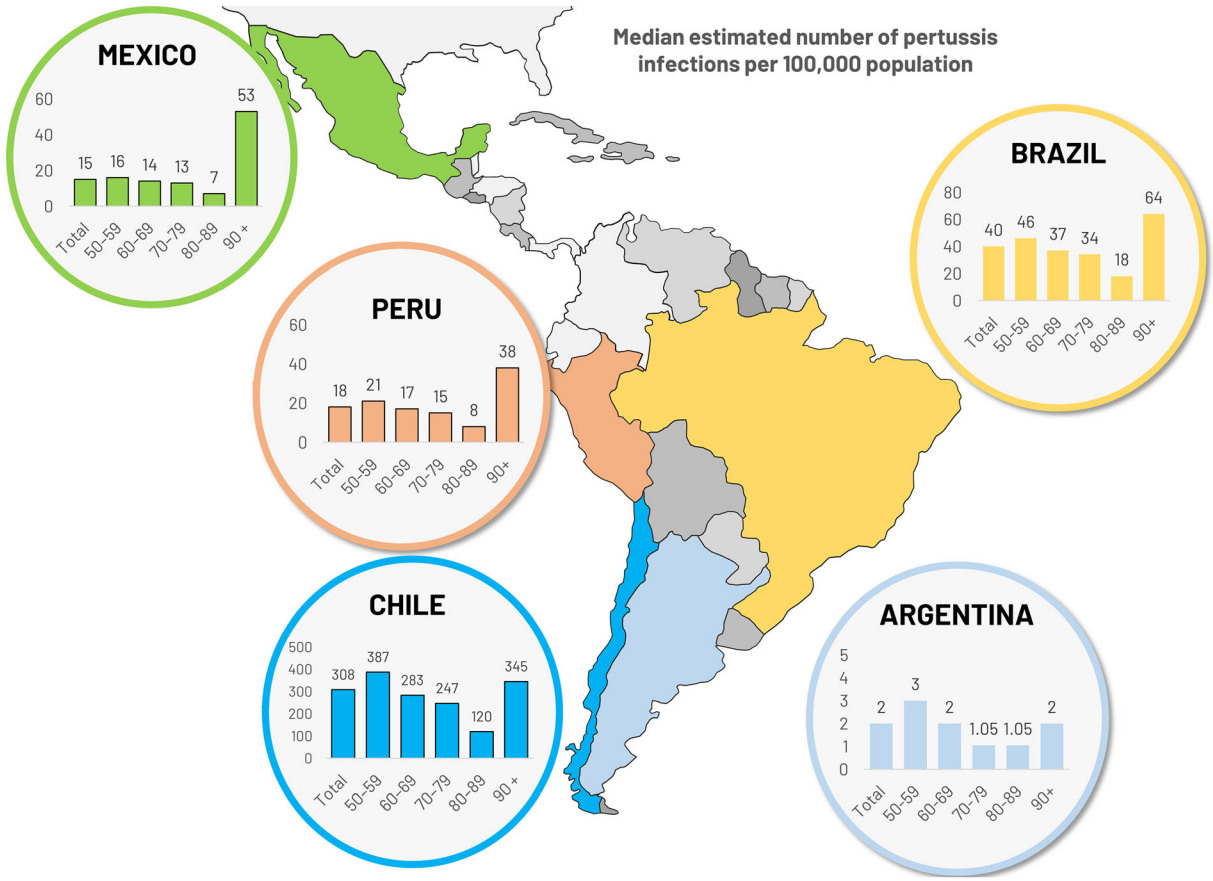

Fig. 3 Median estimated number of pertussis cases per 100,000 population by age group for each country

the incidence of notified clinical pertussis cases [36]. In the Netherlands, pertussis incidence estimated by serology was 6.6% per year for people aged 3–79 years, approximately 685 times higher than the 0.01% annual incidence of notified cases [37]. Our estimated median case numbers of approximately 100 times higher than reported data are somewhat lower than the results from these studies, but the 90% upper limit of our estimates (419 to 482) is similar to the value reported in the Israeli study [36]. Our results are also broadly consistent with a study in the USA that estimated undiagnosed pertussis cases in adolescents and adults with reported acute respiratory disease using clinician notes in an electronic health record database, using a machine learning algorithm [38]. This US study found that accounting for undiagnosed pertussis episodes increased the estimated pertussis incidence by 110-fold on average [38]. This estimate is very similar to our median estimated multiplier of 104–114.

There is a consensus that reported pertussis cases are likely to be considerably lower than the real number of pertussis cases [39]. Underreporting is a particular problem in older age groups, as the only symptom in adults and adolescents may be prolonged cough, for which patients may present late or not at all, and which may be misdiagnosed if clinicians perceive pertussis as a childhood disease [39]. In Italy, the estimated incidence of pertussis based on seroprevalence data in the population aged ≥ 15 years was 3464 times higher than the rate of notified pertussis cases in 2018, while in the population aged 6–14 years the estimated incidence from seroprevalence was 141 times the notification rate [40]. A study in the Netherlands reported a remarkable difference in the age distribution for notified pertussis cases

compared with infection rates estimated from serological data [37]. The incidence of notified cases was highest in infants (77.2 per 100,000 in the first year of life) and young children (87.4 per 100,000 in children aged 3–4 years and 63.1 per 100,000 in children aged 5–9 years), decreasing sharply to around 1–3 per 100,000 in adults aged 20 years or over. By contrast, the estimated incidence was lowest in children aged 3–4 years (3299 per 100,000), reached a peak in young adults aged 20–24 years (10,831 per 100,000), and fluctuated around 6,500 per 100,000 in adults aged 25–54 years and around 4000 per 100,000 in adults aged 55 years or over [37].

The number of pertussis cases per 100,000 population estimated in this study varied between countries, with the highest estimates in Chile. This reflects the higher number of pertussis surveillance reports in Chile, which results in a larger number of cases as the multiplier is similar as a result of a lack of country-specific data for the pertussis inputs in the model. The present study was not intended to make comparisons between the countries. It illustrates the potential magnitude of underestimation of pertussis, and there is considerable uncertainty in the estimates, as indicated by the broad 90% limits around the median values. In a study comparing the number of isolates of invasive pneumococcal disease reported to surveillance with the expected number of cases based on regional disease incidence data, Chile had the highest rate of reporting (43–83%) of the six Latin American countries in the study [41]. Other researchers have reported wide variations in pertussis prevalence between countries; in a study in 12 European countries conducted in 2007–2010, the percentage of adult patients presenting to primary care with acute cough who were found to have *B. pertussis* ranged from 0% in Italy to 6.2% in Sweden [42]. A review of the literature reported rates of pertussis underreporting varying from 5 to 50% in Brazil, Colombia, Spain, and the USA, and in the Netherlands a multiplier factor of 3 for infants and 200 for adults [43]. However, comparison of pertussis incidence between countries is difficult because of factors such as differences in case definitions, diagnosis methods, and reporting systems [39]. Open-source data may provide useful information on pertussis outbreaks globally, especially in countries that lack national surveillance systems [44]. Most studies of the cost-effectiveness of pertussis vaccination in adolescents and adults attempt to take account of underreporting of pertussis cases in these age groups. For example, a review of 27 economic evaluations of vaccination strategies for tetanus–diphtheria–acellular pertussis vaccine (Tdap) in a range of countries found that 18 of the 20 studies that considered adult or adolescent pertussis incidence used some strategy to correct for pertussis underreporting [45].

In most of the countries in the study, the highest number of pertussis cases per 100,000 population was in the oldest age group, aged 90 years or over. The data in Table 1 indicate that the five countries in the study have slightly different population structures, with the percentage of people in the group aged 50–59 years highest in Brazil (45%), Mexico (47%), and Peru (45%). This may indicate a potential future increase in the burden of pertussis in these countries as this group reaches older ages.

The present study has a number of strengths. It used an established model developed by the Centers for Disease Control and Prevention which has previously been applied to influenza [16] and hepatitis [17]. Furthermore, it provides a simplified way to visualize and quantify pertussis underestimation in older adults in Latin America. This should help to increase awareness of the health burden of pertussis in adults among health officials and clinicians, helping to support surveillance and prevention activities.

Nevertheless, the study has a number of limitations. Data for hospitalizations were available for only two countries, Brazil and Chile, and therefore the estimated multiplier for hospitalizations was based only on these two countries as there were no others to construct the probabilistic model. Further data on hospitalizations from other countries would improve the analysis, if such data become available in the future. Surveillance data from Argentina were also limited, with a total of two hospitalizations (one from 2017 and one from 2018)

and zero cases reported across the whole study period. It is not feasible to run the model with a data input of zero, so the model for Argentina was run using the two hospitalized cases as a minimum proxy for ambulatory cases. With these very small numbers, it is possible that even the predicted cases could have a degree of underestimation. The study collected data from 1 January 2017 to 31 December 2021, and this included the period of the COVID-19 pandemic, which could have affected data collection. We constructed the model with the ability to split the analysis into two separate periods, 1 January 2017 to 31 December 2019 and 1 January 2020 to 31 December 2021, so that the COVID-19 pandemic period could be excluded if necessary. However, there was little difference in surveillance results between the two periods, so results are presented across the whole study duration. The analysis involved several assumptions, and data for parameter estimates were sparse, indirect and sometimes limited in geographical scope. Few studies have assessed underestimation in adults with pertussis. In Latin America, we identified only one published source with an estimate of the frequency of healthcare-seeking among adults with pertussis [27], and one reporting results from a Delphi panel [29]. Both these publications were from Brazil, reflecting its position as the largest country in the region. The issues with pertussis diagnosis and testing in adults are similar across all countries in Latin America, so it is likely that data from Brazil will be applicable to other countries in the region. For other inputs, we had to use data from countries outside Latin America, which may not be representative of the countries in the analysis. To account for some of this uncertainty, we used a probabilistic model with a range of values for each parameter. In addition, the case definition of pertussis may have varied between the studies from which parameter values were obtained, and since adults with milder illness may be less likely to seek care or be tested, they may not be fully captured in these estimates. Furthermore, we did not evaluate variability or uncertainty in the model parameters using sensitivity analysis. If more accurate and detailed parameter data become available in the future from surveys of health-seeking behavior, testing practices and policies, this would help to improve the estimates in this study. In the meantime, the estimates presented here should help to support decision-making for the management of pertussis in older adults in Latin America.

CONCLUSION

This analysis investigated the underestimation of pertussis in adults aged 50 years or over in five countries in Latin America, adapting a previously published probabilistic model and data from surveillance systems and the literature. Our results suggest that the number of pertussis cases in adults aged 50 years or over may be approximately 100 times higher than the numbers captured by surveillance systems. These results highlight the substantial disease burden of pertussis in older adults and should help to support decision-making in the management of pertussis disease.

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Data Availability. The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Conflict of Interest. Adriana Guzman-Holst, Jorge A Gomez, Otavio Cintra, Desirée Van Oorschot, Nicolas Jamet and Javier Nieto-Guevara are employees of GSK. Adriana Guzman-Holst, Jorge A Gomez, Otavio Cintra, Desirée Van Oorschot and Javier Nieto-Guevara hold shares in GSK. All authors declare no other financial or non-financial relationships and activities and no other conflicts of interest.

Ethical Approval. Ethics approval was not required as this study was based on published data and therefore did not involve human participants. Data for Chile and Argentina were obtained via Public Data Transparency Laws. All the disease data were extracted from publicly accessible surveillance system databases which report aggregated anonymized data.

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