national schedule. This new schedule reduces how much vaccines are given during clinic visits and allows opportunity to introduce new future vaccines [35].

4.3. Global Disparities in Pneumococcal Vaccine Coverage

Pediatric pneumococcal disease exacts a substantial burden on global health, much of which is vaccine preventable. Despite this considerable burden and the demonstrably high efficacy of PCVs, the overall level of PCV uptake remains concerningly low, especially compared with that of other childhood-recommended vaccines, such as tuberculosis and polio. A wide array of plausible expositions exists for this low uptake, including logistical challenges, psychosocial factors, and cost-effectiveness. Although decisions regarding PCV introduction and recommendation vary by country, an increasing number of both high- and low-income countries now incorporate PCV into their national immunization programs (NIPs). As of March 2019, 147 countries had introduced one or more PCVs into their NIPs (including 136 universal, five subnational, and three special risk programs), and 15 countries had announced plans to introduce a PCV [26]. These 147 countries include 60 low-income countries eligible for international assistance in procuring vaccines that introduced PCV after 2009 (the year in which funding from Gavi, the Vaccine Alliance, became available for PCVs) [36]. **Figure 2** shows global PCV coverage by countries.

Reductions in the worldwide burden of childhood pneumococcal diseases reflect the widespread adoption of pneumococcal vaccines over the past two decades. Within the past 10 years, the total number of countries that have introduced PCVs (in at least one population and at least one region) has more than quadrupled. Despite these recent progress and relative growth in vaccine coverage, the

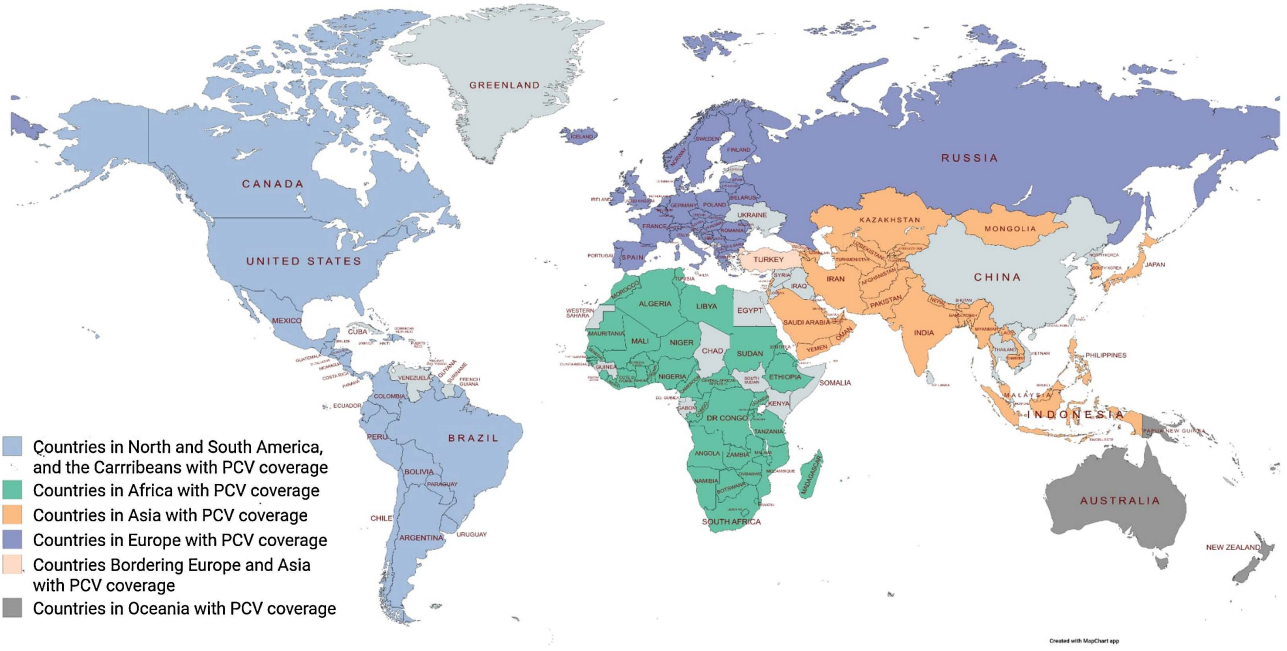


Figure 2. Vaccine coverage map [26]. Countries in grey represent areas without PCV coverage.

universal acceptance level of PCV is still subpar. The World Health Organization (WHO) estimates that global coverage of the third dose of PCV, while notably greater than in 2014, still only reached 48% of its target population in 2018 [37]. Table 4 below describes the percentage of the global population in the last 10 years who were vaccinated annually, and Figure 3 illustrates the trend in annual vaccination during the same period.

Table 4. Global vaccine coverage in the last 10 years according to World Health Organization (WHO) [37].

Year	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023
% population	26	32	38	41	45	48	51	51	51	60	65

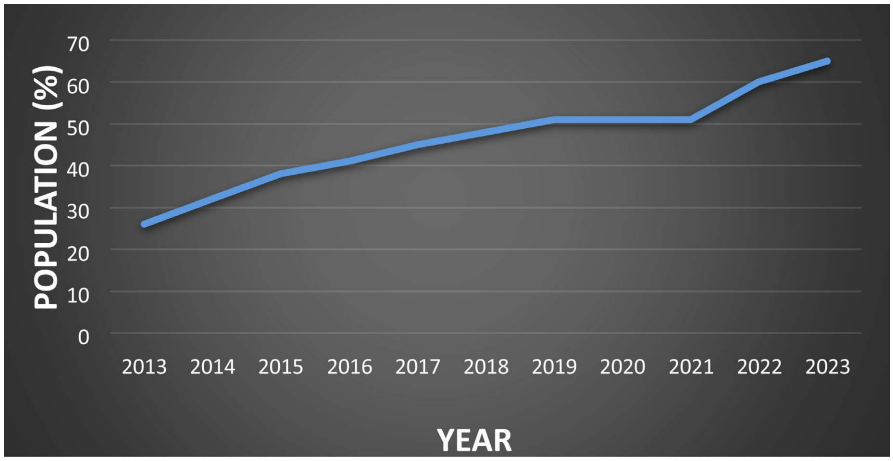


Figure 3. Trends in global vaccine coverage over the last decade [37].

Many barriers and obstacles can impede PCV uptake. From a logistical standpoint, sustaining high coverage rates requires a dependable supply chain network, which has become increasingly challenging due to widening varieties of available vaccines, increasing supply costs, and tightening infrastructure standards. Many existing immunization and supply chain logistics (ISCL) systems are not keeping pace with the changing vaccine landscape, often resulting in stock shortages, inventory unpredictability, the potential administration of ineffective vaccines and avoidable wastage. The WHO estimates that in 2011, cold-chain failures in five countries resulted in the loss of 2.8 million vaccine doses [38].

Even when existing ISCL systems are running smoothly and efficiently for the areas that they serve, accessibility often remains an especially important consideration for uptake in developing and rural areas. In underserviced areas, limitations such as travel opportunity costs, direct costs, and safety concerns may play a larger role in vaccination decisions. Children born to families living farther away from a road or clinic are at demonstrably greater risk of not being fully vaccinated, even where vaccines are reliably available and reimbursed [36]. Accessibility shortcomings and insufficient ISCL system funding both have far-reaching implications for vaccine coverage, uptake, and—in cases of noncompletion—efficacy [38].

Behavioral and psychosocial considerations are also key determinants of vaccination uptake [36]. Vaccine hesitancy is one leading impediment to sustaining high coverage rates and is common worldwide: more than 90% of countries reported some level of vaccine hesitancy [39]. The top three reasons cited for vaccine hesitancy globally in 2016 were 1) risk-benefit concerns (such as vaccine safety concerns, 23% of responses); 2) lack of knowledge and awareness of vaccination and its importance (10%); and 3) religion, culture, gender, and socioeconomic issues regarding vaccines (12%) [39]. The spread of misinformation through anti-vaccination lobbies and the media exerts a powerful influence on parents' vaccination decisions and perceptions of vaccine safety. Another basis of low pediatric PCV uptake is affordability. PCVs are more expensive than earlier generations of vaccines, and their prices have been rising in the United States and globally [40] [41].

One other plausible major and systemic cause of low uptake is economists' and policymakers' tendency to undervalue vaccination in general, particularly PCVs, by adopting a narrow health sector perspective when performing economic evaluations of vaccines. The conventional health sector perspective focuses on two benefit categories of vaccination: healthcare cost savings (stemming from reductions in visits to healthcare professionals, inpatient stays, and prescription drugs) and health gains (the value of reduced morbidity, mortality, and suffering from pneumococcal diseases). These two benefit measures alone are inadequate to establish a panoramic assessment of the value of PCVs, as they do not capture a much broader set of socioeconomic benefits to society [37].

4.4. Challenges and Future Directions for Pneumococcal Vaccination

Despite the increase in vaccination rates with the pneumococcal vaccines, there are still missed opportunities for vaccination, such as at the time of hospital discharge or clinic visits, [1] as well as vaccine hesitancy. Other avenues to offer pneumococcal vaccination include nursing homes and long-term care facilities. Early identification through screening and vaccination of at-risk groups especially in hospitalized populations would remarkably reduce morbidity and mortality from pneumococcal diseases [1]. The lack of a vaccine that can protect against all pneumococcal serotypes as well as the spread of resistant serotypes pose significant challenges for both pneumococcal vaccines and antibiotic-resistant pneumococcus [37]. The CDC recommends that expanding vaccine use can prevent future infections, slow, and even reverse emerging antibiotic resistance [37]. According to Dunne *et al.*, the knowledge gap between host responses, viral and pneumococcal respiratory infections, and the role of PCVs need to be explored further [25]. Cai et all surmised that newer vaccines that target all strains, can reduce disease burden as well as asymptomatic carriage [42]. A non-dependent-serotype protein vaccine is also an advantageous and more affordable pneumococcal vaccine option for children in third world countries, providing extensive coverage against

geographical serotypes against IPDs and other pneumococcal infections, thus curbing the global impact of pneumococcal diseases [23] [24].

Active surveillance will continue to identify populations with vaccine hesitancy, low vaccine uptake, and poor vaccine education as well as growing antibiotic resistance. Constant public reminders such as vaccine education and advocacy on the unparalleled importance of vaccination and herd immunity, will promote active vaccine acceptance and uptake and reduce cost association with antibiotic resistance and treatment of pneumococcal infection.

4.5. Actionable Plans to Improve Pneumococcal Vaccine Coverage

Prioritization of vaccination scheme: this involves initiatives such as pharmacist-led distribution programs, standing orders for nurses to administer vaccines and appropriate protocols for distribution, improved protocols for eligibility (e.g. notification within electronic medical record when accessing a patient's chart, standardized checklist guidelines), and routine vaccination guidelines on a national level. A study by Patel *et al.* showed that pharmacy-led teams in the United States increased national immunizations by an estimated 3.5 million doses per year [43] [44].

Removing practical barriers to immunization such as access: Limited access to vaccination is one of the leading causes to reduced coverage (e.g. limited opening hours, distance to health centers, inconvenient booking system). Improving on the booking system such that individuals can book and receive vaccination same day would increase the rate of vaccination. In addition, the creation of mobile vaccination units will reduce the distance between individuals and vaccination sites [45].

Use of immunization information system: Immunization information systems (IIS) are confidential, computerized, population-based systems that collect and consolidate vaccination data from vaccination providers and provide important tools for designing and sustaining effective immunization strategies at the provider and immunization program levels. These tools include clinical decision support, vaccination coverage reports, interoperability with electronic health record systems, vaccine inventory management, and the ability to generate reminder and recall messages. Patient recall and reminder systems such as sending text messages or phone calls to individuals to remind them of their upcoming vaccination appointment or pending vaccination booking have shown to be an effective way to increase coverage [46] [47].

5. Recommendations

There is great need to increase pneumococcal vaccine uptake in the US and globally. Initiatives to increase vaccine uptake should be prioritized and promoted. For instance, opportunities for vaccinations such as at a clinic visit, hospital discharge, long-term care facilities, nursing homes and general public health promotion should be maximized. Issues of vaccine hesitancy need to be addressed at all levels

of health care services, especially at the primary care level which serves as the patients' medical home and the bridge between community and health care services. Addressing behavioral and psychosocial issues such as health-seeking behaviors; vaccine safety concerns; lack of knowledge and awareness of vaccination and its importance; religion, culture, gender, and socioeconomic issues regarding vaccines; and misinformation are key to solving vaccine uptake barriers such as vaccine hesitancy and nescience.

Despite ongoing research efforts to provide a single vaccine that can cover all serotypes or antigens, policies need to be set in place by health care policymakers to improve vaccination rates. Factors such as barriers to vaccine access; ability to schedule and attend appointments; ability to pay for uninsured vaccine services, limited opening clinic hours are important considerations for policymakers. These are especially important in resource poor communities and populations facing social and health inequities.

6. Conclusion

Though there have been great strides in the evolution of pneumococcal vaccines and its effect on IPDs, there is still much to be done. Vaccine uptake in more developed countries like the US is unsatisfactory, as the prevalence of pneumococcal diseases persists. This is of great public health concern. Areas for future research in pneumococcal vaccines include coverage for all serotypes and NVTs. We believe that public health policies surrounding vaccine advocacy need more attention to encourage PCV accessibility and embrace, while also addressing the issue of its costs.

7. Strength and Limitations of the Study

This study uses moderate quality evidence derived from multiple publications including those from the CDC and WHO, providing a general overview and a practical, comprehensive and pertinent synthesis of diverse literature. It is believed that as research evolves, new serotypes of the pneumococcal disease may develop, and existing serotypes may mutate which would affect the development of new vaccines and the use of existing vaccines. Our study observes gaps in vaccine schedules and coverage, and sets the stage for future research. The study design also includes observational studies based on the effect of the vaccines observed over the years. However, our study lacks methodology, and an exhaustive and systematic review of the data.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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