A narrative review on vaccination rate and factors associated with the willingness to receive pneumococcal vaccine in Chinese adult population

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ABSTRACT
The 23-valent pneumococcal polysaccharide vaccine (PPSV-23) is the only approved vaccine for pneumococcal diseases in elderly Chinese population. Though regional studies explored the PPSV-23 vaccination coverage rates and influencing factors in China, a large-scale, nation-wide epidemiological surveillance studies to understand the different factors impeding pneumococcal vaccination rate are required. Hence, this review summarized PPSV-23 coverage rate, analyzed and identified vaccination influencing factors among elderly population across China by exploring articles published in CNKI, Wanfang and PubMed databases. Pneumococcal vaccination coverage rate was found to be low at around 1.23%~42.10% in China. Co-morbidities, knowledge, attitude, perception toward pneumonia and PPSV-23, education level, socio-economic disparities, health education and local policies were some of the factors associated with vaccination willingness among elderly Chinese population. Interventions or policies like government funding, subsidies, inclusion of PPSV-23 in medical insurance, or systematic encouragement from HCPs as key strategies should be implemented to encourage vaccination.

1. Introduction
Streptococcus pneumoniae (also known as pneumococcus) is the leading cause of invasive pneumococcal disease (IPD), comprising meningitis, bacteremia, and pneumonia, and ranks as the most common causative agent of community-acquired pneumonia (CAP) in adults. Elderly population are at greatest risk of IPD with high morbidity and mortality. Due to the increased size of aging population (>60 years old) in China which accounts 18.1% (253.9 million) by the end of 2019, which further increases by 483 million (35.4%) by 2050, disease burden of pneumococcal pneumonia will be exacerbated and it is believed to be clinically significant. In China, pneumonia is the fourth leading cause of the death in elderly accounting for 125000 deaths every year and infection rates of pneumonia differ regionally, varying from 28.0% to 71.5%.

High antimicrobial resistance to S. pneumonia in elderly people aged ≥ 65 years from China (>40% for erythromycin, cefuroxime and, penicillin) emphasizes the significance of vaccination in this age group in preventing pneumococcal pneumonia. In China, 23-valent pneumococcal polysaccharide vaccine (PPSV-23) was approved to use in elderly population and children with certain medical conditions. PPSV-23 offers protection against diseases associated with 23 common serotypes of S. pneumonia and with its application, reduced mortality rates of CAP and IPD, have been documented in elderly. Recent studies have supported the effectiveness of PPSV-23 vaccine in preventing pneumonia and IPD in adults and recipients aged ≥ 65 years old. In China, a study conducted by Xu et al. reported that vaccination with PPSV-23 in elderly was associated with reduced incidence of lower respiratory tract infection (69.7%), and hospitalization (65.9%) during the subsequent years. Despite amicable evidences, pockets of data from different regions of China indicated that PPSV-23 vaccination coverage among elderly is less than 3.7% in 2019. On contrary, pneumococcal vaccination coverage in Western countries (USA and England) is as high as 60% in elderly. Behavioral intentions were reported to influence the acceptance of pneumococcal vaccination among the elderly.

As the studies on vaccination rates and the factors influencing the administration of vaccines from China were confined to specific regions. Lack of large-scale, nation-wide epidemiological surveillance studies to understand the different factors impeding pneumococcal vaccination rate. Hence, there is an urgent need to identify the evidences addressing the pneumococcal vaccination rate and influencing factors in Chinese adults.

With this background, this review is aimed to summarize the vaccination rate of pneumococcal vaccine and the influencing factors, including the disparity in the availability of free vaccines between different geographic locations among elderly population in China.

2. Vaccination coverage of pneumococcal vaccines among elderly population in China
In China, PPSV-23 vaccine has been used to prevent pneumococcal infections since 1996. Governments of Beijing and Shanghai, Shenzhen implemented policies to provide free vaccination to local elderly residents. However, data from...
local areas show that pneumococcal vaccination coverage rate in elderly is very low (Figure 1 and Supplementary Table 1).

In 2010, a local study from Chaoyang district of Beijing reported that 19.6% of elderly participants aware of the fact that vaccination can prevent pneumonia. However, pneumonia vaccination rates were observed in only 2.1% among elderly (≥ 65 years) in the community. In 2014, data from QingPu District of Shanghai revealed that pneumococcal vaccination rates in the residents aged ≥ 65 years were 1.8%-2%. But, vaccination rate among residents aged ≥ 80 years was slightly higher (4.4%). In 2015, a survey of 1200 randomly selected residents (aged ≥ 60 years) of Chengdu region in China under pneumococcal vaccination subsidy program demonstrated a pneumococcal vaccination rate of 42.1%. A cross-section study from Hangzhou city of China analyzed immunization records of 9,027,977 (aged ≥2 years) residents from 2006–2017 and found a vaccination coverage of PPSV-23 of 2.98%. The vaccine coverage among elderly (aged ≥ 60 years) was between 0.17% to 0.69% with a high rate in urban areas (3.70%) compared to rural areas (3.34%). According to public health records, in Hong Kong, around 34% of the residents aged ≥65 years were vaccinated against pneumococcal diseases in 2015 (retrieved from Hong Kong information services department).

Through a public health projec, Shanghai municipal government provided free vaccination of PPSV-23 for elderly since 2013. A total of 1.56 million elderly population were vaccinated through this program with an estimated coverage of 30%.

2.1. Pneumococcal vaccination coverage in adults with chronic conditions

Adults with co-morbidities such as cardiovascular diseases, diabetes, or pulmonary diseases are at greater risk to develop complications from vaccine-preventable diseases, like IPD. Several previous studies have found a benefit of administering pneumococcal vaccine to elderly and patients with chronic illness and demonstrated that vaccinated patients with co-morbidities had the reduced treatments or hospitalizations. World Health Organization (WHO) and US Centers for Disease Control and Prevention (CDC) recommended to prioritize the pneumococcal vaccination in elderly and patients with co-morbidities.

A retrospective study from Shanghai analyzed the immunization records of 2,531,227 (≥15 years) residents with co-morbidities (hypertension, diabetes and chronic obstructive pulmonary disease [COPD]) from 2013–2017 and found a vaccination coverage of 22.8%. Vaccination coverage was observed highest in elderly aged ≥ 60 years.

In a Chinese COPD surveillance (2014–2015) program, 9067 patients (aged ≥40 years) were assessed for pneumococcal vaccination status. The vaccination rate was found to be 0.3% (95%CI: 0.2%-0.5%) in the patients aged 40 to 59 years and 1.2% (95%CI: 0.3%-2.1%) in the patients aged ≥60 years (P < .05). The vaccination rate was 1.4% in former smokers and 0.6% in current smokers. The vaccination rate was higher in urban area (1.5%) compared to rural area (0.4%). In China, a 2018 questionnaire-based survey of 3000 random patients with type 2 diabetes mellitus found a low pneumococcal vaccination rate (0.79%) and 43.75% patients were willing to receive pneumococcal vaccination.

3. Factors influencing the pneumococcal vaccination among elderly

Vaccination coverage of pneumococcal vaccine in elderly population is influenced by several factors such as knowledge,
beliefs and attitude of elderly toward pneumonia and vaccination, socio-economic status, education level, cost of vaccine and availability health education (Table 1).

Favorable policies, recommendation by physicians or family members, knowing that vaccine is effective and having high education were reported as contributing factors for high vaccination rate of PPSV-23 among elderly in Zhengzhou and Chengdu regions. Whereas, low education, poor economic status and perception on vaccine contributed for very low vaccination rate in Qing Pu district, Chaoyang district and Xi’an city (Supplementary Table 2). The overall awareness of vaccination among Chinese adults is low, which might have led to the low vaccination rate in most regions of China. Some regions might have benefited by related policy thus the vaccination rate would have significantly increased. Other reasons are economic conditions of different regions, and the study design, quality, time of the study may also contribute to the difference in vaccination rate.

Hence, understanding the potential barriers that impend acceptance of PPSV-23 among the elderly is significant to accelerate the vaccination process and to frame required policies.

3.1. Knowledge, perception and beliefs about pneumococcal vaccine

A previous Chinese-based study demonstrated that knowledge has a positive impact on attitudes toward pneumococcal vaccine uptake among elderly. It helps to improve elderly cognition on the performance expectancy of pneumococcal vaccines and also positively correlates to behavioral intention. Trust was another factor that was predicted as significant factor that affects both behavioral intention and uptake of vaccine. To encourage pneumococcal vaccination among elderly in China, it is important to build the trust among the elderly on health care providers, vaccination safety, and health protection intention.

In a study conducted by Liu et al., of 2926 elderly population surveyed, rate of reasonable perceptions about vaccination, including the perception about vaccine efficacy and safety among the elderly, was observed in less than 50%. Around 43.3% believed that vaccination could protect them from pneumococcal disease.

In October 2020, a questionnaire-based survey of 15,066 older adults in Shenzhen City of China reported that 81.3% aware of pneumonia infection (p < .001) and majority of subjects (87.5%) accepted that pneumonia is a life-threatening disease. Around 37.8% older residents believed that pneumococcal vaccination is helpful in preventing pneumococcal pneumonia (p < .001), and 22.8% aware of the local pneumococcal vaccination policy (p < .001).

A cross-sectional study based out of Shanghai interviewed 12000 household elderly aged 60 years and reported that 61.9% were aware of pneumonia and 68.1% knew about PPSV-23 vaccination. Moreover, the awareness rate of vaccination was observed to decline with increasing age, but increased with education level. Around 80% of participants learned about PPSV-23 through television, posters, informed consents, friends and physicians. Subjects who were not aware of PPSV-23 were willing to gain information about it. The survey results emphasized that knowledge is vital factor in decision making of acceptance of pneumococcal vaccine.

In 2017, a survey conducted in Foshan city, Guangdong province found that knowledge about pneumonia and pneumococcal vaccine were some of the influencing factors of pneumonia vaccination in the elderly. In a previous survey of patients with Rheumatic diseases (n = 235) in China, the major reason given for not taking vaccination included, “vaccination is unnecessary” (8.9%) and “troublesome to take vaccine” (8.3%). Patients preferred to take pneumococcal vaccine if they were aware of it before or had knowledge of pneumonia, and had trust in vaccine’s safety and efficacy (p < .05).

A Hong Kong based study investigated 40 elderly people on perceptions and barriers associated with the seasonal pneumococcal vaccination. The belief of vaccine as harmful, negative rumors on vaccine, low perceived risk of contracting the pneumococcal disease, use of traditional Chinese medicine were identified as major factors that prevent elderly from being vaccinated with pneumococcal vaccine.

3.2. Health education and vaccine policies

Health education is an effective strategy to promote the coverage rate of pneumococcal vaccination among the elderly. Physicians and healthcare practitioners (HCPs) play a vital role in bringing awareness in elderly on the importance of pneumococcal vaccination in reducing the risk of pneumonia.

Data from a previous survey of 869 older adults in Ninghai city of China revealed that only 17.61% were recommended to be vaccinated by nearby doctors, and 5.87% were occasionally recommended. Moreover, elderly who had been already vaccinated with pneumonia vaccine, 47.06% were vaccinated based on recommendation of physician. In a recent Chinese population-based survey, recommendation by physicians (adjusted odds ratio = 7.399, 95% CI: 3.472–15.764, p = .008) was found to be one of the main factor for acceptance of pneumococcal vaccine among elderly. It indicates that HOPs play a key guiding role in recommending the elderly to be vaccinated against pneumonia.

A Hong Kong-based cross-sectional study assessed the attitude of general practitioners toward pneumococcal vaccination for elderly population (aged >65 years) and reported that 53.4% of the practitioner would actively recommend pneumococcal vaccination to elderly patients. Main reasons for not recommending pneumonia vaccination by practitioner were consultations not related to pneumococcal vaccine (43.6%), rarity of pneumonia cases in their daily practice (68.4%).

China’s government currently does not provide PPSV-23 among its mandatory vaccines freely available to elderly. Hence, difference in local policies leads to difference in vaccination rates. Shanghai has implemented a policy to provide free vaccine to residents with 60 years or old with PPSV-23 since 2013 which lead to increased vaccination rate (1.56 million people were vaccinated). A questionnaire survey among the elderly residents (aged 50–69 years) in 13 communities in Shanghai in 2020 reported that price sensitivity plays a key role in acceptance of PPSV-23 vaccination.
Table 1. Different factors that impact the pneumococcal vaccination among Chinese elderly population.

| S.No | Influencing factor of pneumococcal vaccination | Impact on pneumococcal vaccination | Study population | Surveyed population | Studied region | Odds ratio with 95% CI | Year of publication | First author name and references |
|------|-----------------------------------------------|------------------------------------|------------------|---------------------|---------------|-----------------------|---------------------|-------------------------------|
| 1    | Recommendation by physicians                   | Recommendation by physicians was positively associated with pneumococcal vaccination rate | 1000             | Elderly ≥60 years   | Hong Kong region | Adjusted OR = 7.399  | 2016               | Huang J et al.13             |
|      |                                               |                                    |                  |                     |               | (95% CI: 3.472–15.764) p = .008 OR = 0.37 |                     | 2016 Zuo Mengmeng et al.12   |
| 2    | Previous vaccination history                    | Previous vaccination history was associated with more acceptance of pneumococcal vaccination | 15,066           | Elderly ≥60 years   | Shenzhen region | Adjusted OR = 3.199  | 2021               | Zhang M et al.12             |
|      |                                               |                                    |                  |                     |               | (1.492–6.860) p = .008 |                     | 2021 Shijun Liu et al.11     |
| 3    | Knowledge, beliefs, trust and attitude toward vaccination | High knowledge, positive attitude and trust on vaccine safety was associated with higher likelihood of pneumococcal vaccination | 600              | Elderly ≥60 years   | Changsha region | OR = 2.00 (95% CI: 1.54–2.59) | 2014               | Liu S et al.13               |
|      |                                               |                                    |                  |                     |               |                       |                     |                               |
| 4    | Education level and occupation                 | Higher education and occupation level in elderly was associated with increased acceptance rate of pneumococcal vaccine | 11,972           | Elderly ≥60 years   | Changsha region, | OR = 22.24 (95% CI: 8.60–57.56) | 2019               | Yang et al.33               |
|      |                                               |                                    |                  |                     |               |                       |                     |                               |
| 5    | Socio-economic disparities                     | Good family economic status was associated with high vaccination rate | 886              | Elderly ≥55 years   | Ninghai County | OR = 1.68 (95% CI: 1.64, 1.71) | 2016               | Zhang Q et al.17             |
|      |                                               |                                    |                  |                     |               |                       |                     |                               |
| 6    | Co-morbidities                                | Previous vaccination history and having multiple co-morbidities was associated with higher likelihood of acceptance of pneumococcal vaccination | 2,531,227        | Individuals ≥15 years | Shanghai region | OR = 0.15 (95% CI: 0.03–0.70) | 2019               | Yang et al.33               |
|      |                                               |                                    |                  |                     |               |                       |                     |                               |

Abbreviations: CI, Confidence Interval; OR, Odds Ratio.
Vaccination willingness was 79.4% (free PPSV-23 for local persons), 54.7% (self-paid PPV23 for non-local persons). Inclusion of PPSV-23 in medical insurance policies or providing vaccine for subsidy may promote the coverage rate of pneumococcal vaccine among elderly.

3.3. Education levels, occupation and income

Previous studies demonstrated that education level plays a major role in acceptance of pneumococcal vaccine. Higher education in elderly was associated with increased acceptance rate of pneumococcal vaccination compared to those with low education levels. Furthermore, data from surveys conducted in multiple regions of China demonstrated that higher education level, occupation and income were positively associated with willing to accept pneumococcal vaccine (p < .05) in elderly. It is possible that the elderly with high educational level usually pay more attention to health care policies and take the initiative to understand the relevant knowledge of pneumonia vaccine.

3.4. Socio-economic disparities

PPSV-23 is a self-paid vaccine in majority of the regions in China, therefore the vaccination rate is affected by personal economic status. Data from a previous survey on willingness to uptake of self-paid pneumococcal vaccine indicated that 92% of the households are not willing to pay market price of pneumococcal vaccine. Low price barrier was associated with uptake of vaccine. Couple of Chinese-based surveys reported that vaccination rate in elderly with good family economic status was relatively high and the cost was acceptable. For the elderly with poor economic status, the vaccine price was too high to bear, which is also an important factor causing the low vaccination rate.

As China rapidly urbanizes, the vaccination rates in migrants from rural areas (also called floating population) and people living in rural areas were reported to be very low.

4. Willingness to get PPSV-23 vaccination against invasive pneumococcal disease

Several factors were reported to be association with the willingness toward pneumococcal vaccination. Having a greater number of chronic diseases in Chinese patients was one of the factor that was associated with higher likelihood of pneumonia vaccination. A study conducted by Liu et al in urban elderly population of China demonstrated that factors such as severity of pneumonia, safety of PPSV-23 vaccination, advice on the vaccination from family members, and pneumococcal vaccination history were found to be independently associated with the willingness to receive PPSV-23 vaccine.

Data from a recent large-scale questionnaire-based survey of 15,066 respondents of Shenzhen city of China revealed that subjects with better knowledge about pneumonia were 1.39 times more likely to get the pneumococcal vaccine compared to subjects with poor knowledge. The perception that pneumonia is a severe disease and pneumococcal vaccination is sufficient to prevent pneumonia were related to the positive attitude toward pneumococcal vaccination. Moreover, subjects with a pneumococcal vaccination history in the past five years were also likely to accept pneumococcal vaccine. Another recent Chinese based study reported that pneumococcal vaccination uptake in elderly was strongly influenced by service accessibility, followed by willingness, price sensitivity, medical history of vaccine-preventable diseases and underlying diseases. A recent meta-analysis evaluated the willingness of 19136 Chinese residents to receive pneumococcal vaccination in elderly population, and found an overall willingness rate of 49%. The vaccination willingness rate was higher in people with undergraduate and above education levels (71%) compared to those with lower education (53%; junior middle school and below, senior high school, technical secondary school). The vaccination willingness rates of the elderly with and without chronic diseases were 49% and 45%, respectively. Public interest in vaccinations generally surges during outbreaks, particularly with regard to diseases like pneumonia and COPD that manifest symptoms similar to those of the pandemic. Heightened willingness in pneumococcal vaccine was observed in China during coronavirus disease 2019 (COVID-19) pandemic. Pneumococcal vaccination in China increased significantly, even if it was self-paid. Since beginning of 2020, China issued around 4.97 million pneumococcal vaccines, a significant increase of 65.2% year-on-year. Another study has demonstrated a peak in global interest in the uptake of pneumococcal vaccine during the early stages of the COVID-19 pandemic (between February and March 2020). Since 2020, the public awareness of health has increased significantly regarding disease symptoms that are similar to that of COVID-19, such as influenza, pneumococcal pneumonia. Furthermore, a recent meta-analysis demonstrated that COVID-19 pandemic has increased intention to vaccine against influenza globally. A recent Chinese based study demonstrated that government promotion, residents perception of the importance of vaccines and the risk of disease were the main reasons for accelerating residents to vaccinate against COVID-19. Overall, it indicates that global pandemics may change public perception about the importance of vaccines.

5. Cost-Effectiveness of pneumococcal vaccine

Cost-effectiveness of vaccine plays an important role in vaccine coverage rate. Couple of previous studies have analyzed the cost-effectiveness of PPSV-23 vaccination program in Shanghai from the health system perspective. Routine vaccination of the elderly population with PPSV-23 was found to be cost-effective. A study conducted by Zhao et al., on people aged ≥ 60 years in Shanghai, China, in 2016 reported that incremental cost-effectiveness ratio of PPSV-23 vaccination compared with no vaccination was $16,699/quality-adjusted life years gained, which was lower than the per capita GDP of Shanghai ($16,840).

6. City immunization program (CIP) in China

Some cities in China have started implementing free pneumococcal vaccination (PPSV-23) for people over 60 years of age. Shanghai was the first city that initiated the CIP in 2013.
Currently, around 15 cities offer the free pneumococcal vaccination in China. In 2019, among the overall pneumococcal doses released, around 16% were covered under CIP (Figure 2).

7. Future directions and measure that can enhance vaccination rate

Considering the sub-optimal coverage of pneumococcal vaccine in elderly population of China, interventions or policies like government funding, subsidies or inclusion of pneumococcal vaccine in medical insurance are some of the suggested strategies to be implemented to encourage vaccination.

Novel and effective strategies are required to strengthen the knowledge, attitudes, perception and beliefs toward pneumonia and PPSV-23 vaccine among elderly population. Health education programs that target elderly people and HCPs should focus on the hazards of pneumococcal disease, the interpretation of the guidelines, the benefits of vaccination and local vaccination policies.

Continuous improvement of the accessibility and equality of vaccination services in rural areas should be considered to further substantially increase the vaccination coverage in Chinese elderly.

8. Conclusion

Vaccination coverage rate among elderly population in China is low compared to vaccination coverage rates in western countries. The vaccination rate of pneumococcal vaccine was 1.23%–42.10% in China. A high vaccination rate in Zhengzhou and Chengdu and Hong Kong regions was observed, on contrary, lowest vaccination rate was observed in Qing Pu district, Chaoyang district, Xi’an city and Hangzhou. The overall awareness of vaccination among Chinese adults is low, which might have led to the low vaccination rate in most regions of China co-morbidities, knowledge, attitude, perception toward pneumonia and PPSV-23 vaccine, education level, socio-economic disparities, health education and local policies were some of the factors that are associated with willingness toward vaccination among elderly population in China. High education levels, recommendation by physician or family members, favorable policies, previous vaccination history, co-morbidities, knowing the fact that vaccine is effective are few major influencing factors that were associated with high vaccination rate in some regions. On contrary, low education, poor economic status, poor awareness and wrong perception on vaccine were the some of the influencing factors that were associated with low vaccination rate in majority of the regions. Routine vaccination of the elderly population with PPSV-23 was found to be cost-effective. More cities in China are anticipated to provide CIPs to increase the coverage of vaccination in high-risk population. HCPs should be involved in the promotion of pneumococcal vaccination among elderly by providing effective health education and inculcating positive attitude toward pneumococcal vaccination.

Acknowledgments

The authors acknowledge Sankara Narayana Doddam, PhD and Vengal Rao Pachava, PhD of Indegene Private Limited, Bangalore, India for providing editorial assistance, which was funded by MSD China, Shanghai, China.

Disclosure statement

Peng Bai is employee of MSD China; all other authors have none to declare.

Funding

This work was supported by the MSD China, Shanghai, China and by 2021 Beijing Key Specialty Program for Major Epidemic Prevention and Control.

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