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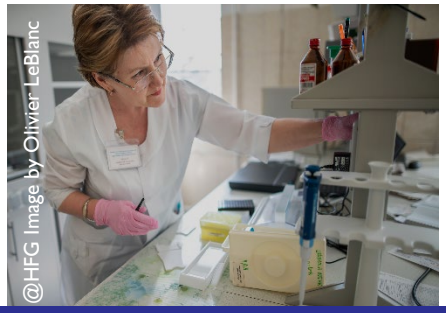

TECHNICAL REPORT: HOSPITAL DRUG EXPENDITURES - ESTIMATING BUDGET NEEDS AT THE REGIONAL LEVEL IN UKRAINE

September 2018

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The Health Finance and Governance Project
USAID's Health Finance and Governance (HFG) project helps to improve health in developing countries by expanding people's access to health care. Led by Abt Associates, the project team works with partner countries to increase their domestic resources for health, manage those precious resources more effectively, and make wise purchasing decisions. As a result, this six-year, $209 million global project increases the use of both primary and priority health services, including HIV/AIDS, tuberculosis, malaria, and reproductive health services. Designed to fundamentally strengthen health systems, HFG supports countries as they navigate the economic transitions needed to achieve universal health care.

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TECHNICAL REPORT: HOSPITAL DRUG EXPENDITURES - ESTIMATING BUDGET NEEDS AT THE REGIONAL LEVEL IN UKRAINE

I. CONTENTS

ACRONYMS

AIC	Akaike Information Criterion
BNF	British National Formulary
DoH	Department of Health
CMS	Centre for Medical Statistics
CI	Confidence Interval
CV	Coefficient of variation
EBM	Evidence-based medicine
EML	Essential medicines list
HFG	Health Finance and Governance Project
ICD	International Classification of Diseases
INN	International non-proprietary name
LRT	Likelihood ratio test
MoH	Ministry of Health
NHSU	National Health Service of Ukraine
NICE	UK National Institute for Health and Care Excellence
OOP	Out of pocket payment
PIM	Potentially inappropriate medications
Quasi-DRG	Case-based payment system for hospitals
SD	Standard deviation
SKU	Stock Keeping Unit
UAH	Ukrainian hryvnia
USAID	United States Agency for International Development
USD	US dollar
WHO	World Health Organization

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EXECUTIVE SUMMARY

Background and objectives

Ukraine has recently embarked on health reforms. Transformation of health financing and health services purchasing is a key element of the reform package. To assist the Ministry of Health with its implementation, the USAID Health Finance and Governance Project (HFG) has supported the design and introduction of health purchasing operating systems, including development of a new case-based payment system for hospitals (quasi-DRG). The HFG supported three oblasts in Ukraine to conduct cost accounting study in 180 multiprofile hospitals. The results were used for the design of case-based payment model. However, the task is complicated by uncertainty around the magnitude of out of pocket payments which affects the calculation of the appropriate payment rates to the providers. Another issue is the practice of prescribing drugs with poor evidence and realization that public money should not cover such products. This study therefore aimed to estimate the magnitude of hospital budget deficit on medications at the regional level and to estimate the costs of inpatient prescriptions with poor evidence.

Methodology

The study was conducted in the Poltava oblast of Ukraine. A cross-sectional retrospective study design was used to achieve the goals. Sampling strategy included multi-level simple random sampling stratified by age. The Poltava hospital discharge information system served as a main source of patient and hospital data. Information on inpatient prescriptions was entered by study hospital staff using the inpatient drug information module hosted by the Centre for Medical Statistics (MOH CMS). Weighted average wholesale and retail prices were purchased from the Morion company. We estimated the regional budget drug needs through econometric modeling. Our approach to assess evidence-based prescribing included the development of an EBM score and categorizing all inpatient prescriptions into 3 major groups of high, moderate and low evidence. The British National Formulary served as the main source of EBM information.

Results

In the 11 study hospitals, 4,127 patients discharged in 2016 were randomly selected for analysis. Females accounted for 56%. The mean age of the study population was 33.7 years (SD=27.9). Average length of stay was 9.6 days (SD=7.7 days). The sample covered 48 of 50 the quasi-DRGs.

The study population had 38,106 prescriptions in total during their hospital stay. The average number of prescriptions was 9.2 (SD=6.7). 24,864 (65.2%) were assigned the high EBM score. 11,668 (30.1%) prescriptions were described as of moderate evidence, while the remaining 1,574 (4.1%) had the low EBM score.

All the 38,106 prescriptions reduced to 759 INNs. Comparing with the 2017 National EML of Ukraine, 153 INNs from the Poltava study list were included in the National EML. 256 more drugs that were in use across the study hospitals and also listed in the BNF were not included in the National EML.

The average drug costs per a discharged patient were UAH 1,175 (USD 46) whereas the average cost of prescription was UAH127 (USD 5). Patients admitted to multiprofile facilities carried a heavier financial burden paying for inpatient prescriptions. The proportion of prescriptions paid by the patients in these facilities ranged from 59% to 94%.

The average OOP payment was considerable at UAH808 (USD 31.6) per hospital stay or at UAH96 (USD 3.8) per day: individuals with the minimal salary would have to work nearly 3 days to cover the drug costs of one day of hospitalization. The total estimated drug budget for 47 inpatient facilities in the Poltava region was UAH291.1mln (USD 11.4mln) for the year of 2016. In contrast, UAH59.3mln (USD 2.3mln) were allocated by the region.

Limitations included the reliance on administrative databases, scan-review as opposed to a more rigorous systematic review of evidence for drugs not listed in the BNF, top 1% truncation of the data in the modeling exercise.

Conclusions and Recommendations

The magnitude of OOP payments for inpatient drugs among hospitalized individuals in the Poltava region presents a substantial financial burden for the households. Also, only 65% of all prescriptions were assigned the high EBM score. The results will be used to adjust the quasi-DRG weights. In the meantime, national policy making efforts should be made to improve the following:

The government should increase allocations to fund inpatient prescriptions with the high EBM score focusing on multiprofile hospitals and facilities providing healthcare in priority areas such pediatrics and maternity.

Expansion of the national EML list should be considered to include other drugs of high evidence as it currently does not cover the needs of hospital physicians.

In parallel, a national dialogue needs to be established to review prescription practices in the country to avoid prescribing medications with poor evidence. Not being included on the NEML (i.e., positive procurement list), these medications are paid OOP causing unnecessary and avoidable financial burden for the patients.

2. INTRODUCTION

A lower middle- income country with a population of 45.5 mln, Ukraine has retained many features of the Semashko model of healthcare system: a state owned nationally controlled structure with a heavy emphasis on inpatient care[1]. Over the years after the independence, decentralization of managerial power was a major fundamental change to the system implemented by the government: in most other respects, the system remains largely unreformed[1]. However, despite many political and economic challenges that have hindered reforms in the past, continuing attempts to introduce much needed structural changes to the system have led to the development of The Health System Reform Strategy for Ukraine 2015–2025. Transformation of health financing and health services purchasing is a key element of the reform package[1].

To assist the Ministry of Health (MoH) with its implementation, HFG has supported the establishment of a Health Purchaser in Ukraine: a strategic single payer for healthcare services. The technical support included the adaptation of a methodology for facility-level cost accounting, introduction of an information system of discharged patients for monitoring provider performance, and development of new purchasing instruments such as a new case-based hospital payment system (quasi-DRG). The ultimate goal is to inform development of national tariffs within the DRG-based payment system and to estimate payment rates for services included in the State Guaranteed Benefit Package.

However, the task is complicated by the high volume of out of pocket payments in the system[2]. These payments are wide spread and are present in many forms at various levels of care: ambulatory services and hospital care, official services fees and informal charges, medical products and drugs. Reportedly, as many as 90.7% of inpatients are paying for at least some inpatient drugs [1 3]. This has implications for any initiatives that seek to reform healthcare financing and provider payment mechanisms. Uncertainty around the magnitude of OOP payment makes it difficult to determine the level of per capita expenditures for inpatient drugs and consequently the appropriate payment rates to the providers. Also, with the current economic situation pushing the drug prices up in Ukraine while the real income of the population decreasing[4], the financial burden can reach catastrophic levels for many patients. This situation jeopardizes the strategic goal set by the MoH which is to provide patients with high quality and affordable medicines across the country[3].

Another aspect to consider when estimating hospital budget needs is presciption practices. Historically, inteference with science and isolation from the West's scientific research have left many post-Soviet countries the legacy of outdated, excessive or ineffective diagnostic and treatment practices[2 5-7]. Administrative and legal mechanisms to support evidence-based medical aproaches are lacking[2]. While a debate on why these practices are still in place is beyond the scope of this report, it is clear that the government should not allocate public money to cover pharmaceutical products of dubious effect. Such prescriptions would need to be identified and accounted for during a budget estimation exercise.

Building on the work completed by the Project and acting upon a request from national and regional HFG partners, this study aimed to

1) To estimate the magnitude of hospital budget deficit on medications at the reigonal level:
    - ❖ Determine the magnitude of out of pocket payments for drugs among hospitalized individuals
    - ❖ Contribute to age-based adjustment of the quasi-DRG weights
2) To estimate the extend of evidence-based prescribing:
    - ❖ Determine the proportion of prescriptions with a high level of evidence of clinical effectiveness
    - ❖ Estimate the costs of inpatient prescriptions with poor evidence.

3. METHODS

3.1 Context and Ethics

This study was conducted in the Poltava oblast of Ukraine. Located in the middle of the country, the region is an industrial and agricultural centre with a population of approximately 1.4 mln [8]. Provision of health care in the region is overseen by the Department of Health of Poltava (DoH). 70 healthcare facilities provide inpatient care at 3 geographical levels (oblast, city, and district). Most of the hospitals are multiprofile.

The MoH selected the region as a key pilot for HFG activities where all strategic purchasing instruments are to be tested and introduced across the multiprofile hospitals. The choice was determined by several factors: high level of information and technical support, political will and progressive leadership of the region, high capacity of clinical, financial and economic staff of the DoH and health facilities.

The study was approved by the Poltava DoH and received an overwhelming administrative support from its officials throughout the study duration. The MoH was kept informed and eventually briefed on the final results of the study at a knowledge translation event. The Center of Medical Statistics (CMS) of the MoH provided technical support in data collection and formation of the patient-level dataset for analysis. Because we used de-identified patient information gathered retrospectively, subject consent was not deemed necessary.

3.2 Sampling Strategy

A cross-sectional retrospective study design was conducted among patients discharged from the Poltava hospitals in 2016. Several principles guided our study design and sampling strategy:

1) To use the available time and resources efficiently, we focused on hospitals that provide care for the majority of the population in the region
2) The selected hospitals should treat a wide range of conditions

3) Some patient categories (e.g., children and pregnant women) are a priority for the government, hence should be accounted for in the study
4) All 3 geographical levels of care must be represented in the sample
5) No comparison group was needed. However, to better adjust the DRG weights, a good representation of main age groups was required for which 7 age categories were created: 0-1, 1-5, 5-18, 18-30, 30-50, 50-65, >65 years of age

The sample size is one of the most important steps in designing a study. It should be large enough to represent the target population. At the same time, efforts to collect the sample data should not result into a wastage of resources and time. In studies not involving comparison (hence no need to detect the size of the difference between the comparators), it is reasonable to adopt an approach commonly used in surveys. The formula takes account of the confidence interval (CI) and the margin of error[9-11]:

$$n = N/(1 + N\ (e^2)),$$

where n = sample size to be estimated, N= population size, e= error margin at a specified confidence interval. We used the 5% margin of error and 95% CI in our calculations. Appendix 1 shows the distribution of sample sizes conditional on these parameters.

Stratified simple random sampling constituted our sampling strategy. It was implemented in several steps. First, we excluded hospitals (n=23) that provided specialized care. Examples are facilities that manage tuberculosis, psychiatric and oncologic diseases. Instead, the focus was on multiprofile healthcare facilities that managed ~220,000 of 309,058 discharged patients in 2016. Second, analysis of discharged cases by the number of ICD10 codes led us to select 5 multiprofile facilities that represented 3 levels of care: Oblast General Hospital, Poltava City Hospital #1, Lubny Central City Hospital, Poltava Central Rayon Hospital, and Gadyach Central Rayon Hospital (Appendix 2). The total sample size needed to be randomly drawn from these 5 multiprofile facilities would be at least 400 subjects. However, to ensure adequate representation of major age groups (or strata), the size for each stratum was inflated up to approximately 400 through random selection within each stratum (total at ~2800=7 age groups X 400). Further, subjects from several mono-profile hospitals were added to the sample to account for priority patient categories: 2 pediatric hospitals (n=~400) and 2 maternity hospitals (n=~400). Also, we added 2 long-term care facilities (n=~400) to evaluate rational drug use using an assessment tool specifically designed for elderly patients. The expected total sample size was 4215 patients from 11 facilities.

3.3 Data Sources, Collection and Formation of a Single Dataset for Analysis

3.3.1 *Patient and hospital characteristics:*

During 2016-2017, HFG supported the introduction of cost analysis tools and development of a hospital discharge information system in the Poltava region. This resulted into creation of a database of all patients discharged from the 70 hospitals across the region. Using data from the #066 hospital report form, the database compiled basic demographic (e.g., age, sex), clinical (e.g., DRG code, length of stay),

and administrative information (e.g., hospital profile, geographical level) on all (n=309,058) hospital admissions during the period of 2016. This database served as the main source of patient and hospital characteristics in the study. Because the 2016 data was most complete, all further data collection and analysis was coducted for this year.

3.3.2 *Inpatient prescriptions*

Information on inpatient prescriptions was collected from entries in the medical records. After we selected patients into our sample, the coded numbers of their medical records were forwarded to designated personnel in the hospitals selected for the study. They accessed the archived medical records and entered information on prescriptions for each patient into the inpatient drug prescription module hosted by the CMS. Key input data points included:

- the Stock Keeping Unit (SKU) for each prescription which includes the drug's brand name, drug form (e.g., pill, ampule, tube, etc), and dosing information
- International Non-proprietary Name (INN)
- Number of units per package
- Source of drug funding (e.g., procured by the hospital, purchased by the patient, covered by insurance or other)
- If the drug was procured by the hospital, the price per SKU was also entered into the system

3.3.3 *Drug prices*

In addition to hospital procurement prices, information on wholesale and retail drug prices was obtained for all SKUs from a local vendor, the Morion company (*http://www.morion.ua/*). The company conducts routine monitoring of drug prices across the country and provides advanced analytical support to the government and industry. We purchased data on two types of prices for each SKU at the national and the Poltava regional level:

- Wholesale: weighted average sell-in 2016 prices per SKU (i.e., price at which drug stores procure from distributors)
- Retail: weighted average sale-out 2016 prices per SKU (i.e., retail drug prices)

We considered obtaining distributors' prices as indicated on their price lists but after consultations with the Morion representative we rejected this source as unreliable: the prices indicated on the price list do not reflect the actual wholesale prices as well as the sell-in prices do.

3.3.4 *Formation of a Master file*

Finally, information from the three databases was combined into a single patient-level dataset for further analysis (See Master file attached).

The most challenging part of its formation was assigning drug prices to each prescription. For most prescriptions, there are several SKUs available on the market. These are very similar in most respects

such as INN, drug form, dose, except for the number of units per package and the price – see Fig. 1 as an example.

When hospital data operators were entering prescription data, they had to pick an SKU from a drop-down menu in the inpatient drug prescription module. Unless the prescribed drug was supplied by the hospital (then the operators knew exactly which SKU to select), they could pick any of those that seemed suitable based on the drug form and dose. Moreover, upon receiving the prescription, the patient could buy any of the SKUs at a drugstore. Therefore, we had to standardize the unit prices for all SKUs by INN, drug form, and drug dose, and calculate an average price per unit across SKUs that were identical. The prices for SKUs were assigned to the prescriptions. This work was conducted in close collaboration with the CMS.

Figure 1: **Example of several SKUs available for similar drugs**

Група АТХ	Міжнародна назва (INN)	Назва та дозування ЛЗ
C05CX	ЛІЗИН	L-ЛІЗИНУ ЕСЦИНАТ®, розчин для ін'єкцій, 1 мг/мл in bulk: по 5 мл в ампулах в коробі картонному
C05CX	ЛІЗИН	L-ЛІЗИНУ ЕСЦИНАТ®, розчин для ін'єкцій, 1 мг/мл по 5 мл в ампулах у блістерах
C05CX	ЛІЗИН	L-ЛІЗИНУ ЕСЦИНАТ®, розчин для ін'єкцій, 1 мг/мл по 5 мл в ампулах у блістерах, покритих плівкою, у пачці
H03AA01	ЛЕВОТИРОКСИН НАТРІЮ	L-ТИРОКСИН 100 БЕРЛІН-ХЕМІ, таблетки по 100 мкг у блістерах
H03AA01	ЛЕВОТИРОКСИН НАТРІЮ	L-ТИРОКСИН 125 БЕРЛІН-ХЕМІ, таблетки по 125 мкг у блістерах
H03AA01	ЛЕВОТИРОКСИН НАТРІЮ	L-ТИРОКСИН 150 БЕРЛІН-ХЕМІ, таблетки по 150 мкг у блістерах
H03AA01	ЛЕВОТИРОКСИН НАТРІЮ	L-ТИРОКСИН 50 БЕРЛІН-ХЕМІ, таблетки по 50 мкг у блістерах
H03AA01	ЛЕВОТИРОКСИН НАТРІЮ	L-ТИРОКСИН 50 БЕРЛІН-ХЕМІ, таблетки по 50 мкг у блістерах в картонній коробці
H03AA01	ЛЕВОТИРОКСИН НАТРІЮ	L-ТИРОКСИН 75 БЕРЛІН-ХЕМІ, таблетки по 75 мкг у блістерах
H03AA01	ЛЕВОТИРОКСИН НАТРІЮ	L-ТИРОКСИН-ФАРМАК®, таблетки по 25 мкг у блістерах
R06AE09	ЛЕВОЦЕТИРИЗИН	L-ЦЕТ®, сироп, 2,5 мг/5 мл по 100 мл у флаконах
R06AE09	ЛЕВОЦЕТИРИЗИН	L-ЦЕТ®, сироп, 2,5 мг/5 мл по 100 мл у флаконах разом з мірною ложкою в картонній коробці
R06AE09	ЛЕВОЦЕТИРИЗИН	L-ЦЕТ®, сироп, 2,5 мг/5 мл по 60 мл у флаконах
R06AE09	ЛЕВОЦЕТИРИЗИН	L-ЦЕТ®, сироп, 2,5 мг/5 мл по 60 мл у флаконах разом з мірною ложкою
R06AE09	ЛЕВОЦЕТИРИЗИН	L-ЦЕТ®, сироп, 2,5 мг/5 мл по 60 мл у флаконі разом з мірною ложкою в картонній коробці

3.4 Estimation of hospital drug budget needs

Hospital drug budget estimation included several steps. First, we calculated the cost of each prescription for all the patients in the sample using the formula:

$$Cost\ per\ prescription = Price\ per\ unit\ (UAH) X\ Quantity\ of\ units\ \ aday\ X\ Duration\ of\ drug\ administration\ (Days);$$

Second, based on the formula, we developed 2 major scenarios to estimate drug costs for each patient in the sample: "observed" and "projected" costs. To accommodate the fact that all prescriptions per patient had various sources of funding, we used a corresponding price per unit and made some assumptions, as explained below. The total drug costs for each patient per admission were calculated by summing up the costs of all separate prescriptions. We used the "observed" drug expenditures to

describe the actual drug costs in the selected 11 hospitals. The "projected" costs were extrapolated to determine the budget needs across 47 hospitals in the region.

1. "Observed" drug expenditures

If a prescription was provided by the hospital, then we used the hospital procurement price for this particular hospital. In the case when a prescription was funded by the patient, we assumed the patient obtained it from a drugstore and applied the average regional retail price. For prescriptions that were funded through other channels (such as insurance), we also applied the average regional retail price.

2. "Projected" drug expenditures

Similar to the previous scenario, we used the hospital procurement price for prescriptions provided by the hospital. However, the costs of all other prescriptions were calculated using the regional wholesale prices assuming that the drugs would be procured by the hospital at these prices had the facility had enough funding.

Third, to calculate the budget needs for 47 hospitals, including the costs for all patients (not only the sample subjects) from the selected 11 facilities, econometric modelling was applied. Econometrics employs statistics methods for estimating economic relationships[12]. We try to find an association between available variables (e.g., age, sex, length of stay, morbidity, etc) and inpatient drug expenditures among patients in the sample by fitting a model:

$$Drug\ costs\ per\ patient = \beta 0 + \beta * var\_1 + \beta * var\_2 + \beta * var\_3 + \mathcal{E};$$

As a result, each variable in the model is assigned a regression coefficient (i.e., β) once the model is fit. The fitted model is then applied to the rest of the patient population to forecast drug costs for each individual in the entire hospital population. Therefore, we calculated the mean annual drug costs per facility and multiplied that by the total number of discharged patients from the facility in 2016 to arrive at the annual budget needs for drug.

We have considered several variables, data for which was available to us (Table1). Generalized linear regression was used to model the drug costs with gamma distribution and log-link function to handle the right-skewed data[13 14]. The choice of gamma distribution was confirmed by the modified Park test[15]. To avoid model convergence issues and improve the model fit, we truncated the top 1 percentile of the data. Selection of the variables was conditional on the significance of the likelihood ratio test (LRT) at p-value <0.05 and the Akaike Information Criterion (AIC: the lower AIC, the better the model is). Analyses were conducted using SAS software version 9.4 (SAS Institute Inc., Cary, NC, USA).

Table 1 **List of variables considered in modelling**

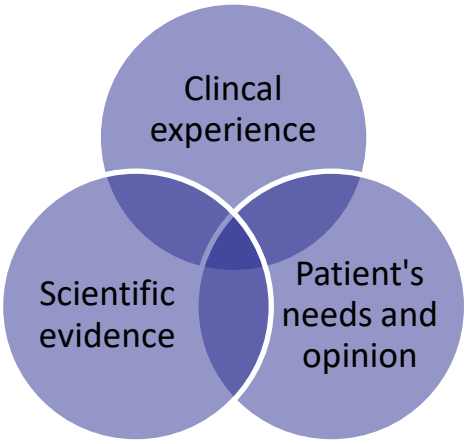
#		Variable name
1		Age (by categories)
2		Sex(M/F).
3		Quasi-DRG (50 groups, based on ICD-10 codes and whether there was a surgical intervention)

4		Length of stay (in days)
5		Type of admissions, urgent (=1) vs planned (=0)
6		Multiprofile facility (yes=1)
7		Level of care (1=rayone, 2=city, 3=oblast)

3.5 Evidence-based prescribing

As defined in the WHO's guideline on how to develop a national drug formulary[16], "Evidence-based drug therapy means integrating the best, currently available clinical evidence from scientific research with the individual clinical expertise of the prescriber to improve patient care" (Figure 2).

Figure 2 **Main pillars of evidence-based medicine**



The available sources of evidence on drug therapy are divided into 3 major categories[16]:

1) Tertiary: major comprehensive reference textbooks that compile all available information on individual medicines, including safety, clinical and cost-effectiveness data. Examples are
    a. Martindale: The Complete Drug Reference (https://about.medicinescomplete.com/)
    b. British National Formulary (https://www.pharmpress.com/BNF)
2) Secondary: reviews of current therapeutic information, including clinical trials, that answer specific and usually narrow research questions. These may be conducted as an independent analysis (e.g., systematic reviews with or without a meta-analysis) or as part of a larger initiative (e.g., clinical guideline). Cochrane Database is known for its rigorous methodology applied to systematic reviews (https://www.cochranelibrary.com/) . The UK National Institute for Health and Care Excellence (NICE) is an example of an agency responsible for developing and updating clinical guidelines for recommended use nation-wide (https://www.nice.org.uk/).

3) Primary: results of individual observational and experimental (such as randomized controlled) studies. Several large bibliographical databases exist (EMBASE, MEDLINE, CINAHLE, etc). Of them, the US National Library of Medicine's MEDLINE database is most commonly used as many publications are available at no charge via the PubMed search engine (*https://www.ncbi.nlm.nih.gov/pubmed/*)

3.5.1 *EBM score*

We assessed the degree of evidence-based prescribing in the sample and assigned a score to each prescription using the following approach:

- If the INN of a prescribed drug was listed in the BNF, then the EBM score was "high"
- If the INN of a prescribed drug was not listed in the BNF but the product was described in the Martindale and/or positive clinical trials were identified in MEDLINE, then the EBM score was "moderate" or grey
- If no or little information of equivocal quality was retrieved for a prescribed product, the EBM score was "low".

Additionally, the Poltava hospital study drug list was compared with the National Essential Medicines List (EML) approved by the order #333 in 2017, with the purpose to evaluate the overlap between the two lists and identify potential gaps.

3.5.2 *EBM prescribing among seniors*

At times, drugs with a high EBM score may still be used inappropriately or incorrectly: e.g., at a wrong dose, in an inappropriate combination, or in a vulnerable population potentially increasing the risk of side effects. Such facts are a target of drug utilization reviews that would scrutinize drug prescriptions trying to identify issues with their rational use[17]. Needless to say, this task would be an enormous undertaking requiring a team of experts at hand and was certainly beyond the scope of this assignment. However, instruments exist that allow researchers to flag potentially inappropriate medications (PIM) in medical records directly or, which is more suitable in our case, in administrative databases that contain information from medical records[18].

One such instrument are the Beers criteria used to identify inappropriate prescribing among seniors, i.e., aged 65+[19]. The criteria were developed in 1992 and have been since revised several times. The last revision was done in 2015. We evaluated the proportion of PIMs among senior subjects using these criteria.

4. RESULTS

4.1 *Patient characteristics*

In the 11 study hospitals, 4,127 patients discharged in 2016 were randomly selected for analysis (Table 2). Female accounted for 56%. The mean age of the study population was 33.7 years (SD=27.9). Average length of stay was 9.6 days (SD=7.7 days). The sample covered 48 of 50 quasi-DRGs, where DRG 7.2 (Diseases of Upper respiratory tract + Diseases of ears, nose, and pharynx), 9.2 (Diseases of cardiovascular system), and 10.1 (Diseases of Lower respiratory tract) were the top 3 most common groups. The two missing clinical groups were 2.2 (Cancer in situ) and 7B.1 (Endocrine surgery).

Missing data included 88 records, most of which (n=60) were for young men undergoing clinical evaluation before service in the military.

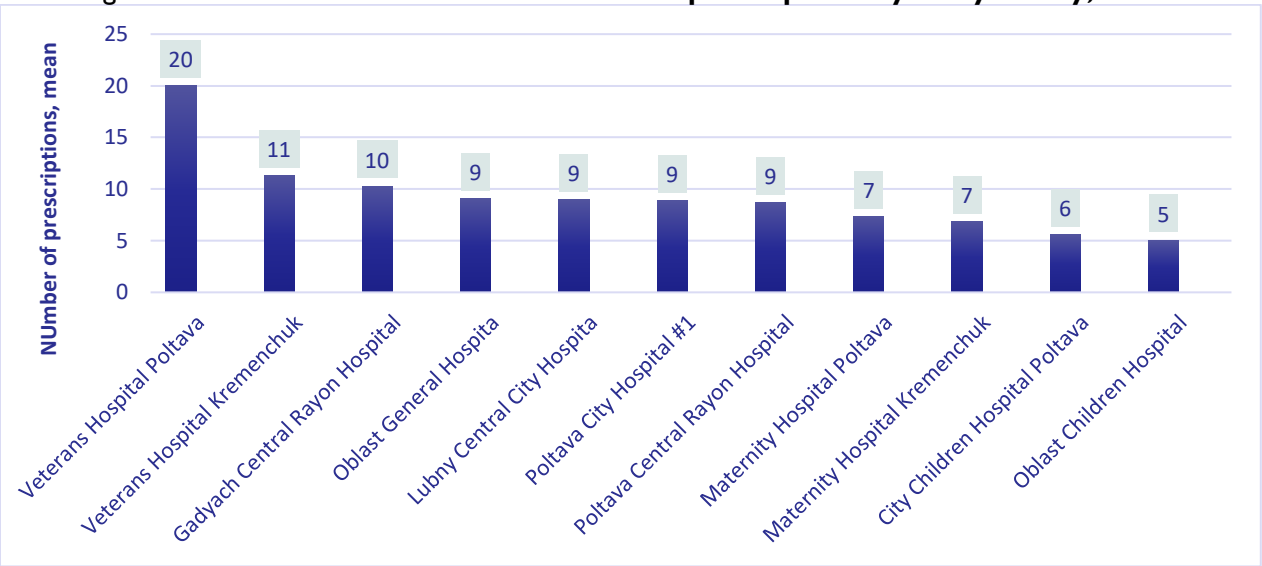
Table 2 **Patient characteristics**

Variable	Description
Age (by categories), number (%)	
0-28d	37 (0.9)
29d-1y	382 (9.26)
1-5y	499 (12.09)
5-18y	622 (15.07)
18-30y	610 (14.78)
30-50y	644 (15.6)
50-65y	484 (11.73)
>65y	849 (20.57)
Sex, number (%)	
Female	2310 (55.97)
Male	1817 (44.03)
Clinical group (top 10), number (%)	
7.2	589 (14.27)
9.2	587 (14.22)
10.1	448 (10.86)
15.1	266 (6.45)
11.1	159 (3.85)
15.3	159 (3.85)
19.1	148 (3.59)
11.2	143 (3.46)
6.1	129 (3.13)
7.1	100 (2.42)
Level of care, number (%)	
District	917 (22.22)
City	1825 (44.22)
Oblast	1385 (33.56)
Hospital type, number (%)	
Multi-profile	2946 (71.38)
Type of admission, number (%)	
Elective	3039 (73.64)
Urgent	1088 (26.36)
Acute length of stay, mean ± SD	9.6 (7.7)

4.2 *Drug Prescription*

The study population (n=4,127) had 38,106 prescription altogether during their hospital stay. The average number of prescriptions was 9.2 (SD=6.7). As expected, patients from the children and maternity hospitals had the lowest number of prescriptions ranging from 5 to 7 on average, whereas seniors hospitalized in the Veterans hospitals had the highest number (Figure 3).

Figure 3 **Distribution of the number of prescriptions by study facility, mean**



The majority of prescriptions (24,864 or **65.2%**) were listed in the BNF, hence had a high EBM score. 11,668 (30.1%) prescriptions were described as of moderate evidence, while the remaining 1,574 (4.1%) had the low EBM score.

Some variation was observed across the study hospitals in the proportion of prescriptions with a different EBM score (Figure 4). We calculated the coefficient of variation (CV) for each EBM category: CV per EBM category =standard deviation of the proportion of prescriptions with an EBM score across the facilities over the average. The CV was the highest for the low EBM score at 31.6% where the proportion of prescriptions with the low EBM score ranged from 1.7% (Veterans Hospital Kremenchuk) to 6.9% (Oblast Children Hospital). The CV for the proportion of prescriptions with the moderate EBM score was at 14.4%. Variation among the proportions of prescriptions with the highest EBM score was the lowest at 7.5% ranging from 59.9% (Poltava Central Rayon Hospital) to 74.5% (Maternity Hospital Kremenchuk).

Figure 4 **Proportion of prescriptions by EBM score, all and by study facility**

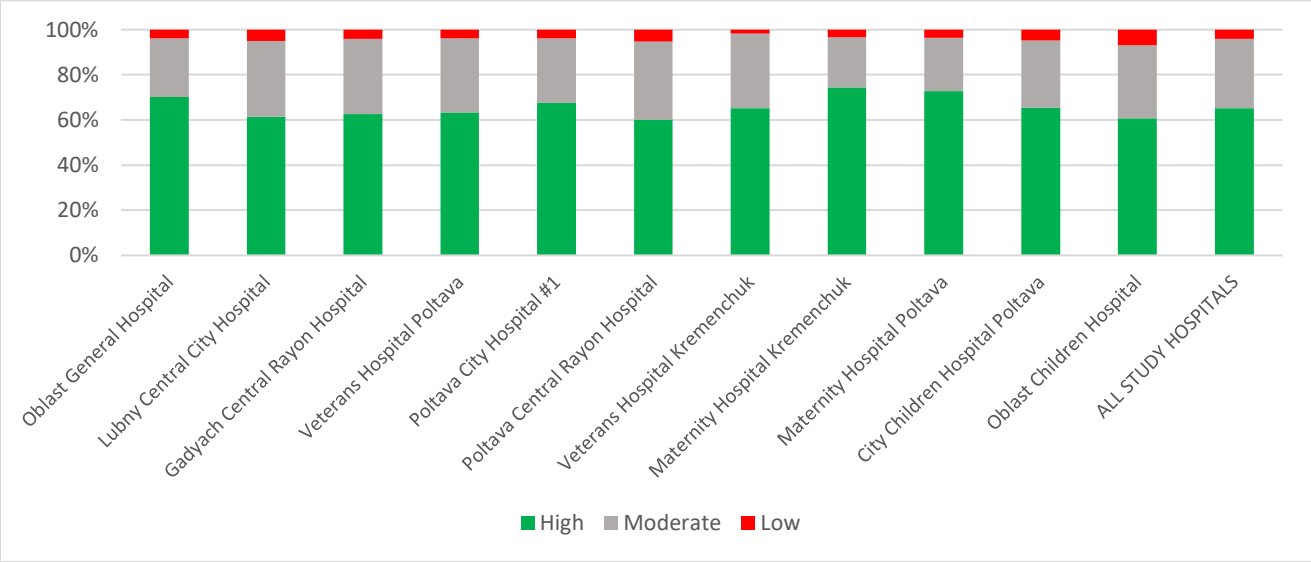
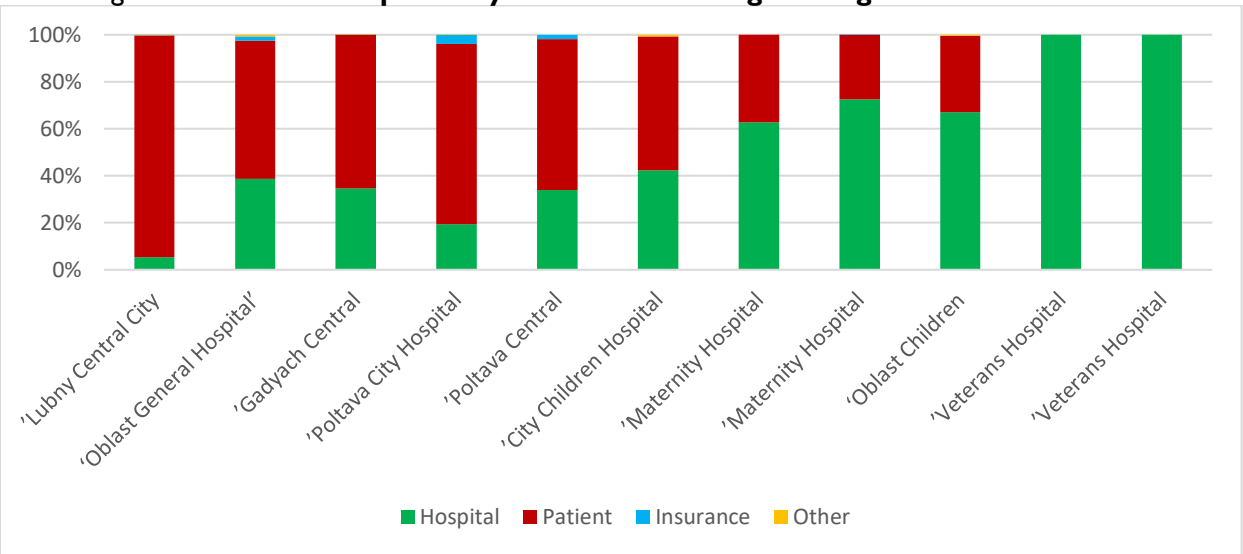


Figure 5 below presents a description of prescriptions by the source of drug funding. All inpatient medications prescribed at two Veterans' hospitals were publicly funded. Most of the prescriptions in the maternity and children hospitals were also funded by the government. However, the proportion of such drugs should probably approximate 100%, given the both are areas of high priority for the government. Patients admitted to the multiprofile hospitals experienced the heaviest financial burden due to OOP on medications. The proportion of prescription paid OOP at these facilities ranged from 58.8% (Oblast General Hospital) to 94.4% (Lubny Central City).

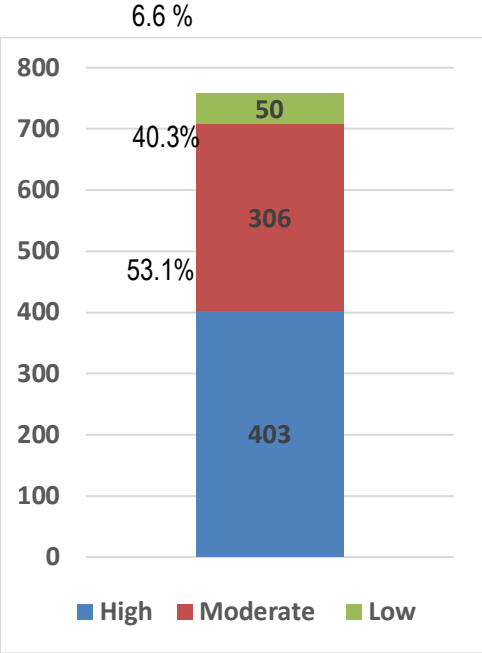
Figure 5 **Prescriptions by the source of drug funding**



4.2.1 *Comparison with the 2017 National EML*

All the 38,106 prescriptions reduced to 759 INNs (Figure 6). Just over half of the prescribed drugs were listed in the BNF (53.1%). 50 medication (6.6%) was assigned the lowest EBM score. The remaining 306 (40.3%) medications were placed in the middle category.

Figure 6 **Distribution of EBM scores among prescribed INNs**



In comparison with the 2017 National EML of Ukraine, 152 INNs from the Poltava study list were included in the National EML. 146 of them had the high EBM score, whereas 6 medications had moderate evidence. 259 drugs used in Poltava hospitals and also listed in the BNF were not included in the National EML. Because the National EML serves as a positive procurement list (i.e., only medications on the list can be procured using public funds), it can cause issues with the hospital supply of drugs of high evidence.

4.2.2 *Proportion of PIMs (by Beers criteria)*

The proportion of PIMs was evaluated in a subset of the study population that were elderly, n=849. The mean age of the elderly patients was 75.5 years (SD=7.5), 52.4% were females. Most of the patients were hospitalized at the rayon level of care (67.3%), to a multiprofile hospital (53%) through a planned admission (91.5%). The mean LOS was 17 days (SD=9.9).

The elderly patients had the total of 10,781 inpatient prescriptions. 1004 prescriptions (9.3%) could be classified as a PIM (Table 3). The most common PIMs were Diphenhydramine (24%), Omeprazole (12.4%), and Phenobarbital (11.6%). The PIM prevalence in the study population is considerably lower compared to hospitalized seniors in other countries[20-23]. It is important to note however that besides the fact of prescription, a few drugs on the list had to meet additional criteria to qualify as a PIM. For instance, omeprazole (and other similar medications) had to be prescribed for >8 weeks. Few patients stayed at the hospital for this long. However, the fact of prescription is still concerning and requires

further exploration, especially that very little research in the area has been done in the post-Soviet countries.

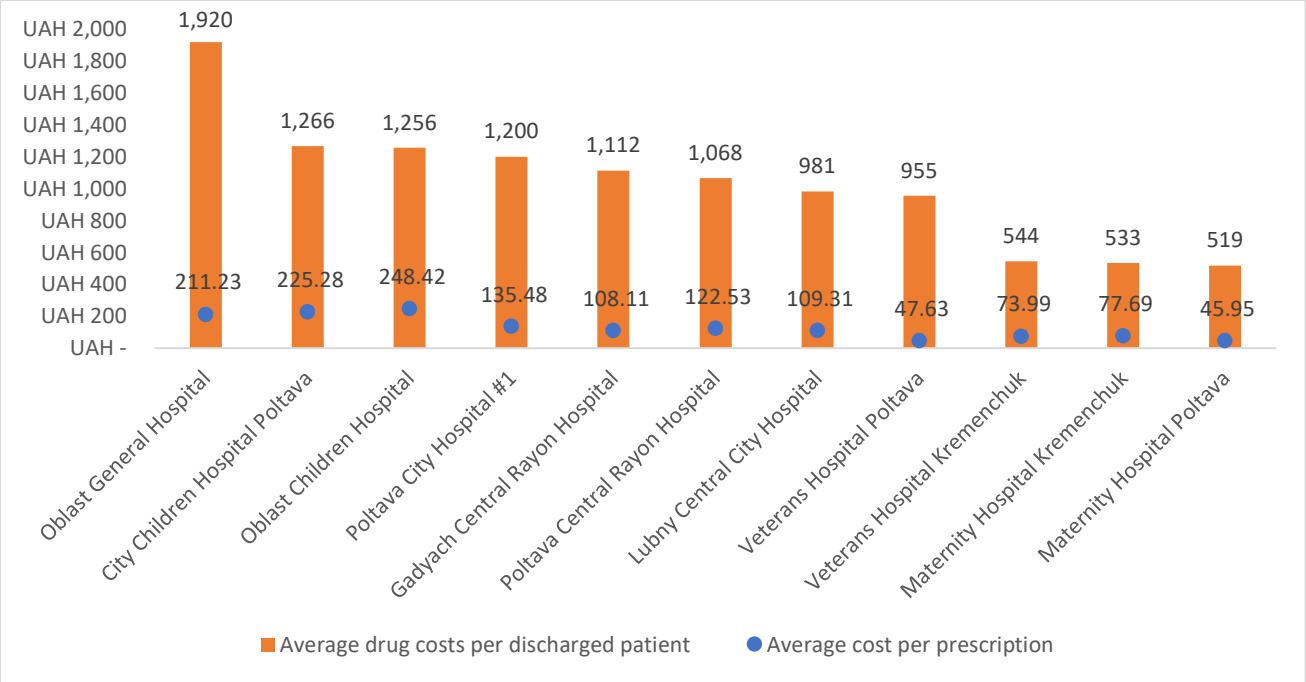
Table 3 **PIMs among seniors**

INN	Count	INN	Count
Diphenhydramine	241	Diazepam	19
Omeprazole	124	Doxazosin	16
Phenobarbital	116	Esomeprazole	12
Dipyridamole	90	Nifedipine	11
Amiodaron	60	Meperidine	11
Metoclopramide	55	Phenazepam	10
Ketorolac	54	Clemastine	5
Pantoprazole	49	Chlorpromazine	5
Gidazepam	38	Clonidine	3
Digoxin	31	Guanfacine	2
Atropine	28	Rabeprazole	2
Insulin	21	Amitriptyline	1
		TOTAL:	**1004**

4.2.3 *Drug costs*

Based on the "observed" costs scenario, the total costs of all the inpatient prescriptions in the study were **UAH 4.9mnln**. The average drug costs per a discharged patient were **UAH 1,175** whereas the average cost of prescription was **UAH 127**. There was substantial variation in drug costs across the study facilities (Figure 7). The drug costs in maternity hospitals were expectedly the lowest (UAH 519 and UAH 533) and nearly 4 time as low as the drugs costs in the Oblast General Hospital (UAH 1,920). However, much of the variation was likely warranted: normal delivery is the most common cause of maternity hospital admissions. It typically does not require drug therapy and have been a target of de-medicalization/de-prescribing efforts[24] [25]. The variation among city and rayon multiprofile hospitals was much less (CV=8%).

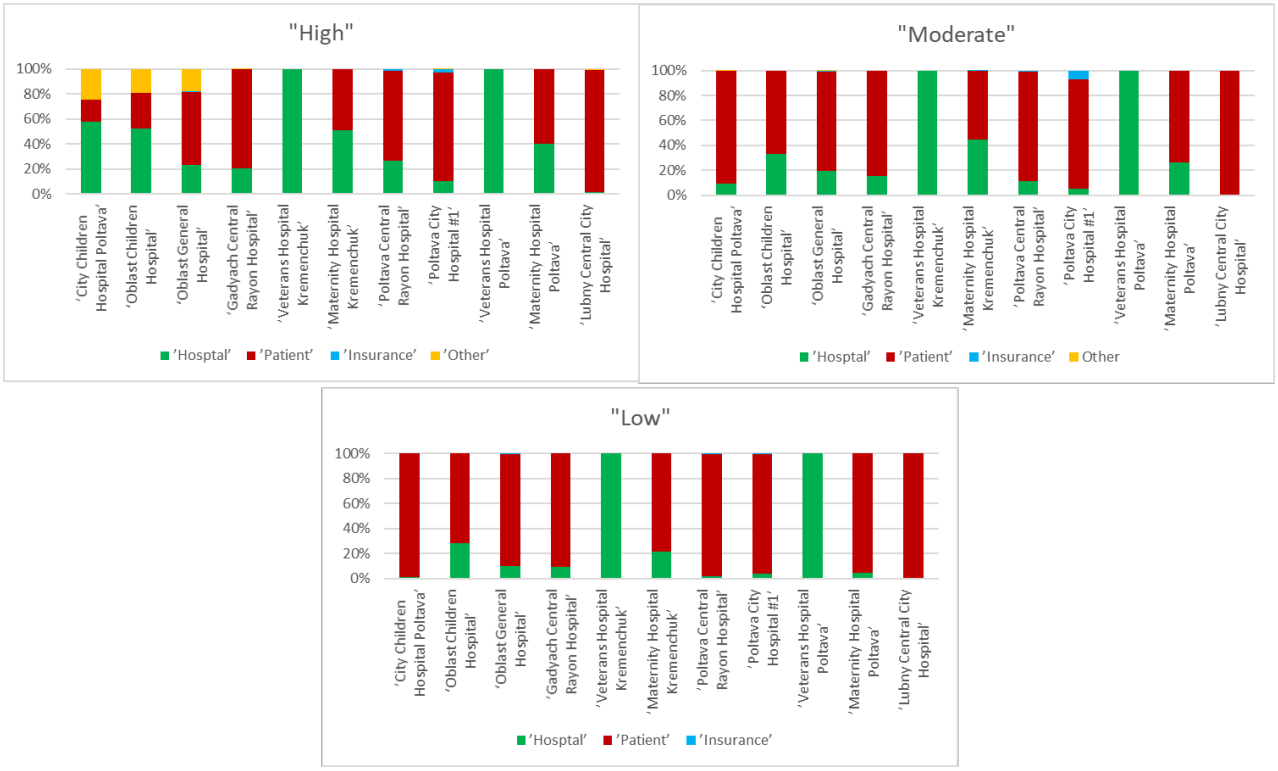
Figure 7 **Average inpatient drug expenditures, by study hospital**



To fulfill its commitment to affordable healthcare across the country, the government should strive to fund inpatient prescriptions with the high EBM score. Unfortunately, the proportion of patients' OOP spending on these drugs is considerable (Figure 8). With the exception of the Veterans Hospitals, it ranges from 17.6% (City Children Hospital Poltava) to 97.4% (Lubny Central City Hospital). It is concerning to see that patients admitted to maternity hospitals have to pay for nearly half of their prescriptions with the high EBM score: 48.8% (Maternity Hospital Kremenchuk) and 59.7% (Maternity Hospital Poltava). At the same time, some hospitals exhibit the practice of procuring medications with poor evidence: this spending, if reversed, could be re-allocated to purchase medications with the high EBM score. Also, reviewing physicians' behavior to stop the practice of prescribing medications with poor evidence could result in savings for the patients as currently they carry most of the financial burden to purchase these drugs.

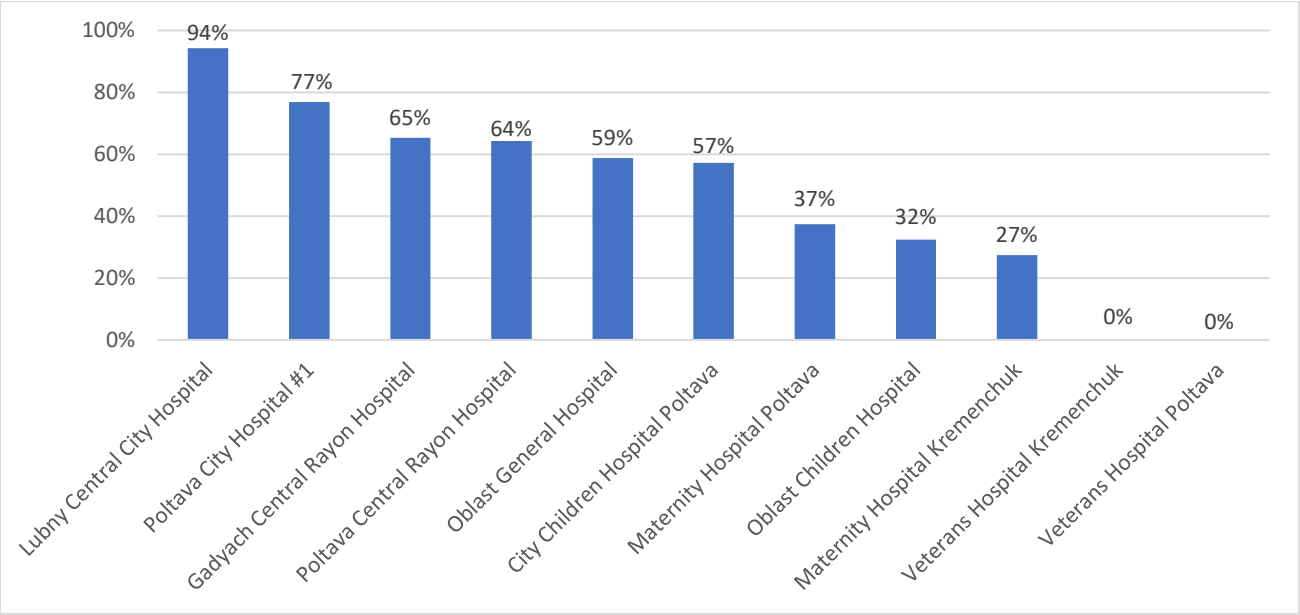
Of note, only 443 prescriptions (out of 38,106) were financed by an insurance company (n=234) or other sources (n=209). However, the costs of medicines in the Other category accounted for 24.7% (City Children Hospital Poltava), 18.8% (Oblast Children Hospital), and 17.4% (Oblast General Hospital). These are attributed to very expensive drugs such as Peginterferon Alfa-2B, Rituximab, and Adalimumab that were supplied by the MoH through a government program.

Figure 8 **Costs for prescriptions by the source of funding and EBM score (High, Moderate, and Low)**



In absolute terms, the OOP payments among hospitalized patients were high. Consistent with the results above, patients admitted to multiprofile facilities carried a heavy financial burden paying for inpatient prescriptions (Figure 9). The proportion of prescriptions paid by the hospitalized patients ranged from 59% (Oblast General Hospital) to 94% (Lubny Central City Hospital).

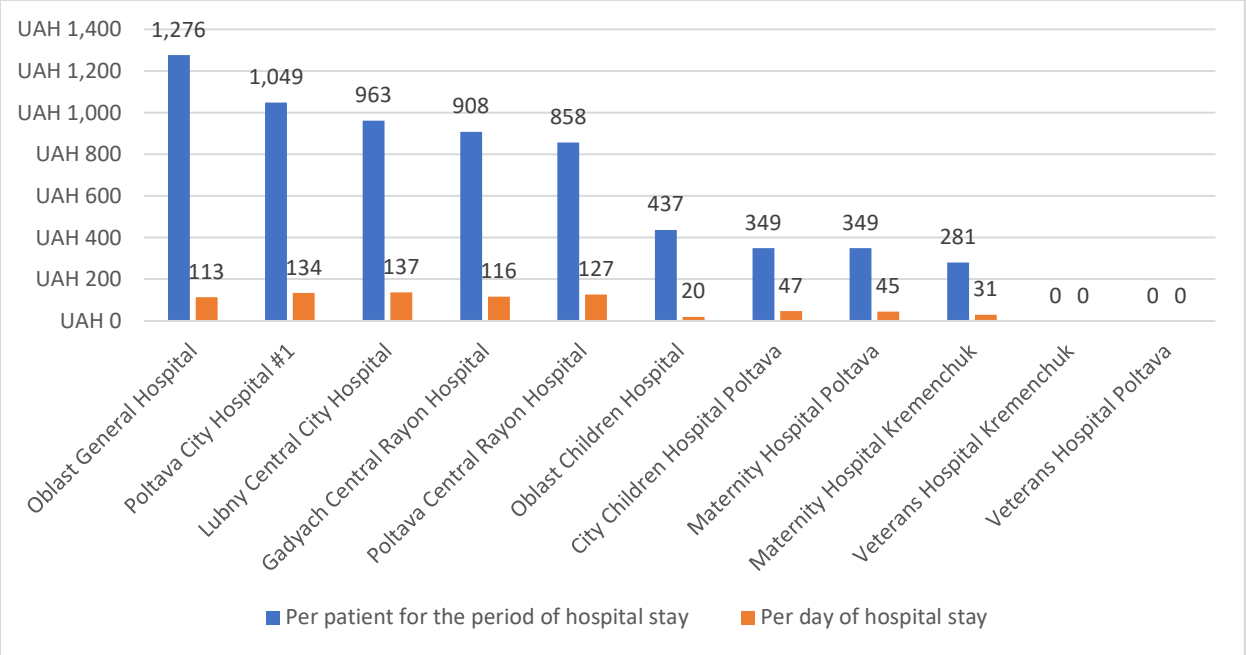
Figure 9 **Proportion of prescriptions paid out-of-pocket**



If the patient had to pay out- of -pocket for inpatient prescriptions, the average cost across the 11 facilities was UAH 808 during the hospital stay or UAH 96 per day (Figure 10). In addition to the lower proportion of prescriptions paid out of pocket, patients admitted to the children and maternity hospitals also incurred the lowest OOP payments ranging from UAH 281 to UAH 437. In contrast, patients hospitalized to the Oblast General Hospital incurred UAH 1,276 on average. Also, patient admitted to rayon or city multiprofile facilities incurred higher OOP costs per day.

When compared with the minimal and average monthly salary in the Poltava region, the OOP payments revealed a critical level of expenditures for the households. The minimal reported 2016 monthly salary in the region was UAH 1,600 (or UAH 53.3 per day) whereas the average salary was reported at UAH 5,673 (or UAH 189.1 per day)[26]. An employee with the minimal salary would have to work nearly 3 days to cover the drug costs of one day of hospitalization.

Figure 10 **Average OOP payment on drugs**



4.2.4 *Forecasting drug costs*

We have forecasted the total drug budget needs for 47 health care facilities using econometric models. Two models have been fit to complete **option A**: costs of all drugs included and **option B**: costs of drugs with the high EBM score only. For both, we modelled inpatient drug expenditures calculated in scenario 2 which assumed that medicines were procured by the hospitals at the average wholesale prices. Out of 7 variables we used in the models, sex and urgency of care were not statistically significant based on the LRT and were excluded from the final models (See Appendix 2 for more detail).

As a check of predictive accuracy, Figures 11-12 below plot drug expenditures for the 11 study hospitals: mean "projected" costs based on Scenario 2 and predicted costs by the models. The mean predicted drug costs are close to the projected means suggesting a good accuracy for most of the hospitals. The exceptions are the children hospitals and the Oblast General Hospital where there is a gap between the projected and predicted means. One possible explanation is that the gap reflects the very expensive drugs supplied by the MOH that were budgeted for in the "projected" costs scenario but were truncated during the model exercise. As a result, the models offer a more conservative forecast of the drug expenditures at these facilities. For budgeting purposes in these and similar facilities (i.e., children hospitals in other towns), health administrators can use the "projected" mean expenditures per facility in calculations.

The forecasted total drug budget for 47 healthcare facilities across the Poltava region was UAH 291.1mln for option A when the costs for all drugs were modelled. The forecasted budget reduced to UAH 179.3mln in option B. Since the reported 2016 drug budget across these facilities was UAH 59.3mln, the estimated budget gap for inpatient medications is at least **UAH 120.3mln** (See Appendices 3-4).

Figure 11 **Projected and model predicted drug expenditures for 11 study hospitals, costs of ALL drugs included**

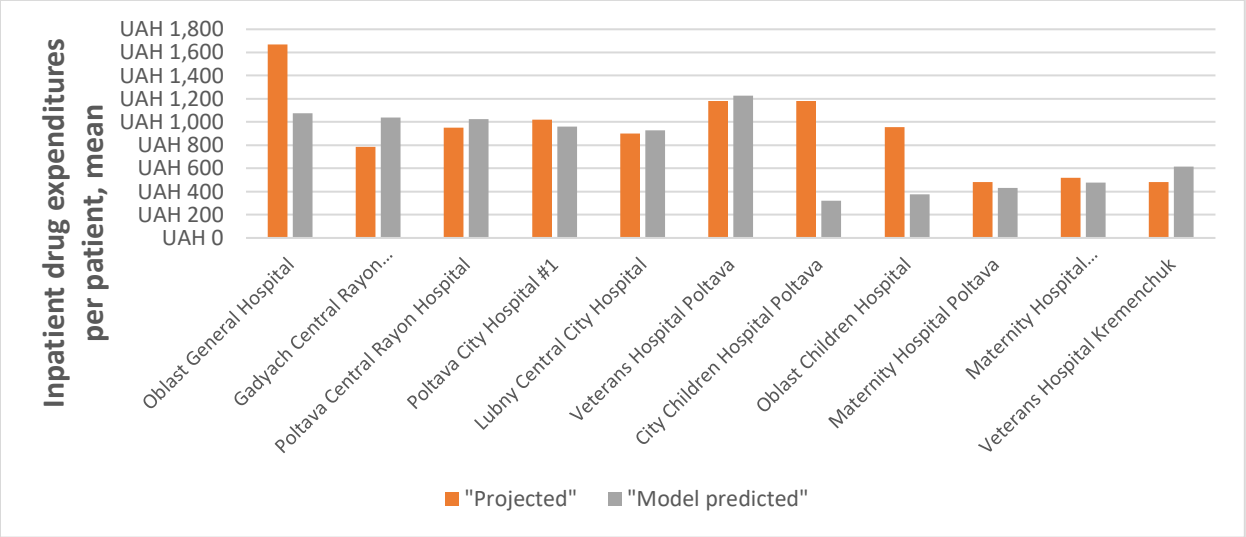
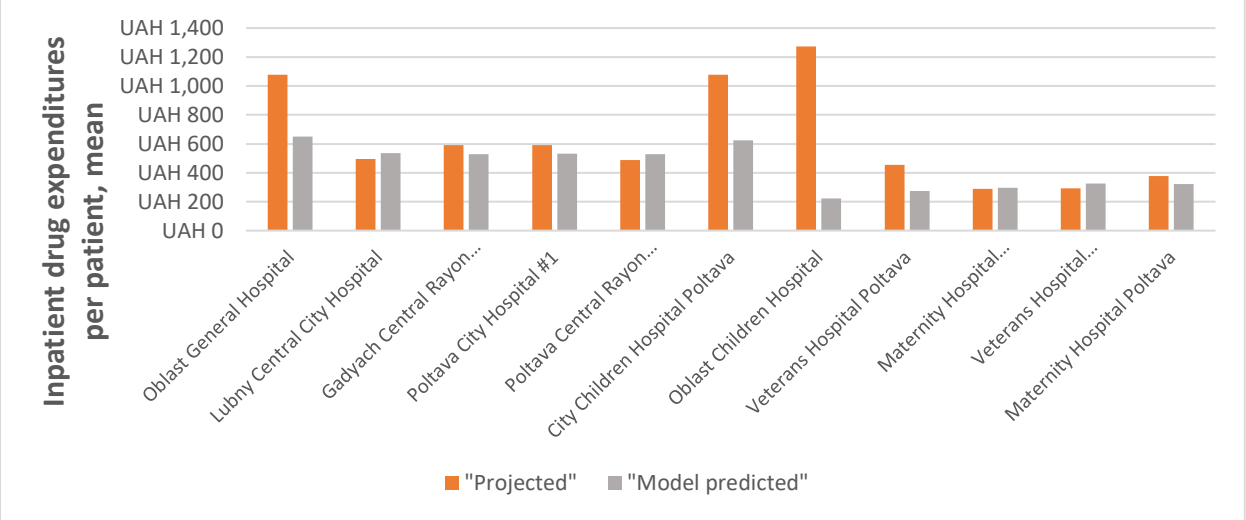


Figure 12 **Projected and model predicted drug expenditures for 11 study hospitals, costs of drugs with EBM score=high**



5. LIMITATIONS

Our study heavily relies on an administrative database. Although they are increasingly used in research, such databases are not designed for it. Data accuracy and missing data are typical concerns[27]. However, the Poltava hospital discharge information system has been subject to data quality contol activities to prevent these issues.

The entry of prescription data into the inpatient drug prescription module by hospital staff was not fully controlled. We did however check entry quality for obvious mistakes and, if errors were identified, the staff members made corrections. Also, hospital staff showed enthusiasm about the study. It was reinforced by clear interest from the local health administrators: they actively participated in all the meetings, encouraged hospital representatives to provide researchers with all the assistance in the study, and created a positive environment around the study activities in general.

The development of the EBM scoring system was based on a scan-review. No systematic review was conducted to identify the best available evidence, especially for prescriptions in the Moderate and Low categories. This limitation however is unlikely applicable to the prescriptions in the High category as listing medicines in the BNF is in itself a rigorous process.

The number of INNs identified in the study may be slightly different. There was a number of herbal or homeopathic items prescribed as a standalone product or a combination of several for which no INNs was available. They were combined under one INN: herbal. This may have some implications on the total number of INNs but no impact on the costs, which was the main objective.

Finally, top 1% truncation in the modelling exercise has affected the predictive values for some hospitals. However, the result was a more conservative estimation of the budget needs.

6. CONCLUSIONS AND RECOMMENDATIONS

This cross-sectional retrospective study has confirmed scarce previous reports: the magnitude of OOP payments for inpatient drugs among hospitalized individuals in the Poltava region is substantial. Patients admitted to multiprofile facilities in cities and rayons, i.e. those that provide most of healthcare in the region, have a higher proportion of prescriptions with OOP payments and incur the highest OOP costs.

The average OOP payment was considerable at UAH 808 per the hospital stay or UAH 96 per day individuals with the minimal salary would have to work nearly 3 days to cover the drug costs of one day of hospitalization. The total estimated drug budget for 47 inpatient facilities was UAH 291.1mln for the year of 2016. In contrast, UAH 59.3mln were allocated by the region.

Only 65% of all prescriptions were assigned the high EBM score, with a modest variation across the study facilities (CV=7.5%). Unfortunately, >90% of these prescriptions were covered out of pocket in some facilities. 152 INNs from the Poltava study list were included in the National EML. 259 drugs used in Poltava hospitals and were listed in the BNF were not included in the National EML.

The results will be used to refine the hospital case-based payment system. In the meantime, national policy making efforts should be made to improve on the following:

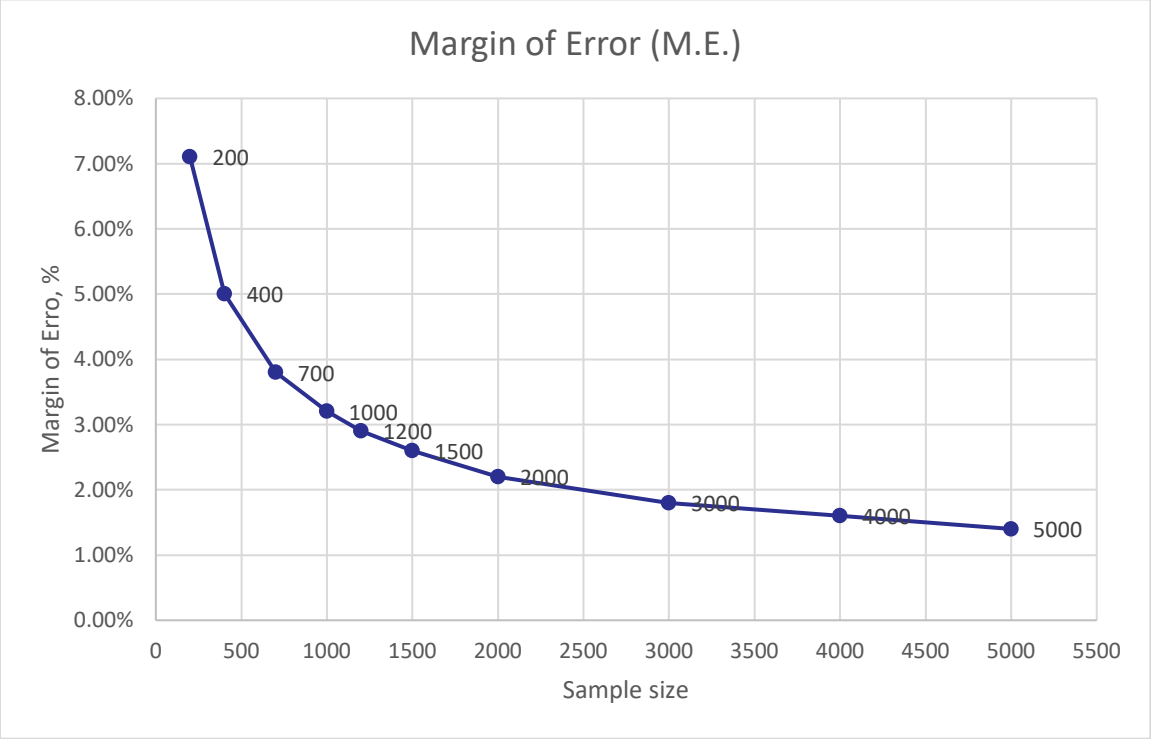
The government should increase allocations to fund inpatient prescriptions with the high EBM score focusing on multiprofile hospitals and facilities providing healthcare in priority areas such pediatrics and maternity.

An expansion of the national EML list should be considered to include other drugs of high evidence as it currently does not cover the needs of hospital physicians.

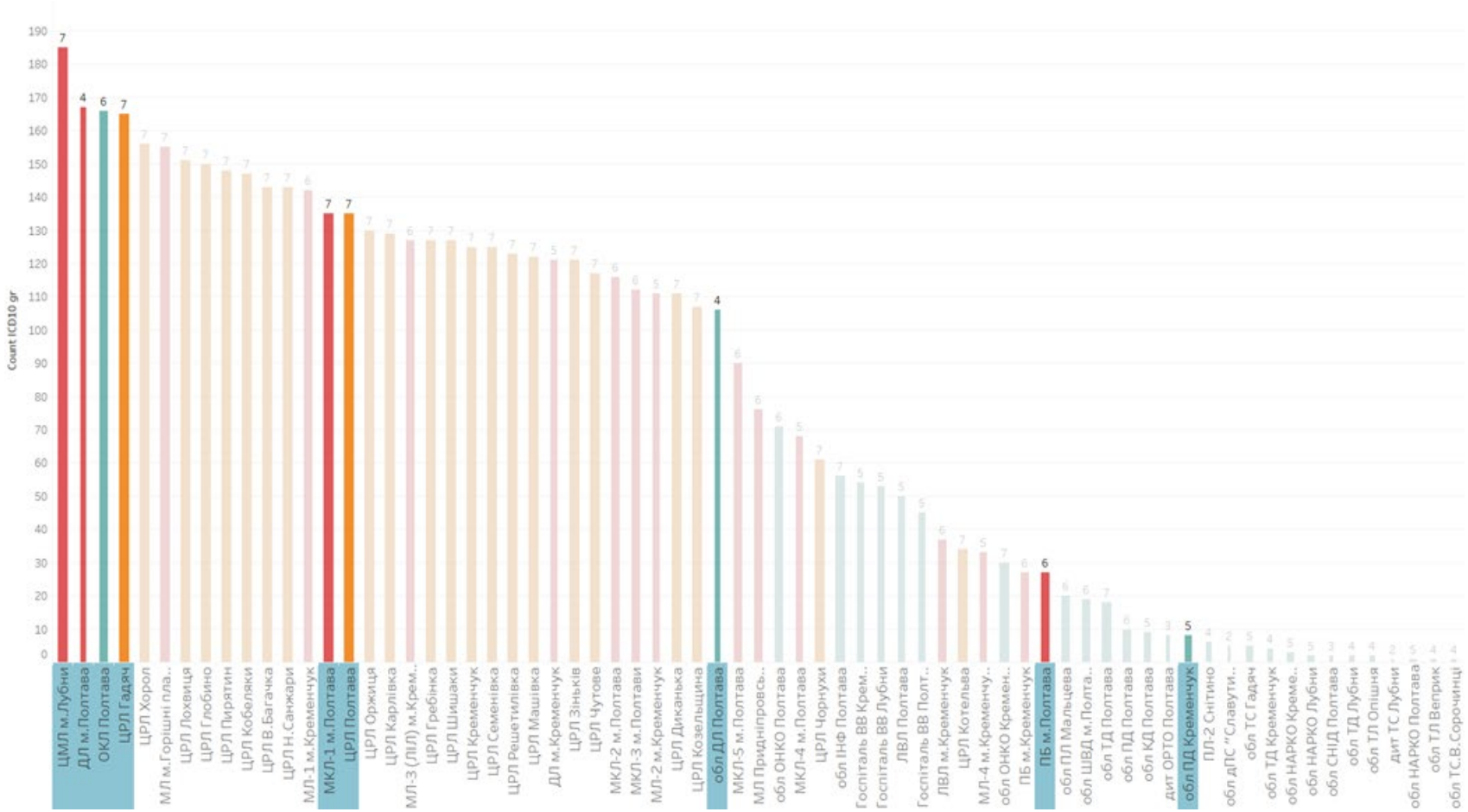
In parallel, a national dialogue needs to be established to review prescription practices in the country to avoid prescribing medications with poor evidence. Not being included on the NEML (i.e., positive procurement list), these medications are paid OOP causing unnecessary and avoidable financial burden for the patients. Improved prescribing can reduce such costs.

7. APPENDICES

Annex 1: Sample size distribution



Annex 2: Number of ICD10 codes managed at the Poltava region hospitals



Annex 3: Model fit characteristics

EBM=all

Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	4022	3638.065	0.9045
Scaled Deviance	4022	4592.604	1.1419
Pearson Chi-Square	4022	4366.652	1.0857
Scaled Pearson X2	4022	5512.354	1.3706
Log Likelihood		-30512.8	
Full Log Likelihood		-30512.8	
AIC (smaller is better)		61145.66	
AICC (smaller is better)		61147.48	
BIC (smaller is better)		61524.5	

LR Statistics For Type 3 Analysis

Source	DF	Chi-Square	Pr > ChiSq
age2	7	96.98	<.0001
drg	47	379.83	<.0001
los	1	727.33	<.0001
level	2	16.48	0.0003
hosp_spec	1	360.02	<.0001

EBM=1

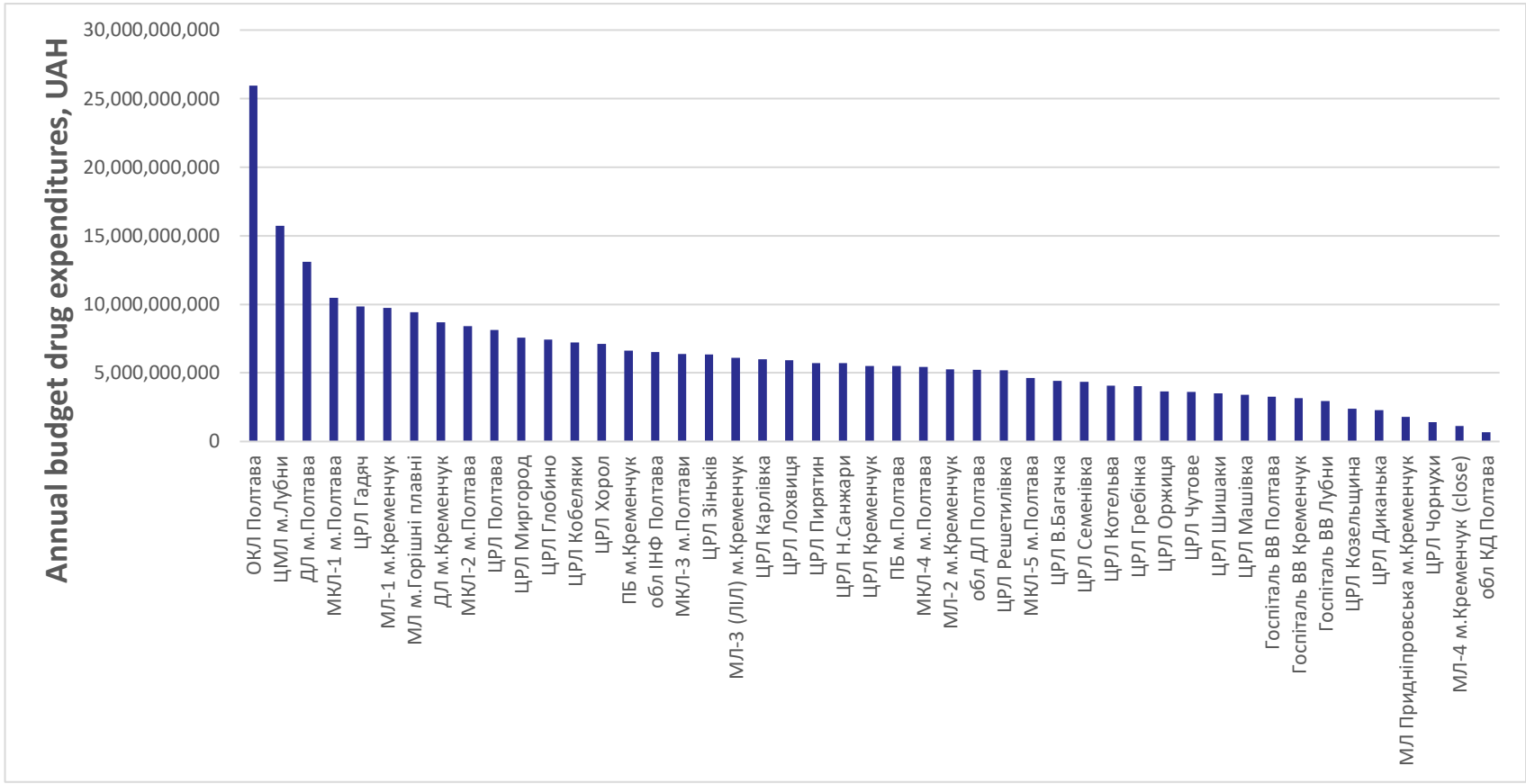
Criteria For Assessing Goodness Of Fit

Criterion	DF	Value	Value/DF
Deviance	3914	4486.305	1.1462
Scaled Deviance	3914	4575.979	1.1691
Pearson Chi-Square	3914	6005.523	1.5344
Scaled Pearson X2	3914	6125.564	1.565
Log Likelihood		-27825.2	
Full Log Likelihood		-27825.2	
AIC (smaller is better)		55770.3	
AICC (smaller is better)		55772.18	
BIC (smaller is better)		56147.54	

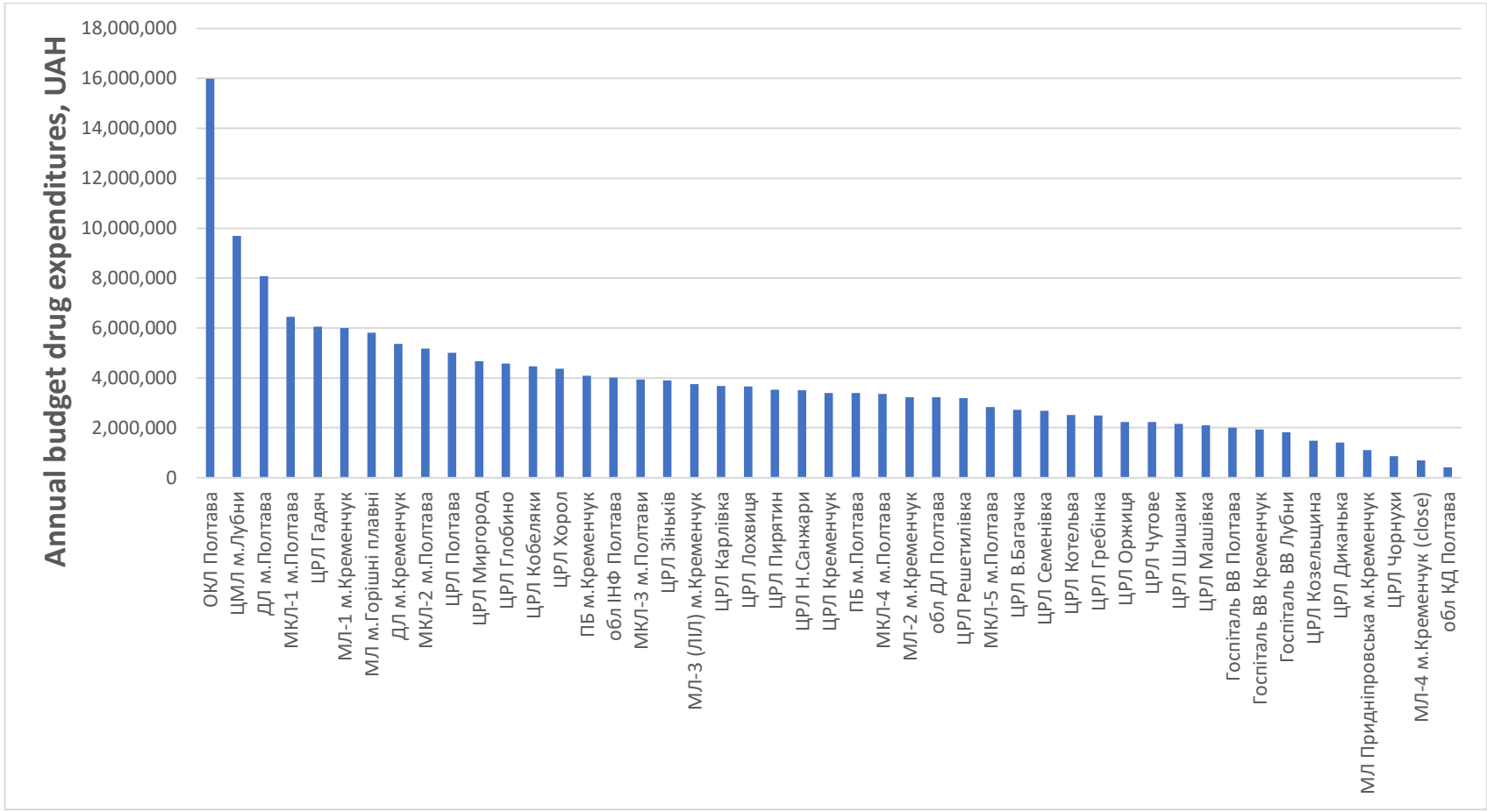
LR Statistics For Type 3 Analysis

Source	DF	Chi-Square	Pr > ChiSq
age2	7	37.05	<.0001
drg	47	442.29	<.0001
los	1	467.42	<.0001
level	2	6.57	0.0374
hosp_spec	1	193.26	<.0001

Annex 4: Budget needs estimation for 47 Poltava region hospitals: all EBM scores



Annex 5: Budget needs estimation for 47 Poltava region hospitals: EBM score=High



ANNEX 7: BIBLIOGRAPHY

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