



## QUANTITATIVE ANALYSIS OF SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITOR FORMULARY INTEGRATION AND DISTRIBUTION IN JORDANIAN MILITARY HOSPITALS: A MULTI-CENTER RETROSPECTIVE STUDY

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### ABSTRACT

**Objectives:** This research will attempt to describe and examine the formulary integration pathway of empagliflozin 25 mg and dapagliflozin 10 mg in the JRMS hospital network by following the average monthly quantities of these medications dispensed from JRMS main warehouses to three strategic hospitals: (1) King Hussein Medical Hospital (KMH), (2) Prince Rashed Bin Al-Hasan Military Hospital (PRBH), and (3) Queen Alia Military Hospital (QAMH), over a five-year period of 2020 to 2024. The research will also aim to find patterns of adoption and varying uptake rates across facilities as well as trends in time which might be indicative of the broader trends of T2DM pharmacotherapy in the JRMS system. The study will also try to produce evidence-based suggestions to help in future formulary management and procurement planning in the JRMS pharmaceutical services.

**Methodology:** A retrospective descriptive design will be used in this study; it will be based solely on the official pharmaceutical dispensing records of the JRMS Pharmaceutical Directorate. The data source will be the amount of empagliflozin 25 mg and dapagliflozin 10 mg issued (annually) in the form of tablets on an average of each of the three target hospitals per month throughout the period of the study. The data will be categorized and assessed in terms of year, name of drug, and institution where it was received. In order to describe the trends in utilization, descriptive statistical values, such as absolute amount, growth rates per year, proportion of hospital contributions, and compound annual growth rate (CAGR) will be computed. Data analysis will also undertake the gradual introduction of empagliflozin compared to the dapagliflozin and the varying adoption behaviors of the three hospitals will be considered to uncover drivers that might have affected adoption of the formulary.

**Conclusion:** This study demonstrated a marked expansion in the integration and utilization of SGLT2 inhibitors within the Jordanian Royal Medical Services healthcare network over the five-year study period. The phased adoption pattern across hospitals reflected the structured formulary implementation strategy within JRMS, with tertiary care centers serving as primary pioneers before wider secondary-care dissemination. The substantial transition from dapagliflozin toward empagliflozin in 2024 highlights the influence of emerging evidence-based clinical guidelines and evolving therapeutic preferences on institutional prescribing behavior. These findings emphasize the importance of proactive procurement planning, dynamic formulary management, and evidence-driven pharmaceutical policy within centralized military healthcare systems. Furthermore, the study provides a valuable pharmacoepidemiological framework for monitoring the institutional uptake of novel therapeutic agents in military and large-scale healthcare networks.

**Keywords:** SGLT2 inhibitors, empagliflozin, dapagliflozin, drug formulary, military pharmacy, JRMS, Jordan, drug utilization, type 2 diabetes mellitus, pharmaceutical management

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## 1. INTRODUCTION:

Type 2 diabetes mellitus (T2DM) is rising worldwide burden at an unprecedented rate, presenting a great challenge for health care systems. The International Diabetes Federation (IDF) estimated that by 2021 about 537 million people were suffering from diabetes worldwide, and expects this to reach 783 million by 2045 (1). The prevalence of diabetes in Jordan is approximately 17.1% in adults, and this prevalence is second highest in the Middle East and North Africa (MENA) region (2), imposing a significant burden of drugs for institutional healthcare providers such as the Jordanian Royal Medical Services (JRMS).

The sodium-glucose cotransporter-2 (SGLT2) family of drugs has become an integral part of contemporary therapeutics for T2DM. They work in a special way, by promote urinary glucose excretion without the involvement of insulin, leading to glycemic, cardiovascular and renal protection (3). Thus, the cardiovascular death risk reduction was 38% relative to placebo in high-risk, T2DM patients seen in the EMPA-REG OUTCOME trial, which studied Empagliflozin (4). Dapagliflozin was evaluated in the DECLARE-TIMI 58 trial and had significantly lower rates of hospitalization for heart failure and renal composite outcomes (5). These results prompted significant changes to international guidelines, seeing both the American Diabetes Association (ADA) and European Association for the Study of Diabetes (EASD) defining SGLT2 inhibitors as the first-line treatment for type 2 diabetes in those at established risk for cardiovascular disease or established cardiovascular disease. (6)

Formulary management in the institutional (hospital) setting is a systematic and evidence-driven approach to ensure optimum medication accessibility, cost-effectiveness and therapeutic safety. The JRMS has an integrated pharmaceutical supply chain with one main warehouse that supplies all affiliated hospitals and allows the quantitative monitoring of the quantity of medicines dispensed as a measure of the extent of formulary adoption.

The first investment of dapagliflozin into JRMS formulary came in the form of dapagliflozin 10 mg, and initial distribution of the drug was made to King Hussein Medical Hospital (KHMH) as early as 2020. In 2022, the drug Empagliflozin 25 mg. followed. The delay in introducing the drug in the three hospitals, KHMH, Prince Rashed Bin Al-Hasan Military Hospital (PRBH) and Queen Alia Military Hospital (QAMH) and the different use patterns across these hospitals offers a unique natural experiment for formulating conclusions about how to integrate pharmaceutical formulations

within a structured military health care system. While further research evaluating the use of SGLT2 inhibitors has emerged in the world, little literature exists to assess the adaptation of the SGLT2 inhibitors in Middle Eastern Military Healthcare Systems to which this study applies.

## 2. LITERATURE REVIEW:

### 2.1 Pharmacological Profile of SGLT2

**Inhibitors:** The action of SGLT2 inhibitors inhibit the reabsorption of glucose into the bloodstream in the proximal convoluted tubule, thereby increasing the excretion of glucose in the urine (3). This is an insulin-independent mechanism which is unique and of great benefit in patients with suboptimal insulin action or secretion. Both Dapagliflozin (Forxiga®) and empagliflozin (Jardiance®) have been approved by the FDA in 2014 and they have been extensively studied in this class of agents (8). When used combined with other medications, Empagliflozin 25 mg lowers HbA1c by 0.8-1% and offers drop in body weight and systolic blood pressure (9) whereas Dapagliflozin 10 mg averages 0.5-0.8% decrease in HbA1C with a minimal risk of hypoglycemia (10). Both agents have been charged with increased cardiac indications for ejection fraction, HFrEF, and for chronic kidney disease (CKD), expanding the clinical and formulary significance (11).

### 2.2 Cardiovascular and Renal Evidence:

Empagliflozin has shown significant reduction in the three-point MACE composite (14%), cardiovascular death (38%), and hospitalization for heart failure (35%) over placebo in the EMPA-REG OUTCOME (2015) trial in more than 7,000 T2DM patients who already had cardiovascular disease (4). DECLARE-TIMI 58 (2019) included >17,000 patients, where Dapagliflozin resulted in a 27% decrease in hospitalization for heart failure or cardiovascular-related death and an important renal protective effect (5). The DAPA-CKD trial also paved the way for dapagliflozin to be approved for CKD with or without diabetes, representing a paradigm shift in the treatment of nephrology-related diseases (12).

### 2.3 Formulary Integration and Drug Utilization in Military Settings:

There is a need for established framework with evidence based systems to evaluate, approve and monitor the addition of new pharmacological products to the formulary. Pharmacy and Therapeutics (P&T) committees consider clinical evidence, safety profile, cost-effectiveness considerations, and therapeutic alternatives before approving a new agent (7). Clinical trial data for SGLT2 inhibitors has typically been a catalyst for speeding up institutional adoption of these drugs, though levels of acceptance of the drugs within institutional settings will depend on

drug-to-drug interactions, structural characteristics of the drug, prescribing culture, and budget and patient population characteristics (13).

A key advantage of military health care systems (HCS) for conducting research on drug utilization is that they have a centralized drug procurement system, a standardized formulary, and the ability to document all drug transactions from the provider side of the system (17). Similarly a recent study reported that durations of SGLT2 inhibitor prescribing grew significantly after the large-scale cardiovascular outcomes trials, demonstrating the influence that trial data can have in a large, 'bureaucratic' healthcare system (14). A Saudi Arabian study reported progressive additions of SGLT2 inhibitors to the list of drugs available in the facilities of the Ministry of Health, depending on guideline changes, and found a wide spread of utilizations between facilities (15). Such shift toward newer antidiabetic drugs was also observed in a Jordanian study of usage of antidiabetic drugs in public hospitals (16). To date, however, there have been no studies looking in detail at the adoption of this class of medications in the JRMS or like regional military system-specific drug formularies.

### 3. METHODOLOGY:

**3.1 Study Design and Setting:** A descriptive analytical approach with retrospective study design is implemented, where the dispensing data of drugs maintained in the JRMS Pharmaceutical Directorate is taken into account, covering the period from January 2020 to December 2024 based on the existing drug utilization research (DUR) methods set forth by the World Health Organization (WHO) (20).

The main data source is the official annual average monthly quantity of the medicines ( in tablet units)

dispensed from JRMS central warehouse at three receiving hospitals (KHHM is largest JRMS hospital and the major tertiary care hospital, PRBH is a secondary care base hospital in northern Jordan in Irbid governorate and QAMH is a secondary care hospital in Amman). The presence of these three institutions makes it possible to make meaningful comparisons across institutions to reflect the diversity of service levels in JRMS.

**3.2 Data Variables and Analysis:** The following data was collected for each calendar year: medication name, strength of the medication; and the average number of tablets issued to each hospital per month. Any hospital-year combination that had no record of issuance had zero values recorded for it.

Analytical parameters calculated were: annual average monthly issuance quantities, year-over-year (YoY) percentage change, cumulative issuance, proportional contribution of each hospital to total network issuance and compound annual growth rate (CAGR) which was calculated using the formula:  $CAGR = [(Ending\ Value / Beginning\ Value)^{(1/n)} - 1] \times 100$ , where n represents the number of years. All analyses are done at an aggregate level with the official institutional records. A request for ethics committee review was necessary for retrospective administrative data analyses even though no individual patient data were used, and JRMS ethics committee review was obtained.

### 4. RESULTS AND DISCUSSION:

**4.1 Raw Data:** The raw data for annual average monthly volume of issuance is presented in Table (1) for both of the SGLT2 inhibitors during the period of study.

**Table 1: Annual average monthly issuance quantities (tablets) of SGLT2 inhibitors from JRMS main warehouses, 2020–2024.**

Year	Medication	KHHM	PRBH	QAMH	Total Network
2020	Dapagliflozin 10 mg	229	0	0	229
2021	Dapagliflozin 10 mg	870	15	0	885
2022	Dapagliflozin 10 mg	2,052	80	284	2,416
2022	Empagliflozin 25 mg	485	0	0	485
2023	Dapagliflozin 10 mg	3,663	338	399	4,400
2023	Empagliflozin 25 mg	948	0	0	948
2024	Dapagliflozin 10 mg	1,340	920	0	2,260
2024	Empagliflozin 25 mg	6,195	281	261	6,737

**4.2 Dapagliflozin 10 mg: Adoption Trajectory:** In 2020, the pioneer drug Dapagliflozin 10 mg was added to the JRMS formulary and was provided exclusively to the resources rich , largest care site,

KHHM (229 tablets/month); typical of a first phase of adoption where a new drug is first added to the formulary at the primary site and then subsequently to secondary care sites (Table 2).

**Table 2: Year-over-year growth in average monthly dapagliflozin 10 mg issuance by hospital, 2020–2024**

Year	KHMH	YoY Change	PRBH	YoY Change	QAMH	YoY Change	Total Network
2020	229	—	0	—	0	—	229
2021	870	+280.0%	15	New	0	—	885
2022	2,052	+135.9%	80	+433.3%	284	New	2,416
2023	3,663	+78.5%	338	+322.5%	399	+40.5%	4,400
2024	1,340	-63.4%	920	+172.2%	0	-100%	2,260

In 2021, total network issuance reached 885 tablets per month (+286.5%) on the network and started distributing limited quantities for the first time to PRBH (15 tablets/month). In total, 2416 tablets/month were issued by 2022, a 173.0% higher rate than in 2021, corresponding with the increased and widespread uptake of updated guidelines suggesting using SGLT2 inhibitors in T2DM of cardiovascular risk (6). Increased dapagliflozin use peaked in 2023 with a monthly consumption of 4,400 tablets (+82.1%) with KHMH accounting for 83.2% of the network consumption.

However, in 2024 this was reversed with total dapagliflozin issuance dropping by 48.6% to 2260

tablets/month. KHMH's issuance fell (-63.4%) and PRBH's issuance remained increasing with a slight increase (+172.2%) while QAMH got zero issuance. This reduction occurred with a huge increase in the number of empagliflozin prescriptions, which might have been a result of clinical substitution (see section 4.4).

**4.3 Empagliflozin 25 mg: Adoption Trajectory:** Empagliflozin 25mg was introduced to the JRMS formulary in 2022, at the KHMH site only (485 tablets/month), reflecting typical sequencing as one of the newer agents which would be tried after the pioneer agent (Table 3).

**Table 3: Year-over-year growth in average monthly empagliflozin 25 mg issuance by hospital, 2022–2024**

Year	KHMH	YoY Change	PRBH	YoY Change	QAMH	YoY Change	Total Network
2022	485	New	0	—	0	—	485
2023	948	+95.5%	0	—	0	—	948
2024	6,195	+554.0%	281	New	261	New	6,737

Between 2022 and 2023, issuance at KHMH increased by almost 100%, with no issuances at PRBH or QAMH, reflecting a similar phased launch that was observed with early dapagliflozin. The most captivating aspect of the data appears to be the rapid surge in the number of tablets dispensed in 2024: KHMH dispensed 6,195 tablets/month (+554.0%), and PRBH received it for the first time, with 281 tablets dispensed/month, as did QAMH

with 261 tablets dispensed/month. Total network of empagliflozin issued increased to 6,737 tablets per month in 2024 after being introduced in the system in 2022, CAGR increasing by ~272.5% from its introduction in 2022.

**4.4 Comparative SGLT2 Inhibitor Dynamics: The 2024 Inflection Point:** When plotted together, there is a dramatic change in the relative use of the two agents (Table 4).

**Table 4: Combined total SGLT2 inhibitor issuance and proportional contribution of each agent, 2020–2024**

Year	Dapagliflozin	Empagliflozin	Total SGLT2	Dapagli % Share	Empagli % Share
2020	229	0	229	100.0%	0.0%
2021	885	0	885	100.0%	0.0%
2022	2,416	485	2,901	83.3%	16.7%
2023	4,400	948	5,348	82.3%	17.7%
2024	2,260	6,737	8,997	25.1%	74.9%

Since the launch of empagliflozin in 2022, dapagliflozin has held an overall share of 82–83% of the SGLT2 network from 2020 to 2023 due to its dominance of the system for this class. By 2024 it was the opposite, 74.9% of the total was from empagliflozin compared with just 25.1% from dapagliflozin.

There are a number of possibilities to consider. However, the fact that the results of the EMPEROR-Reduced trial have been disseminated broadly since 2020 and have shown empagliflozin's cardiovascular benefits in HFrEF could have hastened its use among cardiologists and endocrinologists taking care of JRMS patients with

a concurrent heart failure diagnosis (21). Second, measures governing medical benefit distribution, such as clinical use preference in certain situations and a formulary interchange protocol, could have been influential in causing distribution shifts. Third, the procurement and pricing for pharmaceuticals in the JRMS pharmaceutical cycle may have had an impact on relative availability. An empagliflozin heart failure meta-analysis presented by Zelniker et al (22), suggested numerically lower amounts of cardiovascular death in high-risk groups, which could have also affected prescriber choice at those tertiary care military center.

**4.5 Cross-Hospital Adoption Patterns:** The primary pioneer for both the SGLT2 inhibitors was consistently KMH as expected since it is the principal tertiary institution with the largest number of specialist physician and complex patients in the JRMS centers.

PRBH showed a stepwise trajectory with minimal quantities (15 tablets/month) of dapagliflozin in 2021, followed by a gradual increase to 920 tablets/month by 2024, before getting its first allocation of empagliflozin in 2024. This is akin to that of KMH where dapagliflozin paved the way for the SGLT2 inhibitor and now empagliflozin is just starting to be adopted into clinical use.

The numbers were most varied with QAMH showing a first time issuance of dapagliflozin tablets in 2022 (284 tablets/month), then in 2023 continued to use dapagliflozin tablets (399 tablets/month), followed by a reception of no dapagliflozin tablets in 2024 in tandem with a first reception of empagliflozin tablets/month). This full substitution at QAMH is not consistent with mere prescribing preference shift, rather it is a formulary level transition.

**4.6 CAGR Analysis and Overall Growth:** When applied to KMH, for dapagliflozin the CAGR for the growth phase (2020–2023) was ~148.6% and the overall CAGR was 55.5%, which was lower due to the drop in 2024. For empagliflozin at KMH, the 2022–2024 CAGR was 257.5%. Total network CAGRs were 76.9% for dapagliflozin (2020–2024) and approximately 272.5% for empagliflozin (2022–2024).

A significant trend over the last five years within JRMS shows tremendous transformation in the use of combined SGLT2 inhibitors from the network including 229 tablets/month in 2020 to 8997 tablets/month in 2024 (approximately 3829% increase).

**4.7 Implications for Formulary Management:** The trends found in this study have a number of important implications in the way JRMS pharmaceutical management. First, the paradigm

shift in the use of SGLT2 inhibitors highlights the need for comprehensive procurement planning and flexible forecasting models that take into consideration historical trends and future indications' growth. Secondly, the large difference between the rates of adoption at PRBH and QAMH in comparison to KMH points to the need to implement more structured methods of disseminating to other secondary care facilities to encourage earlier uptake.

Thirdly, the choice of dapagliflozin over empagliflozin in 2024 should be subjected to the JRMS P&T committee's formal review to decide if this switch is clinically sound and cost-effective. Given that there is no clinical outcome data to allow for the establishment of therapeutic relevance from issuance criteria only, clinical audit data are required to support this. Last but not least, the different rates of adaptation between hospitals underscore the importance of setting up a clinical pathways for T2DM and promoting the use of cardioprotective agents across all healthcare settings based on the best evidence to guide clinical decision making. Medication management programs by clinical pharmacists have been shown to be effective in the military population by expediting appropriate SGLT2 use and resulting in better outcomes in military–beneficiary patient populations through the successful incorporation into clinical practice and outcomes (23).

## 5. CONCLUSIONS:

The present study aimed to analysis SGLT2 inhibitor issuance data from the JRMS warehouses and showing how the pathways of the medication on SGLT2 group, namely empagliflozin 25 mg and dapagliflozin 10 mg, have been incorporated into the Jordanian Royal Medical Services (JRMS) network, at the institutional level, over the past 5 years. The study highlighted a gradual and step-wise adoption over time that commenced with the introduction of dapagliflozin at KMH in 2020 and extended to a network-wide adoption of both agents until 2024, with a remarkable change in relative utilization, shifting towards empagliflozin.

As the tertiary care center, KMH was the institution that was first to adopt both agents. The expected stepwise rollout of the formulary was reflected in the time differences mentioned, ending with PRBH and QAMH. The most analytically relevant observation was the 2024 parallel significant increases in empagliflozin's use (554% at KMH and a first-ever expansion to all three hospitals) and corresponding decreases in dapagliflozin's use, due to presumed clinical need for using empagliflozin versus dapagliflozin, possibly driven by the growing body of evidence on

the former's superiority in reducing CV death as well as expanding use in HFrfEF and CKD.

The total inhibitor issuance of SGLT2 inhibitor treatment via JRMS increased from 229 tablets/month in 2020 to 8,997 tablets/month in 2024—an almost 40-fold increase, driven by changes in the pharmaceutical model of the JRMS according to international evidence-based guidelines and the growing recognition of SGLT2 inhibitors as essential cardiorenal-protective agents. The results highlight the need for introducing a practice model for proactive demand forecasting; institution of structured transition protocols from

formulary to secondary care in JRMS and implementation of a system of evidence based extrapolation of tertiary to secondary care. These administrative data should be complemented with clinical outcome studies (COs) that clearly demonstrate the therapeutic effects of the uptake of SGLT2 inhibitors translating through improved outcomes in the JRMS beneficiary population. This is one of the few studies on How to Manage a Drug Formulary in the Military Healthcare System developed to date and a methodological approach for monitoring the uptake of new therapeutic agents in a centralized institutional pharmacy network.

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**CONFLICT OF INTEREST REPORTED: NIL; SOURCE OF FUNDING: NONE REPORTED**