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ORIGINAL RESEARCH

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Herd immunity in older adults from a middle-income country: A time-series trend analysis of community-acquired pneumonia mortality 2003–2017

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Abstract

Background and Aims: Community-acquired pneumonia is responsible for substantial mortality, and pneumococcus is commonly accepted as a major cause of pneumonia, regardless of laboratory confirmation. Child immunization programs have reported success in decreasing pneumonia mortality: directly in young children and indirectly (herd immunity) in unvaccinated adult populations in some countries. We assess changes in mortality trends for all-cause pneumonia in older adults associated with the introduction of pneumococcal vaccination for children in Peru.

Methods: This is a secondary analysis on administrative data collected periodically by the Peruvian Ministry of Health. An observational retrospective time series analysis was conducted using longitudinal population-based data from death certificates in Peru between 2003 and 2017. The time series includes 6 years before and 9 years after the introduction of the pneumococcal-conjugated vaccines in the national child immunization program in 2009. Monthly frequencies and annual rates for all-cause pneumonia deaths in children under 5 years of age and adults over 65 years of age are presented. Linear and quadratic trends are analyzed.

Results: Deaths among older adults accounted for 75.6% of all-cause pneumonia mortality in Peru, with 94.4% of these reporting "pneumonia due to unspecified organism" as the underlying cause of death. Comparing pre- and post-child immunization program periods, annual average mortality rates from unspecified pneumonia decreased by 22.7% in young children but increased by 19.6% in older adults. A linear trend model supports this overall tendency, but a quadratic curve explains the data better.

Conclusion: Pneumococcal-conjugated vaccines are developed using serotypes prevalent in selected countries from less common (invasive) pneumococcal disease and expected to prevent mortality worldwide from widespread (noninvasive) pneumonia. Our results do not support the presence of herd immunity from pneumococcal vaccination of children for community-acquired pneumonia in the

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increasingly ageing population of Peru. This should direct future research and could influence public health policy.

KEYWORDS
aged population, mortality, Peru, pneumonia, pneumococcus-conjugated vaccine

1 | INTRODUCTION

Acute respiratory infections caused by viruses, bacteria, fungi, or a combination of these represent a high demand for health services worldwide, especially in children under 5 years of age[1] and people over 60 years of age.[2] Pneumonia, an acute infection of the lower respiratory tract, is a major cause for long-term complications and death, ranking among the 10 leading causes of death and being the most common cause of death due to an infectious disease in the United States.[3] Pneumonia in older adults has higher morbidity and mortality than in younger populations,[4] probably due to underlying comorbid conditions common in this age group that affect the etiology and the outcome of pneumonia episodes.[5] Community-acquired pneumonia (CAP) is caused by an acute infection acquired outside of a hospital setting,[6] in persons who have not been hospitalized recently and have not had regular exposure to the healthcare system.[7] Incidence, fatality, and likelihood of hospitalization for CAP increases with age,[8] and the annual incidence of CAP is higher among older (65–79 years of age) adults and highest among the oldest (over 80 years of age) adults.[9] CAP mortality rates are usually low in outpatients, but reach between 10% and 25% for hospitalized patients,[10] and those who died are older with more chronic comorbidities.[11]

There is some geographic distribution for CAP. In the United States, nearly one million older adults are hospitalized for CAP every year and over a third of these die within 1 year.[12,13] Similarly, CAP incidence rates were highest in participants over 65 years of age and the overall 1-year mortality was 24.9% in three cities in South America.[14] CAP incidence varies widely by country in Europe (case-fatality rate: <1%–48%), increases with age, and is higher in men.[15] In general, CAP mortality rates are higher in Central and Eastern European countries, compared to those reported by Western European Union countries.[8] Outside of recent COVID-19 studies, we are not aware of any CAP study in older populations in Peru.

Etiology is important for prevention and treatment of pneumonia. Historically, *Streptococcus pneumonie* (pneumococcus) has been proclaimed as the most important global cause of pneumonia, but in the United States the frequency with which pneumococcus is implicated as a cause of CAP has declined from 95% in the era before antibiotics, to 10%–15% of inpatient cases.[7] Currently, proving the pneumococcal etiology of pneumonia is difficult and isolation of pneumococcus occurs only in a minority of pneumococcal pneumonia cases.[16] A multicenter study in the United States reported 62% had "no pathogen detected" among 2259 hospitalized CAP patients (median age: 57 years). In this study, *S. pneumoniae* was present in only 5% of pneumonia patients and was not the most common pathogen for CAP.[9] A meta-analysis of 24,423 CAP episodes in 15 European countries (average age: 62.1 years) reported 19.3% of episodes attributed to *S. pneumoniae*.[17] Even studies reporting pneumococcus as the most common culprit sometimes overlook the number of unsolved cases. The etiology of 359 hospitalized CAP patients (mean age: 62 years) was reported mostly due to pneumococcus in 15.3% cases, but twice that amount (32.9% of patients) remained with "unknown" etiology.[18] In a review of 13 European countries, pneumococcus was the most frequently isolated pathogen causing CAP (range: 11.9%–68.3%), but in 9 of the participating countries the mean percentage of "no pathogen identified" was similar or higher (range: 35.3%–67.3%) than that reported for pneumococcus.[15] This tendency is concurrent with a proposed global decline in the quality of microbiology analysis, with few studies reportedly identifying any likely pathogen in 50%–70% of pneumonia cases.[19] Systematic reviews support pneumococcus as a major cause of CAP in adults in developed countries,[20] but its prevalence varies significantly across European countries,[17] and seems less important in certain parts of Asia,[21] where other CAP-associated etiological pathogens like *Klebsiella pneumoniae* and *Burkholderia pseudomallei* are predominant.[22]

Key points

- The most prevalent etiology of community-acquired pneumonia can vary among populations and is usually unknown. This is not a problem only in Peru.
- Many studies fail to address this limitation and report only on cases with laboratory-confirmed diagnosis, ignoring the large percentage of uncertainty within the population that limits targeted prevention and treatment policies.
- Extrapolating vaccine efficacy (including direct and indirect effects) without laboratory surveillance could generalize an unverified assumption that may not justify the continuous incremental expense of immunization programs. A plausible explanation to the study results is that pneumococcus is not a major contributor to pneumonia mortality in Peru.

Community/collective immunity, also referred to as herd immunity, is possible when most of the people in a community/population are immune to a disease (either by vaccination or natural infection), thereby preventing further spread of a disease, and has been described for many pathogens.[23] Immunization eliminates the carriage of certain pneumococci from the respiratory tract in children, thus reducing its presence in the community, and potentially benefiting everyone. If enough children are vaccinated, susceptible/unvaccinated individuals can be considered statistically more likely not to become infected and are indirectly protected. This indirect benefit derived from the vaccination of infants and young children with pneumococcal conjugate vaccines (PCVs) has been reported to lead to a significant decrease in pneumococcal disease in all age groups.[24] Following PCV introduction in the United States in 2000, early studies reported a drop in the incidence rate (cases per 100,000 people) of invasive pneumococcal disease (IPDs), including adults over 65 years of age and older, although the largest decline was reported in children under 2 years of age.[25,26] Using projection models, PCV was estimated to have even prevented more than twice as many IPD cases through indirect effects than through its direct effect of protecting vaccinated children.[26] However, reports suggesting indirect effects of PCVs over IPDs by comparing control populations retrospectively may not be able to differentiate such effects from a secular trend.[27] Further, the extrapolation from IPDs to pneumonia is not straightforward since the most common type of pneumonia is noninvasive, and pneumococcal serotypes causing invasive disease may differ significantly from those causing non-invasive pneumonia in adults.[28] Etiological diagnosis using non-invasive microbiological laboratory procedures is not always definitive or even achievable,[29] resulting in only a "probable" diagnosis. Thus, the actual proportion of adult pneumonias caused by vaccine-serotype pneumococcus and therefore the fraction that could be prevented by PCVs is largely unknown.[30] Estimating the adult burden of pneumococcal disease from bacteremic pneumococcal pneumonia data alone significantly underestimates the true burden of disease in adults since it has been estimated that for every case of bacteremic pneumococcal pneumonia, there are at least three additional cases of non-bacteremic pneumococcal pneumonia.[20] From a public health standpoint, the percentage of pneumococcus causing CAP[31] and the proportion of non-bacteremic pneumonia due to pneumococcus[32,33] are more relevant to the impact of any vaccine than whether the vaccine prevents pneumonia caused by the specific serotypes included in it.

Epidemiological data on pneumonia at the population level are scarce in low-income countries,[6] and there are limited data from developing countries demonstrating the impact of widespread childhood PCV immunization on adult pneumonia.[34] In Peru, after the introduction of PCVs into the Peruvian national child immunization program in 2009, protective effect for the (mostly unvaccinated) older adult population could be reasonably anticipated, with a consequent decrease in pneumonia mortality in this high-risk age group. Statistically quantifying this indirect effect is complicated and sometimes controversial, but time series analysis can help identify trends. The purpose of this study is to assess changes in mortality trends for all-cause pneumonia in people 65 years of age and over in the context of the introduction of PCV immunization for children in Peru.

2 | MATERIALS AND METHODS

2.1 | Study design

An observational retrospective time series analysis was conducted using longitudinal death certificate data from Peru between 2003 and 2017.

2.2 | Data collection

We performed secondary analysis on a governmental healthcare administrative data set to evaluate the change in trend for mortality due to all-cause pneumonia in a high-risk group. Data sets from the Peruvian Ministry of Health are considered public domain and are available upon official request. The system involves hardcopy data that have been digitalized and collects nationwide information on all deaths. Since 2018, online reporting significantly changed data collection procedures and is analyzed separately.

2.3 | Study population

Potential cases were selected among records from adults over 65 years of age who reported pneumonia as the "underlying cause of death" in the death certificate according to the tenth revision of the International Classification of Diseases (ICD-10): codes J12 to J18. Our case definition (participants) included adults over 65 years of age who died reported "pneumonia due to unspecified organism" (ICD-10 code J18) as the basic cause of death in Peru between 2003 and 2017. This category represented almost exclusively all deaths due to all-cause pneumonia, so other, much more infrequent ICD-10 pneumonia categories were considered outliers with a potential selection bias due to uncommon access to specific diagnostic technologies.

2.4 | Statistical analyses

Descriptive statistics included monthly death frequencies and estimated annual mortality rates (per 100,000 population) at the national level using demographic projections for Peru from 2009[35] to standardize the effect of population growth during the study period. Time series analysis of monthly frequencies and annual rates was performed using linear and quadratic trend models. Statistical estimates and modeling were achieved using IBM SPSS Statistics v.23.

TABLE 1 Basic cause of death, for adult people over 65 years of age, Peru, 2003–2017 (N = 820,064).

ICD-10 code	Condition or disease	Frequency	Percentage
J18	Pneumonia, organism unspecified	119,108	14.5
A41	Other sepsis	59,375	7.2
I21	Acute myocardial infarction	50,439	6.2
I10	Essential (primary) hypertension	30,083	3.7
J84	Other interstitial pulmonary diseases	29,422	3.6
I50	Heart failure	26,985	3.3
C16	Malignant neoplasm of stomach	26,197	3.2
J96	Respiratory failure, not elsewhere classified	25,337	3.1
N18	Chronic kidney disease	19,844	2.4
K74	Fibrosis and cirrhosis of liver	18,297	2.2
C61	Malignant neoplasm of prostate	17,817	2.2
E14	Unspecified diabetes mellitus	17,581	2.1
I64	Stroke, not specified as hemorrhage or infarction	17,196	2.1
Various	Other underlying cause of death	36i2,383	44.2

Ethical considerations are minimal, this is a secondary analysis of public domain datasets without personal identifiers that were collected for administrative purposes.

3 | RESULTS

Among all death certificates in Peru (N = 1,420,631) during the study period 2003–2017, adults over the age of 65 accounted for 57.7% (n = 820,064): 49.6% were female and 55.5% were 80 years of age or older. Table 1 lists the most common underlying causes of death for this age group: "pneumonia due to an unspecified organism" represents 14.5% (n = 119,108) of deaths among adults 65 and over: 50.8% were female and 68.9% were 80 years of age or older. This unspecified pneumonia category accounted for 94% of all-cause pneumonia fatalities in older adults (n = 126,215), while pneumonia due to *S. pneumoniae* was reported in 0.04% of all-cause pneumonia deaths in this age group (Table 2).

Regarding the chain of events (diseases, injuries, or complications) that contributed to death due to unspecified pneumonia in older adults (n = 119,108): 20.8% reported unspecified pneumonia as the single basic or immediate cause of death. Among death certificates reporting one or more conditions leading to death due to unspecified pneumonia (n = 91,837): 21.3% reported unspecified pneumonia, 27.4% reported "respiratory failure" (ICD-10 code J96), 18.9% reported "other sepsis" (ICD-10 code A41), and 11.0% reported "cardiac arrest" (ICD-10 code I46) as the immediate cause of death.

Annual frequency of deaths and mortality rates at the national level for pneumonia without a specified organism were calculated for all ages (n = 157,575), for children under 5 years of age (6.5%, n = 10,242), and for adults over 65 years of age (75.6%, n = 119,108), and plotted in Figure 1 where we can appreciate that the standardized annual mortality rate is also much higher for the older group, on average 20 times (range: 14.1–33.9 times) on any given year than that for young children. Figure 1 suggests two secular trends over time during the study period, a marked positive (increasing) trend for the older adult fatalities and a subtle negative (decreasing) trend for young child fatalities. These annual trends are better explained in Figure 2, which plots a regression line (green) and a curve (orange) to fit the trends for pneumonia annual mortality rates. Besides the difference in scale and direction, the change in trend (the inflection point) is plotted approximately around 2007 for children, and around 2011 for older adults. Figure 2 also suggests trends may be better explained by a curve in both age groups, suggesting a more complex (nonlinear) relationship over time.

TABLE 2 All-cause pneumonia cases reported as the basic cause of death for adult people over 65 years of age, by ICD-10 categories, Peru, 2003–2017 (n = 126,215).

ICD-10	Influenza and pneumonia	Frequency	%
J12	Viral pneumonia	952	0.8
J13	Pneumonia due to *Streptococcus pneumoniae*	48	0.0
J14	Pneumonia due to *Haemophilus influenzae*	2	0.0
J15	Bacterial pneumonia	6,040	4.8
J16	Pneumonia due to other infectious organisms	59	0.0
J17	Pneumonia in diseases classified elsewhere	6	0.0
J18	Pneumonia, organism unspecified	119,108	94.4
	Total	126,215	100.0

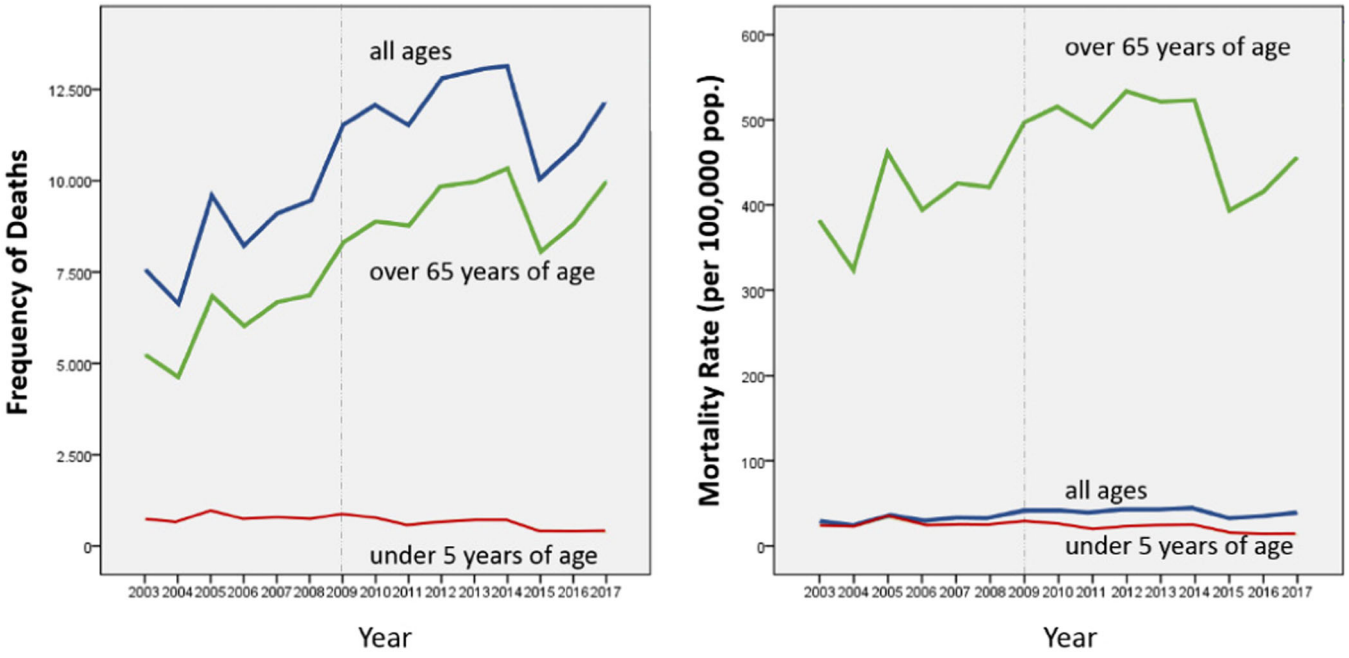

FIGURE 1 Annual frequency of deaths and mortality rates for pneumonia due to unspecified organism (ICD-10 code J18), by high-risk age group, Peru 2003–2017.

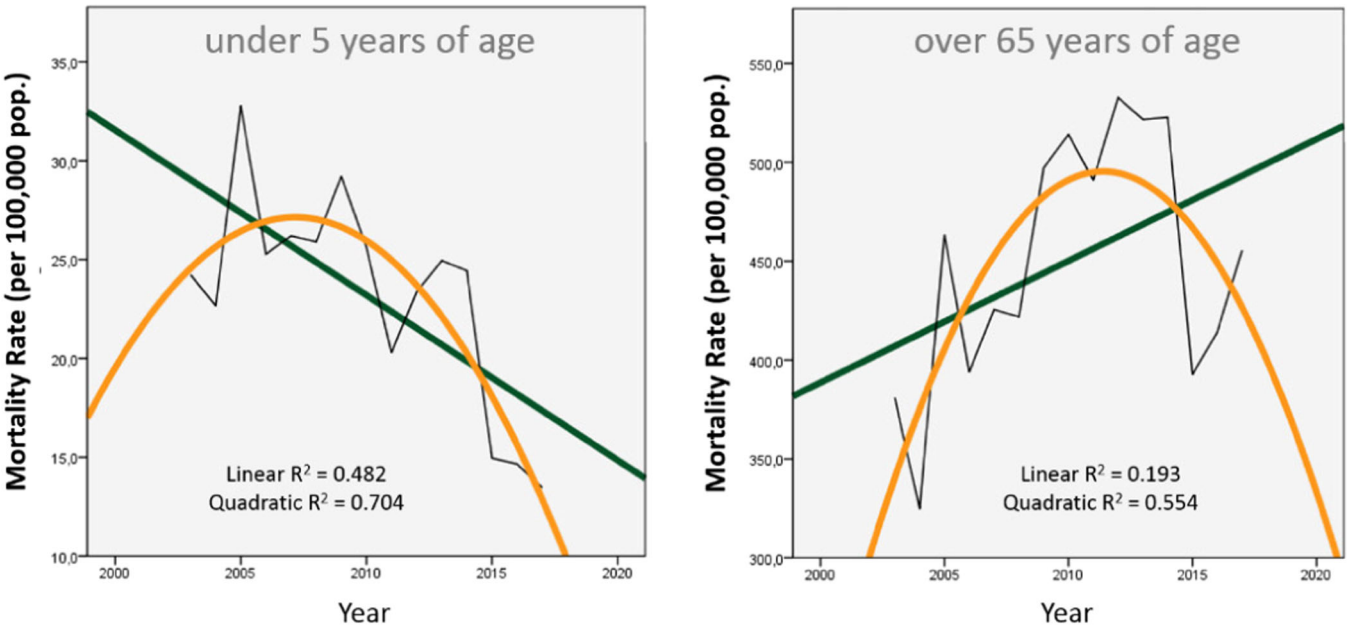

FIGURE 2 Trends in annual mortality rates for pneumonia due to unspecified organism (ICD-10 code J18), by major risk group; Peru 2003–2017.

Figure 3 plots the monthly frequencies of unspecified pneumonia deaths (ICD-10 codes J18) for both risk groups. The simple linear regression (green) follows the same secular trend reported for annual mortality rates in both groups: decreasing for children and increasing for older adults. The quadratic curve (orange) in Figure 3 also suggests a change in monthly mortality trends of around 2008 in young children and around 2012 in older adults.

For comparison, Figure 4 plots the annual mortality frequency from the three most common underlying causes of death in older adults: the increasing pneumonia mortality trend is not shared by other major causes of deaths: deaths due to sepsis seem to have a decreasing trend while deaths due to acute myocardial infarction seem to remain within a certain range during the study period.

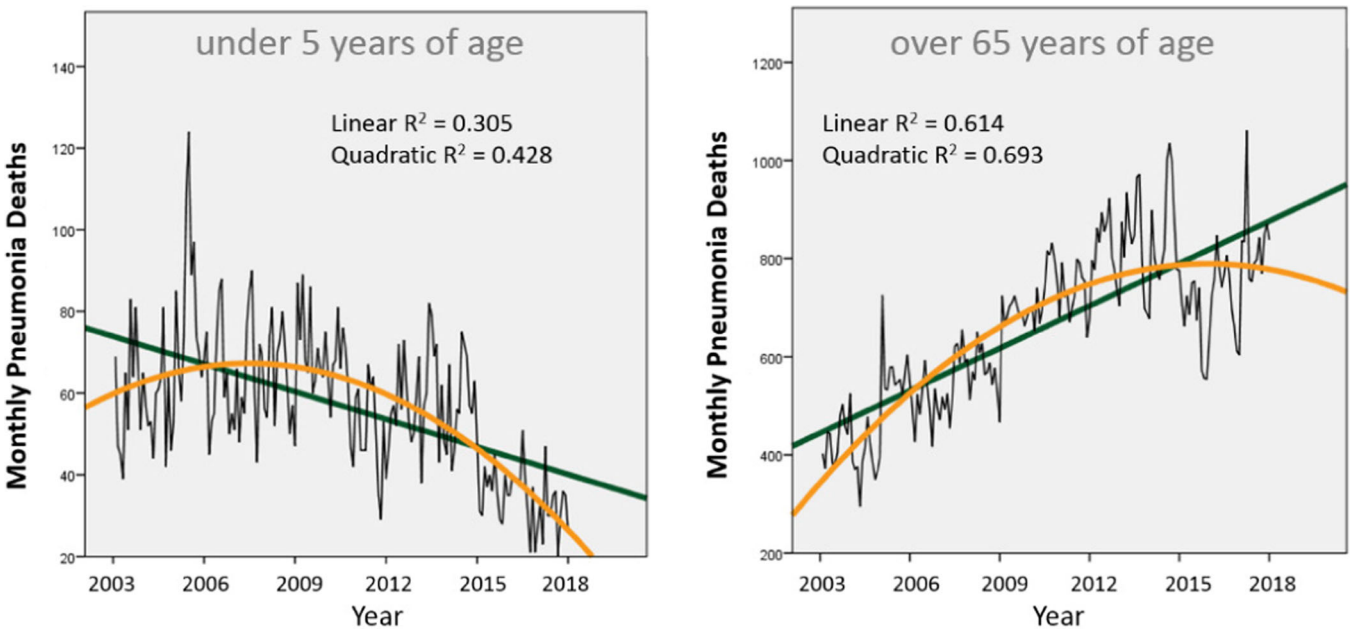

FIGURE 3 Trends in monthly frequency of pneumonia deaths due to unspecified organism (ICD-10 code J18), by major risk group; Peru 2003–2017.

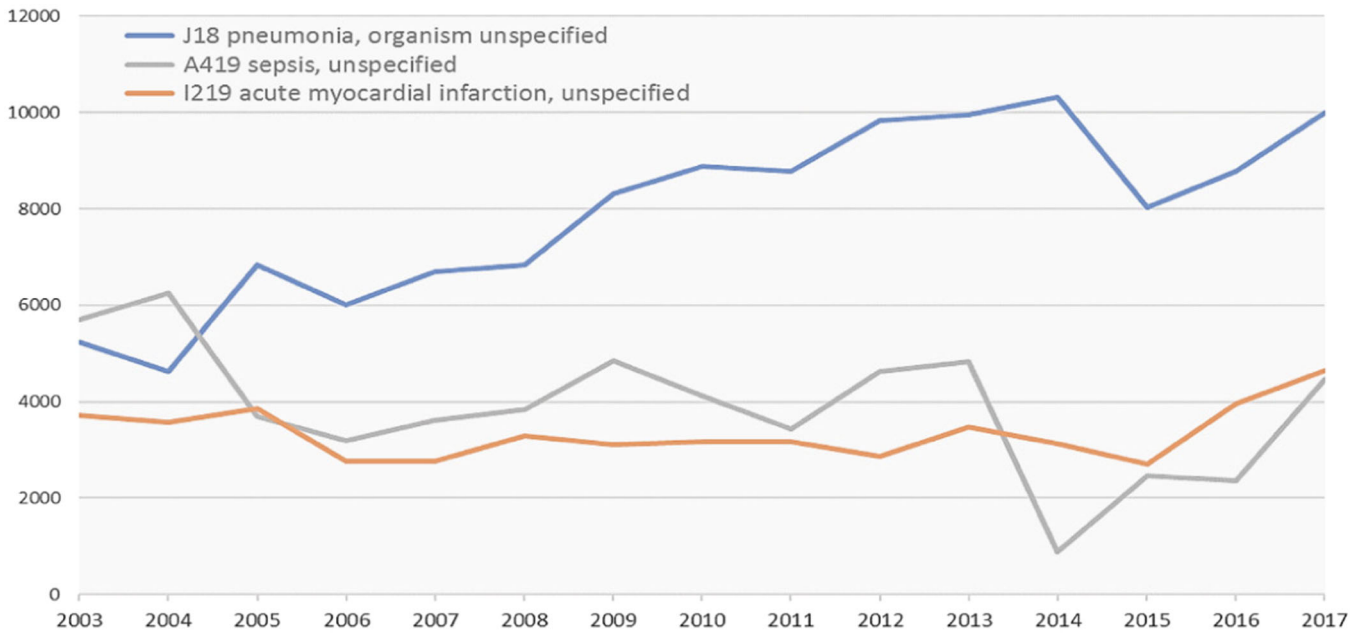

FIGURE 4 Annual frequency of deaths from the three most commonly reported underlying causes of death for people 65 years of age and over; Peru 2003–2017.

Comparing the pre- and post-vaccination periods, the average monthly frequency of deaths due to unspecified pneumonia in people older than 65 years of age increased by 54.5%: from 503 deaths per month (range: 295–726) during 2003–2008 to 777 deaths per month (range: 555–1061) during 2010–2017. The annual number of deaths due to unspecified pneumonia nearly doubled during the study period, and the average annual mortality rate due to unspecified pneumonia increased by 19.6%: from 401.7 deaths per 100,000 population (range: 324.8–463.4) before PCV introduction to 480.6 deaths per 100,000 population (range: 392.6–532.8) after. During the same period, the average annual mortality rate for children under 5 years of age decreased by 22.7%: from 26.2 deaths per 100,000 population (range: 22.7–32.8) in the pre-vaccination period to 20.2 deaths per 100,000 population (range: 13.5–25.6) in the postvaccination period.

4 | DISCUSSION

PCVs are important public health tools that are promoted by the World Health Organization (WHO) and are incorporated into national child immunization programs all over the world.[36] Immunologic protection from PCVs is mediated through antibodies directed against specific bacterial capsular polysaccharides (serotypes) that are covalently bonded (conjugated) to an immunogenic carrier protein to induce immunologic memory and response. It is well documented that PCVs prevent vaccine-type pneumococcal disease in children,[24,37] and have reduced the incidence of vaccine-type disease in all age groups, including older adults,[28] but vaccine-type pneumococcal disease is only a fraction of all pneumococcal disease in adults.[20] For example, it has been cited that adults in contact with a vaccinated child are significantly less likely to have vaccine-type CAP compared with adults in contact with an unvaccinated child.[38] However, in that study a serotype was identified in 64.1% of pneumococcal CAP patients which represented 36.3% of 1130 hospitalized adults with CAP. The sample size for the vaccine-type calculation was 112 (9.9%) of the original cohort.[38] In another study, *S. pneumoniae* was detected in 13.8% of 710 pneumonia subjects (median age: 65.4 years), but a specific serotype was detected in only 11.0%.[28] In our data set, more than 94% of all-cause pneumonia fatalities among older adults had no etiology, potentially being caused by virus, bacteria, or a combination of both. Therefore, mortality directly attributed to pneumococci, let alone any specific serotype, is largely unknown and increasing in Peru (Figure 1). This universal lag in laboratory identification of causal pathogens for pneumonia has been reported in many countries,[19] but it is especially concerning in low-income countries.[16] It has been proposed that this is a consequence of a lack of disease awareness in the general public and healthcare professionals with no disease advocacy strategies, and different priorities in pharmaceutical companies, that have contributed to unchallenged international guidelines that have not changed much in decades.[39] It is hard to fathom the impact of any antipneumococcus vaccination without having specific knowledge of the prevalence of pneumococcus serotypes in CAP episodes within a specific population.

Circulating pneumococcal serotypes in young children are also important since the impact on the incidence of vaccine-type pneumococcal diseases in older adults is influenced by the vaccine effectiveness of childhood vaccination.[34,38,40] In Peru, before the arrival of PCVs, a multicenter study in five sentinel hospitals designed for pneumonia etiology surveillance reported: 1.5% *S. pnemoniae* and 0.8% *Haemophylus influenzae* among 1210 pneumonia patients under 5 years of age. However, this report also failed to specify that the majority (97.7%) of the laboratory samples included in the study did not identify any infectious agent.[41] This can be explained by local laboratory limitations, but another plausible explanation is that pneumococcus is not a predominant causal agent for pneumonia in children in Peru which would also explain the lack of any evident indirect effects in our results. Regardless, next-generation vaccines for children were approved by WHO based on comparative immunogenicity with PCV7, which in turn was based on predominant invasive pneumococcus serotypes from high-income countries,[42] and national child immunization programs were sequentially implemented in Peru using PCV7, PCV10, and PCV13 in 2009, 2012, and 2015, respectively. The uncontested increasing costs for these next-generation PCVs are also a concern to countries like Peru that need to allocate scarce resources more efficiently.

Potentially, vaccines can prevent pneumonia mortality in older adults in two major ways: directly or indirectly. The direct approach is through vaccination, but this is controversial,[40] and is not completely unrelated to child immunization. A meta-analysis of 25 studies involving 12,7146 adult participants reported that pneumococcal polysaccharide vaccines (PPVs) prevented IPD in adults, but not all-cause pneumonia or mortality.[43] Similarly, PCV13 was not able to significantly prevent all-cause pneumonia compared to placebo (vaccine efficacy: 5.1%) in a major clinical trial involving 84,496 adults 65 years of age or older with CAP; the study did report better values for certain specific vaccine-type strains (vaccine efficacy: 45.6%) and IPDs (vaccine efficacy: 75.0%).[44] Early systematic reviews did conclude that PCVs in older adults can be cost effective,[45] but vaccine efficacy in this group is known to wane over time,[46] and others have pointed out the high cost of implementing PCV13 in adults without any benefit in mortality.[47] Economic evaluations using hypothetical cohorts favor PCVs over PPVs for older adults, but acknowledging this benefit depends on PCV13 effectiveness against non-bacteremic pneumococcal pneumonia and the magnitude of potential indirect effects from childhood PCV13 on pneumococcal serotype distribution.[48] A more recent systematic review concluded that pneumococcal vaccination in older adults may not be cost effective when children are vaccinated with higher-valent PCVs (PCV10 and PCV13) if there is a rapid decline in vaccine-type pneumococcal disease.[40] In Peru, vaccines for older adults are available but not mandatory and are not part of a national immunization program, so this is an unmeasured cofactor and not an alternative explanation for the increasing all-cause mortality trend in older adults.

The second potential approach for vaccines to prevent pneumonia mortality in older adults would be the indirect protection implied by "herd immunity." Older adults have been reported to indirectly benefit from the introduction of PCVs in the pediatric population,[24,34] especially for vaccine-type pneumococcal disease,[49] and more than 90% of the reduction in model-attributed pneumococcal pneumonia hospitalizations and deaths was attributed to herd immunity among adults.[50] In fact, indirect effects from childhood vaccinations have a major impact on cost-effectiveness estimates for vaccines,[40] and statistical models are encouraged to include indirect effects when evaluating the cost-effectiveness of PCVs.[45] A cost-effectiveness model in Argentina reported cost-saving results for adult vaccination by considering a hypothetical 50% reduction of vaccine serotype coverage after the introduction of childhood vaccination.[51] A study in Italy acknowledged significant herd protection in the unvaccinated adult population after the introduction of PCV7 but only a very limited protection after PCV13.[52]

Conversely, a systematic review of economic evaluations of pneumococcal vaccines for adults aged 50 years or older in low- and middle-income countries raised questions about potential bias in studies and whether conclusions hold after including the impact of indirect protection.[53] The magnitude of herd protection after implementation of a pneumococcal conjugate immunization program will depend on the immunization strategy, the coverage achieved, the reduction in carriage of vaccine serotype pneumococci among vaccinees and their contacts, the proportion of pneumonias caused by vaccine serotypes, and the population composition.[30] Differences in vaccine-type serotypes, disease severity and comorbidities can further limit the country-specific health and economic impact of any vaccine.

Studies on herd immunity induced by PCV introduction in developing countries should be an essential part of vaccination impact measurement,[50] due to differences in CAP mortality rates and in the prevalence of etiologic agents.[16] The incidence of disease and serotype coverage varies greatly between countries and are major drivers of the cost-effectiveness ratios, so different countries can benefit differently from the implementation of a national vaccination program with PCVs and comparisons between outcomes of models from different countries should be made with caution.[40] A systematic review on herd immunity after the introduction of PCVs concluded that most studies that reported either statistically significant reduction or insignificant changes in IPD and pneumonia disease rates in adults were from developed countries, while the few studies that reported a statistically significant increase in pneumococcal disease rates were mainly from countries with low PCV coverage rates and/or inadequate surveillance.[34] Population-based surveillance can contribute to the limited evidence available on the burden of pneumococcal pneumonia (indirect impact of PCVs) among adults in a resource-limited setting.[54] Indeed, population-based data from Peru does not support a major contribution from herd immunity to pneumonia mortality in older people. Our results suggest that the trend over time for all-cause pneumonia mortality is not a linear one (Figures 2 and 3), but rather a complex tendency where other cofactors have not been identified.

Improvements in vaccines against pneumococci and increased rates of immunization are expected to result in continued reductions in the incidence of infections due to this common pathogen, but not necessarily in all populations. Risk factors for morbidity (affecting who requires hospitalization) may be different from those for mortality (affecting who dies from the infection). Vaccine impact may limit the exposure to vaccine-type pathogens in the community, but once infected, immunization may not influence disease progression in a high-risk population like people over 65 years of age, and other factors (like access to healthcare) can become vital. For example, the reduction in pneumonia admissions (a proxy measure of disease severity) after PCV introduction can provide an estimate of the proportion of pneumonias attributable to *S. pneumoniae* that are vaccine preventable, but this can vary among age groups. A study comparing trends in monthly hospital admission rates before and after routine immunization of children with PCV7 in the United States from 1997 to 2004 reported a 30% statistically significant decline in all-cause pneumonia admissions in adults aged 18–39 years (95% confidence interval [CI], 9–47), but the difference was not significant for adults 65 years or older.[55] Is disease severity in older adults unaffected by child immunization or are other unknown factors involved? In the case of the aforementioned study, pneumococcal pneumonia was only reported in 4% of all-cause pneumonia admissions.[55] If half of hospitalized patients with CAP are reported as having "no causative organism," it is unclear what proportion of these can be attributed to infection by so-called typical or atypical bacterial pathogens, oral flora, viruses, or other pathogens.[7] In one multicenter study, the most frequent cause of definable pneumonia in hospitalized patients was indeed pneumococcus, but among those who died, half were infected with *Staphylococcus aureus*,[18] and *Legionella* has also been associated with CAP mortality.[10] If the "unspecified" pneumonia diagnosis hides co-infections by other bacteria (perhaps even acquired in the healthcare setting), the presence of immunization against pneumococcus would make little difference in the outcome (since healthcare-associated infections are commonly drug resistant). Due to lack of efficient laboratory surveillance, we do not know if this is the case in Peru.

Our study has limitations. Population-based studies must rely on data that were not collected to answer a specific research question, and databases collected for other purposes imply no ability to control for the "quality" of the data collection process, classification, manipulation, or registration. Still, these are official data that public health authorities use to make decisions, and data do go through internal quality control. Even if we assume data quality may be compromised to make accurate estimations (i.e., missing data, misclassification, or underreporting), the overall trend of the time series may still prevail if any bias occurs randomly across the study period. We propose that, if a public health intervention has any real impact on the population, that impact should be reflected in precisely this type of data that are systematically collected and reported periodically. Further promoting the use of these data might also help to improve data quality and timeliness in the future.

5 | CONCLUSION

The importance of the prevalence of pneumococcus as a local causal agent of CAP has implications for the impact (direct and indirect) of pneumococcal vaccines in specific locations. More recent scientific reviews and meta-analysis are reporting other predominant pathogens in different parts of the world. Our results do not support the concept of herd immunity in pneumonia mortality among people over 60 years of age associated with PCV child vaccination. At no detriment toward efforts to prevent pneumonia mortality among children, we propose a renewed interest to identify effective prevention strategies for pneumonia mortality among the growing aging population. As Peruvians live longer and natality rates continue to decrease, this high-risk age group will continue to become an important target for prevention of CAP mortality in the future.

AUTHOR CONTRIBUTIONS

Carlos A. Sanchez: Conceptualization; data curation; formal analysis; investigation; methodology; writing—original draft; writing—review & editing. **Oriana Rivera-Lozada**: Resources. **Michelle Lozada-Urbano**: Funding acquisition. **Pablo Best-Bandenay**: Supervision; writing—review & editing. All authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Carlos A. Sanchez had full access to all of the data in this study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis. The data that support the findings of this study are available upon request from the Peruvian Ministry of Health.

TRANSPARENCY STATEMENT

The lead author Carlos A. Sanchez affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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