Identifying Cohorts of Patients With Type 2 Diabetes Mellitus Initiating Dapagliflozin in Three Data Sources

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BACKGROUND

- Dapagliflozin is a sodium-glucose cotransporter-2 (SGLT2) inhibitor used to treat type 2 diabetes mellitus (T2DM).
- A multidatabase study of dapagliflozin using United Kingdom (UK)– and United States (US)–based data sources identified historical cohorts of patients with T2DM initiating dapagliflozin in the context of evaluating the renal safety of dapagliflozin.
  - The data sources differ in patient populations, data systems, and health care delivery and practice.
- A common protocol and statistical analysis plan were applied with data source–specific adaptations to identify and describe patients initiating dapagliflozin.

DISCLOSURES:
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OBJECTIVE

- To describe patient characteristics and initiation patterns among new users of dapagliflozin with T2DM in three data sources.

METHODS

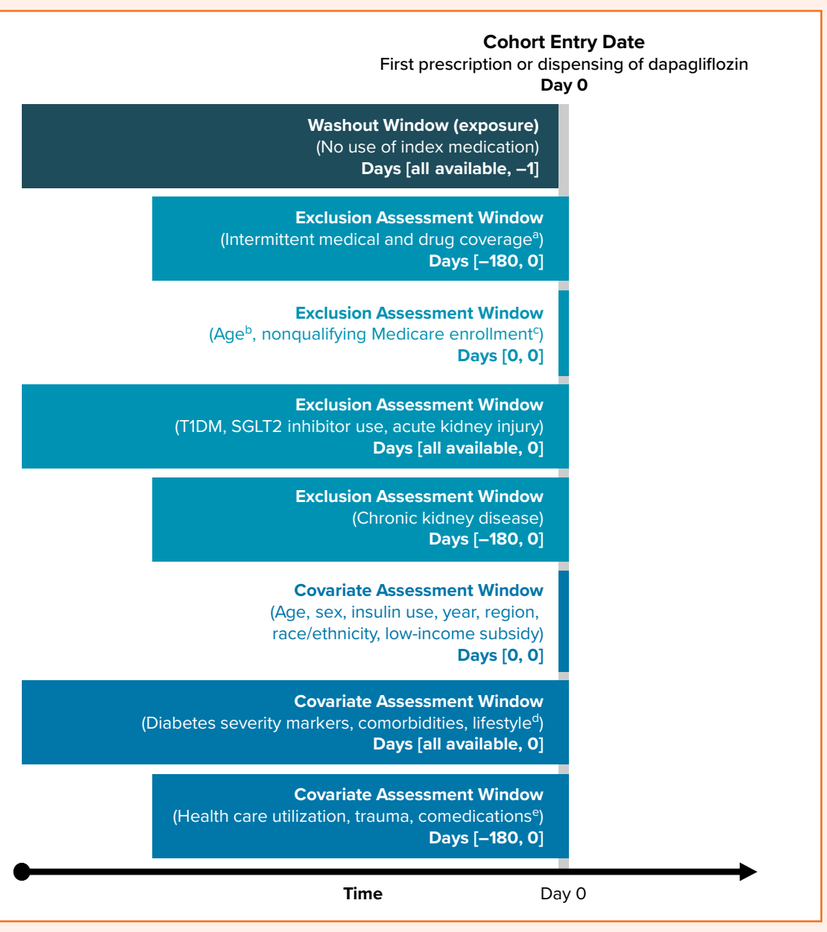
- We used the following three existing health care data sources (Table 1):
  - Clinical Practice Research Datalink (CPRD), UK
  - HealthCore Integrated Research Database (HIRD), US
  - Medicare Research Identifiable files, US
- We identified adults initiating dapagliflozin at the first issued prescription (UK) or pharmacy dispensing (US) for dapagliflozin during the data source-specific study period (Figure 1).
  - Eligibility requirements for database enrollment were adapted to each data source (e.g., registered in a participating practice in CPRD vs. continuing insurance coverage in HIRD and Medicare Parts A, B, and D).
  - Other eligibility criteria based on age, comorbidities, and previous medication use were evaluated.
- Clinical and demographic characteristics of the resulting study cohorts were described and evaluated across data sources as follows:
  - In CPRD, general practitioner (GP)–recorded information
  - In HIRD and Medicare, using recorded diagnoses, procedures, and pharmacy claims from submitted administrative billing information

Table 1. Characteristics of Selected Data Sources

Characteristics	CPRD	HIRD	Medicare
Country	United Kingdom	United States	United States
Included study years	Jan 2012-Dec 2018	Jan 2014-Feb 2019	Jan 2014-Dec 2017
Study population ages	Aged ≥ 18 years	Aged 18-64 years	Aged ≥ 65 years
Data type	GP records	Administrative claims data from commercial, employer-sponsored insurance	Administrative claims data from government-sponsored insurance
Medication information	GP-prescribed medications	Pharmacy-dispensed prescriptions	Pharmacy-dispensed prescriptions
Medication date	Date prescription issued	Date prescription dispensed	Date prescription dispensed
Lifestyle risk factors	Included, with missing data	None	None
Coding system	Read	ICD-9-CM, ICD-10-CM, CPT, HCPCS	ICD-9-CM, ICD-10-CM, CPT, HCPCS
Outpatient visits	As recorded by GPs	Yes, one or more diagnoses on submitted claims	Yes, one or more diagnoses on submitted claims
Hospitalization data	Partial linkage to HES; as recorded by GPs	Yes, one or more diagnoses on submitted claims	Yes, one or more diagnoses on submitted claims
Specialist visits	Information from referral letters	Yes, one or more diagnoses on submitted claims	Yes, one or more diagnoses on submitted claims
Emergency room visits	As recorded by GPs	Yes, one or more diagnoses on submitted claims	Yes, one or more diagnoses on submitted claims

CPT = Current Procedural Terminology; HCPCS = Healthcare Common Procedure Coding System; HES = Hospital Episode Statistics; ICD-9-CM = *International Classification of Diseases, 9th Revision, Clinical Modification*; ICD-10-CM = *International Classification of Diseases, 10th Revision, Clinical Modification*.

Figure 1. Schematic of Study Design and Variable Assessment Windows Relative to Medication Initiation



T1DM = type 1 diabetes mellitus.

[a] CPRD, registered in an up-to-standard participating general medical practice. HIRD, complete pharmacy and medical coverage in a health insurance plan with no enrollment gaps greater than 30 days; Medicare, enrolled in fee-for-service insurance in Parts A, B, and D.

[b] CPRD, ≥ 18 years; HIRD, 18-64 years; Medicare, ≥ 65 years.

[c] Medicare, enrolled because of disability or end-stage renal disease; nonresident of a US state or the District of Columbia; enrolled in managed care coverage.

[d] Diabetic nephropathy or renal insufficiency; peripheral neuropathy; peripheral vascular disease; retinopathy; coronary heart disease; cerebrovascular disease; amputation; kidney and genitourinary stones; hypertension; heart failure; liver disease; other cardiovascular disease; chronic obstructive pulmonary disease, emphysema, respiratory insufficiency; systemic connective tissue disorders; rheumatoid arthritis; other autoimmune disorders; osteoarthritis; polymyalgia rheumatica; urinary infections (chronic or recurring); colon polyps; Crohn's disease; ulcerative colitis; pancreatitis; immunosuppressive diseases; peptic ulcer disease; dementia; asthma; hyperlipidemia; all malignancies other than non-melanoma skin cancer; body mass index; smoking history; alcohol use; alcohol abuse; socioeconomic deprivation.

[e] Number of hospitalizations; trauma; antihypertensives/diuretics; antiarrhythmics; digoxin; nitrates; lipid-modifying agents; non-steroidal anti-inflammatory drugs; systemic corticosteroids; inhaled systemic corticosteroids; zoledronic acid; acetaminophen; antibiotics (all types); anticonvulsants; antifungal agents; antituberculars; methotrexate; antineoplastic agents other than methotrexate; systemic antivirals; aspirin and antiplatelets other than clopidogrel; anticoagulants; HbA1c tests (number performed and value); outpatient visits; emergency department visits; specialty care visits.

Note: figure template available at www.repeatinitiative.org.

RESULTS

- We identified 51,303 dapagliflozin initiators across the data sources (Table 2).
- The distribution of insulin use among dapagliflozin initiators was similar across data sources.
  - The proportion of patients adding dapagliflozin to existing treatment with other oral antidiabetic medications was much higher in CPRD.
- There was an expected observed relationship between mean age and levels of markers of T2DM disease severity and comorbidities.
  - The Medicare cohort was restricted to patients aged ≥ 65 years, thus the mean age is greater than those in other data sources, and Medicare patients had higher proportions of most markers of T2DM severity and comorbidities.
  - Patients in HIRD were restricted to those aged < 65 years and generally had lower proportions of T2DM severity markers and comorbidities.
- CPRD contained patients across the entire spectrum of adult ages, age 18+, though there were characteristics in the CPRD that differed from both US-based data sources.
  - Characteristics present in a higher proportion of patients in CPRD included comedication use, including the use of the following: systemic, noninhaled corticosteroids; lipid-modifying agents; and acetaminophen.
  - Characteristics present in a lower proportion of patients in CPRD included history of peripheral vascular disease, hypertension, and chronic or recurring urinary tract infections, as well as antibiotic use.

Table 2. Selected Characteristics of Patients with Type 2 Diabetes Mellitus Initiating Dapagliflozin in Three Separate Data Sources

Characteristics	CPRD N = 12,051	HIRD N = 21,173	Medicare N = 18,079
Age, mean (SD)	56.9 (10.4)	51.7 (8.5)	70.7 (5.0)
Sex, %			
Male	58.5	54.8	49.7
Female	41.5	45.2	50.3
Antidiabetic treatments, %			
Insulin use	13.5	13.8	17.1
Dapagliflozin as add-on oral therapy	89.2	75.8	72.0
Dapagliflozin as oral monotherapy	2.2	8.0	9.8
Markers of diabetes severity, %			
Retinopathy	28.1	23.8	36.1
Peripheral neuropathy	3.4	1.9	5.8
Peripheral vascular disease	3.1	22.6	35.8
Coronary heart disease	12.0	9.5	30.6
Cerebrovascular disease	4.3	1.7	12.4
Comedication use, %			
Antihypertensives/diuretics	70.7	68.2	80.8
Systemic, noninhaled corticosteroids	13.8	9.9	9.8
Lipid-modifying agents	77.9	61.8	77.0
Antibiotics	29.4	34.7	35.8
Prescription acetaminophen	30.1	16.0	15.5
Comorbidities, %			
Hypertension	54.0	70.5	89.8
Heart failure	1.6	1.8	8.2
Respiratory disease	5.2	2.7	10.7
Other cardiovascular disease	8.5	3.1	14.2
Chronic or recurring urinary tract infections	2.4	6.3	14.5

SD = standard deviation.
Note: A complete list of all covariates is shown in the footnotes to Figure 1. Characteristics presented in Table 2 were selected to represent different patterns of covariate distribution between the three data sources.

DISCUSSION

- Characteristics of patients with T2DM initiating dapagliflozin vary based on the source population and data source.
  - Dapagliflozin appears to be prescribed somewhat differently in the UK, with higher proportions of the dapagliflozin users using dapagliflozin as add-on therapy.
  - These differences may be largely due to differences in age, data coding systems, source of health records, and clinical practice patterns.
    - For some characteristics, the distributions in the CPRD and HIRD cohorts were similar (e.g., antihypertensive use, coronary heart disease), likely due to the similar age structure of the patients.
    - Despite differences in age between the HIRD and Medicare cohorts, both of these patient populations had higher prevalences of peripheral vascular disease, hypertension, and antibiotic use, likely reflecting the characteristics of the US population, treatment patterns, and claims-based data.
- The patterns of dapagliflozin initiation in CPRD differed from the US samples, which could be due in part to differing diabetes treatment approaches in the two countries.

CONCLUSIONS

- The characteristics of patients with T2DM initiating dapagliflozin vary between the three study populations, reflecting underlying differences in the use of dapagliflozin across age groups and countries.

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