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An Impact Evaluation of the Rollout of the Pneumococcal Conjugate Vaccine in Uttar Pradesh State, India. 2017-2019

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Abstract

This paper is aimed toward examining whether methods currently being rolled out to administer the pneumococcal conjugate vaccine to children in the Indian state of Uttar Pradesh is effectively reducing morbidity and mortality. The fundamental question regarding this current effort is if it proves to be useful at reducing the prevalence of *Streptococcus Pneumoniae* and whether the surveillance methods examining the efficacy of healthcare interventions are helpful. Both rural and urban India are troubling areas for public health surveillance to reach, though many diseases of poverty and respiratory illnesses such as pneumonia flourish there. With no true quantification of burden, it is challenging to implement interventions and distribute resources. The data for this paper is challenging because it was collected through surveillance networks whose efficacy is yet to be determined. As further analysis was conducted it became apparent that the surveillance data utilized in this paper is not a strong indicator of occurring cases of pneumonia, however through time series analysis, regression analysis, and spatial analytics, useful general trends appeared. The Pneumococcal Conjugate Vaccine rollout is new and success is yet to be determined in the short time period since 2017. Through this detailed analysis of available information details arose that describe the holistic effectiveness of the program and can inform directions for the future. Overall mortality rates hinge on access to care, and this paper will integrate quantitative data analysis with a qualitative review of the systems involved. The results require follow up of several more years to account for disparities between districts and weakness of the data. However, an investigation into the districts where the vaccine was rolled out, which also experienced the heaviest burden of cases, revealed that the PCV rollout has the potential to achieve a tentative level of success. The complication is that as
surveillance improves, death counts of previously invisible individuals will ruse. The full effect of this effort will not be seen for 2-4 years due to the age of vaccination and the retooling of health systems. With proper administration, data management, and surveillance systems in place, a shift in vaccine access has a capacity to reduce childhood mortality.
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Introduction

Rollout

According to research at the International Vaccine Center at Johns Hopkins University, a child dies every 8 minutes of pneumococcal disease in India\[1\]. The launch of the free Pneumococcal Conjugate Vaccine is following a time of extreme need. As a greater understanding of the state of public health in the developing areas in a nation of one billion grows, the importance of joining 120 other countries in the fight against this disease is critical. The government of India made an official promise in May of 2017 to launch the PCV under the Universal Immunization program. The Union Minister for Health and Family welfare Shri J P Nadda declared the government’s commitment to reducing morbidity and mortality in young children\[2\]. As pneumonia kills more children under five than any other infectious disease in the region, the government considered this movement a long-term investment in the future of India and the 27 million children born each year. Of that figure, 2 million of those children do not make it past the age of five\[3\]. This effort is a part of a larger movement under President Modi to expand healthcare to bolster India’s status on the path of development. Overall vaccine coverage has also been improved according to the Minister for Health, growing from protecting against 6 preventable infectious diseases to 12. The government is promoting the program heavily through posters, TV commercials, and radio [2].

In addition to two other states, the six districts in the northern state of Uttar Pradesh that were determined to have the most “need” by the government were Balrampur, Bahraich, Kheri, Sitapur, Siddharthnagar and Shravasti. [12]. The overall burden of disease was paired with the prevalence of secondary risk factors such as poverty, illiteracy rates, housing security, poor sanitation conditions, and lack of healthcare access for consideration [13]. The vaccines would be available starting June 10, 2017 for free for children under one at six weeks old, fourteen weeks old, and nine months. The government determined that the economic offset of the reduction of healthcare and hospitalization costs due to infections would justify the cost of the free vaccine. The PCV rollout was modeled on existing vaccine campaigns that were used to eradicate polio under the Universal Immunization Program [14].
Complications arise from the fact that a significant amount of background information comes from the Indian government itself, which has strong interests in making efforts to improve quality of life. As a rising global economy, public health is a key part of developing infrastructure. However, much of the data describing the extent of the reach of the vaccine program has come from the government itself. The prevalence statistics provided by the National Health Profile of India do not supply sources and methodologies. There is a concern among the global community that countries like India understate their poor health outcomes in order to build power. However, it is the thought of this paper that understatement is inevitable, because the systems to account for every community effectively do not exist. The WHO and individual research studies also carry their own figures. Further discussion is needed on which source should be the touchstone for the global health community as severe knowledge gaps exist. My data will be coming from private efforts from HMIS, which will be further discussed in the methods section. This paper will reflect community and local based surveillance and healthcare delivery approaches that are common in the region.

**Burden of Pneumonia**

No national review of this issue exists in India. As stated above, exact counts of sickness and death are challenging and disparate reporting exists. According to the Million Death Study the statistics in the above Rollout section are confirmed with some slight discrepancies in the thousands[4]. Further research under this study revealed that a higher percentage of rural children suffered than urban children, though only by a slight margin: 28.9% as opposed to 25% [4]. Cases within slums lie in a grey area, which is problematic considering the ties of slum life to risk indicators. Cases also vary by state, though our scope will be limited to the state with the most severe situation. These distinctions will be considered.

**Host Factors**

There is extensive research on the risk indicators and implications of childhood pneumonia. Environmental and behavioral circumstances integrate to shape the susceptibility of communities and children. Some of the primary indicators for pneumonia mortality are whether or not the child is breastfed, low birth weight, malnutritioned, experiencing poor air quality outdoors and indoors, living in overcrowding, and failed to receive measles immunization[5].
Some publications rank these risk factors by severity, but for the purposes of this paper risk factors will be supplemental information. Further epidemiological evidence revealed that time trends are incredibly important when conducting a review of both cases and mortality, which supports the work done in this paper. Another study identified socioeconomic status as an indicator that should be taken under consideration, especially given India’s wealth gap[6]. An important trend that literature also revealed is very few studies identify the etiology of pneumonia cases. Like this paper, diagnostics are often the main source of detection. When diagnostics are weak and healthcare access is poor, portions of the populations are missed and direct links to risk factors are challenging to establish.

**Antibiotic Treatment**

Though the biological causes of pneumonia are known, various serotypes of *S. pneumoniae* are rarely distinguished[7]. Considering the high prevalence and death rate, a conundrum exists over whether to prescribe antibiotics when testing resources are not available. Antibiotics can also simply be purchased over the counter in India with no confirmation that the infection isn’t actually viral, rendering the treatment ineffective. This is a similar challenge all over the world when care providers must decide between protecting the child and the fight against antimicrobial resistance. AMR appeared in several pieces of literature, identifying in-vitro resistance to commonly used antibiotics, with penicillin resistance low and cotrimoxazole resistance high and growing steadily since 2000[8]. AMR could render some treatments ineffective within a number of years, however neglecting to provide treatment to suspected cases of pneumonia is a difficult moral choice. Further, communities that live in poverty far from healthcare facilities do not even encounter this situation and die unseen by treatment providers. Increased detection could lead to increased antibiotic use, which also carries the secondary risk of AMR, even when appropriately used. Oversight of dosage and adherence to the entire prescription would need to be established to address this problem.

**Solutions**

The PCV vaccine exists to mitigate these systemic problems. There are several systematic reviews identifying high efficacy when full vaccine doses were administered, however confirmation diagnostics were inconsistent across the literature[9]. In India, available
data reported that the PCV covers around half of the serotypes responsible for disease, however this varies on whether the PCV-13 is replacing the PCV-7[10]. It appears that the largest defining factors in pneumonia mortality is the overall burden within the community and the effectiveness of the vaccine and its boosters. This paper examines both the impact of the current rollout of the vaccine and the capabilities of surveillance networks in place. Currently, guidelines for administration are yet to be reviewed for this new rollout, though community-based management is favored and has been proven effective in past efforts[11].

Methods

This is a cross sectional study, examining cases and deaths from pneumonia during 2017 to 2019 after the onset of the PCV rollout. The population under observation is represented by data grouped by districts in India. The population under observation are children under five within the state of Uttar Pradesh and its 76 districts, which included both rural and urban areas. Exact counts for the population were pulled from 2011 census data. Data in this paper includes death rates for pneumonia and upper respiratory infections as well as the percentage of the population that receives their booster shots. This sample size is broad to determine if district and state level surveillance is an effective measurement of the impact of the PCV vaccine on childhood mortality.

The data analysis was conducted in RStudio and ArcGIS to measure the fluctuation of reported cases and deaths over time. A time series analysis was created to give an overall picture of the fluctuations in deaths over time, first viewing the data from the beginning of the investigation in 2008 and then narrowed down to the time frame decided upon to increase specificity. Then, utilizing geographic information and census information, maps were created in order to visualize cases. The data was formatted for compatibility, and then the death rate was divided by the population of the districts to discover prevalence rates, and multiplied by 1 million.
Further, I used a Poisson Regression framework. I fit a regression where there was a dummy variable for whether the observations are from pre or post vaccine. My outcome variable was whether or not there was a decrease in death rates per year. The interaction term was created to inform if there is a change. In order to visualize the differences in deaths before and after the rollout of a vaccine we also looked at rate ratios for how different pre and post vaccine status looks and if they are different in places that did or didn’t introduce the vaccine. Data is sourced from HMIS. An intensive qualitative research process provided context to our results.

Results

Time Series

These analyses are preliminary and only cover one of the three states involved in the rollout at this time- Uttar Pradesh. Time series analytics were run on the overall state (figure 1) and on each individual district.
The initial time series revealed a large spike at the onset of our study period in 2017, though previous vacillations existed previously to program rollout. The further time series for each of the 76 individual districts showed distinct patterns over time through visual inspection.

**Spatial Analysis**

In order to display the distribution of deaths due to pneumonia across the state, maps were created to visualize prevalence. The resulting maps displayed unique patterns and geographic paradigms throughout Uttar Pradesh.
Pre rollout in 2017, cases were centralized in the mid-east of the state, particularly clustered in the most populous districts. Bahraich, Sonbhadra, and Maharajganj all contained the highest prevalence in the state (figure 2). The main overlaps in intensity occurred in the north. The map displaying PCV rollout indicates its occurrence in the districts of Lakhimpur Kheri, Sitapur, Siddharthnagar, Bahraich, Balrampur, and Shrawasti.

In 2018 (figure 8), cases intensified in the same regions and rose significantly compared to previous years. Note in the figures that the gradient follows a relative natural break pattern and not set high/low values. Deaths were still particularly high in the vaccine rollout region in the north. In 2019 deaths (figure 10) dropped significantly throughout the state for both pneumonia and upper respiratory infections. The geospatial trends have several potential influences that will be discussed.
Figure 8. 2018 Pneumonia deaths per 1 million

Figure 10. 2019 Pneumonia deaths per 1 million
Regression Models

For further analysis of the influence of the PCV on deaths a regression was run against pneumonia deaths and upper respiratory infection hospitalizations as a comparison factor. The model accounted for disparities between districts. The model regarding upper respiratory infections as a point of comparison found a statistically significant connection between those deaths and the introduction of the PCV vaccine. However, the main analysis with deaths from pneumonia showed no significant relationship. The strength and fit of this model were moderate.

A rate ratio determined that districts who received the vaccine had a 50% less chance of death than others. All of our data has severe limitations that hinder the quantitative interpretation of the results. Qualitative context is critical to understand and theorize implications.

Discussion

Early Impact Evaluation

The foundation of the results of this analysis is that our interpretation of the data has to consider the strength of the data itself before any takeaways can be definitively stated. To begin, pneumonia deaths in fact rose in the first year of reporting, 2018, post PCV rollout (figure 8). The national initiative to improve data quality brought more cases and deaths to light, causing a spike in deaths that was most likely not a spike at all. Instead, increased visibility of deaths creates the perception that they are actually increasing. As surveillance efforts were escalated to reach more people post 2017, this rise could be due to improved recording of previously unseen cases. This phenomenon has the potential to confound early impact evaluations. As mentioned, there was a significant drop in 2019 (figure 10), however there is uncertainty on the completeness of 2019’s data. No relationships could be proven at this time to be statistically
significant, but that further strengthens the idea that increase surveillance will hinder early trend analytics because the populations dynamics differ year to year.

Due to the young age of the children receiving vaccination (>1 year), the reflection of their specific health status in general mortality will be severely underrepresented until they grow older and higher in numbers to represent more of the population. The PCV can be administered to older children, but for now the rollout is focused on infant and under 5 mortality [15]. As pneumonia is a large killer of children under five, we can assume to see impact in 2-4 years. A decline in deaths per million began in 2019 as vaccination continued, particularly in the districts receiving the vaccine. Because of the prevalence of disease there is higher impact potential in these districts compared to the state itself. Isolating the districts that received the vaccine showed a concentrated amount of increased cases in 2018, averaging around 8-22 per million, with the exception of one district, Shravasti, that has a lower population.

Deaths from pneumonia require a more specific diagnosis as well as records that mainly take place at a hospital. Pneumonia deaths are significantly less prevalent because of these weaknesses in the surveillance system and a lack of access to diagnostic materials [16]. URIs experienced a relatively high hospitalization rate in the same areas as the pneumonia deaths. However, they followed similar fluctuation patterns during the analysis, indicating that risk factors for both general URIs and pneumonia are related and consistent.

Differences of the conditions in the individual districts that received the vaccine could account for fluctuations in death counts. The GIS data indicates consistent changes among 5 of the 6 districts (figures 8 and 10). For example, Siddharthnagar was named as one of the most “backwards” districts in the region [19]. Balrampur has been listed as a “Minority Concentration District,” which indicates below average socioeconomic status and a lack of basic amenities [20]. The district of Kheri has a literacy rate of 43% compared to the national average of 59.5% [22]. Sitapur is a high transportation hub, which has the potential to escalate transmission [24]. Finally, Shrawasti has many historic sites where relooks followers make pilgrimages, which has the potential for surrounding travelers to carry and bring in disease [25].

Another geographic phenomenon is the significantly higher death rates in the districts that border Nepal. Nepal’s PCV rollout took place two years before India’s and early research
supports its growing success [26]. The border is an open international border [27], so transmission events may have occurred between the two. The less severe districts that received the vaccine border low population areas that also experience lower rates of deaths per million. This trend continues in districts to the south, west, and east that border other states. Geospatial analytics are highly recommended for the future of PCV impact research.

**Statistical PCV Impact Evaluation**

My regression model determined that the rollout of the PCV did not have a statistically significant influence over changes in death rates from pneumonia in any of the districts. The most likely cause of this result is because of the confounding issues I discussed above. The recorded death counts are bound to rise during a pointed, national campaign to build data capacity. There may not be enough data from the pre to post vaccine period to draw a conclusion in such a short amount of time. It will be a challenge to effectively quantify impact and increase visibility of pneumonia deaths at the same time. More sophisticated methods to account for this trend are recommended.

A comparison model using general URI hospitalization did find statistical significance related to the vaccine rollout, indicating secondary impacts. My hypothesis that URI prevalence could serve as an indicator for missed pneumonia cases. This could be tested further in a few years after more data is collected. It is not sound to compare hospitalization rates against death rates, but it is possible that undiagnosed pneumonia cases had been grouped incorrectly with general upper respiratory infections. Upper Respiratory Infection hospitalization rates could have also been significant because they represent a healthcare interaction and are more easily recorded. Pneumonia deaths do not always touch the healthcare system, which can result in misrepresentation in the data. The same weaknesses in surveillance capacity in the region impacts surveillance of upper respiratory infections as well.

**Evaluation of Socioeconomic, Structural, and Cultural Barriers to PCV Implementation and Pneumococcal Surveillance**

Identifying the risk factors of pneumonia as indicators of limitations to data collection and surveillance can make it easier to conceptualize the situation in these densely packed cities.
While there is an aggressive advertising campaign in support of PCV implementation, those who experience poverty lack access to radio, internet, and television may be missing the message. Issues such as poverty, lack of access to care, lack of access to sanitation and water for hygiene, illiteracy, and compact urban living directly feed into the points of failure in accounting for people who require vaccination or care [4]. Slums are challenging to navigate and in many parts of Uttar Pradesh data on addresses are weak, though the census efforts are attempting to correct this and create stronger accounting for citizens [17]. However, a portion of the 2021 census is expected to be collected via smartphone, which only 63% of slum dwellers own [30]. However conventional methods will still be used in partnership with the new initiative [18]. This effort will be particularly important as India’s new Universal Healthcare policy which will provide funding for the poor is implemented.

More specifically, many births and deaths occur at home [4] and it is extremely challenging for public health entities to gather reports of deaths outside of the major cities. HMIS data could not record these individuals. Anecdotal evidence from residents of smaller villages report never visiting a hospital, even in dire circumstances [21]. This presents a challenge as the first rollout of the PCV will only be available at hospitals [11]. Healthcare seeking culture is remarkably low in these areas as mistrust of healthcare abounds because of lack of support from local government and the privatization of healthcare resources beyond their economic reach [21]. Uttar Pradesh is the most populous state in India [4], which presents a challenge in accounting for the health of every life. The rate of doctors and hospitals per capita are lower, with 1 doctor per 1800 citizens [22]. High poverty is directly associated with poorer health outcomes [4], and the specific limitations of India’s healthcare system exacerbate the figures represented in existing research. While there is a strong research infrastructure in many Indian Universities, it is nearly impossible to account for those considered invisible by society who have never interacted with the healthcare system.

This brings us to the problem of the quality of the surveillance itself. The data was not age stratified, which represents the weakness of the data in terms of the focus on child mortality. Overall death counts are broad and nonspecific in terms of targeting specific groups. For example, high population areas experienced higher rates of infection according to visual inspection, however there was no specification between location in or out of major cities that
contain more hospitals or any data on socioeconomic status. It is challenging to suggest improvements or new surveillance tactics without this specific data. Previously discussed research supports the connection between poverty and poor reporting, but assumptions without further scientific investigation only contributes to the shakiness of the data.

Analysis of surveillance methods are needed to explain disparities in the observed year to year deaths. Potential for further analysis as the years progress may bring more trends to light. India has yet to implement their own impact evaluation of the PCV rollout because they consider the data as still pending [28]. The potential future data provided by the government will have strengths and weaknesses. Their own analysis will most likely be stronger than HMIS data because of a higher knowledge of the areas and citizen behaviors. However, there have been many criticisms and concerns of underreporting in order to maintain a positive perception of their recent public health efforts [29].

Conclusion

Ultimately there is groundwork for a meaningful pattern despite the small window of time. The time series analysis of deaths in Uttar Pradesh have shown some improvements in representing deaths post 2017. However, the estimated death counts are still lower than existing research would anticipate in areas with research supported indicators for poor health outcomes. The data in this paper is chaotic in nature, which serves as both a barrier in analysis and the heart of the issue at hand. Surveillance needs to be strengthened in order to identify any valid patterns. A further rollout to other states is expected by 2022 [28], so the opportunity to make systematic improvements has a small window. The prepared expansion of Universal Healthcare by Prime Minister Modi potentially serves as an opportunity to build a stronger picture of public health in India and increase access significantly, however plans for implementation have a weak budget and vague language [2]. India is an extremely interesting challenge for public health because of its size, population, transitional stage of development, and varied cultures and practices between districts and states. Despite the weak data in this paper, determining the weaknesses are just as important as determining the strengths.
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