AD and a Shifting Paradigm: A New Approach to Care for Type 2 Diabetes

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- Speaker has no conflict of interests

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Who We Are

- **Illinois Academic Detailing Visits And New Evidence CEnter**

- Illinois Public Act 101-0278

- 30+ clinical pharmacists

Which of the following is an important consideration when determining an appropriate agent to initiate in patients with Type 2 diabetes?

A1C (blood test measuring the average blood glucose level over the past 3 months)

Comorbid ASCVD (atherosclerotic cardiovascular disease)/ High-risk for ASCVD

Comorbid heart failure

Comorbid CKD (chronic kidney disease) /DKD (diabetic kidney disease)

All of the above

A Standing Ovation

PARIS, France ***(UPDATED)***–Dapagliflozin, when given on top of standard therapy, markedly reduces the risk of worsening heart failure events and cardiovascular death and improves symptoms among heart failure patients with reduced ejection fraction (HFrEF), full results from the DAPA-HF trial show.

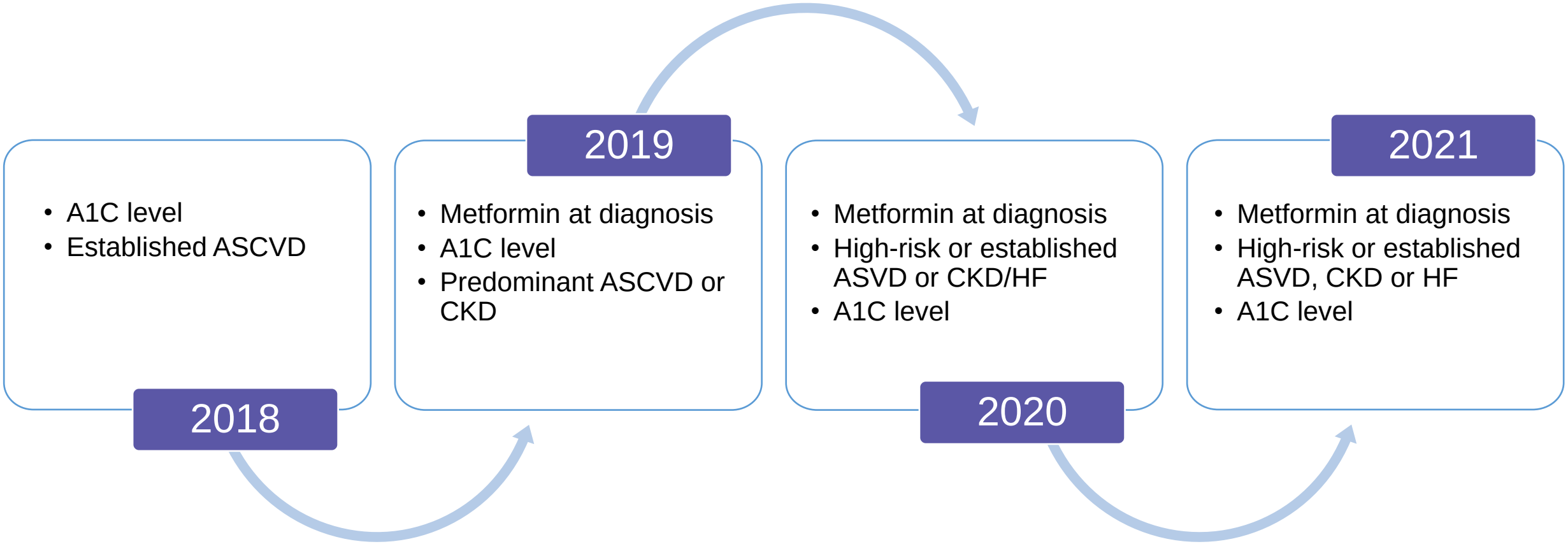
Importantly, the relative and absolute risk reductions in death and hospitalizations were consistent across subgroups, which included patients both with and without diabetes, presenter John McMurray, MD (University of Glasgow, Scotland), said here at the European Society of Cardiology Congress 2019, prompting hoots of surprise and scattered applause from the audience. McMurray's concluding remarks were met with sustained applause and at least one man gave the results a standing ovation.

This is What Academic Detailing Was Made For

Diabetes Evidence Changing Rapidly

EMPA-REG OUTCOME (2015)	LEADER (2016)	SUSTAIN-6 (2016)	CANVAS (2017)
REWIND (2019)	DECLARE-TIMI 58 (2019)	CREDENE (2019)	DAPA-HF (2019)
	DAPA-CKD (2020)	EMPEROR-REDUCED (2020)	

Guidelines Changing Rapidly



The Campaign

January 2021

43 visits and counting…

Studies, studies and more studies

Benefits of SGLT2i and GLP-1 RAs

The Topics

Care Evolution	Atherosclerotic Cardiovascular Disease (ASCVD)	Chronic Kidney Disease (CKD)	Heart Failure (HF)
Background information	33% of patients with T2DM	20-40% of patients with T2DM	2x higher risk of developing HF in patients with T2DM

The Brochure

- Treatment algorithm
- Results of meta-analyses
- Forest plot
  - Includes 5 agents that are FDA-labeled

ATHEROSCLEROTIC CARDIOVASCULAR DISEASE

Patients With High Risk For or Established ASCVD [3,6,7,9-13]

1 Metformin + Lifestyle + DSMES

Independent of A1C

Add GLP-1 RA or SGLT2i with proven CV benefit*†

Contraindicated, not tolerated, or A1C above goal

2 Add agent from alternate class not used above†

A1C above goal

3 Add agent demonstrating CV safety

*Liraglutide, semaglutide, dulaglutide, empagliflozin, canagliflozin
†See package inserts for renal dosing recommendations

Clinical guidelines emphasize comprehensive management of both glycemic goals and CV risk factors.

Many glucagon-like peptide-1 receptor agonist(s) (GLP-1 RA) and sodium-glucose co-transporter 2 inhibitor(s) (SGLT2i) have demonstrated **statistically significant reductions in risk of major adverse cardiovascular events (MACE) independent of glucose control.**

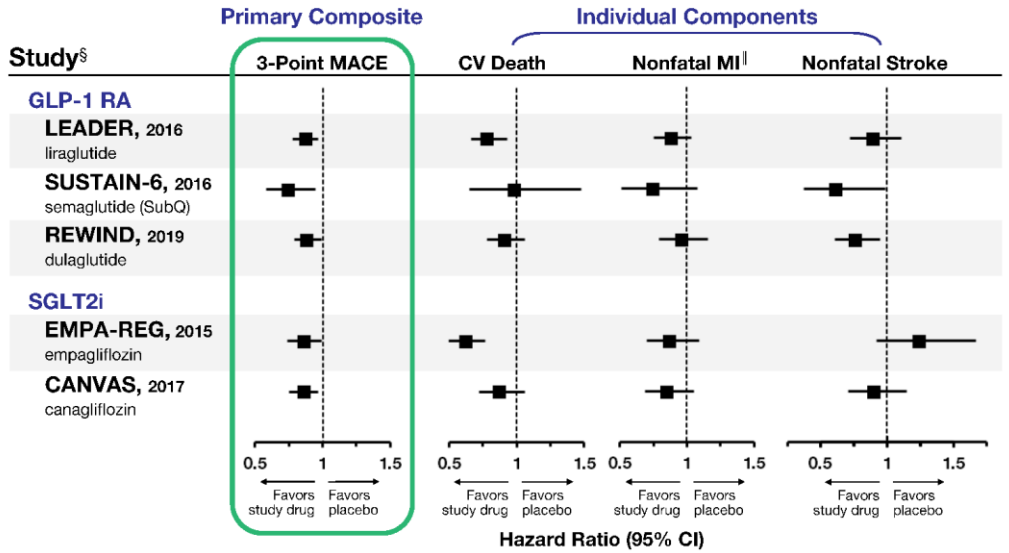
Overall, meta-analyses of CVOT showed:

- GLP-1 RA reduce the risk of MACE by 13% versus placebo (HR 0.87; 95% CI 0.80-0.96)‡
- SGLT2i reduce the risk of MACE by 12% versus placebo (HR 0.88; 95% CI 0.82-0.94)

‡*HR* hazard ratio, *CI* confidence interval

GLP-1 RA and SGLT2i That Have Shown CV Benefit [3,9,11,14-18]

The medications in the following trials reduce CV risk to a similar degree in patients with T2DM and ASCVD.



§Study designs and patient populations differ. EMPA-REG refers to the EMPA-REG OUTCOME trial. See supplemental table for details regarding individual studies.
‖*MI* myocardial infarction

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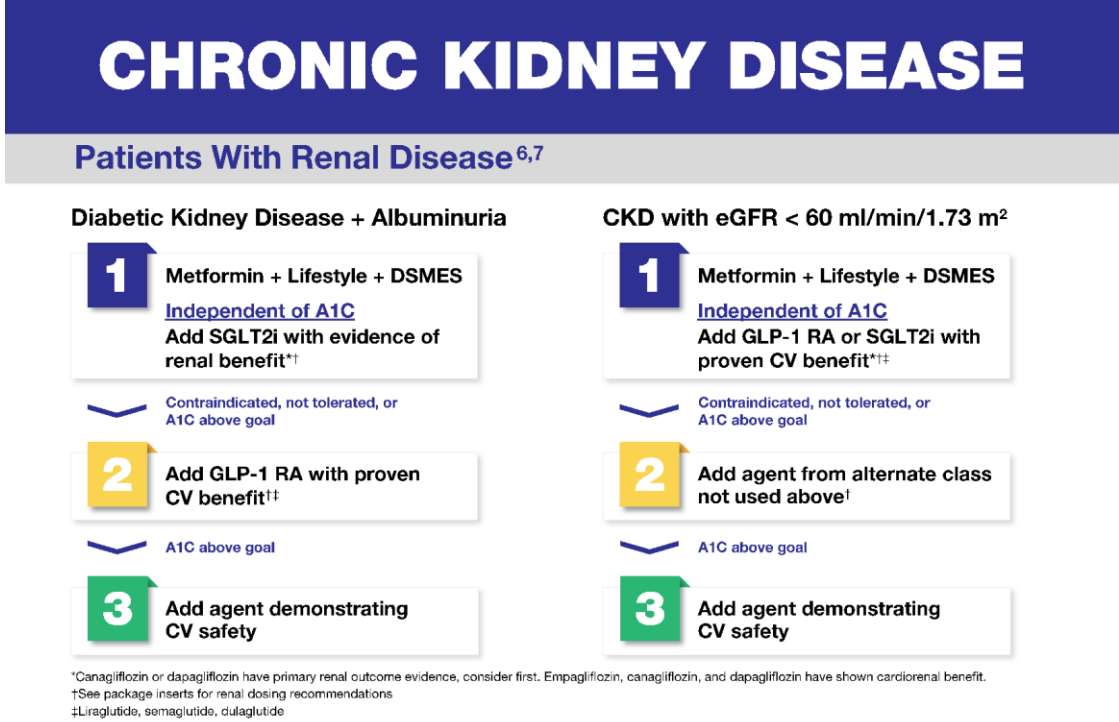
The Brochure

- Treatment algorithm
- Results of individual studies
  - CREDENCE
    - Patients with T2DM
  - DAPA-CKD
    - Patients with and without T2DM



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The Brochure

- Supplementary document
- Additional information on individual studies

SELECT GLP-1 RA AND SGLT2i TRIALS

Trial Design, Median Duration	Population	Relevant Background Therapies	Intervention	Primary Endpoints HR (95% CI); *P* value	Other Select Endpoints HR (95% CI); *P* value
ASCVD Outcome Trials—GLP-1 RA					
LEADER[1] (2016) R, DB, PC, MC, ITT 3.8 years	**N = 9,340** T2DM (100%) eCVD (72.4%)	Antithrombotic (~67.8%) Statin (~72.2%) ACEi/ARB (~82.9%) Beta-blocker (~55.5%) Metformin (~76.5%)	Liraglutide 1.8 mg (or maximum tolerated dose)	**3-Point MACE*** 0.87 (0.78-0.97); *P*<0.001 for NI and *P*=0.01 for S	**CV death** 0.78 (0.66-0.93); *P*=0.007 **Nonfatal stroke** 0.89 (0.72-1.11); *P*=0.30 **Nephropathy** 0.78 (0.67-0.92); *P*=0.003
SUSTAIN-6[2] (2016) R, DB, PC, PG, MC, ITT 2.1 years	**N = 3,297** T2DM (100%) eCVD (58.8%)	Antithrombotic (76.3%) Statin (72.8%) ACEi/ARB (83.5%) Beta-blocker (57.4%) Metformin (73.2%)	Semaglutide 0.5 mg,1 mg	**3-Point MACE*** 0.74 (0.58-0.95); *P*<0.001 for NI and *P*=0.02 for S	**CV death** 0.98 (0.65-1.48), *P*=0.92 **Nonfatal stroke** 0.61 (0.38-0.99); *P*=0.04 **New or worsening nephropathy** 0.64 (0.46-0.88); *P*=0.005
REWIND[3] (2019) R, DB, PC, MC, ITT 5.4 years	**N = 9,901** T2DM (100%) eCVD (31.5%)	Antiplatelet (~54%) Statin (~66.1%) ACEi/ARB (~81.5%) Beta-blocker (~45.6%) Metformin (~81.2%)	Dulaglutide 1.5 mg	**3-Point MACE*** 0.88 (0.79-0.99); *P*=0.026	**Renal composite†** 0.85 (0.77-0.93); *P*=0.0004 **Nonfatal stroke** 0.76 (0.61-0.95); *P*=0.017 **CV death** 0.91 (0.78-1.06), *P*=0.21
ASCVD Outcome Trials—SGLT2i					
EMPA-REG OUTCOME[4] (2015) R, DB, PC, MC, mITT 3.1 years	**N = 7,028** T2DM (100%) eCVD (>99%) HF (~10.2%)	Anticoagulant (~89.2%) Statin (~76.7%) ACEi/ARB (~80.6%) Beta-blocker (~64.7%) Diuretic (~43.2%) Metformin (~74.1%)	Empagliflozin 10 mg, 25 mg	**3-Point MACE*** 0.86 (0.74-0.99); *P*<0.001 for NI and *P*=0.04 for S	**4-Point MACE‡** 0.89 (0.78-1.01); *P*<0.001 for NI and *P*=0.08 for S **CV death** 0.62 (0.49-0.77); *P*<0.001 **All-cause mortality** 0.68 (0.57-0.82); *P*<0.001 **HHF** 0.65 (0.50-0.85); *P*=0.002
CANVAS Program[5] (2017) R, DB, PC, MC, ITT 126.1 weeks (~2.4 years)	**N = 10,142** T2DM (100%) eCVD (65.6%) HF (14.4%)	Antithrombotic (73.6%) Statin (74.9%) RAAS inhibitor (80%) Beta-blocker (53.5%) Diuretic (44.3%) Metformin (77.2%)	Canagliflozin 100 mg, 300 mg	**3-Point MACE*** 0.86 (0.75-0.97); *P*<0.001 for NI and *P* = 0.0158 for S	**All-cause mortality** 0.87 (0.74-1.01); *P*=0.24 **CV death** 0.87 (0.72-1.06); NA **HHF** 0.67 (0.52-0.87); NA **Progression of albuminuria** 0.73 (0.67-0.79); NA
DECLARE-TIMI 58[6] (2019) R, DB, PC, MC, ITT 4.2 years	**N = 17,160** T2DM (100%) eASCVD (~40.6%) HF (~10%)	Antiplatelet (~61.1%) Statin or ezetimibe (~75%) ACEi/ARB (~81.3%) Beta-blocker (~52.6%) Diuretic (~40.6%) Metformin (~82%)	Dapagliflozin 10 mg	**3-Point MACE*** 0.93 (0.84-1.03); *P*=0.17 **Composite (CV death or HHF)** 0.83 (0.73-0.95); *P*=0.005	**CV death** 0.98 (0.82-1.17); NA **HHF** 0.73 (0.61-0.88); NA **All-cause mortality** 0.93 (0.82-1.04); NA **Renal composite§** 0.53 (0.43-0.66); NA

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What We've Learned

Insurance	• Coverage of medications is a major hurdle
A1C	• Primary driver of care
Medications	• Managing side effects • Understanding nuance between medications
Patient factors	• Communicating value of cardiorenal benefits • Resistance to change

Looking to the Future

Online Toolkit

Frequently asked questions

Additional educational resources

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Collaborating with prescribers to ADVANCE evidence-based healthcare