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**GENERAL**

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**ANTIBACTERIAL DRUG PRESCRIPTION FOR OUTPATIENTS:  
AGE, SEASONAL AND PULMONARY DISEASE DEPENDENCY****DOMINIK R. DZIURDA<sup>1\*</sup>, SEBASTIAN POLAK<sup>1</sup>; AGNIESZKA SKOWRON<sup>1</sup>,  
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**Abstract:** The goal of this study was to analyze antibacterial drug prescribing in the 1-million-plus, strictly defined population in Poland. For the 2002-2005 years, data from National Health Fund on outpatient purchasing of antibiotics in Lubuskie's Province were collected and expressed in DDD per 1-thousand inhabitants per day (DID). In the period 2002-2005 the average rate of antibiotics purchasing was 19.8 DID. During the 3-year period, at least 64.3% of the population had prescribed antibiotics. 22.7% of patients purchased 62.6% of a three-year total purchasing of antibacterial drugs in the province. A tiny 1.9% of the population purchased 10.0% of the total. From the different age-group, the study showed that special attention should be paid to two different and relatively small groups of patients – those utilizing significant percentage of the year's supply, and group of 5-9 year-old children. Seasonal variation in antibiotic prescribing was strictly linked with the age of patients. Pulmonary diseases were indentified as a factor considerably elevating antibacterial drugs purchasing frequency. A useful way to present recurring patterns in this frequency has been proposed.

**Keywords:** age dependent antibacterial pharmacotherapy, antibiotics, drug policy

In Poland, as in other countries, increasing bacterial pathogens resistance occurs (1-4). This process is, to a large degree, linked with excessive, often ungrounded prescription of antibiotics (5). The Polish National Health Fund (NHF) – a health insurance organization which is the major public source of health care financing – records a continuous increase of spendings on antibacterial treatment (6). This problem is of interest to specialists of multiple health care disciplines (7, 8). It is also reflected in numerous publications attempting to present quantitative and qualitative trends in the use of antibiotics in treatment of different diseases (9, 10). These publications provide information about the level of utilization of these drugs, seasonal variations and long term trends in antibacterial pharmacotherapy using defined daily dose (DDD) methodology.

Available studies have been based on a few basic types of data of varying reliability: including

survey data, data provided by companies analyzing the pharmaceutical market, insurance companies wholesale reports, as well as hospitals' and pharmacies' records. These sources provide general information referring to populations of entire countries or regions. There is a lack of an in-depth analysis of antibiotics utilization pattern within studied populations. This probably stems from the difficulty in acquiring reliable data which would fully describe drug consumption in a large, strictly-defined population (11). Thus, two aspects remain unidentified, the first one being the level of consumption of antibiotics and its seasonal variations in different age groups, the other one being identification of the patient population having the key influence on the drug reimbursement system, in relation to antibacterial pharmacotherapy. There is also a lack of studies presenting the relation between drugs for obstructive airway diseases consumption and antimicrobial therapy frequency.

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The goal of this study was to analyze a prescription pattern of antibacterial drugs, based on data from a large, age-defined population of the Lubuskie's Province in Poland. We have showed the relation between the antibacterial drugs use, the frequency of ambulatory treated infectious diseases, and the age of the patients. The unique character of the available data has allowed to create a map representing the frequency of the antibacterial therapy.

## Methods

### Data

The following sources of information were used during the study: the data from the Lubuskie's Regional Unit of the NHF (12) and the demographic data from the Central Statistical Office (GUS) (13).

The regional units of the National Health Fund gather information about the sales volume of the reimbursed drugs in order to refund the money to pharmacies. In the Lubuskie's Province, the collected data included a PESEL, a unique number for each Polish citizen, identifying among others the age of each patient who has been prescribed a drug. This allows tracking the reimbursed drugs Sales Operation (SO) in relation to every individual patient.

Data from the NHF (approximately 25 million records) – each one corresponding to a single sale of a reimbursed drug in a pharmacy (SO) – were used. SO of reimbursed drugs has been recorded for 975.6 thousand patients during the study period. Of the NHF records, 3.2 million refer to the antibacterial for systemic use (J01<sup>1</sup>). Finally the study database consisted of 3.034 million records (SO), corresponding to 699.7 thousand patients. The rest of the records were deleted during preprocessing due to technical reasons. Within the study population 86.7 thousand patients were recognized as treated with drugs for obstructive airway diseases (R031). They were divided into two groups, according to intensity of drug therapy – Patients Occasionally Treated (POT) and Patients Extensively Treated (PET), the groups comprising 72.5 and 14.2 thousand patients, respectively – methodology described elsewhere (14).

According to the demographic data, the analyzed population consisted of 1.009 million inhabitants – this value did not change by more than 0.1% in the study period.

The data used in the study, in spite of different methods of collection, and a potential information processing error, were compatible with official publications of the National Health Fund (15). What draws attention, after juxtaposing the structure of consumption with the data from the whole of Poland, is a lower use of furazidin and cefuroxime in the Lubuskie's Province. The population of the Lubuskie's province exhibits antibiotics consumption about 5% lower than the national average (16). Taking this into consideration the data were estimated as representative for the whole country.

The presentation of the results is based on the ATC/DDD classification systems (WHO, ATC/DDD version 2006) (17) and expressed in DDD per 1000 inhabitants per day (DID) as well as percentage of total drugs consumption (% DDD). The results referring explicitly to the sales operation (SO) were expressed in SO per 1000 inhabitants per day (SOID) as well as in the percentage of SO (% SO).

The results were rounded up to the first digit after the decimal point. Microsoft Office software as well as Statistica for Windows v. 6.0 (StatSoft, Poland), and the SPSS v.14 (SPSS Inc.) packages were used.

### Terms used

*Sale operation (SO)* – refers to every single purchase of an antibacterial drug by a patient.

*Antibiotic therapy course (ABC)* – refers to a single case of purchase of an antibacterial drug by a patient, each case being separated by a 30-day period of time from one to another. If in the defined period more than one event of an antibacterial drug sale occurred, it was treated as belonging to one course.

*Recurrent course of antibiotic therapy (RABC)* – refers to at least one event of purchase of an antibacterial drug by a patient in the 6 successive 6-months-subperiod from August 2002 to July 2005. Patients were classified to the appropriate RABC group (1-6) according to the number of subperiods in which they have purchased a drug.

## RESULTS

The average level of antibiotics purchasing (2002-2005) was 19.8 DID in the population of the Lubuskie's province. School age patients (5-19

<sup>1</sup> Anatomical Therapeutic Chemical (ATC) classification system (17)

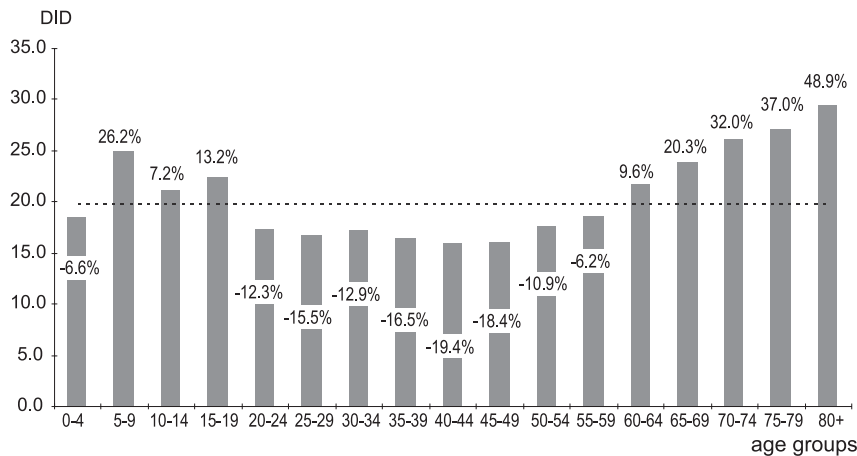


Figure 1. Average yearly antibiotics consumption in different age groups. The average consumption level in the analyzed population was 19.8 DDD/1000 inhabitants/day (DID) – dotted line. Percentage values indicate deviation from average consumption in different age groups. Based on 1.009 million population.

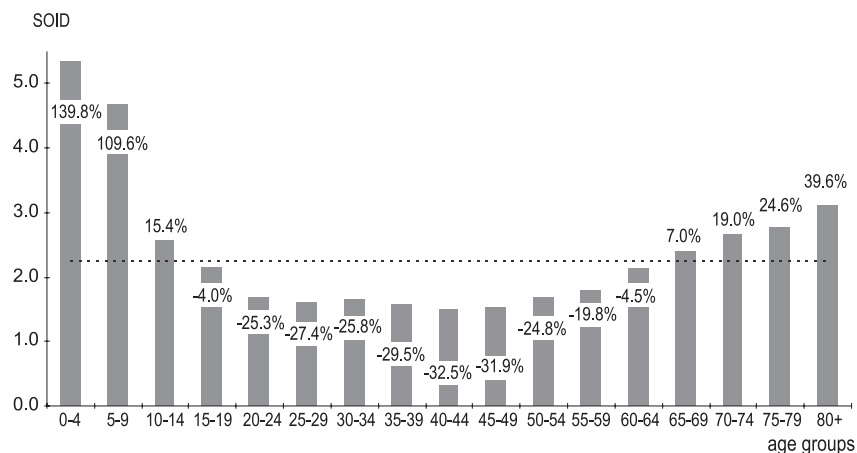


Figure 2. Average yearly antibiotics SO in different age group. The average consumption level in the analyzed population was 2.2 SO/1000 inhabitants/day (SOID) – dotted line. Percentage values indicate deviation from average SO in different age groups. Presented data are almost equal with amount of dispensed packages of drugs (packages/1000 inhabitants/day). Based on 1.009 million population.

year-old), as well as people aged 60-year or older, rank above the average of DID (Figure 1). The maximum deviation from the estimated average was observed for the oldest patients (over 75 year-old). The analysis based on the criterion of registered SO and the quantity of dispensed packages of drugs revealed that 20-59 year-old patients are characterized by a stable average of SO, equal to 1.6 SOID (Figure 2). The amount of SO gradually rose with the age of patients and reached the level of 3.1 SOID for patients over 80 years old. The highest amount of SO was recorded for patients below 10 years old (5.4 SOID in a group of patients below age of 4).

Using the accumulated data (not presented on Figure), it was observed that the age group 0-9 years, while constituting only 10.2% of the population, generated 23.6% of all recorded SO, whereas the group of the oldest patients (65 year olds plus), amounting to 11.6% of the population, generated 13.9% of total amount of the recorded SO.

The estimated seasonal antimicrobial drug purchasing fluctuations (for the Lubuskie's province population as a whole) (Figure 3) follow the pattern described in other publications (2, 18). The patient population was not homogenous in terms of the seasonal changes concerned. In all age groups, the

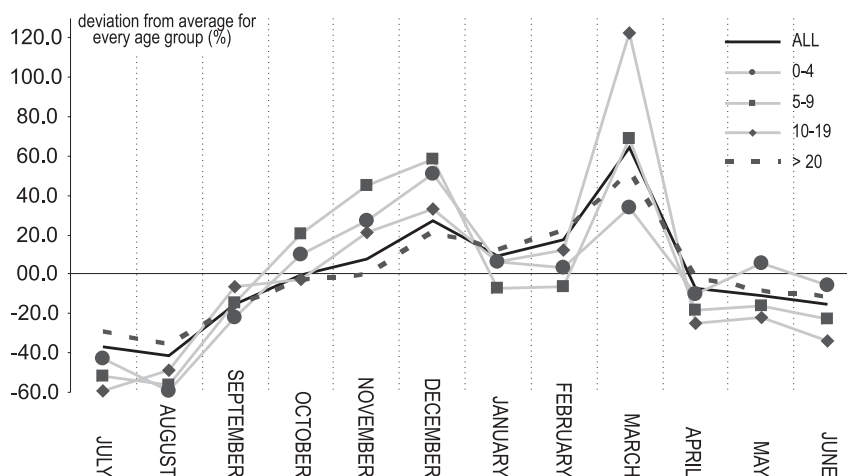


Figure 3. Comparison of seasonal variations in consumption of antibiotics in different age groups. Percentage deviations from yearly average were calculated separately in every age group and for the whole population. Based on 1.009 million population.

months of the largest purchasing were December and March, whilst the lowest level was recorded in the summer months of June, July and August. There was a significant peak of purchasing for the youngest patients (0-4 years old) at the beginning of the winter season (December), when the sales of antibiotics were 3.7 times higher than in August, which was the month of the lowest purchasing. There was tendency for two purchasing peaks for children aged 5-9 in the months of December and March. It was 3.8 and 4.0, respectively, times higher than in the lowest purchasing months. Patients aged 10-19 showed a significant peak of consumption in March (5.5 times higher than in July; (222.7% of average yearly consumption). The seasonal values curve shows a strong tendency to be flatter for the older age groups. Patients who were 20 years old or more, had a single peak incidence in March, when the level of purchasing was 2.4 times higher than in August (the lowest purchasing during the year March +52.1%; August -36.1% of the average this age group purchasing).

The incidence of ambulatory treated infectious diseases was based on Antibiotic Therapy Courses (ABC) (Figure 4). The average yearly incidence of ABC for patients in the age group 20-59 was 30.2% rising to 48.3% for the eldest patients (over 75 year-old). The maximum of ABC was recorded for the age group 5-9 (67.2%).

The DDD methodology was used to estimate the size of the high consumption group. In every calendar year, at least one SO was recorded for an average of 38.2% of Lubuskie's Province population (385.0 thousand patients). These number con-

stitutes a yearly-treated population (YTP) (Figure 5). 10% of that population purchased 30.9% DDD of the total antibiotics consumption whereas 50%, characterized by the lowest consumption level, used only 20.9% DDD of these medications (Figure 5). The number of Recurrent Antibiotic Therapy Courses (RABC) for particular patients was calculated for a 36-month period, divided into 6-month subperiods. At least one purchase of an antibiotic in each of the successive subperiod was recorded as a RABC (see terms used). 6-month subperiods were used in order to facilitate comprehension – raw data were available daily. Medical visits resulting in the

Table 1. 36-month incidence of Recurrent Antibiotic Therapy Courses (RABC) of the Lubuskie's province inhabitants. Comparison of antibiotics use (DDD methodology) and the number of SO during 36-month analysis period in different groups of patients corresponding to RABC classification. Based on 1.009-million population.

Number of RABC	% of patients <sup>1</sup>	% of DDD <sup>2</sup>	% of SO <sup>3</sup>
6	1.9	10.0	12.1
5	3.7	13.8	15.2
4	6.5	17.8	18.2
3	10.6	20.9	20.1
2	17.4	21.8	20.2
1	24.2	15.5	14.1
0	35.7	0	0

<sup>1</sup> Population size 1.009 million people

<sup>2</sup> Total consumption 23.69 million DDD

<sup>3</sup> Total Sales Operations 2.74 million SO

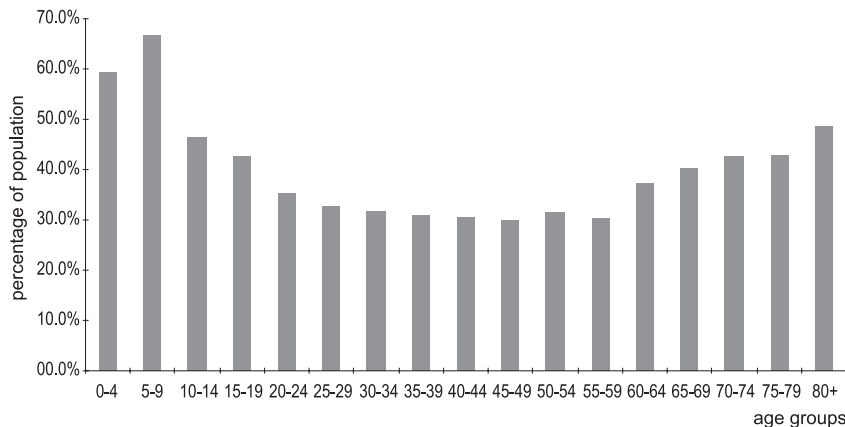


Figure 4. Yearly percentage of patients treated with antibacterial drugs in different age groups. Average data for 2002-2005 periods. Based on 1.009 million population.

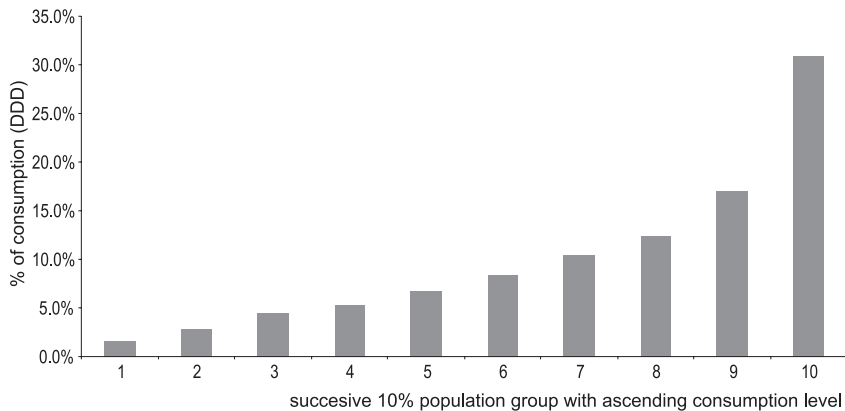


Figure 5. Average percentage of antibiotics consumption purchasing by successive 10% group of one year treated population (YTP). Patients were set in order of increasing yearly antibiotics consumption, then divided into 10 equal groups (every 38,543 thousand treated patients). Average data for every one year period (2002-2005) in DDD. Based on 1.009 million population.

prescription and subsequent purchase of an antibacterial drug were recorded during the 36-month analyzed period for 63.4% of Lubuskie's Province population (Table 1). Solely 1.9% of population purchased 10% of the total three year antibacterial drugs purchasing.

Comparing the yearly data of consecutive year to the 3-year data, it was observed that 10% of the most frequently, or most severely ill patients purchased 59,6% DDD and 35,2% DDD of a total purchasing of antibacterial drug, respectively.

Age distribution in different RABC group varied. In 5 and 6 RABC category 44.8% of patients were below 15 years old. 5-9 year old group was a dominant population in those categories. It was very characteristic that the oldest patients have very sta-

ble, high contribution in every disease recurrence group (Figure 6).

Belonging of the subject to the population treated with drugs for obstructive airway diseases was a strong factor implicating frequency of antibacterial drugs purchasing. These patients constituted 33% of total RABC-6 subpopulation; the above mentioned percentage showed stable tendency to decrease among lower RABC groups: from 5 to 1.

The comparison between two groups of POT and PET patients in combination with the RABC factor, showed significant change in antimicrobial drugs purchasing among more intensively treated patients. Histogram analysis revealed that 43% of PET and 31% of POT patients belonged to the 4, 5 and 6 RABC-group population (Figure 7). There

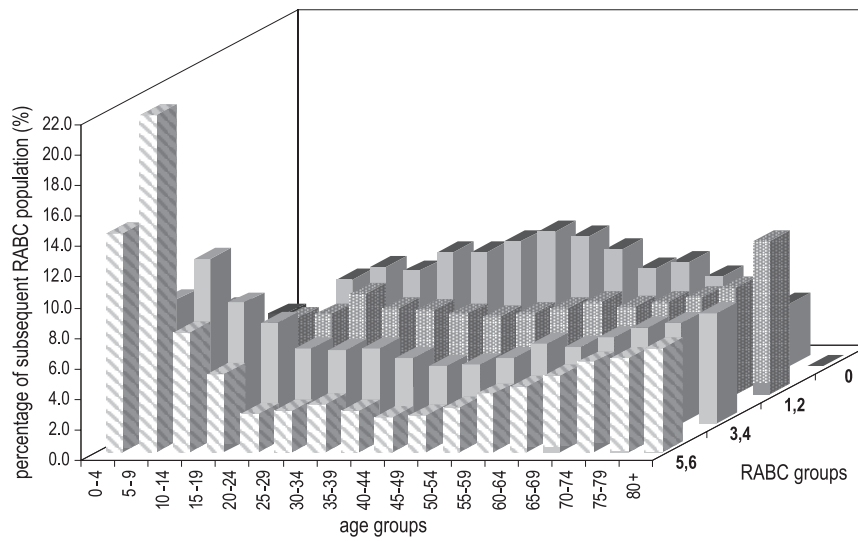


Figure 6. Patients age histograms for different Recurrent Antibiotic Therapy Courses group (according to Chart 6). Based on 1.009 million population.

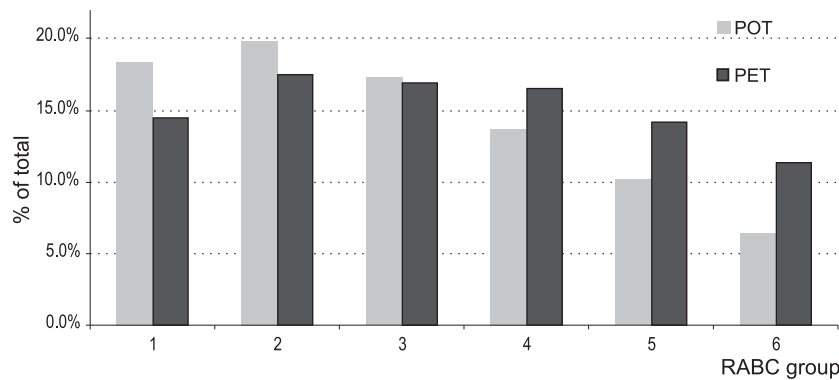


Figure 7. Two groups of patients – occasionally (POT) and extensively (PET) treated – stratification between different Recurrent Antibiotic Therapy Courses (RABC) groups populations.

were two factors identified, namely diagnosed obstructive pulmonary disease and drugs for obstructive airway diseases usage, which influenced the antibacterial drug purchase.

**DISCUSSION**

We would like to divide the discussion for two parts; methodological and descriptive. Taking under consideration usefulness of the DDD methodology it may be stated that it provides unquestionable advantages in studies of drug use, ensuring the comparability of the analyses made in different countries and by different researchers. Despite its advantages, the DDD methodology, as reported in numerous publications, fails to accurately describe drug consump-

tion in children. In the presented study, in the DDD methodology differentiation of consumption in different age groups does not exceed 48.9% deviation (the oldest patients) from the average for the studied population. Whereas, using the number of purchased medication packages or the frequency of the SO as the consumption indicator methodology, one can observe 139.8% deviation in the youngest group (0-4 years old).

These observations were corroborated by the analysis of the yearly variations of antibiotics consumption in different age groups. In the case of young patients, their caretakers expect a quick recovery from the infection and the doctors are under pressure to prescribe an antibacterial drug. A very significant increase of antibiotic prescriptions

in periods of epidemic viral infections among the youngest patients, as well as school children, shows that the potentially most effective target groups for educational actions were their parents, caretakers and doctors (8).

The two key points of the study were the analysis of the consumption level in a one-year periods and creation of a useful way showing the infectious disease incidence in a 36-month period in a large, closed population (Table 1). We demonstrated that a group constituting 20.9% of population was responsible for the use of 62.6% of a three year supply of antibiotic therapy in the province. Notably, it was possible to isolate 1.9% of the population which used over 10% of the supplies and showed an almost chronic use of antibiotics. It is worth to mention that this group encompassed two different subpopulations – children in pre-school and primary school age and, the oldest people with significantly high level of drugs for obstructive airway diseases. In general, the existence of a particularly frequently treated group, might be related to therapeutic errors, the identification of which will trigger actions aiming to rationalize the treatment to be taken. Creation of the incidence map is, in the authors' opinion, their unique contribution to the knowledge of antibacterial drug consumption. Creating comparable studies in populations from different countries, as well as the possibility of observing timelines in this discipline, would facilitate to draw broader conclusions concerning the health of the society.

The data collected by payers of the health system is a very important source of information for pharmacoepidemiological studies. The fact that the payer's (NHF) is centralized with most antibiotics eligible for reimbursement, is crucial to the actions that need to be taken. Being centralized, NHF is able to carry out reliable analysis of the health care system. We are conscious of some bias in the sources, which limited our study. The system of reimbursed treatment encompasses most of the J01 drugs registered in Poland (98%), but not 100%.

During the period of the study, the main differences as far as drug inclusion into the system of refunded treatment was concerned, occurred in two groups: J01E (sulfonamides and trimethoprim) and J01M (quinolone antibacterials) of the ATC system. Most of the antibiotics which were excluded from the refunded treatment system belong to these two groups.

The data concerning consumption of the drugs belonging to these therapeutic groups might not reflect the actual total consumption. The underestimation error might apply to patients who made only

one purchase of a drug from the ATC J01 group during the period of the study, and is strictly linked to the data preprocessing methodology. The weakness of the information from the insurance systems is a lack of information about drugs outside of the reimbursement system (patients without insurance, drug sale within the pharmaceutical prescriptions).

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## NOTES



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