RESEARCH ARTICLE

ISSN 2307-9266 e-ISSN 2413-2241

Scientific and Practical Journal
PHARMACY & PHARMACOLOGY

PHARMACOECONOMIC EVALUATION OF ANTI-PNEUMOCOCCAL VACCINATION IN RISK GROUPS FOR THE PREVENTION OF COMMUNITY-ACQUIRED PNEUMONIA AMONG ADULTS IN THE ASTRAKHAN REGION

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Received 28 May 2020 Accepted 25 Oct 2020

The aim. To evaluate the economic efficiency and the choice of the vaccination strategy in the respiratory pneumococcal infection risk groups among the adult population of the Astrakhan region.

Materials and methods. The data for the period of 2015–2018 were analyzed on the number of registered diseases in the patients living in the service area of the medical organizations (Form No.12, Federal State Statistics Service Orders No. 591, dated 27 November, 2015; No. 679, dated 22 November, 2019). The following working directives were studied: the base medical examination documentation submitted by medical institutions (Form No. 030/y "Dispensary Monitoring Checklist"; lists of the persons subjected to medical observation in the reporting year; Orders of the Ministry of Health of the Russian Federation: No. 1344, dated 12 December, 2012; No. 173n, dated 29 March, 2019). Statistical materials of the territorial fund for compulsory medical insurance of the Astrakhan region on the payment of medical care to 12,970 patients who had pneumonia in 2015–2018, were analyzed. The financial support of vaccination based on the results of tenders for the procurement of pneumococcal vaccines organized by the regional Ministry of Health, was considered. The calculations were carried out in accordance with the guidelines of "Cost-effectiveness of vaccine prophylaxis" (Methodological guidelines 3.3.1878-04, dated 04.03.2004).

Results. The prospective calculation of the vaccination cost showed that the benefits of vaccination with pneumococcal conjugate vaccine Prevenar13 (PCV13) and pneumococcal polyvalent vaccine Pneumovax 23 (PPV23) with a 95% vaccination coverage, are recorded after 2 years. The economic benefit of vaccination by reducing the possible number of pneumonias at the end of 2028 will be 968.2 million rubles.

Conclusion. The economic feasibility of vaccine prophylaxis of the adult contingent with an increased risk of developing pneumococcal infection has been established. The sequential strategy of PCV13 and PPV23 application provides the most effective localization of pneumococcal infection. The research results should be widely introduced into the long-term plans for vaccination and healthcare practice in the Astrakhan region.

Keywords: vaccine prophylaxis; vaccination, pneumococcal infection; community-acquired pneumonia; PCV13; PPV23; risk groups; pharmacoeconomic analysis; Astrakhan region

Abbreviations: PN – pneumonia; PCV13 – pneumococcal conjugate vaccine "Prevenar 13"; PPV23 – pneumococcal polyvalent vaccine "Pneumovax 23"; CAP – community-acquired pneumonia; PI – pneumococcal infection; COPD – chronic obstructive pulmonary disease; CHD – coronary heart disease; CHF – chronic heart failure; DM – diabetes mellitus; HIV – human immunodeficiency virus.

For citation: E.A. Orlova, I.P. Dorfman, M.A. Orlov, M.A. Abdullaev. Pharmacoeconomic evaluation of anti-pneumococcal vaccination in risk groups for the prevention of community-acquired pneumonia among adults in the Astrakhan region. *Pharmacy & Pharmacology*. 2020;8(6):436-445. **DOI:** 10.19163/2307-9266-2020-8-6-436-445

Для цитирования: Е.А. Орлова, И.П. Дорфман, М.А. Орлов, М.А. Абдуллаев. Фармакоэкономическое обоснование проведения антипневмококковой вакцинации в группах риска для профилактики внебольничных пневмоний среди взрослого населения Астраханской области. *Фармация и фармакология.* 2020;8(6):436-445. **DOI:** 10.19163/2307-9266-2020-8-6-436-445

Научно-практический журнал
ФАРМАЦИЯ И ФАРМАКОЛОГИЯ

ОРИГИНАЛЬНАЯ СТАТЬЯ

DOI: 10.19163/2307-9266-2020-8-6-436-445

ФАРМАКОЭКОНОМИЧЕСКОЕ ОБОСНОВАНИЕ ПРОВЕДЕНИЯ АНТИПНЕВМОКОККОВОЙ ВАКЦИНАЦИИ В ГРУППАХ РИСКА ДЛЯ ПРОФИЛАКТИКИ ВНЕБОЛЬНИЧНЫХ ПНЕВМОНИЙ СРЕДИ ВЗРОСЛОГО НАСЕЛЕНИЯ АСТРАХАНСКОЙ ОБЛАСТИ

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Получено 28.05.2020 Принята к печати 25.10.2020

Цель. Обосновать экономическую эффективность и выбор стратегии вакцинопрофилактики в контингентах повышенного риска развития респираторной пневмококковой инфекции среди взрослого населения Астраханской области.

Материалы и методы. За период с 2015 по 2018 гг. проанализированы данные о числе зарегистрированных заболеваний у пациентов, проживающих в районе обслуживания медицинских организаций (форма № 12, Приказы Росстата № 591 от 27.11.2015; № 679 от 22.11.2019). Изучена основная документация по диспансеризации, представленная медицинскими учреждениями (форма № 030/у «Контрольная карта диспансерного наблюдения», списки лиц, подлежащих диспансерному наблюдению в отчетном году, Приказы МЗ РФ № 1344 от 21.12.2012; № 173н от 29.03.2019). Проанализированы отчетно-статистические материалы территориального фонда обязательного медицинского страхования Астраханской области (ТФОМС АО) по оплате медицинской помощи 12970 пациентам, перенесшим пневмонию в 2015–2018 гг. Для финансового обеспечения вакцинопрофилактики учитывались результаты конкурсных торгов по закупкам пневмококковых вакцин, организованных региональным министерством здравоохранения. Расчеты выполнялись в соответствии с методическими указаниями «Экономическая эффективность вакцинопрофилактики». МУ 3.3.1878-04 от 04.03.2004.

Результаты. При проспективном расчете затрат на реализацию вакцинопрофилактики установлено, что окупаемость вакцинации с применением ПКВ 13(«Превенар 13») и ППВ 23 («Пневмовакс 23») в условиях 95% охвата прививками регистрируется через 2 года. Экономическая выгода вакцинопрофилактики за счет снижения возможного числа пневмоний (ПН) по окончании 2028 года будет составлять 968,2 млн руб.

Заключение. Установлена экономическая целесообразность проведения вакцинопрофилактики взрослого контингента с повышенным риском развития пневмококковой инфекции. Наибольшей эффективностью для ограничения распространения пневмококковой инфекции характеризуется стратегия последовательного применения ПКВ13 и ППВ23. Результаты исследования подлежат широкому внедрению в перспективные планы вакцинопрофилактики и практику здравоохранения Астраханской области.

Ключевые слова: вакцинопрофилактика; вакцинация; пневмококковая инфекция; внебольничная пневмония; ПКВ 13; ППВ 23; группы риска; фармакоэкономический анализ; Астраханская область

Список сокращений: ПН – пневмония; ПКВ13 – пневмококковая конъюгированная вакцина «Превенар 13»; ППВ23 – пневмококковая поливалентная вакцина «Пневмовакс 23»; ВП – внебольничная пневмония; ПИ – пневмококковая инфекция; ХОБЛ – хроническая обструктивная болезнь легких; ИБС – ишемическая болезнь сердца; ХСН – хроническая сердечная недостаточность; СД – сахарный диабет; ВИЧ – вирус иммунодефицита человека

INTRODUCTION

Community-acquired pneumonia (CAP) has a leading position in the structure of morbidity and mortality from infectious diseases in the world. In terms of treatment costs, community-acquired pneumonia leads to significant economic losses suffered by the state. There are 3.9 cases of this disease in 1000 people per year among people over 18 years of age in Russia [1, 2]. However, these indicators do not reflect the true prevalence of CAP in Russia. According to various sources, it reaches 14–15% and comprises about 1.5 million people [3]. The most vulnerable categories for the pneumococcal infection (PI) development are young children and adults with chronic diseases of the lungs, cardiovascular system, liver, kidneys, diabetes mellitus (DM) and immunodeficiency diseases [4, 5]. The studies show that the risk of PI developing is significantly increased in patients with background diseases, aged 50–64 years. In comparison with somatically healthy individuals, the risk of PI developing is 13.3 times higher in oncohematological patients, 9.8 times higher in chronic obstructive pulmonary disease (COPD), 6.5 times higher in HIV infection, and 5.8 times higher in immunosuppressive conditions and chronic liver diseases. The risk of PI developing is

also increased by smoking by 4.4 times, in cardiovascular diseases by 4.2 times, in chronic kidney diseases and diabetes, respectively, by 4.2 and 3 times [6, 7].

In Russia, out of 500 thousand cases registered per year, 76% of adults and 90% of children under 5 years of age have pneumococcal etiology [8]. The current situation already calls for specific vaccination in risk groups. In cases of COPD, vaccination reduces the number of exacerbations, stabilizes the performance of functional tests, it also helps slow down the progression of respiratory failure [9, 10]. The relevance of vaccination increases with comorbid pathology. Thus, in 1/3 of cases, COPD is comorbid with an ischemic heart disease (IHD). The total mortality of patients with a chronic heart failure (CHF) with pneumonia development increases by 1.8-4.6 times, and the risk of death increases by 49.5%. It was established that in this category of patients, pneumonia contributes to the progression of circulatory failure by 17.7%, increases the risk of acute coronary syndrome by 14.1% and any rhythm disturbance by 5.3% [11–13]. A significant increase in economic losses due to direct and indirect costs up to 61.6 billion rubles is a negative contribution due to progressive COPD [14]. PI contributes to the sensitization and exacerbation of chronic non-specific inflammation in the bronchi, increases their hyperreactivity in the patients with bronchial asthma [15, 16]. In the presence of kidney diseases, PI is more common than generally in the population, and it is more severe, with possible fatal outcomes. Pneumonia and sepsis frequently develop in the patients with chronic renal failure, especially in those receiving long-term hemodialysis. It should be pointed out that the risk of death from pneumonia in this situation increases by 14–16 times [17, 18].

The need for vaccination against PI in DM and metabolic syndrome has been proved. These categories of patients are known to have defects in immunological protection against all types of microbial infection, including infections of pneumococcal etiology. Their risk of developing invasive forms of PI is 6 times higher in comparison with healthy individuals [19]. Furthermore, Streptococcus pneumoniae is one of the most frequent pathogens of recurrent pneumonia in patients with diabetes mellitus, which often develops with oropharynx or stomach content microaspiration due to esophageal paresis [20]. Unfortunately, researches show that immunization against PI in the already mentioned category of patients still does not correspond to the sufficient volume [21, 22].

Among the general range of problems related to the prevention of PI, the priority has been given to specific vaccination, which prevents the spread of antibiotic-resistant strains and reduces the development of the most severe clinical forms of pneumonia. Vaccination is not only effective but also costly. It is especially true in the countries with limited material resources that are not able to provide a sufficient vaccination coverage of the population. However, the damage from pneumococcal diseases that can be prevented by widespread immunization of the population is higher than expected. This statement specifically determines the high cost-effectiveness of vaccination. Thus, the solution of the problem lies in the prospective regional vaccination programs development in PI risk groups. These programs have a convincing pharmacoeconomical justification.

THE AIM of the study was to evaluate the economic efficiency and the choice of the vaccination strategy in the respiratory pneumococcal infection risk groups among the adult population of the Astrakhan region.

MATERIALS AND METHODS

The study was conducted in the Astrakhan region (according to Federal State Statistics Service, the population is 1005,967 people). Astrakhan has a population of 504,501. He overall population at risk of PI, is represented by adult patients of 18 years and older with chronic forms of cardiovascular (CHD, cardiomyopathy) and bronchopulmonary diseases (COPD, chronic bronchitis, bronchial asthma), patients with DM and obesity, convalescents after acute otitis media, as well as meningitis. Smaller groups included patients with chronic liver, kidney diseases and hemoblastoses (Table 1).

In total, the number of people in risk groups for the period of 2015–2018, amounted to an average of 99,228. If there were chronic diseases that required monitoring and treatment, all of them were assigned to the 3-rd group of dispensary registration.

To select patients for risk groups, verify their clinical diagnoses and plan vaccinations, normative legal documents were used. The data were analyzed for the period of 2015–2018 on the number of registered diseases in the patients living in the service area of the medical organizations (Form No. 12)[1,2]. The basic prophylactic medical examination documentation submitted by medical institutions, was studied (Form No. 030 / "Dispensary Monitoring Checklist", lists of persons subjected to medical observation in the reporting year)[3,4]. Statistical

[1] Order of Rosstat No. 591, dated 27.11.2015 (as amended on 31 December 31, 2020) "On approval of statistical tools for the organization of the Ministry of Health of the Russian Federation of federal statistical observation in the field of health". Available at: http://www.consultant.ru/document/cons_doc_LAW_190056 / (in Russian)

[2] Order of Rosstat No. 679, dated 22.11.2019 "On approval of the federal statistical observation form with instructions for filling it out for the organization by the Ministry of Health of the Russian Federation of federal statistical observation in the field of health protection". Available at: http://www.consultant.ru/document/cons_doc_LAW_338995/ (in Russian)

[3] Order of the Ministry of Health No. 1344, dated 21.12.2012 "On approval of the dispensary observation". Available at: http://www.consultant.ru/document/cons_doc_LAW_142423/. (in Russian)

[4] Order of the Ministry of Health No. 173, dated 29.03.2019 "On approval of the procedure for conducting dispensary observation of adults". Available at: http://www.consultant.ru/document/cons_doc_LAW_323527/ (in Russian)

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DOI: 10.19163/2307-9266-2020-8-6-436-445

materials of the territorial fund for compulsory medical insurance of the Astrakhan region on the payment of medical care to 12,970 patients who had had pneumonia in 2015–2018, were analyzed.

Implementation of prophylactic measures in medical organizations was evaluated in accordance with the national calendar of preventive vaccinations[5].

In vaccination costs calculating the results of competitive tenders for the purchase of pneumococcal vaccines carried out by the regional Ministry of health in 2015–2018, were taken into consideration. In 2015, the cost of PPV23 ("Pneumovax 23") amounted to 2,500 rubles; in 2016, it decreased to 1,800 rubles. The cost of PCV13 ("Preventar 13") remained unchanged in 2017–2018 and corresponded to 1,700 rubles.

Pharmacoeconomic analyses of the already carried out (retrospective) and future (prospective) preventive measures, were used in the interpretations of the research results gained. The calculation algorithm was based on the guidelines "Cost-effectiveness of vaccine prophylaxis"[6]. To determine the components of vaccination economic evaluations, formulas 1–18 were sequentially applied. For obtaining the results of initial regional indicators changing in the calculation algorithm, the MS Excel software base was used.

The sequential calculation of the costs associated with the implementation of the selected vaccination strategies and prevention of damage, was carried out in stages. The main stages of the computational algorithm were:

– A retrospective analysis of the incidence and vaccination coverage of adult patients at risk for PI in the Astrakhan region for 2015–2018;

– A retrospective analysis of the incidence of pneumonia in adult patients and calculation of actual financial costs associated with the treatment in dynamics for 4 years;

– A prospective calculation of costs for the pneumonia treatment, depending on the economic feasibility of applying vaccination in the alternative variations – "without vaccination" and "with vaccination";

– A comparison of "costs" and "benefits" based on the final results of the divariant analysis of vaccination and determining its effectiveness in the prospect of 10 years.

RESULTS AND DISCUSSION

At the first stage of the study, the analysis of incidence for the development of PI in risk groups among the adult population of the Astrakhan region for the period of 2015–2018, was carried out. The annual growth trend in the total number of patients was revealed. Special attention was paid to cardiovascular diseases. The increase in its indicators after 4 years amounted to 17,117 registered cases, and in relation to the initial 2015 year, it reached 46.5%.

The second place was taken by the patients with DM and obesity who made up 30.8% of the total number of the patients in risk groups in 2018. The trends in the growth of chronic diseases of lungs, ENT organs and liver were also revealed. In comparison with 2015, their indicators at the end of 4 years had increased by 18.3%, 6.9% and 17.8%, respectively. Thus, the annual increase of incidence in the above-mentioned risk groups is a determining condition for the optimization of preventive measures and mandatory use of modern technologies for immunoprophylaxis.

The annual average growth rate (Agr_a) of the patients' number in risk groups were calculated using the formula [23]:

$$Agr_a = (N_f - N_i)^{\frac{1}{S}} - 1,$$

where: N_f – the number of people in risk groups in the last year of observation; N_i – the number of people in risk groups in the previous year of observation; S – the number of years of observation.

The calculations performed showed that the average rate of the PI development in the risk groups (the quantitative growth) for the period of 2015–2018, was 5,981 people (6.3%). The obtained result, based on the analysis of initial indicators for 4 years, demonstrates the need for urgent solutions to the issues of vaccination.

The second stage of the study retrospectively analyzed the incidence of pneumonia (PN) among the adult population of the Astrakhan region, and calculated the cost of the treatment implemented in 2015–2018. The total number of the patients, who had had PN, was 12,970 people during this period. The cost of the treatment they had receied was calculated using the formula [24]:

$$Cost_{PN} = Cost_{1PN} \times N,$$

where: $Cost_{PN}$ – the cost of PN treatment; $Cost_{1PN}$ – the cost of one treatment case; N – the number of cases.

According to Table 2, the average cost of one pneumonia treatment case was 20,156.23 rubles. Therefore, the total financial costs reached a significant amount of 265,234,598.53 rubles.

Thus, the ongoing trends towards an increase in the incidence of PN for 4 years and rise in the financial costs for the treatment, characterize the current region's situation, which clearly indicates the requirement to optimize measures for the prevention and treatment of this disease. According to clinical practice, immunoprophylaxis with the use of modern pneumococcal vaccines is one of the ways to increase the effectiveness of treat-

[5] Order of the Ministry of Health No. 125n, dated 21 March 2014 "On the approval of the national calendar of preventive vaccinations and the calendar of preventive vaccinations for epidemic indications "with amendments to Appendices No. 1 and No. 2, dated 2016, and federal clinical recommendations" Vaccine prevention of pneumococcal infections in adults", dated 2018. Available at: http://www.consultant.ru/document/cons_doc_LAW_162756/. (in Russian)

[6] Methodological guidelines 3.3.1878-04 "Cost-effectiveness of vaccine prophylaxis", dated 04.03.2

ment, preventive measures and influence on the PN incidence.

Based on this position, the possibility of the annual vaccination coverage of the adult population from the PI risk groups, and the average annual increase in the PN incidence in the region's population over 4 years (Table 3), was analyzed. 2015 is considered the beginning of vaccination with PPV23 against PI among the adult population of the Astrakhan region. Due to the risk of developing PI, 2,185 people were vaccinated during this year. In 2016, this indicator was the lowest and represented by 176 people. In 2017, the strategy of preventive vaccination changed due to the use of two vaccines. In total, 2289 people were vaccinated with both vaccines: 635 with PPV23 and 1654 with PCV13. In 2018, a group of 2,197 people were only vaccinated with PCV13.

The results on the vaccination status obtained in risk groups indicate the required prospective planning of vaccination measures with the most efficiency.

On the one hand, the PI preventive vaccination has started to implement into the real regional health practice, and on the other hand, vaccination coverage in the risk groups remains low. Considering the average annual increase in incidence, it should be assumed that the amount of newly registered PN cases among the adult population is just increasing. The PN is considered a human disease with reduced immunological reactivity of the body; therefore the role of vaccination in the situation of the Astrakhan region becomes even more relevant.

At the next stage of the study, the estimated number of people in risk groups for the next 10 years has been calculated. The calculation was based on the average growth rate of patients amount (Tgr_a) in the PI risk groups from 2015 to 2018. This approach made it possible for us to calculate comparable indicators representing the number of individuals in risk groups in the period of 2019–2028, prospectively (Table 4).

The role of alternative strategies "without vaccination" and "with vaccination" in the prevention of probable PN cases should be also evaluated in a comparative aspect. Considering the low level of vaccination in 2015–2018 (an average of 1.7%), we chose this temporary episode to be a period without vaccination. Based on the strategy of non-interference ("no vaccination"), to calculate an annual incidence PN rate (with newly registered cases during the year), the following formula was used [9]:

$$K_{avrg} = \frac{k_{avrg}}{n_{avrg}} \times 100000,$$

where: K_{avrg} – an average incidence rate; k_{avrg} – a average number of diseases for the period; n_{avrg} – an average number of vaccinated, expressed in absolute terms.

Here of it follows that for the period of 2015–2018 K_{avrg} of PN incidence in the Astrakhan region amounted to 3,268 people. The resulting indicator was also relevant for calculating the probable number of PN cases that would have occurred without preventive vaccination after 2018 for 10 years (Table 4). Based on the aforementioned, the calculation was carried out according to the following formula [10]:

$$m_i = K_{avrg} \times n_i / 100000,$$

where: m_i – an average number of cases during the period without vaccination; K_{avrg} – an average incidence rate; n_i – n number of people expressed in absolute values.

Thus, the data obtained can witness that there are interrelated trends towards an increase in the number of people in risk groups and probable PN cases, which are generally caused by a low coverage and a low effectiveness of vaccination. There is no doubt that strategies with the absence of vaccination are better to remain as versions of go-ahead events, but the predicted increase in the PN incidence during the next 10 years, is already a wake-up call on the present day. An increase in the financial costs for providing medical care to patients, always causes aggravation of the economic aspects of the regional PN problem.

The data for the prospective calculation of PN cases treatment costs with a research horizon of 10 years providing a non-intervention strategy "without vaccination", are presented in Fig. 1.

It should be pointed out that the cost of PN treatment among insured individuals in the Astrakhan region will significantly increase throughout the 10 years of the study. According to the results of a financial costs prospective calculation on the background of an alternative strategy "without vaccination", the medical care provided to this category of patients, can be estimated at the amount of 1.31 billion rubles.

In order to predict the delayed outcomes of preventive measures in the "with vaccination" option for 10 years ahead, the costs of vaccination and the damage prevented by it were calculated. The cost of vaccination calculation in this alternative version was carried out using the following formula [24]:

$$Cost_v = Cost_d \times N,$$

where: $Cost_v$ – the cost of the preventive vaccination; $Cost_d$ – the cost of the drugs; N – the number of vaccinated.

The cost of vaccination was calculated in accordance with the current vaccination scheme in the country. Patients are vaccinated with PCV13 once-in-a-lifetime according to the national calendar. The individuals, who join the list of risk groups each year, will also need to be vaccinated with PCV13. At the end of the first year, the primary vaccination with PPV23 takes place, and the patients are subjected to the booster vaccination with the same vaccine five years later.

Planned for the next 10 years, vaccination seems a

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DOI: 10.19163/2307-9266-2020-8-6-436-445

Table 1 – Nosological features and the number of patients at risk for pneumococcal infection

Risk groups (people), years	2015	2016	2017	2018
Cardiovascular diseases	36839	43898	49782	53956
Chronic lung diseases	10680	11899	12008	13076
Diabetes and obesity	30357	32394	32117	33874
Acute otitis media, meningitis	6610	7417	7554	7064
Liver disease, including liver cirrhosis	2247	2452	2467	2648
Kidney diseases, chronic kidney failure	238	266	285	273
Hemoblastoses	678	698	8428	809
Total number of patients in risk groups:	86118	97433	103318	110042

Table 2 – Number of reported pneumonia cases and treatment costs

Period, years	2015	2016	2017	2018	Final result
Cases of pneumonia	2,766	3,234	3,193	3,777	12,970
Cost of 1 case, RUB.	15,420.93	22,638.17	19,525.00	23,040.81	20,156.23
The total cost of treatment, RUB.	42,654.292.38	73,211,841.78	62,343,325	87,025,139.37	265,234,598.53

Table 3 – Results of vaccination in risk groups and the average annual increase in the pneumonia incidence in adults of the Astrakhan region

Period, years	2015	2016	2017	2018
Total number of vaccinated people	2.185	176	2.297	2.197
Vaccination coverage, %	2.5	0.2	2.2	2
Increase in the pneumonia incidence, %	Initially: 2,766 of pneumonia cases	16.9	15.4	36.5

Table 4 – Dynamics of quantitative indicators in risk groups and pneumonia incidence in the Astrakhan region, in a 10-year prospective calculation

Years	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028
Risk groups, people	11,6997	12,4392	13,2253	14,0612	14,9499	15,8948	16,8994	17,9675	19,1031	20,3105
Probable PN cases	3,823	4,065	4,322	4,595	4,885	5,194	5,522	5,871	6,242	6,637

Table 5 – The number of prevented pneumonia cases and the cost of prevented damage within a 10-year prospective

Period, years	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028
Probable cases of pneumonia without vaccination (m)	3,823	4,065	4,322	4,595	4,885	5,194	5,522	5,871	6,242	6,637
Probable cases of pneumonia against the background of vaccination (including the vaccinated and unvaccinated) (L)	118	95	47	86	91	98	77	71	75	93
Prevented pneumonia cases (a)	3,705	3,970	4,275	4,509	4,794	5,096	5,445	5,800	6,167	6,544
The cost of prevented damage, million rubles	74.6	80.0	86.2	90.9	96.6	102.7	109.7	116.9	124.3	131.9

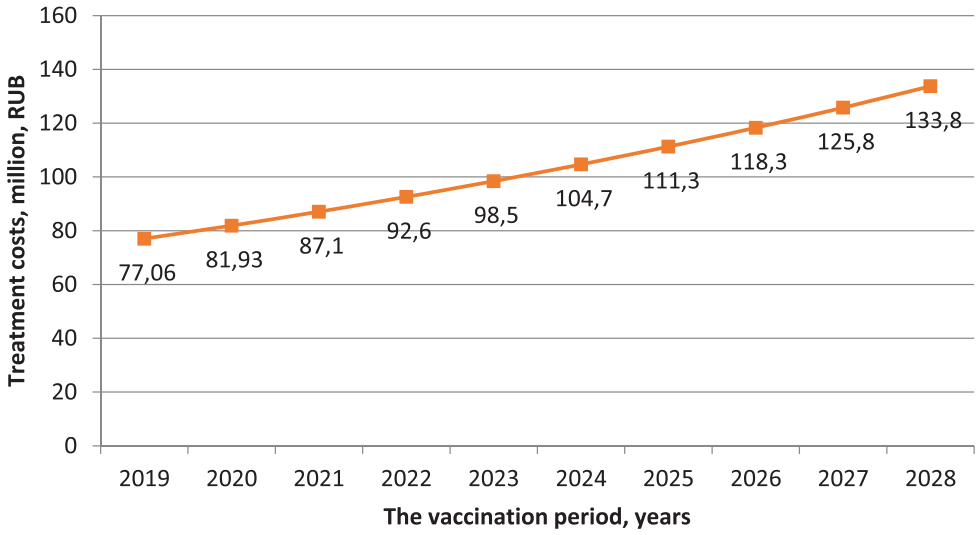

Figure 1 – Prospective calculation of insured pneumonia cases treatment costs in the Astrakhan region with the use of «without vaccination» strategy

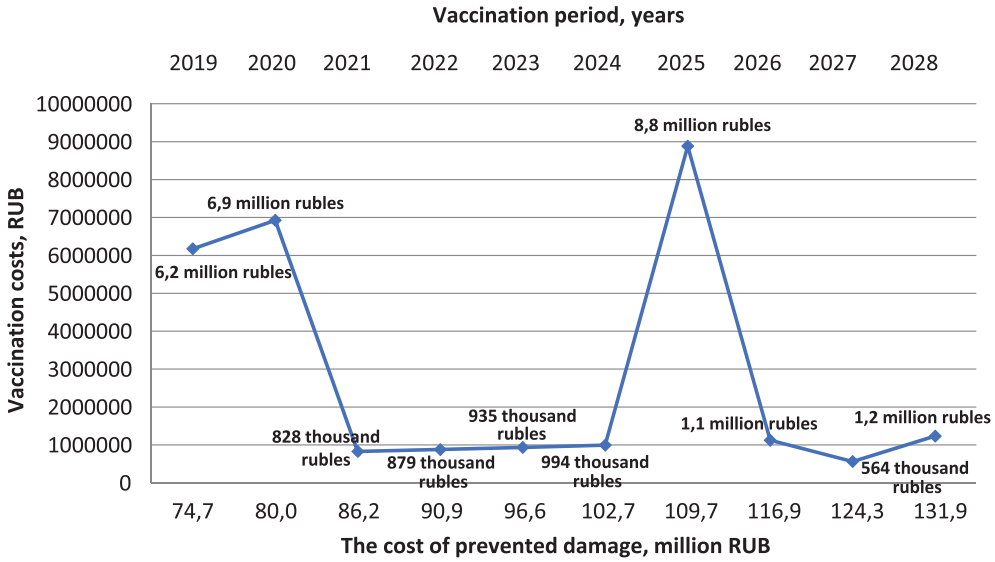

Figure 2 – Ratio of planned vaccination costs to prevented damage in the period of 2019–2028

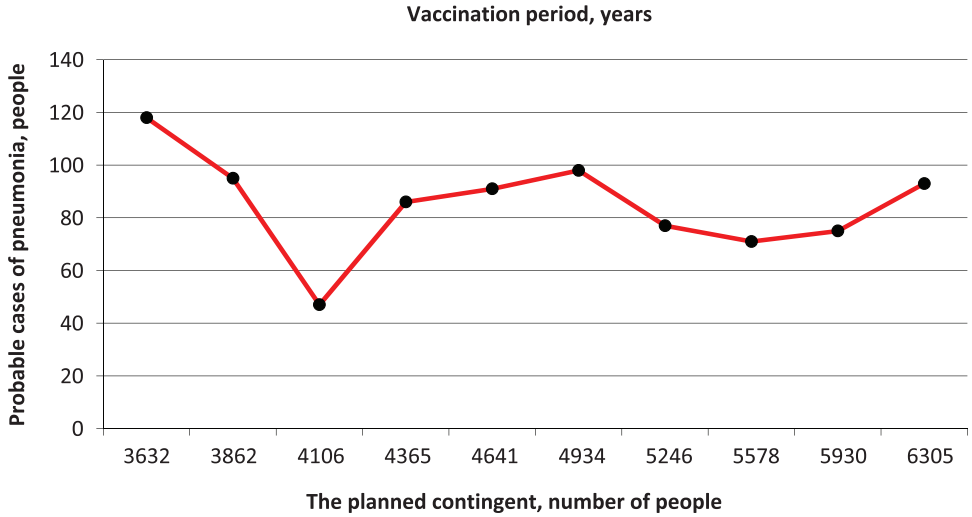

Figure 3 – Estimated indicators of probable PN cases among the vaccinated population

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DOI: 10.19163/2307-9266-2020-8-6-436-445

highly economical and accessible preventive measure that can have a significant impact on reducing the number of PN cases. The use of two non-replaceable polysaccharide vaccines, PPV23 and PCV13, was the pacing factor for improving the effectiveness of PI vaccination. According to the estimated data, in 2019, only the results of primary PCV13 vaccination, conducted in 3,632 people, should have been expected. In 2020, the same individuals were vaccinated with PPV23, and the newly presenting 230 patients were primarily vaccinated with PPV13. Thus, the potentiated effects of the two vaccines began to be realized that year when the biological effect of PPV23 developed against the background of the PCV13 vaccine inoculated in 2019. An overall trend of preventive vaccination during the entire 10-year period will be a regularly repeated event in which the first use of PCV13 in the individuals who annually join the risk groups, is followed by the primary vaccination with PPV23 in another calendar year. Considering the calculations carried out, the number of individuals enrolled into the risk group for the suspected PN each year, will range from 230 to 375 people. It should be notified that the planned number of the vaccinated population will increase in 2028 about twice in comparison with the initial parameter of 2019, and it will amount to 6,305 people. An important feature of the planned vaccination will be the booster vaccination of PPV23 in 2025, covering 4,641 people. For this reason, beginning from 2026, vaccination with PCV13 and PPV23 will proceed in accordance with the established procedure for newly presenting patients. This change in the vaccination schedule also involves a decrease in the financial cost of purchasing drugs within 5 years, i.e. till the next booster vaccination of PPV23. A prospective calculation showed that for PI vaccination based on the requirements of the national calendar of preventive vaccinations, an amount of 28.5 million rubles will be required within the space of 10 years (Fig. 2).

A significant component of the economic evaluation of the preventive vaccination was the calculation of the prevented damage. The number of PN cases prevented during the year, with a 95% coverage of pneumococcal vaccination, was calculated according to the formula (18):

$$a_i = m_i - L_i,$$

where: a_i – the number of prevented PN cases within a year; m_i – the probable number of PN cases that would have occurred each year without preventive vaccination; L_i – the number of people with PN (including the vaccinated and unvaccinated).

Table 5 shows that probable PN cases against the background of preventive vaccination have acquired a one-way downward trend at the end of 2020. However, the probability of developing PN in 2028 will remain increased in the newly presenting patients in the risk groups and receiving only the primary PCV13 vaccination.

This category includes 375 people who are scheduled for the primary PPV23 vaccination in 2029, which is out of time proportion of this study, Nevertheless, in 2028, 352 more people who will join the risk groups in 2027, will be able to be vaccinated with PPV23.

Thus, the evaluation of the prevention strategy benefits “with vaccination” comes from the prevented costs, presented as the economic damage associated with the spread of PN cases that had been prevented as a result of vaccination with PCV13 and PPV23. In order to specify this financial aspect, the prevented costs were determined, calculated as multiplying one case average cost of disease by the number of prevented cases. As a result of the calculation, the total prevented economic damage was 1.14 billion rubles

As Fig. 3 shows, the number of probable PN cases in vaccinated and unvaccinated individuals in the presence of “with vaccination” strategy, has generally decreased positively, and along with them, the cost of treatment has decreased.

At the final stage of this study, the difference between the cost of vaccination in the selected PI risk group and the damage prevented during its implementation within the space of 10 years was calculated. The planned vaccination coverage was 95%. The comparison of the “vaccination costs” and the “benefits” in terms of costs, was the main approach to evaluating the economic parameters of vaccination.

An important aspect of the planned process of preventive vaccination modeling was taking into account all vaccinated persons, including those who are joining the risk groups, adjusting for the annual average growth rate (Tgr_a). As mentioned above, the financial cost of vaccination increased up to 8.8 million rubles due to the booster vaccination with PPV23 in 2025. At the same time, the prevented damage amounted to 109.7 million rubles in financial terms and continued to increase, reaching 131.9 million rubles in 2028. An early index for the efficacy of preventive work should be taken as the fact of vaccination self-sufficiency in 2 years, when the cost of performing it for the first time decreased to 828 thousand rubles. (Fig. 2).

The total economic benefit indicator was calculated as the difference between the prevented damage (1.14 billion rubles), the amount of costs for vaccination (28.5 million rubles) and the cost of PN cases treatment in vaccinated and unvaccinated patients (17.1 million rubles). Based on the obtained result, it is possible that at the end of 2028, the net economic benefit will amount to 968.2 million rubles.

CONCLUSION

In this study, the possibilities of improving the PI vaccination efficiency in the adult population of the Astrakhan region and approaches to the pharmacoeconomical analysis of vaccinoprophylaxis, have been examined. In order to objectify the current situation, the dynamics

of morbidity in risk groups for the PI development in the period of 2015–2018, was analyzed. It has been established that there are no positive trends in the diseases of the cardiovascular system. For the past 4 years, their total increase has reached 46.5%. The next most important indicators were diabetes and obesity, which made up 30.8% of the total structure of pathology at the end of 2018. A special focus is on increasing chronic bronchopulmonary pathology. After 4 years, the indicator has increased by 22.4%. The number of patients with hemoblastosis, chronic liver and kidney diseases increased slightly during the above period. In total, the number of people in risk groups for PI developing was an average of 99,228 people, which is quite a significant indicator in the Astrakhan region.

CAP is a widespread disease of adults that develops against the background of reduced immunological reactivity of the body. The prognosis of CAP in patients with COPD is especially unfavorable. In adult patients, the risk of developing fatal outcomes from CAP is much higher in comorbid pathology: CHD, DM, and CHF. All these factors are particularly relevant in risk groups, which create a "threat situation" for the CAP development against the background of each abovementioned disease.

At the end of the period of 2015–2018, the study of the pneumonia disease dynamics among the population of the Astrakhan region, revealed an increase of PN cases by 36.5%. The absolute indicator of the total number of patients, who had PN, was 12,970 people. A retrospective calculation of the treatment costs for all reported cases during 4 years showed a quite impressive value, which amounted to 265.23 million rubles. An increase in PN incidence and the financial costs of its treatment required a reconsideration of approaches to the prophylaxis and treatment of this disease. Extremely low efficiency of preventive measures in 2015–2018 was demonstrated by a vaccination coverage in risk groups that did not exceed 2.5%.

In the study, this period was considered a "without vaccination" period. To get an answer to the question about the amount of possible damage when there is no vaccination, a prospective calculation of PN treatment costs in such conditions for the next 10 years (2019–2028), was conducted. According to the final results of calculating financial costs, the PN treatment against the background of an alternative strategy "without vaccination", can be estimated at the amount of 1,31 billion rubles.

To prove the economic feasibility of the strategy "with vaccination", the prevented costs were calculated as the equivalent of the prevented economic damage. As a result of the sequential calculations, the total amount of prevented damage against the background of vaccination with a duration of 10 years can reach 1.14 billion rubles. The estimated cost of vaccination is 28.5 million rubles, and the PN cases treatment costs among vaccinated and unvaccinated individuals, is 17.1 million rubles. Thus, 968.2 million rubles are returned to the healthcare budget.

FUNDING

This work did not have funding from outside organizations.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

AUTHORS' CONTRIBUTION

E.A. Orlova – data collection, text writing and editing; I.P. Dorfman – data collection and editing;
M.A. Orlov – text writing and editing; M.A. Abdullaev – text writing and editing.
All authors made a significant contribution to the search and analytical work and preparation of the article, read and approved the final version before the publication.

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