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THE EFFECTIVENESS OF THE USE OF SCHEMES FOR THE TREATMENT OF BRONCHIAL ASTHMA AND COPD ON THE EXAMPLE OF THE CNCE “VINNYTSIA CITY CLINICAL HOSPITAL №1”

Abstract. Bronchial asthma (BA) and chronic obstructive pulmonary disease (COPD) remain among the most common and socially significant diseases of the respiratory system, which significantly affect the quality of life of patients and the economic burden on the healthcare system. Optimization of treatment regimens for these conditions, taking into account the individual characteristics of patients, is a key factor in increasing the effectiveness of therapy. Analysis of the effectiveness of modern diagnostic and treatment methods implemented in multidisciplinary medical institutions allows us to assess their practical significance. Research on therapeutic approaches contributes to the improvement of existing protocols and provides opportunities for improving the long-term results of treatment of these common pathologies. The aim of the study was to conduct a comparative analysis of the effectiveness and cost-effectiveness of different treatment regimens for bronchial asthma and chronic obstructive pulmonary disease in patients of the pulmonology department of the CNCE “Vinnytsia City Clinical Hospital №1”. The disease histories and dates of the next exacerbation of the disease of these patients were analyzed using a medical information system. The treatment regimens Symbicort Turbuhaler (formoterol + budesonide) and Seretide Diskus (salmeterol + fluticasone) were selected for the study. The effectiveness assessment included an analysis of technical efficiency according to the Farrell index and cost-effectiveness for each regimen, taking into account dosage, resource consumption and the influence of concomitant factors such as age, sex, and year of observation. The analysis showed that only 4 out of 172 patients demonstrated optimal basic therapy regimens, and the optimal dosage was found in only 1 patient. Patients with asthma

showed a higher level of prescription effectiveness compared to patients with COPD. Analysis by treatment regimens revealed a significant advantage of the first regimen over the second in both technical efficiency and cost-effectiveness. At the same time, the allocative efficiency of all regimens was optimal, without disparities between the main and accompanying therapy. Comparative analysis showed that the cost-effectiveness of the first regimen deteriorated over time, and for the second regimen, the length of hospital stay was a significant influencing factor. Overall, existing treatment regimens require revision to improve the adaptation of therapy to the needs of patients. Further research should be aimed at improving dosing and developing individualized approaches.

Keywords: treatment effectiveness, broncho-obstructive syndrome, treatment schemes, chronic obstructive pulmonary disease, bronchial asthma.

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ЕФЕКТИВНІСТЬ ЗАСТОСУВАННЯ СХЕМ ДЛЯ ЛІКУВАННЯ БРОНХІАЛЬНОЇ АСТМИ ТА ХОЗЛ НА ПРИКЛАДІ КНП «ВІННИЦЬКА МІСЬКА КЛІНІЧНА ЛІКАРНЯ №1»

Анотація. Бронхіальна астма (БА) та хронічне обструктивне захворювання легень (ХОЗЛ) залишаються одними з найпоширеніших і соціально значущих захворювань дихальної системи, що суттєво впливають на якість життя пацієнтів та економічне навантаження на систему охорони здоров'я. Оптимізація схем лікування цих станів, що враховують індивідуальні особливості пацієнтів, є ключовим фактором у підвищенні ефективності терапії. Аналіз ефективності сучасних методів діагностики та лікування, впроваджених у багатопрофільних медичних закладах, дозволяє оцінити їхнє практичне значення. Дослідження терапевтичних підходів сприяє вдосконаленню існуючих протоколів і забезпечує можливості для покращення довгострокових результатів лікування цих поширених патологій. Метою дослідження було провести порівняльний аналіз ефективності та витрати-ефективності різних схем лікування бронхіальної астми та хронічного обструктивного захворювання легень у пацієнтів пульмонологічного відділення КНП «Вінницька міська клінічна лікарня №1». Проаналізовано історії хвороб та дати наступ-

ного загострення захворювання даних пацієнтів за допомогою медичної інформаційної системи. Для дослідження відібрані схеми лікування Симбікорт Турбухалер (формотерол + будесонід) та Серетид Діскус (сальметерол + флутиказон). Оцінка ефективності включала аналіз технічної ефективності за індексом Фаррела та витрати-ефективності для кожної схеми з урахуванням дозування, витрат ресурсів і впливу супутніх факторів, таких як вік, стать, та рік спостереження. У результаті проведеного аналізу встановлено, що лише 4 із 172 пацієнтів демонстрували оптимальні режими базисної терапії, а оптимальне дозування виявлено у лише 1 пацієнта. Пацієнти з БА показали вищий рівень ефективності призначень порівняно з пацієнтами з ХОЗЛ. Аналіз за схемами лікування виявив значну перевагу першої схеми над другою як за технічною ефективністю, так і за витратною ефективністю. Водночас алокативна ефективність усіх схем була оптимальною, без диспропорцій між основною і супроводжувальною терапією. Порівняльний аналіз показав, що витратна ефективність першої схеми погіршувалася з роками, а для другої схеми значущим фактором впливу була тривалість перебування в стаціонарі. В цілому, існуючі схеми лікування вимагають перегляду з метою підвищення адаптації терапії до потреб пацієнтів. Подальші дослідження мають бути спрямовані на вдосконалення дозування та розробку індивідуалізованих підходів.

Ключові слова: ефективність лікування, бронхообструктивний синдром, схеми лікування, хронічне обструктивне захворювання легень, бронхіальна астма.

Statement of the problem. Bronchial asthma (BA) and chronic obstructive pulmonary disease (COPD) remain among the most common respiratory diseases in the world, with a significant impact on the quality of life and health of the population. The prevalence of BA continues to increase, especially in developed countries, which is largely due to changing environmental and social factors [1]. The situation is complicated by the high probability of comorbid conditions, which is characteristic of patients with BA. This increases the risk of complications and requires a multidisciplinary approach to treatment [2].

The epidemiology of COPD, as indicated by Diaz-Guzman and Mannino, indicates its high prevalence among adults worldwide, especially among the elderly. The disease is associated with high levels of disability and mortality [3]. Risk factors for the development of COPD include smoking, exposure to harmful substances in the workplace, air pollution and genetic predisposition. The high incidence requires active measures for prevention, early detection and treatment [4].

The main goals of asthma and COPD treatment are to reduce symptoms, prevent exacerbations, and improve patients' quality of life. In the context of modern medicine, there is a need for an individualized approach to COPD therapy with a focus on preventing exacerbations [5]. For patients with asthma, treatment is based

on the use of inhaled corticosteroids in combination with β 2-agonists, as well as on the control of trigger factors [6].

Modern diagnostics of both diseases involves a detailed study of the clinical picture, the use of lung function tests, and, if necessary, imaging methods. At the same time, treatment should be based on clinical recommendations that take into account individual patient characteristics, including their age, comorbidity, and risk factors.

These data emphasize the importance of further research into the effectiveness of therapeutic regimens aimed at optimizing the treatment of asthma and COPD, which will improve the prognosis and quality of life of patients.

Connection of the publication with planned scientific research works. The work was carried out as part of the research work of the National Pirogov Memorial Medical University, Vinnytsya: “Effectiveness and safety of chemotherapeutic agents and metabolic correctors in conditions of comorbid pathology” (state registration number 0119U000069).

The purpose of the article – using the example of patients treated at CNCE “Vinnytsia City Clinical Hospital №1” to determine the effectiveness of the use of regimens for the treatment of bronchial asthma and chronic obstructive pulmonary disease.

Research objects and methods. 208 medical histories and 208 extracts from the medical information system were analyzed regarding subsequent deteriorations in the condition of patients based on the pulmonology department of the Municipal Non-profit Enterprise “Vinnytsia City Clinical Hospital №1” who were treated for bronchial asthma and chronic obstructive pulmonary disease. Information on the cost of drug treatment regimens (in US dollars at the time of drug prescription) for 1 month was used for the analysis. The following treatment regimens were selected for the study: Symbicort Turbuhaler (manufacturer AstraZeneca AB, Sweden): Formoterol + Budesonide (123 patients) and Seretide Diskus (manufacturer Glaxo Wellcome Production, France): Salmeterol + Fluticasone (23 patients).

Committee on Bioethics of National Pirogov Memorial Medical University, Vinnytsya (protocol № 7 from 08.11.2022) found that the studies do not contradict the basic bioethical standards of the Declaration of Helsinki, the Council of Europe Convention on Human Rights and Biomedicine (1977), the relevant WHO regulations and laws of Ukraine.

For statistical processing of the obtained results, we used the analytical system R, version 4.3.1 (2023-06-16) GNU GPL license v.(≥ 2) svn.rev 84548, using the “aarch64-apple-darwin20” platform, the “Benchmarking” library “, “readxl”, “ggplot2”, “AER”, DEA analysis functions `eff()`, `dea()`, `cost.opt()`, `dea.boot()`, `sdea()`, `slack()`, statistical test functions `ks`, `Test()`, `qf()`, tobit regression function `tobit()`.

Efficacy was determined by volume to establish dosing inefficiencies. The optimal doses were determined as the ratio of E indices according to CRS (Constant Returns to Scale) to those according to VRS (Variable Returns to Scale). Optimality is achieved by the value of the ratio 1. Insufficient or excessive dosage is determined

by comparing the VRS index with that according to DRS (Decreasing Returns to Scale), namely if $VRS < DRS$, we have insufficient dosage, and when $VRS = DRS$ and the efficiency due to the volume is less than one we determine the excess dosage. And technical efficiency by distance to the frontier.

The study of the effectiveness of the main treatment (basic therapy) of AB and COPD was carried out on the basis of the technical efficiency of product production with constant resources, i.e. output efficiency according to the Farrell index

We also studied both the efficiency of resource use, i.e. input efficiency according to the inverse Farrell index E , and the technical efficiency of product production with unchanged resources, i.e. output efficiency according to the Farrell index (Farrell efficiency, $F \sim 1/E$). The indicated indices were determined using DEA (Data Envelopment Analysis), namely the resource efficiency index, which is sought by their (x) minimization:

$$E^0 = E((x^0, y^0); T^*) = \min\{E \in \mathbb{R}_+ | (Ex^0, y^0) \in T^*\}$$

and the Farrell index by maximizing the produced product (days to the next exacerbation):

$$F^0 = F((x^0, y^0); T^*) = \max\{F \in \mathbb{R}_+ | (x^0, Fy^0) \in T^*\}$$

We determined the cost-effectiveness index, which has a scale from 0 (zero efficiency) to 1 (100% efficiency). The cost-effectiveness criterion takes into account not only the resources, the produced product, but also the prices of resources, that is, it adds a price component to the consideration, and therefore it is considered preferable. It is calculated as the ratio of optimal costs for a given frontier to those observed for the same manufactured product.

Analysis of factors that significantly modified the cost-effectiveness criterion according to treatment schemes was carried out on the basis of tobit regression ("AER" library of the international analytical system R). The analysis was performed only for the first and second schemes that had a sufficient number of patients. The basic formulation of the model works is presented below, α is the vector of model coefficients presented in the article, ε are the residuals of the model with a standard normal distribution, i.e. $\varepsilon \sim N(0, \sigma^2)$. The estimate of the scaling parameter σ , or rather the logarithm of the estimate, is presented in the last line as the effect "Log(scale)".

$$E = \begin{cases} 0, & \text{if } az + \varepsilon \leq 0 \\ az + \varepsilon & \text{if } 0 < az + \varepsilon < 1 \\ 1 & \text{if } az + \varepsilon \geq 1 \end{cases}$$

Presentation of the main material.

Research results and their discussion. Analysis of the technical effectiveness of treatment with the main drug. Analysis of the effectiveness of treatment by input efficiency showed that the frontier of effectiveness was formed by only 4 patients out of 172 included in the analysis, which is evidence that the regimens for prescribing basic therapy are poorly adapted to patients.

Analysis of efficiency due to volume. Only in 1 out of 172 patients the doses were optimal. The result showed that of all patients with efficiency due to volume less than 1, namely $172-1=171$ patients, 100 had excessive dosages, and in 71 doses were lower than optimal.

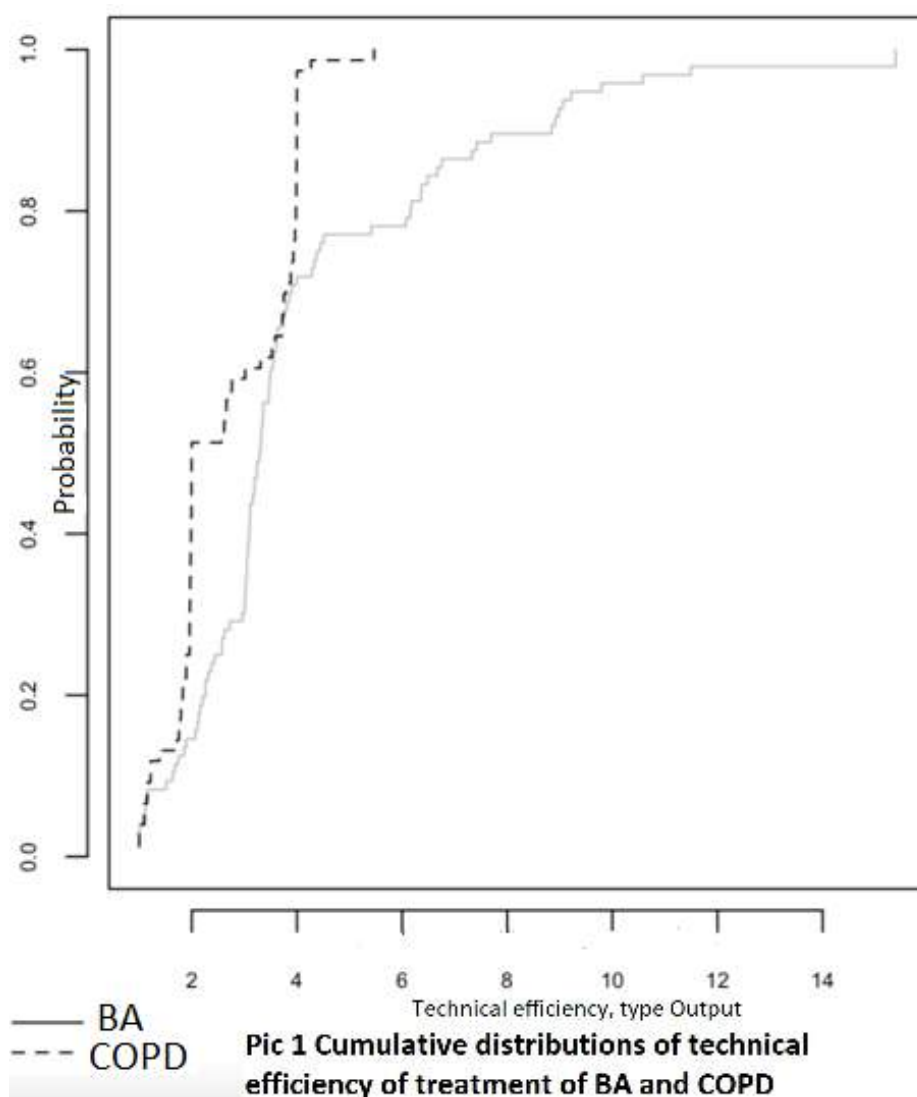
Study of the effectiveness of the main treatment (basic therapy) of AB and COPD. It turned out that only 3 out of 96 patients with asthma formed the frontier of technical effectiveness according to the Farrell index, i.e. had optimal prescriptions. 3 out of 76 patients with COPD had optimal prescriptions, i.e. formed the frontier. The percentiles of the Farrell index distributions of patients with asthma and COPD are shown in Table 1.

Table 1.

Summarized data of the analysis of the efficiency of resource use, efficiency due to volume and efficiency of the main treatment of patients with broncho-obstructive syndrome in CNCE "Vinnytsia City Clinical Hospital №1".

	Min	25%	50%	Mean	75%	Max
Input E	0.0021	0.1221	0.1831	0.2477	0.2869	1
By volume	0.05	0.3368	0.4343	0.4882	0.6451	1
BA Farrell	1	2.540	3.296	4.136	4.392	15.387
COPD Farrell	1	1.942	1.996	2.693	3.935	5.466
Scheme 1 Farrell	1	1.459	1.957	2.144	2.575	4
Scheme 2 Farrell	1	1.650	2.315	2.444	2.616	7.085
Scheme 1 CE	0.1250	0.3085	0.5026	0.4987	0.5807	1
Scheme 2 CE	0.1105	0.1936	0.3394	0.4230	0.5306	1

It can be seen that 50% of patients were characterized by an efficiency index of less than 0.1831, and in a quarter the index did not exceed 0.1221. From these distributions, we can conclude that the better efficiency of prescriptions for patients with asthma is achieved. Graphically, the cumulative distribution functions of the Farrell index values for patients with asthma and COPD are shown in Fig. 1.



The rather wide area between the curves indicates large differences, which were tested using both the parametric Fisher test (F) and the nonparametric Kolmogorov test of the difference between the two cumulative distributions. The results of the two tests are given in Table 2.

Table 2.

Analysis of the effectiveness of prescriptions for patients with broncho-obstructive syndrome at CNCE "Vinnytsia City Clinical Hospital №1".

	Kolmogorov's test	F - test	95% CI
BA - COPD, Farrel	D = 0.36732, p-value = 1.267e-05	1.852298	0.7413575 - 1.356138
Scheme 1 vs 2, Farrel	D = 0.3298, p-value = 0.02222	0.7920486	0.6604525 - 1.62339
Scheme 1 vs 2, CE	D = 0.38317, p-value = 0.004468	0.8688075	0.6604525-1.62339

The value of the Kolmogorov test statistic $D=0.36732$ with $p=1.267e-05$ indicates the presence of highly reliable differences in the curves, as does the Fisher parametric test with a test statistic of 1.852298, which is outside the 95% confidence interval of the F-distribution, namely 0.7413575 - 1.356138. This indicates that a significantly better effectiveness of basic therapy for patients with asthma has been established.

Comparative analysis of the effectiveness of treatment regimens based on basic therapy according to Farrell criteria.

We took into account both basic and accompanying therapy, that is, we considered treatment in a complex, although the scheme was determined by the basic therapy. Two such common schemes were found, with the corresponding number of patients 123 and 23. It is clear that the technical efficiency of Output was studied according to the Farrell criterion. Table 1 shows the centiles of the distributions of the Farrell index of patients according to two treatment schemes. The first scheme is clearly better, which has lower values of the Farrell index at all centiles of the distribution, which indicates its regularly higher efficiency. The results of the application of the nonparametric Kolmogorov and parametric F tests are given in Table 2. There is a significant difference in efficiency between the first and second groups according to the Kolmogorov test ($D=0.3298$), the p-level of reliability is high ($p=0.02222$), the Fisher criterion estimate is 0.7920486, but it is close to the lower limit of the 95% confidence interval 0.6604525 - 1.62339.

Comparative analysis of treatment regimens based on basic therapy according to cost-effectiveness (CE) criteria.

The analysis cannot be performed for patients with asthma and COPD, since different regimens are used for each group of nosologies. However, it can be done by treatment regimens. We also took into account both basic and concomitant therapy, and the regimen was determined by the basic therapy, i.e. the two basic regimens described above. Accordingly, the regimens included 123 and 23 patients.

As in the case of Farrell's technical efficiency, the cost-effectiveness index favors the first treatment regimen (see Table 1), where 9 out of 123 patients had an

index value exceeding 0.999. For the second regimen, this number was 3 out of 23. These differences are regular across all centiles, i.e. they apply to the distributions as a whole. Statistical tests indicate a significantly worse cost-effectiveness of the second treatment regimen. Thus, the significantly lower cost-effectiveness of the second scheme compared to the first scheme was confirmed by the Kolmogorov test with statistics $D = 0.38317$, $p\text{-value} = 0.004468$. The Fisher exact test estimate is 0.8688075, but is close to the lower limit of the 95% confidence interval 0.6604525 - 1.62339.

Allocative effectiveness of treatment regimens based on basic therapy.

It turned out that all schemes have optimal allocative efficiency, i.e. the best combination of the sizes of the main and accompanying therapy. Moreover, no “tail” (slack) was observed for any patient, i.e. there were no discrepancies in the sizes (disproportions) of the prescriptions of the volumes of the main and accompanying therapy. That is, in most cases, both the main and accompanying therapies were used in excess amounts, as was established above, but the excess was proportional.

Analysis of factors that significantly modified the cost-effectiveness criterion by treatment regimens.

The factors that significantly modified the cost-effectiveness criterion by treatment regimens were determined, since the influence of factors may be different. These factors were: patient age and sex, place of residence (village; city), employment, length of hospital stay, diagnosis (BA; COPD), year of observation. Of all the criteria, we chose cost-effectiveness as multi-dimensional and, therefore, the most informative. The results of the regression work are given for the first and second treatment regimens, respectively, in Tables 3 and 4.

Table 3.

Analysis of the influence of factors on the cost-effectiveness of the first treatment scheme by tobit regression.

Effect	Coefficient	Error	z	p
Constant	0,8785	0,1386	6,3378	2,33E-10
Age	-0,0019	0,0014	1,3405	0,1801
Sex	0,0270	0,0414	0,6516	0,5147
Living in the village	-0,0110	0,0837	0,1314	0,8954
Employment	0,0084	0,0119	0,7045	0,4811
Duration of inpatient treatment	-0,0081	0,0073	1,1217	0,2620
Diagnosis	-0,0371	0,0458	0,8101	0,4179
Year	-0,0506	0,0135	3,7465	0,0002
Log(scale)	-1,6319	0,0638	25,595	1,71E-144

It is clear from Table 3 that the only factor included with a significant effect is the year of observation. The negative value of the regression coefficient suggests that the cost-effectiveness of the first scheme deteriorated over the years 2019 to 2024.

Table 4.

Analysis of the influence of factors on the cost-effectiveness of the second treatment scheme by tobit regression.

Effect	Coefficient	Error	z	p
Constant	1,0606	0,3229	3,2841	0,0010
Age	-0,0029	0,0037	-0,7675	0,4428
Sex	-0,1149	0,1164	-0,9867	0,3238
Living in the village	-0,0209	0,0427	-0,4895	0,6245
Employment	-0,0638	0,0192	-3,3234	0,0009
Duration of inpatient treatment	0,0901	0,1243	0,7248	0,4686
Diagnosis	0,0494	0,0492	1,0039	0,3154
Year	-1,5162	0,1474	-10,2831	8,40E-25

Analysis of the impact of factors on the cost-effectiveness of the second treatment regimen using Tobit regression shows that the only significant factor was “duration of inpatient treatment”, namely the cost-effectiveness of the second treatment regimen worsened with a decrease in the duration of hospital stay $\alpha = -0.0638$, $p = 0.0009$. All other factors considered did not have a significant impact on the cost-effectiveness of the second treatment regimen.

Studies aimed at assessing the cost-effectiveness of asthma and COPD treatment indicate a significant financial burden of these diseases on health care systems. According to an analysis by Punekar et al., the cost of COPD management in primary care in the UK is closely related to the frequency of exacerbations. Patients with more than two exacerbations per year spend on average £2,033 more on treatment than those with a lower frequency of exacerbations [7]. A systematic review by Gutiérrez Villegas et al. supports this finding, noting that the average annual cost of COPD treatment ranges from \$1,521 to \$9,047, depending on the country and severity of the disease. A significant proportion of these costs are attributable to hospitalizations and pharmacotherapy [8].

The use of single-inhaler triple therapy (FF/UMEC/VI) for patients with symptomatic moderate to severe COPD may be more cost-effective than tiotropium monotherapy. This strategy reduces overall costs by \$1,200 per patient per year while providing better symptom control [9].

The DOSE index proposed by Li et al. is an effective tool for predicting healthcare costs in COPD. Patients with higher index values (≥ 4) have significantly higher annual treatment costs (\$5,723) than those with $\text{DOSE} \leq 2$ (\$2,144) [10]. This index may help identify patients who require more intensive monitoring and treatment.

In asthma, mepolizumab has been shown to be cost-effective in the treatment of severe eosinophilic asthma. A cost-benefit model estimated the cost per quality-adjusted life year (QALY) at \$68,500, which is within the acceptable range for innovative treatments [11]. An analysis by Nunes et al. also confirms the high economic importance of asthma, noting that in Europe the direct and indirect costs of treating the disease amount to €72.2 billion per year, a significant proportion of which is due to lost productivity [12].

The effectiveness of long-term use of omalizumab in patients with uncontrolled allergic asthma was confirmed in a systematic review by Lai et al. Patients treated with this drug had a 32% reduction in exacerbation rates compared with the control group, which resulted in a significant reduction in hospitalization costs [13]. Overall, the analysis of different treatment regimens for asthma and COPD demonstrates that a personalized approach to treatment using modern therapeutic strategies can significantly reduce the economic burden of these diseases. These results highlight the importance of further research to optimize therapy, taking into account clinical effectiveness and financial feasibility.

Conclusions. 1. Analysis of the effectiveness of existing basic therapy regimens for the treatment of bronchial asthma and COPD revealed a low level of adaptation of prescriptions to the needs of patients. Only a small proportion of patients received optimal doses of drugs, while in most cases significant deviations were observed - both in the direction of excessive dosage and insufficient intensity of therapy. This indicates the need for more careful selection of doses, taking into account the individual characteristics of patients. Each of the schemes is well thought out and contains optimal therapy ratios in terms of allocative efficiency.

2. The results of a comparative analysis of two common treatment regimens showed a stable advantage of the first regimen in terms of technical and cost-effectiveness. This indicates its feasibility for wider use, while demonstrating the need to revise approaches to the use of the second regimen. Highly reliable differences in the effectiveness of the regimens emphasize the importance of multifactorial analysis for improving therapeutic strategies.

3. The study established the influence of individual factors on the effectiveness of treatment. For the first regimen, the key modifier was the year of follow-up, indicating a deterioration in efficacy over time, while for the second regimen, the duration of inpatient treatment was important. These results highlight the need for systematic review of treatment standards to take into account dynamic changes in medical practice and patient needs.

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