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# The comparison of use of antibiotics due to acute respiratory infections in the rural population of primary care in 2010 and 2017

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## ABSTRACT

Respiratory tract infections are the most common reason because of which patients report to a family doctor. The role of the family doctor is to assess both the symptoms suggesting the aetiology of infection, as well as performing additional tests, in order to make a definitive diagnosis. An increasing clinical problem is antibiotic resistance. Therefore, the objectives of this study were to assess and compare antibiotic use due to acute respiratory infections in the rural primary care population for over a 7-year period.

A retrospective examination of electronic medical records covered 4355 declared patients in 2010 and 3959 patients declared in 2017. The analysis included advice - medical consultations due to acute respiratory infections, related or not related to the antibiotic prescription. In 2010, 2531 such consultations were given, and in 2017 - 1687.

The results of our analysis indicate that in the surveyed rural population there was a decrease in both the frequency of consultations for respiratory infections (58.12% vs 42.61%) and the frequency of prescribing antibiotics / chemotherapeutics for this reason (50.8% vs 34, 6%). The type of antibiotic, which was most often used in the diagnosis of J06 (dominating both in 2010 and in 2017), has changed as well - from azithromycin to amoxicillin. The structure of diagnoses of respiratory tract infections systemized by ICD-10 has also been slightly changed.

The reducing frequency of prescribing antibiotics as well as the change of the "first choice" antibiotic in the treatment of acute respiratory infections is a favorable trend and may result from the doctors' greater awareness of antibiotic resistance. Likewise, the change in the structure of diagnoses made by doctors from unspecified to specific ones may indicate greater awareness, resulting in treating specific diseases with targeted antibiotics. Further studies are needed to assess the choice of antibiotic therapy by the general practitioner.

**Key words: antibiotics, infection, rural region, primary care**

## INTRODUCTION

Respiratory infections are the most common reason of GP’s consultations [1]. Physiological immaturity of developing respiratory system, being in nurseries or kindergartens and allergies are the reasons why the most exposed group of patients are children below 5 years of age. [2]. The second group of patients which is more susceptible to respiratory infections are the elderly - people over 60 years of age. The coexistence of many diseases (COPD, heart failure, immunodeficiency connected to aging), exposure to pathogenic factors during hospitalizations or living in nursing homes and treatment modulating the functions of the immune system are resulting in frequent infections [3].

The division of respiratory infections can be conducted considering their etiology. The most frequent subgroup is viral infections. They are caused most often by rhinoviruses, adenoviruses, coronaviruses, influenza and parainfluenza viruses, RS virus and enteroviruses. The mechanism of their action is damaging the structure of the airway epithelium, which

causes an inflammatory reaction, and sometimes also bronchial hyperresponsiveness. Moreover, by weakening the natural immune barrier and impairing mucociliary transport, they can lead to bacterial infections. Due to the seasonality of viral infections, the largest number of patients suffering from respiratory infections is observed in the autumn and winter. In the case of bacterial infections, the etiological factor depends on the age, the place of infection and risk factors.

In everyday practice colonization of the nasopharyngeal cavity with pathogenic bacteria (according to estimates, about half of children under 2 years of age is colonized with S. pneumoniae) is a problem often leading to unnecessary implementation of antibiotic therapy in viral infections [4].

The role of the family doctor is to assess both the symptoms suggesting the etiology of infection, as well as performing additional tests in order to make a definitive diagnosis. An increasing clinical problem is antibiotic resistance. The mass prescription of these drugs without indications, often in viral infections, increases the amount of resistant bacteria. The common presence of antibiotics and chemotherapeutic agents in the environment leads to acquiring the resistance mechanisms by bacteria. It is estimated that 80% -90% of antibiotics in the USA are prescripted by family doctors [5]. In Australia in 2014 as many as 46% of inhabitants were treated with antimicrobial drugs at least once and in 2016 family doctors ordered 88% of all prescribed antibiotics [6]. The phenomenon of increasing antibiotic resistance forced a gradual rationalization of the use of these drugs. Basing the indications for antibiotic treatment on current guidelines and changing the beliefs of patients who are sometimes convinced that they need to be treated with this type of drugs (even in case of viral infections) seem to be important. However, these changes must be introduced systemically to ensure that the rules are applied as widely as possible [5]. Therefore, the objectives of this study were to assess and compare antibiotic use due to acute respiratory infections in the rural primary care population for a 7-year period.

## MATERIAL AND METHODS

### *Location*

Non-public Healthcare Center (NZOZ) REMED in Borzęcin, which was established in January 2009, provides free primary care services to the local community on conditions included in the contract with the National Health Fund (NFZ). Over 90% of patients declared to doctors and nurses in REMED are residents of the rural commune of Borzęcin. At the end of 2017 there were 3959 patients declared to 2 physicians in the facility, 4308 patients declared to 4 family nurses and 2248 patients declared to family midwife. The data includes only patients with confirmed health insurance.

### *Research material*

A retrospective examination of electronic medical records covered 4355 declared patients (adults and children) in 2010 and 3959 declared patients (adults and children) in 2017 (Table 1). The analysis included medical consultations due to acute respiratory infections, related or not related to the antibiotic prescription. In 2010 - 2531 such consultations were given, and in 2017 - 1687. As the study was retrospective and concerned only the analysis of the electronic medical records, it did not require the consent of the Bioethics Committee.

Diagnosis of the acute respiratory infection was based on the International Statistical Classification of Diseases and Related Health Problems in the relevant group "J" with the range J00-J22, where J00 means Acute nasopharyngitis [common cold], J01 - Acute sinusitis, J02 - Acute pharyngitis, J03 - Acute tonsillitis, J04 - Acute laryngitis and tracheitis, J05 - Acute obstructive laryngitis [croup] and epiglottitis, J06 - Acute upper respiratory infections of multiple and unspecified sites, J10 - Influenza due to identified seasonal influenza virus, J11 - Influenza, virus not identified, J12 - Viral pneumonia, not elsewhere classified, J13 - Pneumonia due to Streptococcus pneumoniae, J14 - Pneumonia due to Haemophilus influenzae, J15 - Bacterial pneumonia, not elsewhere classified, J16 - Pneumonia due to other infectious organisms, not elsewhere classified, J17 - Pneumonia in diseases classified elsewhere, J18 - Pneumonia, organism unspecified, J20 - Acute bronchitis, J22 - Unspecified acute lower respiratory infection.

The type of recommended antibiotics and chemotherapeutics was also analyzed obtaining 7 groups: penicillin, cephalosporins, aminoglycosides, tetracyclines, macrolides, lincosamides and sulfonamides. In addition, amoxicillin and penicillin were isolated from the group of penicillins, cefaclor and cefuroxime from the group of cephalosporins, and from the group of macrolides - azithromycin and clarithromycin.

## RESULTS

*Table 1. Comparison of demographic characteristics of REMED patients in 2010 and 2017.*

| **POPULATION OF REMED** | | |
|---|---|---|
| Age group | **2010** | **2017** |
| 0 - 6 | 270 | 179 |
| 7 - 19 | 879 | 524 |
| 20 - 39 | 2904 | 1063 |
| 40 - 65 | | 1453 |
| 66 - 75 | 302 | 370 |
| Above 75 | | 370 |
| Aggregate | **4355** | **3959** |

*Analysis of the year 2010*

Out of 4355 patients, 2531 (100%) consultations concerned respiratory infections. The most common diagnosis was J06 - 71.8% of all consultations. The second most frequent was J03 (14.6%) and the third J00 (8.1%). The least frequent diagnoses were J11 and J18 (0.3% each) (Table 2).

Respiratory tract infections were treated with antibiotics and chemotherapeutics in more than a half of cases (50.8%). Antimicrobial drugs were used most often in the treatment of acute tonsillitis (78.3%), acute bronchitis (62.3%) and acute rhinosinusitis (52.6%) (Table 3).

1285 packages of antibiotics and chemotherapeutics were prescribed. The most frequently prescribed group of antibiotics were macrolides (555 packs), of which azithromycin was the most common (41.3% of all antibiotic packaging discharged). In the second place, amoxicillin (38.1%) and the third cefuroxime (13.3%). The lowest rates were for cefaclor and clindamycin (0.1% and 0.2%) (Table 4).

Azithromycin in almost 80% of cases was administered in J06 (acute upper respiratory infections of multiple and unspecified sites). The same diagnosis was the cause of cefuroxime use in 47% and amoxicillin in 41% of cases (Table 5).

*Analysis of the year 2017*

Out of 3959 patients, 1687 (100%) consultations concerned respiratory infections. The most common diagnosis was J06 - 65,6% of all consultations, the second most frequent J00 (12.9%) and the third J03 (11.9%). The least frequent diagnoses were J22, J11 and J18 (0.1%, 0.2% and 0.2% respectively) (Table 2).

Respiratory tract infections were treated with antibiotics and chemotherapeutics in over a third of cases (34.6%). These drugs were most often used in unspecified respiratory tract infection (100%), acute tonsillitis (70.7%) and acute bronchitis (56.3%) (Table 3).

583 packages of antibiotics and chemotherapeutics were prescribed. The most frequently prescribed group of antibiotics were penicillins (345 packs), of which amoxicillin was used in the first place (58.7% of all antibiotic packaging discharged). In the second place azithromycin (23.8%) and in the third cefuroxime (11.3%) were administered. The least frequently used antimicrobial drugs were phenoxymethyl penicillin, amikacin and sulfamethoxazole + trimethoprim (0.5% each) (Table 4).

Amoxicillin was the most preferred antibiotic - in 66% it was used in acute upper respiratory infections of multiple and unspecified sites (J06). This diagnosis was the reason for using azithromycin in 38% and cefuroxime in 4.1% of cases (Table 5).

*Comparison of the year 2010 and 2017*

The number of consultations due to respiratory tract infections decreased from 2531 in 2010 to 1687 in 2017 as the population decreased. Nonetheless, taking into consideration the percentage of these consultations in reference to the size of the population, the difference was over 15% (58.12% vs. 42.61%).

The frequency of treating the respiratory tract infections with antibiotics has decreased - from more than half of cases in 2010 to nearly one-third in 2017 (50.8% vs 34.6%). Furthermore, acute rhinosinusitis was treated with antibiotics in more than half of the cases in 2010, comparing to 40% in 2017. Similarly, in the case acute upper respiratory infections of

multiple and unspecified sites, there was a decrease from 48.5% of cases treated with antibiotics to 32.1% in 2017.

The structure of diagnoses has also changed to some extent. Although the dominant diagnosis in both years was J06, its frequency decreased in 2017 by 6.2% (71.8% vs. 65.6%). There was also a change in the diagnosis of J03, which was the second in frequency in 2010, but the third in 2017 (14.6% vs 11.9%) and J00, which ranked third in 2010 and second in 2017 (8.1% vs. 12.9%). A rare diagnosis was J22. The only two cases were registered in 2017.

The type of antibiotics used has also changed. Although azithromycin (41.3%) was the most commonly used in 2010, especially when diagnosed with J06 (80% of cases), in 2017 amoxicillin (58.8%) was most commonly used for the same diagnosis. Cefaclor remained in the third position in both years. However, among the least used antibiotics and chemotherapeutics, the use of sulfamethoxazole with trimethoprim changed from 4.1% in 2010 to 0.5% in 2017.

*Table 2. Comparison of the frequency of diagnoses from group J by ICD-10 in 2010 and 2017 in relation to the number of all consultations due to respiratory tract infections.*

| **Diagnosis type** | **Diagnosis frequency in 2010** | | **Diagnosis frequency in 2017** | |
|---|---|---|---|---|
| | **n** | **%** | **n** | **%** |
| **J00** | 206 | 8,1 | 218 | 12,9 |
| **J01** | 49 | 1,9 | 90 | 5,3 |
| **J02** | 11 | 0,4 | 41 | 2,4 |
| **J03** | 369 | 14,6 | 201 | 11,9 |
| **J04** | 10 | 0,4 | 10 | 0,6 |
| **J06** | 1817 | 71,8 | 1102 | 65,6 |
| **J11** | 8 | 0,3 | 3 | 0,2 |
| **J18** | 8 | 0,3 | 4 | 0,2 |
| **J20** | 53 | 2,1 | 16 | 0,9 |
| **J22** | - | - | 2 | 0,1 |
| **Razem** | 2531 | 100% | 1687 | 100% |

*Table 3. Frequency of antibiotic or chemotherapeutic prescription during the infection in different types of diagnoses.*

| Diagnosis type | Antibiotic usage in 2010 | | Antibiotic usage 2017 | |
|---|---|---|---|---|
| | n/N | % | n | % |
| **J00** | 39/206 | 18,9 | 15/218 | 6,9 |
| **J01** | 29/49 | 52,6 | 36/90 | 40,0 |
| **J02** | 3/11 | 27,3 | 22/41 | 53,7 |
| **J03** | 289/369 | 78,3 | 142/201 | 70,7 |
| **J04** | 4/10 | 40,0 | 1/10 | 10 |
| **J06** | 881/1817 | 48,5 | 354/1102 | 32,1 |
| **J11** | 3/8 | 37,5 | 0/3 | 0,0 |
| **J18** | 4/8 | 50 | 2/4 | 50 |
| **J20** | 33/53 | 62,3 | 9/16 | 56,3 |
| **J22** | - | - | 2/2 | 100 |
| **Razem** | 1285/2531 | 50,8 | 583/1687 | 34,6 |

*n – cases in which antibiotic was administered, N - frequency of diagnoses according to ICD-10*

*Table 4. Comparison of the frequency of administering different types of antibiotics and chemotherapeutics in 2010 and 2017.*

| **Antibiotics and chemotherapeutics** | **Frequency in 2010** | | **Frequency in 2017** | |
|---|---|---|---|---|
| | **n** | **%** | **n** | **%** |
| Penicillins: amoxicillin | 490 | 38,1 | 342 | 58,7 |
| Penicillins: phenoxymethyl | 0 | 0 | 3 | 0,5 |
| Cephalosporins: cefaclor | 1 | 0,1 | 0 | 0 |
| Cephalosporins: cefuroxime | 171 | 13,3 | 66 | 11,3 |
| Aminoglycosides: amikacin | 0 | 0 | 3 | 0,5 |
| Tetracyclines: doxycycline | 13 | 1,0 | 9 | 1,5 |
| Macrolides: azithromycin | 531 | 41,3 | 139 | 23,8 |
| Macrolids: clarithromycin | 24 | 1,9 | 13 | 2,2 |
| Linosamides: clindamycin | 3 | 0,2 | 5 | 0,9 |
| Sulfonamides: sulfamethoxazole + trimethoprim | 52 | 4,1 | 3 | 0,5 |
| Aggregate | 1285 | 100% | 583 | 100 % |

*Table 5. The comparison of frequency of administering the three most popular antibiotics in the three most popular diagnoses.*

| **Antibiotic/ chemiotherapeutic type** | **2010** | | | **2017** | | |
|---|---|---|---|---|---|---|
| | J06 | J03 | J00 | J06 | J03 | J00 |
| Macrolides: azithromycin | 420 (79%) | 49 (9,2%) | 15 (2,8%) | 67 (48%) | 57 (41%) | 5 (3,6%) |
| Penicillins: amoxicillin | 201 (41%) | 186 (38%) | 21 (4,3%) | 226 (66%) | 68 (20%) | 8 (2,3%) |
| Cephalosporins: cefuroxime | 80 (47%) | 52 (30%) | 3 (1,8%) | 27 (4,1%) | 14 (2,1%) | - - |

***% - value relative to total antibiotic/chemiotherapeutic consumption in a given year***

## DISCUSSION

The results of our research showed differences in the amount of consultations due to respiratory tract infections in general community from 2010 and 2017 (58.12% vs 42.61%), as well as the decreased frequency of prescribing antibiotics / chemotherapeutics for this reason (50.8% vs 34.6%). The type of antibiotic which was most frequently used in 2010 and in 2017 in the diagnosis of J06 also changed (from azithromycin to amoxicillin). A slight change in the structure of diagnoses (ICD-10 classification) was also noticed.

Presented analyzes were conducted in order to assess the use of antimicrobial drugs administered by primary care doctors in the rural population. Reports of increasing antibiotic resistance and its implications usually affect doctor's treatment and result in the rationalization of the use of antibiotics. Several European science projects were exploring this phenomenon. E. coli resistance varied eighteen-fold between Sweden (1.0%) and Greece (18.2%). The difference was even more significant in the case of K. pneumoniae - in Switzerland - 0.7%, and in Greece - 64.1% [7]. Nowadays it is widely known that the extent of antibiotic resistance is directly influenced by the increased consumption of antibiotics. The measure of this consumption in 2010 were 18.3 daily doses per 1,000 inhabitants per day (DID). The highest value for Greece (39.4 DID), the lowest in the Baltic countries (11.1) and the Netherlands (11.2) [8]. In a further study even greater consumption of antibiotics were found in Turkey, at the level of 42.3 DID [9]. Reduction and rationalization of the use of antibiotics reduces antibiotic resistance. A study conducted in Finland concerning S. pyogenes resistant to macrolides showed that in 3 years (1997-2000) this resistance decreased from 9.2% to 7.4%, which was correlated with reduced administering of macrolides [10].

Antibiotics are of great significance to modern medicine therefore we should limit their presence in the environment in order to minimize the augmentation of resistance. Swedish scientists analyzing water taken from one of the rivers in India near the industrial zone proved that the concentration of ciprofloxacin was higher than the therapeutic level in human blood during treatment with this antibiotic. This contamination was caused by discharging sewage from the factory producing medicines directly to the river [11]. Subsequent genetic tests indicated that the bacteria present in the tested water were not only resistant to ciprofloxacin, but also to fluoroquinolones, beta-lactams, aminoglycosides, sulfonamides, and others [12]. The bacterial genetic material can be transferred to other bacteria during reproduction or horizontal gene transfer resulting in antibiotic resistance within many types of bacteria [12].

Numerous studies comparing the diagnostics and treatment of respiratory tract infections in Poland and in the world have been conducted. In the Happy 2 study the aim was to analyze the additional tests conducted in the primary care and the methods of subsequent treatment of respiratory diseases. One of the differences noticed among polish doctors is lower frequency of conducting additional tests. Rapid Streptococcus tests in Poland were performed in 0.4% of cases (European average is 4.45%), CRP concentration in 2.2% of cases (European average 14.2%), and chest X-ray in 2, 3% of cases (Europe average 14%). All of these tests can be useful in order to distinguish viral and bacterial infection and to avoid unnecessary antibiotic therapy. Another observation noticed in the study Happy 2 is less frequent use of narrow spectrum antibiotics by doctors in Poland. Among the prescribed antibiotics fenoxymethylpenicillin was used by physicians in Poland only in 6.7% of cases (in Sweden it was over 70% of prescribed antibiotics). The majority of antibiotics used in Poland were amoxicillin (28.9%), amoxicillin with clavulanic acid (24.4%), macrolides (22.4%) and cephalosporins (12.1%) [13].

The effect of amoxicillin therapy on the course of lower respiratory tract infection (when pneumonia is not suspected) proved to be controversial. During one of the scientific studies, patients who were presenting to the family doctor were swabbed. Based on the evaluation of these tests' patients were assigned to groups with bacterial, viral and mixed etiology. Subsequently, the course of the disease was evaluated in patients treated with amoxicillin (3x1g for 7 days) and those taking placebo, the criteria were: duration of symptoms, their intensity and the presence of possible deterioration of the patient's health condition (defined as an additional consultation or presenting to the hospital). In none of the groups there was a statistically significant reduction in the duration of symptoms. In patients with bacterial infection administered with antibiotic the intensity of symptoms was lower than in the placebo group (mean intensity of symptoms lower by 0.26 points), in this group also the number of patients reporting deterioration was lower (0.47 vs 0.46). In the group of patients with mixed etiology of infection, the use of antibiotics contributed to lowering the frequency of deterioration of patients' health from 32% to 10% [14].

Another study was conducted similarly but patients were additionally divided into people over 60 years of age, comparing their results with the total number of participants. In this study no swabs were collected from patients. Patients above 18 years of age with lower respiratory tract inflammation and cough for less than 28 days were randomly assigned to the amoxicillin treated group (3x1g for 7 days) or placebo. The duration of severe symptoms and their average intensity during infection did not differ significantly between groups. The presence of deterioration or appearance of new disease symptoms were more frequent in the placebo group (19.3% vs. 15.9%). In the study there were also noticed the side effects of

antibiotic therapy. Nausea, rash or diarrhoea were observed more often among patients treated with amoxicillin (28.7% vs. 24%) and in this group there was also one case of anaphylaxis. In the group of people over 60 years of age there were no more benefits from the implementation of antibiotic therapy observed, than in the general population [15].

The influence of measuring CRP concentration and training conducted via the Internet (describing situations in which antimicrobial treatment should be used and presenting methods of communication with the patient) on the therapeutic decisions of GPs were also the subject of research. Doctors were divided into groups: control (without any intervention), a group trained in using CRP concentration (specific indications were identified in which the test was conducted: presence of auscultatory changes, fever, dyspnoea and uncertain situations in the doctor's opinion. In this group, training in communicating therapeutic decisions to the patient was also conducted), a group with extended communication training (the training concerned obtaining information from the patient, communication between the doctor and the patient, doctors also received informers containing guides about: symptoms, situations in which the patient should be consulted again, antibiotic therapy and antibiotic resistance) and a group that was trained in both measuring the CRP concentration and in extended communication techniques. In the group trained in measuring the CRP concentration the frequency of antibiotics administration was 15% lower, and in the group after extended communication training lower by 9%, compared to the control group. The result in the group of doctors trained in both courses was not statistically significant. The intensity of symptoms experienced by patients in the following days of therapy was similar [16].

Nowadays, doctors have at their disposal more and more tests. It is helpful in making the right diagnosis and administering proper treatment. However, in case of pneumonia the most important are still symptoms, signs and physical examination conducted by the doctor. One of the publications described results of the experiment, which compared the effects of measuring CRP and procalcitonin levels on the diagnosis of pneumonia. CRP or procalcitonin levels were correlated with the symptoms presented by patients. Within seven days after the consultation, the patient underwent an X-ray examination (which in its assumption determined the accuracy of the diagnosis). Among the traditional symptoms, the most important were: no rhinitis, dyspnea, abnormalities during auscultation, tachycardia and fever. Different cut-off values were tested for CRP concentration, it was considered that the concentration> 30 mg / l would be an optimal indicator of the ongoing inflammatory process that can be localized in the lower respiratory tract. Correlating the results of the physical examination with the concentration of CRP above this cut-off point, allowed to diagnose correctly 28% more patients than in the case of the physical examination itself. The measurement of procalcitonin concentration did not provide any relevant diagnostic information [17].

## CONCLUSIONS

The decreasing frequency of prescribing antibiotics in the treatment of acute respiratory infections is a favourable trend which may result from greater awareness of antibiotic resistance. Likewise, the change in the structure of diagnoses made by doctors (from

unspecified to specific ones) may indicate greater awareness in the case of treating specific diseases with targeted antibiotic treatment. Further studies are needed to assess the choice of antibiotic therapy by the general practitioner.

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