Common Data Model for Interoperability of Observational Health Data: Bulgarian Diabetes Register Pharmacology Case Study

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***Abstract*—This paper demonstrates the potential of a standard common data model to facilitate access to observational data and extract knowledge. The common data model enables platform interoperability for computational health technologies allowing assessment of the burden caused by the pharmacology costs on the healthcare system. It helps understanding the trends and effects in using different classes of drugs for diabetes treatment by exploring clinical data from the Bulgarian diabetes register. Unlike most regularly published reports on diabetes prevalence, the research results are obtained from a population-based study rather than applying aggregated statistical estimates. The Bulgarian Diabetes Register is a public common data model implementation allowing to overcome platform interoperability problems. It contains the latest and complete dataset of outpatient records of 501,065 distinct patients with diabetes in Bulgaria in 2018. The pharmacology case study reports new results for better assessment of the cost burden created by prescribing drugs for diabetes. Two major groups of drugs are considered- drugs for treatment of diabetes and related comorbidities. Novel drug diabetes therapies are just evolving in 2018, while the Metformin prescriptions prevail significantly. The costs are evaluated both at patient-centric level and at high level in terms of cost distributions among the drug classes in each group. The results are graphically visualized, discussed and compared in relation to existing public sources.**

Keywords-observational data; platform interoperability; Common Data Model; diabetes register; pharmacology cost analysis.

I. INTRODUCTION

Modern healthcare more than ever depends on computer information technologies for data processing and exchange of medical information. Huge amounts of data are generated by people and digital devices that participate in the execution of almost all business processes in the healthcare system. For example, national diabetes registers maintain data describing the health status of diabetics. Such clinical data are collected routinely during health care procedures under real-world conditions. This kind of clinical data is collectively referred to as observational health data. Electronic Health Records (EHR) are used to accumulate systematically observational data, as well as other medical information like prescribed medications, allergies, laboratory test results and demographics data about the patient in digital format [1]. Unlike the EHR, an Electronic Medical Record (EMR), such as the Outpatient Record (OpR) provide a narrower view of the patient's medical history than the EHR because it is maintained by a single Healthcare Provider (HP) [2]. Similarly to EHR, the OpR captures rich observational data about the health status of a patient and allows the HP to follow it while prescribing treatment activities and procedures across time. In the general case, an EHR comprises the patient's EMRs from potentially different HPs. Thus, the EHR enable sharing of knowledge, skills and experience through communication between the actors in the healthcare system, provide a basis for research and education, satisfy organizational and legal requirements [3]. Nowadays, all of these opportunities for utilizing EHRs cannot be fully exploited. The reason is the lack of platform and data interoperability among the heterogeneous and proprietary nature of the software applications used by multiple HPs. Such interoperability problems stem from the primary distinction between EHRs and EMRs. EHRs are introduced for the purpose of sharing health data among organizations while EMRs serve the needs of a single HP. Therefore, the EMRs and in particular, the OpRs of a patient cannot be seamlessly integrated in the EHR of that patient.

Considerable research efforts have been made in the last twenty years to resolve the interoperability issues in the exchange of clinical data [4]. Data exchange schemas and standards for reference models have been introduced for sharing EHR data across clinicians, patients and communities [5] [6] [7] . This approach allows disparate health information systems to effectively communicate, exchange data and process the exchanged data within and across the organizational boundaries. Services for accessing and sharing EHRs may accommodate their requirements with respect to three distinct levels of interoperability- foundational, structural and semantic interoperability [8]. Foundational

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interoperability is limited to the availability of information technology, allowing EHR data exchange. Structural interoperability upgrades foundational interoperability with requirements for representing the exchanged data in predefined syntax and thus, allowing interpretation of data at individual data field level. Most often interoperability at that level is used for exchange of observational data represented in terms of a Common Data Model(CDM) where the physical implementation could be a relational database or an XML Schema [9] [10]. The semantic interoperability level employs standard terminologies, classifications and vocabularies to encode EHR clinical data so that the receiving information systems can correctly interpret the clinical meaning such data without human intervention [11] [12]. It is noteworthy that the clinical meaning is inferred not from the individual data values themselves rather from the way in which such data are linked together as compound clinical concepts, hierarchically structured terms, problems or associated with preceding healthcare events. This interoperability level preserves the semantic context of the exchanged clinical data by representing clinical concepts in terms of standard reference models, such as ISO/EN 13606 and HL7 FHIR. Therefore, the exchange of EHR extracts usually implements such semantic interoperability standards.

In this paper, we consider a pharmacology case study that illustrates the potential of CDM to facilitate access to observational data and enhance population- based statistical research. It is motivated by the need for accumulating evidence on cost effectiveness and budget impact through Health Technology Assessment (HTA) [13]. The objective is to assess the burden of pharmacology costs spent for treatment of diabetes in a nationally- representative dataset. The data source for this study is the Bulgarian Database Register(BDR) that is an Observational Medical Outcomes Partnership (OMOP) CDM standardized database publicly available at the EHDEN Portal [14] [15]. This database contains observational data (observation period 01.01.2018-31.12.2018) of all the outpatient records (6,887,876) issued in Bulgaria to patients with diabetics (501,065). The outpatient records are compiled by the General Practitioners (GPs) and the specialists from ambulatory care for every patient encounter. In this case study, the CDM appears to be the optimal solution for imposing structural interoperability in dealing with disparate data sources such as the variety of software applications employed to produce the outpatient records. Thus, the dataset of the BDR can be accessed remotely in order to receive aggregated results after executing analytical code locally in the secure environment of the data custodian.

This paper is divided into sections as follows. In the following section, we make a brief overview of the existing CDM that enhance big medical data analytics [16] [17] [18] and elaborate on the OMOP CDM of the BDR. In Section III, we present aggregated results obtained by executing the analytical code. In Section IV we discuss the obtained results and compare them with existing research work [19]. Section V makes a conclusion and provides remarks on future work.

II. METHODS AND MATERIALS

This paper considers a case study where the original data sources are outpatient records created by a large number of GPs and specialists from ambulatory care using heterogeneous databases and client applications with disparate programming interface for data access, management and analysis. It entails problems caused by poor data interoperability, such as patient-matching with observational data, pseudonymization of records, satisfying requirements for integrity and consistency of clinical data. The development of software tools for analysis and assessment of data in distributed dataset environment is rather complicated and inefficient as well. The need for imposing some kind of unification of these disparate data sources focused our attention on using CDM in this research.

The literature review provides convincing evidence that CDM are the preferred solution in cases of poor data interoperability when simultaneous analysis of disparate data sources is required [10] [20]. There are three most widely used CDMs for observational data research, namely, the OMOP CDM, the Sentinel and the Patient Centered Outcomes Research Institute (PCORNet). Each one of these CDMs has its strengths and weaknesses.

The PCORNet CDM [16] introduces its own standard organization and representation of EHR data for a distributed network of nine population- based Clinical Research Networks of data contributors (14 billion diagnoses, 2.6 billion medication orders and 9.8 billion laboratory results) [21]. A major weakness of this CDM is the missing support for clinical outcome measures, as well as data linkage, for example, queries cannot “de-duplicate” patients appearing in multiple networks.

The Sentinel CDM was introduced in 2007 by the Federal Drug Agency (FDA) to monitor drug safety and includes EHR and register data in the following core subject areas utilization, enrollment, pharmacy, demographics, lab, death and vital signs (more than 365 million unique patient identifiers, 16 billion pharmacy dispensings, 15 billion unique medical encounters, 45 million laboratory test results) [17] [22]. This CDM is extensible to any data source because data is represented as detailed as possible. Thus, the Sentinel CDM is flexible about demands for running data queries in any type of analysis. Queries are processed in a distributed pattern as follows. Query requests are distributed to the data partners where the queries run locally. Next, query results with direct identifiers removed are returned to the central server for aggregation and final processing. It entails keeping copies of large amounts of data and time-consuming data synchronization even for simple queries. Other weaknesses include limited data mapping, extensions of the CDM affect data usability, data granularity entails loss of information and local knowledge and finally, ongoing model refinements are driven entirely by the FDA.

The OMOP CDM was introduced about the same time as the Sentinel CDM for the purpose of studying the effects of medicinal products. Currently, it is extensively used in the US and Europe where it is underpinned by the Observational Health Data Sciences and Informatics (OHDSI) network and

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the EHDEN project of the EU (118 EHDEN data partners, more than 1,12 billion unique patient identifiers) [23]. Similarly to Sentinel and PCORNet, the OMOP CDM maps disparate data sources to a "patient-centric" relational database with predefined tables linked directly or indirectly to patients. The tables correspond to the CDM core subject areas, such as person, visit occurrence, drug exposure, measurement, observation, death. There are also tables describing device exposure cost, as well as standardized vocabularies for normalizing the meaning of data within the CDM. Thus, the OMOP CDM has the potential to meet the requirements of HTA.

The OHDSI OMOP CDM is well supported by software tools assisting the Extract-Transform-Load (ETL) process and ensuring data quality during the mapping steps. This has allowed us to map to OMOP CDM health data from 6,887,876 outpatient records issued in Bulgaria to patients 501,065 with diabetes during their encounters to GPs or HPs in 2018 [15]. Meta data of the thus obtained OMOP CDM of the Bulgarian Diabetes Register are published in the EHDEN Portal (Figure 1).

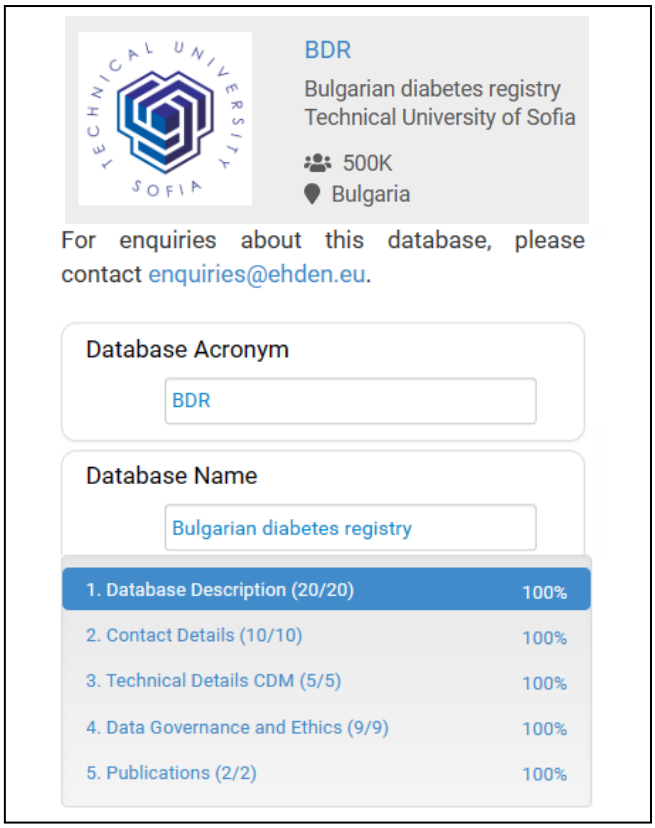

Figure 1. Link to the OMOP CDM of BDR inside the EHDEN Portal.

The distribution of diabetics (Type 1 and Type 2) relative to the population of the corresponding administrative region is displayed in Figure 2. This figure shows that most of the people living in the northern part of the country and especially, in the north-west part, suffer from diabetes. These are the least populated regions of the country. It motivates us to explore the burden of costs spent for reimbursement of drugs for treatment of diabetes and its related comorbidities (cardiovascular drugs, drugs for disorders of the eyes or the nervous and urological system), for the purpose of comparing it with related research work.

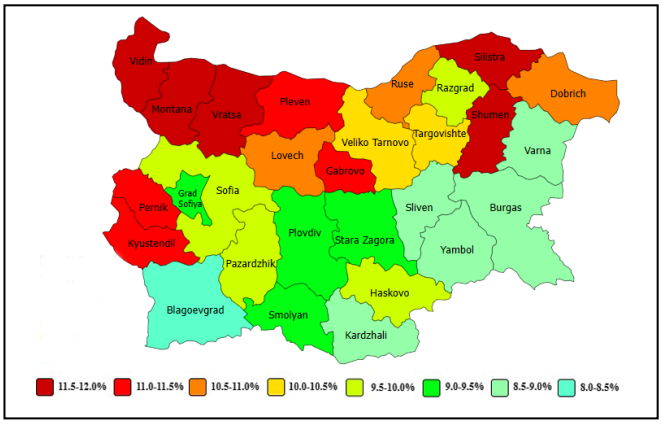

Figure 2. Distribution of patients with diabetes in Bulgaria in 2018.

The original pseudonymized outpatient records have been provided in XML format that needed data processing for making them valid against a single XML schema. For convenience, the adapted XML instances of outpatient records were loaded in a relational database that served as a source for the ETL process (Figure 3).

These records contain administrative data and encoded clinical data describing health status or procedures, such as:

- ✓ Date and time of the visit occurrence
- ✓ Administrative data
- ✓ Personal data, age, gender
- ✓ Patient visit-related information
- ✓ Diagnoses in ICD-10
- ✓ ATC drug codes for medications that are reimbursed
- ✓ Encodings for examinations and procedures
- ✓ Codes describing specialized health care
- ✓ Codes describing hospitalization need
- ✓ Codes for planned consultations,
- ✓ Laboratory tests and medical imaging

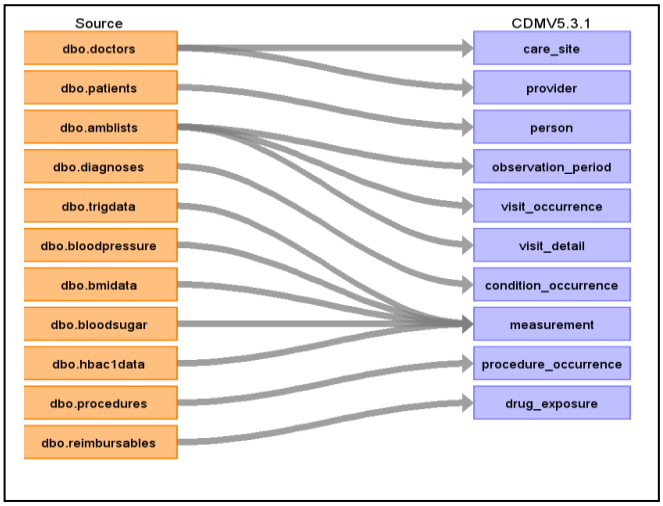

Figure 3. Mapping of outpatient records to OMOP CDM.

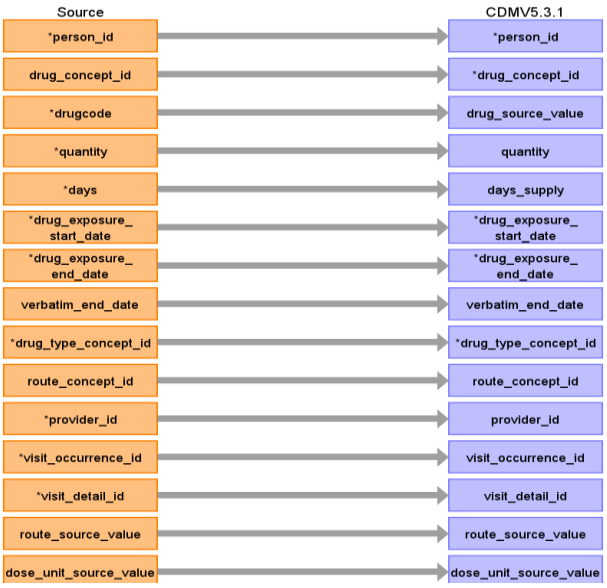

Figure 4. Mapping to table *drug_exposure* of the OMOP CDM.

Observational data like patient state, height, weight, Body-Mass-Index, blood pressure were provided in the outpatient records as unstructured data in natural language (Bulgarian text).

Special interest in this study represent the fields in the OMOP CDM table *drug_exposure* shown in Figure 4 where field *drug_concept_*id encodes the drugs prescribed to diabetics. It is noteworthy that the Bulgarian national drug codes are linked to the ATC hierarchical classification system. Therefore, the standard vocabularies of the BDR are linked to ATC drug codes through *drug_concept_id*.

TABLE 1. DRUG CLASSES FOR TREATMENT OF DIABETES.

Code	Drug class	International Nonproprietary Name (INN)
T1	Insulin	Insulin unique analogues and combination regimens
T2	Sulfonylureas	Glyburide, Glipizide, Glimepiride, Gliclazide, Tolbutamide,Chlorpropamide, Tolazamide
T3	Biguanides	Metformin
T4	Alpha-Glucosidase Inhibitors	Acarbose, Miglitol, Voglibose
T5	Thiazolidinediones	Troglitazone, Rosiglitazone, Pioglitazone
T6	Incretin-Dependent Therapies	Incretin , Exenatide, Liraglutide, Dulaglutide, Albiglutide",Lixisenatide, Semaglutide, Sitagliptin, Saxagliptin, Linagliptin,Alogliptin
T7	Meglitinides	Nateglinide, Repaglinide
T8	Sodium-Glucose Cotransporter Type 2 Inhibitors	Canagliflozin,Apagliflozin,Empagliflozin, Ertugliflozin
T9	Statin-Dependent therapies	Simvastatin, Lovastatin, Ravastatin , Fluvastatin, Atorvastatin, Cerivastatin, Rosuvastatin, Ppitavastatin

The existing literature distinguishes several distinct classes among the drugs for diabetes treatment [19] [24]. These classes are presented in Table 1 where the custom *Code* introduced for shortness and for the purpose of referencing the obtained results in the following section.

It is noteworthy, that currently, the drug class denoted as T8 in Table 1 is considered to be the most modern and promising [19]. This is another reason to find out what is the share of sales of these drugs. Similar interest represents the distribution of sales of drugs prescribed for treatment of diabetes comorbidities. For convenience in referencing these drugs we introduce the drug encodings displayed in Table 2 for the most frequently encountered comorbidities among patients with diabetes. By means of these codes, it will be easier to quote these classes of drugs in the obtained results.

TABLE 2. DRUG CLASSES FOR DIABETES COMORBIDITY TREATMENT.

Code	Drug class for comorbidity treatment	ATC code prefix
A	Cardiovascular drugs	C01, C03, C07, C08, C09, C10
A1	Antithrombotic agents	B01
N	Nervous system disorders	N01-N07
G	Urological disorders	G04
S	Ophthalmolotical disorders	S01
L	Endocrine disorders	L02
M	Ttreatment of bone diseases	M05
R	Asthma drug categories	R03

In addition to table *drug_exposure* the analytical code in this study makes use of tables *person*, *condition_occurence*, *observation_period*, *visit_occurence* of the CDM. The results of executing this code are presented in the following section.

III. RESULTS

The BDR contains huge amounts of data that can provide rich information for treatment of diabetes. First of all, we get an accurate estimate for the diabetes prevalence (9.77%) in Bulgaria in 2018 (4.43% male and 5.35% female). Unlike other public data, the diabetes prevalence is computed accurately taking into consideration the total number of individual patients with encounters registered by GPs or HPs and not by statistical estimates based on the total population of the country.

Once we know the diabetes prevalence, it is important to learn what is the cost for diabetes treatment. The available data in the BDR allows to get detailed information on this issue from different viewpoints. For shortness, here we present summary results that demonstrate the potential of HTA by limiting the scope of our research to drugs that are reimbursed by the National Health Insurance Fund as they are described in Table 1 and Table 2. The Total Cost (TC) of drugs prescribed to diabetics in Bulgaria in 2018 is 160,766,702 euros where 96,171,943 euros is the amount for prescribed drugs from Table 1. It makes about 321 euros per diabetic patient, where 129 euros and 192 euros are spent on the average for drugs for treatment of diabetes comorbidities

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(Table 2) and the diabetes itself (Table 1). Accordingly, 59.82% of the TC are for drugs prescribed for diabetes treatment (Table 1), where 61.51% is the share of the insulin class of drugs.

In the beginning, we have explored what is the share of modern drugs for diabetes treatment among all the prescribed drugs for diabetes treatment. Such are, for example, the drugs encoded as T8 in Table 1. Figure 5 shows that these drugs are rarely prescribed for diabetes treatment in Bulgaria during 2018 (0.69% of all the prescribed drugs from Table 1). Metformin drugs are the most frequently prescribed (T3 in Table 1). These kind of drugs are usually prescribed for initial treatment of Type 2 diabetes and besides, the number patients with this diabetes type prevail significantly over the patients with Type 1 diabetes. This explains the peak value in the prescriptions for Metformin drugs.

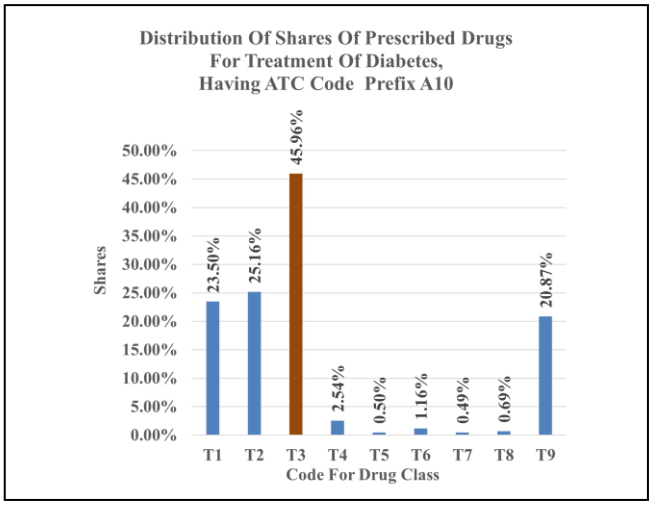

Figure 5. Shares of prescriptions for diabetes treatment.

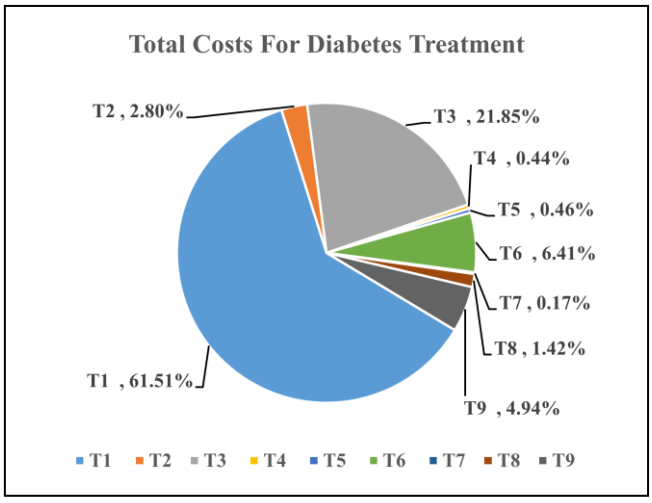

Figure 6. Total costs of drugs for diabetes treatment.

In terms of costs the shares of the drugs in Table 1 change as it is displayed in Figure 6. We notice that the largest expenses are attributed to the insulin class of drugs (T1 in Table 1) although it is the third most prescribed class of drugs in Figure 5. Note that the average price in Bulgaria for the insulin drug class has been about 60 euros against 16 euros for the Metformin drug class in 2018.

The above results provide evidence that the treatment of comorbidities accompanying the diabetes illness is almost as expensive as the treatment of the diabetes itself. Therefore, it is important to understand what are the costs for treatment of the most frequently encountered comorbidities.

In the existing literature there is enough evidence that the cardiovascular diseases, the disorders of the nervous system and the ophthalmological disorders are some of the most frequent comorbidities of diabetes. At the same time, little is known about the relative shares of these disorders with respect to the overall expenses for treatment diabetes comorbidities.

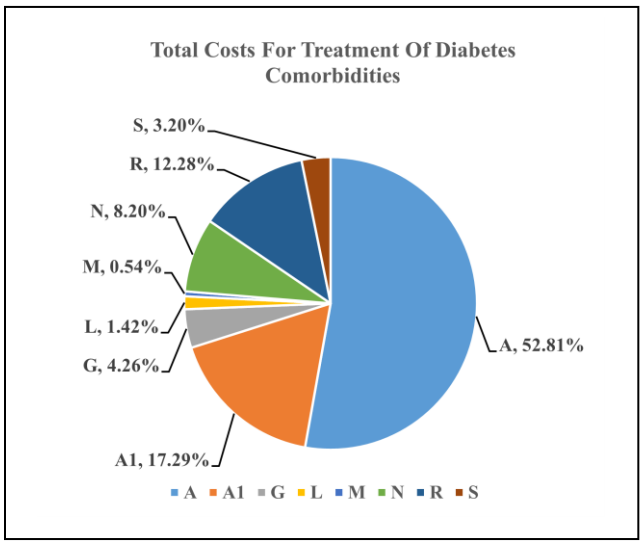

Figure 7. Total costs of drugs for treatment of diabetes comorbidities.

Figure 7 confirms that drugs for cardiovascular disorders and drugs with antithrombotic agents (code A and A1 in Table 2) have the greatest weight (70.10%) in the TC for treatment of comorbidities. The drugs for treatment of asthma of (code R in Table 2) are at the second place (12.28%) in the TC with average price of about 51 euros in 2018, where most of the prescriptions are for medical products costing above the average value. For comparison, the drugs for treatment of disorders of the nervous system (code N in Table 2) are at the third place with 8.2% share in the TC with average price of about 130 euros. Unlike the drugs prescribed for asthma treatment, most of these prescriptions are for medical products with prices significantly below the average for all the products with code N in Table 2. Such an increase in the costs for drugs prescribed to diabetics for treatment of accompanying asthma disorders is observed for the first time and it should be taken in consideration in regulatory decision making.

In conclusion, note that Table 1 and Table 2 entries do not exhaust all the drugs classes prescribed to diabetics. For example, drugs that are given to diabetics but not mentioned in these two tables are drugs for treatment of rare diseases or disorders caused by immune deficiency. Most of these drugs

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are rather expensive and represent a huge burden in the overall amount reimbursed to patients for treatment of diabetes (135% of the TC of drugs from Table 1 and Table 2). In case we add these extra costs to the TC then we get average 675 euros per diabetic patient expenses for prescribed drugs.

IV. DISCUSSION

This paper reports results that are obtained by processing nationally-representative data mapped to an OMOP CDM. The BDR is a physical implementation of that CDM with meta data published on the EHDEN Portal. It allows transparency in accessing data and verifying the integrity and consistency of these results. The BDR contains huge amount of pseudonymized observational data that allows to investigate diabetes treatment from different views through health assessment technologies.

The pharmacology case study considered here is just one example of the potential for exploring the health data. Without a restriction, data exploration could be extended to provide details with different level of granularity about the prescription of selected drugs or to group drug prescription by age and gender. In this regard, we must outline the following limitations that have to be taken in consideration.

First, it is rather difficult to find public literature with numeric data from population-based studies evaluating the burden of costs in diabetes treatment. In one such rare publication [24] we found evidence that matches close with our findings. Although this publication refers to data from 2014 and involves 312,223 patients from Italy, we established close correlation at several issues. For example, the share of costs on insulin drugs (T1 in Table 1) reported in this publication is 58.90% against the above quoted percentage 61.51%. Another match is established in the reported share of cardiovascular drug costs with respect to all drug costs 33.5% against 34.2 % found in our study. There is, however, a great difference in the average cost per diabetic patient, 1066 euros against 675 euros established from data in the BDR. This difference could be attributed to the known differences in the standard of life (and price levels) between both countries at that time.

Another issue that must be taken in consideration is that the NHIF does not reimburse always the full costs for prescribed drugs, while the amounts above quoted refer to the full drug costs. Since the finance reports of NHIF are public [25], we managed to calculate the amounts really reimbursed by the NHIF for diabetic drugs (Table 1) to be 67,208,241 euros in 2018. As expected, this amount is about 30% less than the amount reported in the above section (96,171,943 euros). Here we must take in consideration that only a fraction of all the prescribed drugs in 2018 are dispensed to patients in the same year. Besides, the quantities of the prescribed drugs are usually greater than the quantitates of the reimbursed drugs. Thus, we can conclude that the results reported in this paper are consistent with the real-life practice.

V. CONCLUSION AND FUTURE WORK

This paper demonstrates the potential of the OMOP CDM to facilitate access to observational data accumulated from heterogenous datasets and extract knowledge using standard statistical tools. The assessment of the burden caused by the pharmacology costs on the healthcare system is important for regulatory decision making, as well as for drug suppliers in planning their market strategies. The obtained results help to understand the trends and effects in using different classes of drugs for diabetes treatment and especially, the trends in applying novel drug therapies for diabetes treatment. Public diabetes surveillance reports with such results are rather rare to find in the existing literature primarily because most often the datasets are heterogenous in terms of structure and lack of interoperability of the data sources. Unlike most regularly published reports in the public space, this paper reports results obtained from a population- based study rather than applying aggregated statistical estimates.

The BDR implements an open- source OMOP CDM that allows to overcome poor interoperability among heterogeneous and often, incompatible data providers. It contains the latest and complete dataset of outpatient records issued to 501,065 distinct patients with diabetes in Bulgaria at every encounter to GP or HP in 2018. Among the other CDM briefly reviewed in this paper, the OMOP CDM proves the best potential for applying health assessment technology in obtaining reliable, transparent and verifiable results though analysis of observational data.

The pharmacology case study makes public lot of new results that help understand better the burden of costs generated in the process of prescribing drugs for diabetes treatment. Two major groups of drugs are considered- drugs for treatment the diabetes and drugs for treatment of diabetes comorbidities. Numerical evidence shows that novel drug therapies of diabetes in this country are just beginning to evolve in 2018, while the prescriptions of Metformin drugs prevail significantly among all the rest. Contrary to the expectations, the costs of prescribed drugs for treatment of comorbidities in diabetes caused by asthma surmount the costs of prescribed drugs for therapy of the nervous system or urological disorders. The costs are evaluated both at patient-centric level, as well as at high level in terms of cost distributions among the drug classes in each one of the two groups. The results are graphically visualized, discussed and compared in relation to existing public sources.

In our future work we focus on exploring the trends in using novel drug therapies for diabetes in Bulgaria. Preliminary results based on new public data sources during 2018-2021 show a significant and rapid increase in prescriptions of novel drug class therapies (T8 in Table 1), decrease in other prescriptions (T7 in Table 1) and stable interest in other (T3 in Table 1). Moreover, we work on updating the BDR with fresh data once it becomes available.

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