A call for action: optimizing treatment in CKD

Meg Jardine, MD, PhD Sydney, Australia

4 Things to know about CKD and SGLT2i



A call for action: optimizing treatment in CKD

Meg Jardine

NHMRC Clinical Trials Centre, University of Sydney

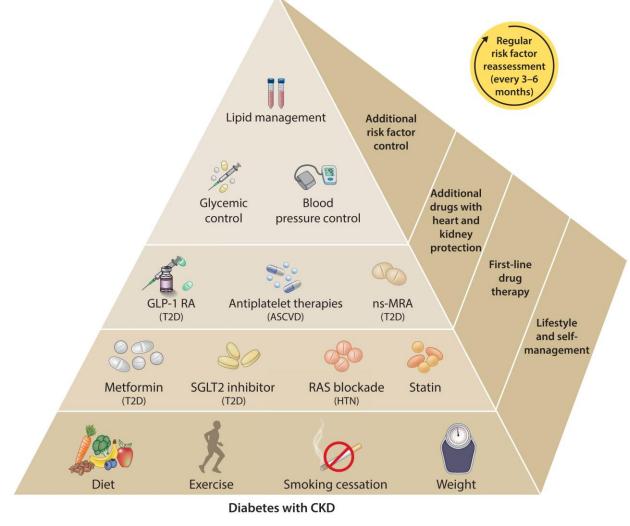
Concord Repatriation General Hospital

Disclosures

- Global Scientific Lead and Steering Committee member CREDENCE, trial sponsored by Janssen
- Advisory Boards and Scientific Presentation fees from Astra Zeneca & Boehringer Ingelheim, companies who make SGLT2 inhibitors
- Responsible for research projects that have received funding from Amgen, Baxter, CSL, Dimerix, Eli Lilly, Gambro, and MSD
- Have received fees for advisory, steering committee and/or scientific presentations from Akebia, Amgen, Astra Zeneca, Baxter, Bayer, Boehringer Ingelheim, Cesas Linx, Chinook, CSL, Janssen, Medscape, MSD, Occuryx, Roche and Vifor
- All consultancy, honoraria or travel support paid to my institution

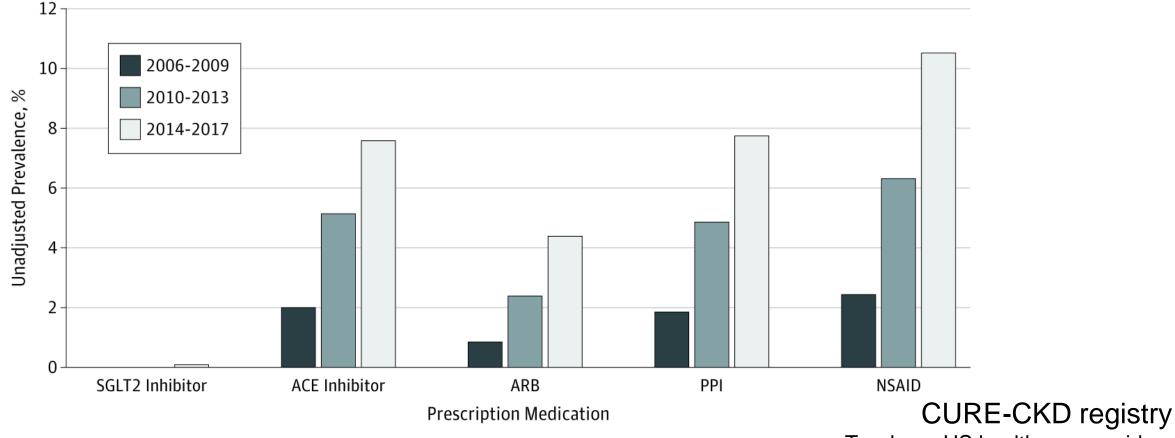


KDIGO 2022 DKD updated guideline



Time course for uptake of RAASi in CKD

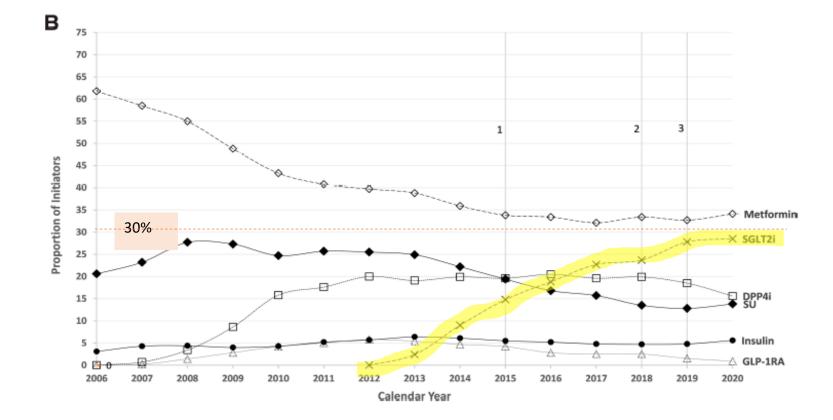
Use of ACEi/ARB in adults with CKD - 20.5%



Two large US healthcare providers

Tuttle KR et al. JAMA Netw Open 2019;2:e1918169

UK: Increasing SGLT2i use in T2DM without CKD

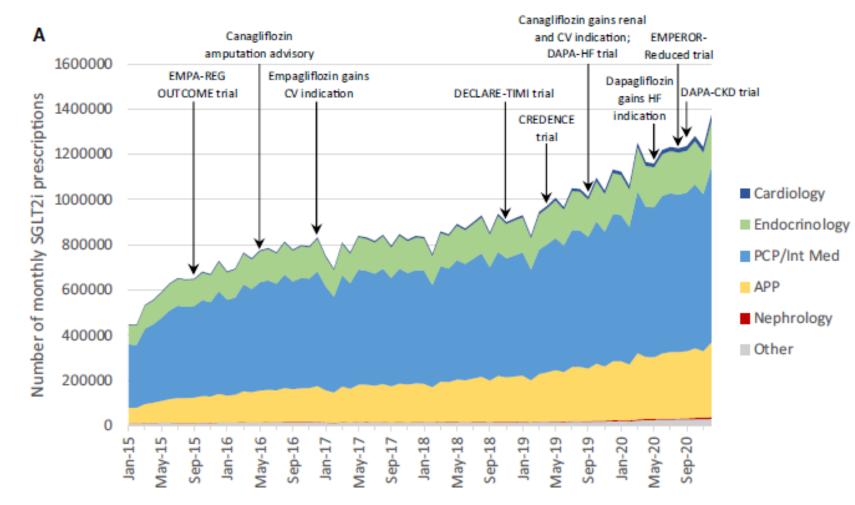


Method

UK Clinical Practice Research Datalink (2006–2020)

Patients with T2DM with CKD (n = 38,622) or without CKD (n = 230,963)

Who's prescribing SGLT2 inhibitors - US

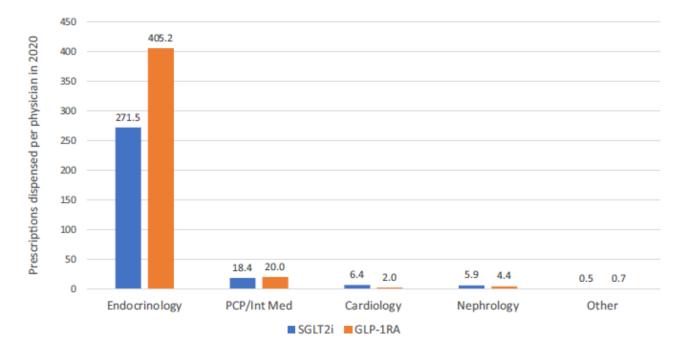


Methods: serial, cross-sectional data, IQVIA National Prescription Audit, audit capturing ≈90% of US retail dispensing

R Adhikari et alJ Am Heart Assoc. 2022;11:e023811. DOI: 10.1161/JAHA.121.023811

Who is prescribing SGLT2i, GLP1RAs in the US

- This analysis of a near-census-level audit of the US retail prescriptions shows that since 2015, cardiologists have increased use of SGLT2is and GLP-1RAs 12-fold and 4-fold, respectively.
- Nonetheless, cardiologists accounted for <2% of all SGLT2i and GLP-1RA use in 2020.



Prescriptions dispensed per physician in 2020

Methods: serial, cross-sectional data, IQVIA National Prescription Audit, audit capturing ≈90% of US retail dispensing

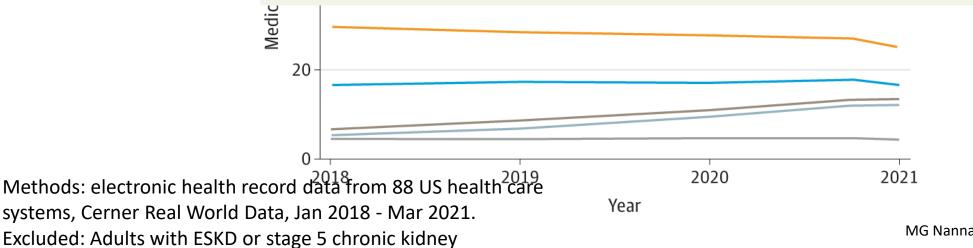
R Adhikari et alJ Am Heart Assoc. 2022;11:e023811. DOI: 10.1161/JAHA.121.023811

Prescription in high risk patients

SGLT2i/GLP1RA use in US Atherosclerotic CV Disease, Diabetes, 2018-2021



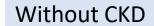
Meaning In this study, despite increases in use of both SGLT2i and GLP-1 RA, the majority of patients with atherosclerotic cardiovascular disease receiving medical therapy for type 2 diabetes were not taking either.

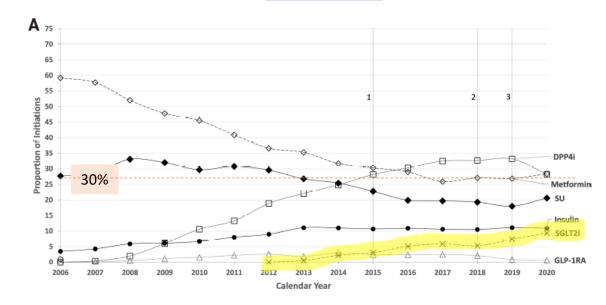


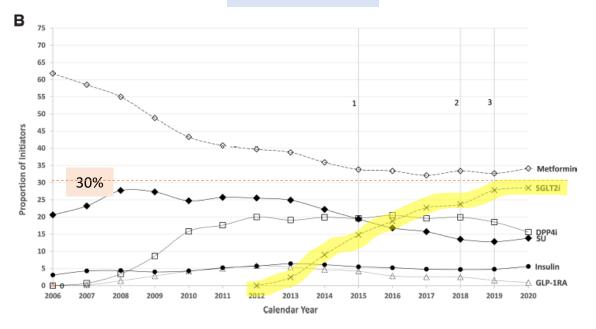
MG Nanna et al *JAMA Cardiol*. 2023;8(1):89-95. doi:10.1001/jamacardio.2022.3839

UK: SGLT2i prescription in CKD

With CKD







Method

UK Clinical Practice Research Datalink (2006–2020) Patients with T2DM with CKD (n = 38,622) or without CKD (n = 230,963)

Conclusions

SGLT2i use increased among patients with T2DM, but this increase was largely driven by patients without CKD.

J Liaw et al Diabetes Care 2022;45:2316–2325 | https://doi.org/10.2337/dc22-0224

Patient Characteristics of Those Treated in the US

Variable associated with SGLT2i use	More Likely	Less Likely
Age	Younger age	Older age
Sex	Male sex	Female sex
Race	White, Asian	Black or African American
Ethnicity	Hispanic or Latino	Non-Hispanic or Latino
Weight	Higher weight	Lower weight
HbA1c	Higher HbA1c	Lower HbA1c
Clinical scenario	Other kidney or Cardioprotective meds	CKD, Prior MI, prior stroke/TIA, any PAD, AF, Heart failure * Hospitalised in last year
Setting	Academic centre setting	
Insurance	Private insurance	
Not Associated with SGLT2i use		
	Encounter year (2018-21), Outpatient encounter in last year	

Methods: electronic health record data from 88 US health care systems, Cerner Real World Data, Jan 2018 - Mar 2021. Excluded: Adults with ESKD or stage 5 chronic kidney

Medication adherence in the trials

Trial	Median Fu		Adherence SGLT2i	Adherence Pbo
CREDENCE	2.6 years	84%		
DAPA-CKD	2.4 years		87.3%	85.6%
EMPA-Kidney	2.0 years		83.1%	80.6%

Adherence and persistence in real world

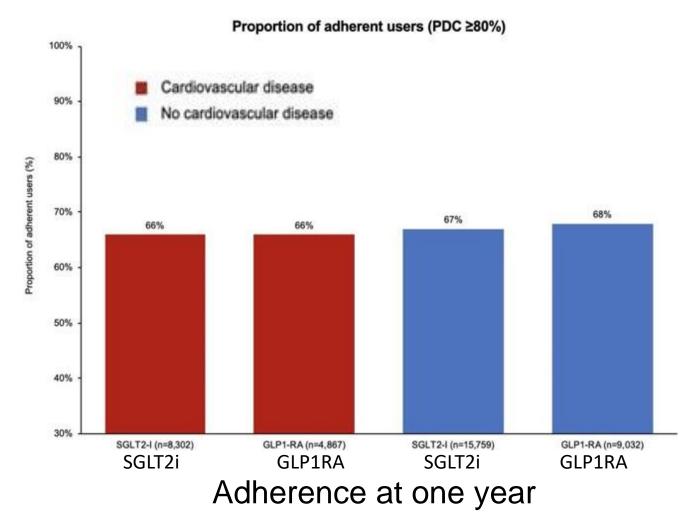
Meta-analysis (to Oct 2019): results of proportion adherent, and the proportion persistent at selected follow-up periods

Outcome	Number of studies	Number of cohorts	Sample size	Pooled results (95% CI)	ľ
% Adherent (PDC ≥0.80)					
6 months	4	7	34 667	59.5 (52.9-65.9)	9
1 y	5	10	28 808	49.0 (42.3-55.8)	9
% persistent					
1 y					
All definitions	10	16	79 181	61.8 (57.8-65.7)	9
≥90-day gap	6	11	33 729	58.9 (53.1-64.6)	9
2 у					
All definitions	4	5	51 510	45.9 (35.5-56.5)	9
≥90-day gap	2	2	7182	34.7 (33.6-35.8)	0

^aSome studies did not report SD and therefore could not be included in the meta-analysis.

Abbreviations: CI, confidence interval; PDC, proportion of days covered.

Adherence to SGLT2i and GLP1RA in Denmark



Malik. *Pharmacology and Pharmacotherapy – Cardiovascular Pharmacotherapy 2022*/43/Supplement_2/ehac544.2692/6746166

Clinician barriers to uptake

Survey SGLT2i prescribing patterns among nephrologists globally and identify barriers to SGLT2i prescribing

49% nephrology fellows or graduates \leq 5 years, 51% practicing > 5 years

64% of total respondents, 68% of trainees/recent graduates said knew

53% from the US vs. 80% outside the US responded that they knew

33.6% of respondents said they prescribe SGLT2i to>50% of patients

153 survey participants

indications for SGLT2i very well

meeting requirements for SGLT2i.

52% university hospital, 48% private practice

indications of SGLT2i very well (P 0.001).

42% US, 58% outside US

Most common N barriers to prescribing he SGLT2i

Mechanisms that helped in prescribing SGLT2i

Lack of time and personnel to manage the side effects (11%)

Lack of experience or comfort in prescribing sglt2i (29%)

Cost of medication or high co-pay (34%) Participation in professional conferences (18%)

Readily available medical knowledge through social media (26%)

> Professional Guidelines (29%)

Nephrologists Survey to Learn Prescribing Patterns of Sodium-Glucose Cotransporter 2 Inhibitors (SGLT2i) Tripti Singh,1 Tingting Li,2 Didier A. Mandelbrot,1 Ali Poyan-Mehr.3 *1University of Wisconsin-Madison, Madison, WI; 2Washington University in St Louis, St Louis, MO; 3Kaiser Permanente, Oakland, CA.*

KDIGO Tool for SGLT2i initiation

KIDNEY DISERS

Practical provider guide to initiating SGLT2 inhibitors in patients with type 2 diabetes and CKD

	Assessment	Intervention	Follow-up
Patient selection	Eligible patients: • eGFR ≥20 ml/min/1.73 m ² High priority features: • ACR ≥200 mg/g [≥20 mg/mmol] • Heart failure Potential contraindications: • Genital infection risk • Diabetic ketoacidosis • Foot ulcers • Immunosuppression	SGLT2 inhibitor with proven benefits: • Canagliflozin 100 mg • Dapagliflozin 10 mg • Empagliflozin 10 mg Education: • Sick day protocol* • Perioperative care [†] • Foot care	 Assess adverse effects Review knowledge Anticipate an acute drop in eGFR, which is generally not a reason to stop the SGLT2 inhibitor
Glycemia	Hypoglycemia risk? • Insulin or sulfonylurea • History of severe hypoglycemia • HbA1c at or below goal	Education: • Hypoglycemia symptoms • Glycemia monitoring Consider insulin/sulfonylurea dose reduction	 Ask about hypoglycemia Reduce sulfonylurea or insulin if needed
Volume	Volume depletion risk? Concurrent diuretic use Tenuous volume status History of AKI 	Education: • Volume depletion symptoms Consider diuretic dose reduction	 Re-assess volume Reduce concomitant diuretic if needed

De Boer, Rossing et al. *Kidney International* 2022 102S1-S127

Conclusions

• SGLT2 inhibitors safely provide kidney and cardiac protection for people with

diabetes and/or with CKD (eGFR \geq 20 mL/min/1.73 m²)

- Uptake appears better than for RAASi but is patchy
- Ways to safely keep patients on proven treatments needs better understanding
- Implementation trials and activities for both uptake and maintenance warranted