

## Diabetes and CKD

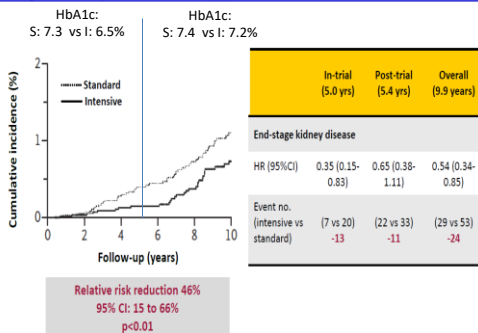
- 25% of individuals with diabetes have CKD (DKD)
- 20% of DKD cases are due to low GFR in the absence of an increase in AER
- Consider AER and GFR as complementary rather than obligatory manifestations of DKD
- Classify patients according to CKD/DKD stage

Kidney Function Stage	GFR (mL/min/1.73m <sup>2</sup> )	Albuminuria Stage		
		Normal (A1) (urine ACR mg/mmol) Male: < 2.5 Female: < 3.5	Microalbuminuria (A2) (urine ACR mg/mmol) Male: 2.5-25 Female: 3.5-35	Macroalbuminuria (A3) (urine ACR mg/mmol) Male: > 25 Female: > 35
1	>90	Not CKD unless haematuria, structural or pathological abnormalities present		
2	60-89			
3a	45-59			
3b	30-44			
4	15-29			
5	<15 or on dialysis			

## Assessing glycaemic control in CKD

- Erythrocyte turnover increases as eGFR declines (red cell survival time is shorter)
- Treatment with erythrocyte-stimulating agents lowers HbA1c values
- Patients with CKD are at higher risk of hypoglycaemia than non CKD patients
- Aim for HbA1c 7-8% in stage 4-5 CKD (although limitations of HbA1c interpretation are appreciated)
- May be able to achieve tighter targets in CKD stage 3 patients
- Ultimately HbA1c results should be interpreted carefully in conjunction with self-monitoring of blood glucose levels
- Role of Fructosamine?

## Long-term benefits of intensive glucose control for preventing end-stage kidney disease in type 2 diabetes: ADVANCE ON



## Guidelines on glycaemic targets in CKD

Guideline	Date	Recommendation
NKF/KDOQI: Practice Guidelines of diabetes and CKD (Am J Kidney Dis 2012, 60:850)	2012	<ul style="list-style-type: none"> <li>• Target HbA1c of approximately <b>7.0% (53mmol/mol)</b> to prevent or delay progression of DKD</li> <li>• <b>Not</b> treating to an HbA1c &lt; <b>7.0% (53 mmol/mol)</b> in patients at risk of hypoglycaemia (insulin/SU and/or advanced CKD)</li> </ul>
ERA-EDTA Clinical Practice Guideline on management of patients with diabetes and eGFR < 45 ml/min (NDT 2015, 30 iii1)	2015	<ul style="list-style-type: none"> <li>• Determine HbA1c target <b>7.0-8.5% (53-64 mmol/mol)</b> according patient characteristics and glucose lowering agent used.</li> </ul>
ADA Standards of Medical Care (Diabetes Care 2017,40: suppl 1, S1)	2017	<ul style="list-style-type: none"> <li>• Optimize glucose control to reduce the risk or slow the progression of DKD.</li> <li>• With prevalent DKD and substantial comorbidity, target A1C levels should be &gt; <b>7% (53 mmol/mol)</b></li> </ul>

## Insulin + CKD

- Insulin clearance decreases in parallel with eGFR decline
- As eGFR declines, gluconeogenesis from the kidney decreases
- Exogenous insulin requirements also decrease on dialysis due to decreased insulin resistance
- Some patients reduced insulin doses by up to 50% on dialysis days

## Metformin + CKD

- Metformin use should be re-evaluated if eGFR < 45
- Suggested maximum dose is 1000 mg/d below the above eGFR threshold
- Discontinue metformin when eGFR falls to < 30
- Advise all patients to cease metformin if they have nausea and vomiting

## Sulfonylureas + CKD

GLICLAZIDE MR	- Generally well tolerated - Initiate 30- 60mg/daily - ESRD √
GLIPIZIDE	- No dose adjustment - ESRD √
GLIMEPIRIDE	- Initiate conservatively at 1mg/day (ESRD √)
GLIBENCLAMIDE	- Avoid (hypoglycaemia)

## DPP-4 inhibitors + CKD

SITAGLIPTIN	- 100mg if eGFR > 50 - 50mg if eGFR 30- 50 - 25mg if eGFR < 30 - ESRD √
SAXAGLIPTIN	- 5mg if eGFR > 50 - 2.5mg if eGFR ≤ 50 - ESRD √
LINAGLIPTIN	- No dose adjustment - ESRD √
ALOGLIPTIN	- 25mg if eGFR > 60 - 12.5mg if eGFR 30- 60 - 6.25mg if eGFR < 30 - ESRD √

## SGLT-2 inhibitors + CKD

DAPAGLIFLOZIN	- Avoid if eGFR < 60
EMPAGLIFLOZIN	- Avoid if eGFR < 45

Advise all patients to cease SGLT2 inhibitors if they have nausea, vomiting, abdominal pain or are fasting for a procedure

## GLP-1 receptor agonists

EXENATIDE	- Not recommended if eGFR < 30 - Avoid in ESRD
DULAGLUTIDE	- No dose adjustment - OK in ESRD
LIRAGLUTIDE	- No dose adjustment - Cautious use in ESRD - Only limited studies in patients with eGFR < 30

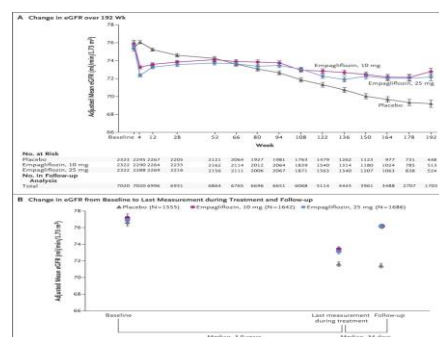
## T2D + CKD

PIOGLITAZONE	- No dose adjustment - Watch for fluid retention - ESRD OK with caution
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## Alpha-glucoside inhibits + CKD

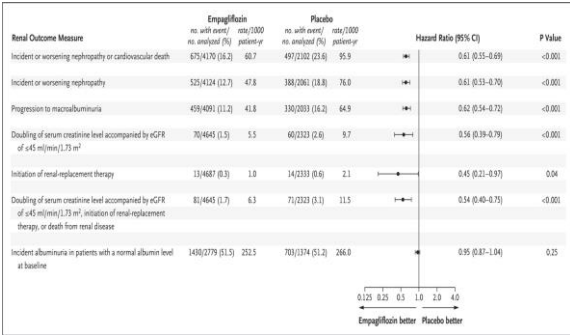
ACARBOSE	- Avoid if eGFR < 30
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## Change in eGFR with empagliflozin (EMPA-REG STUDY)



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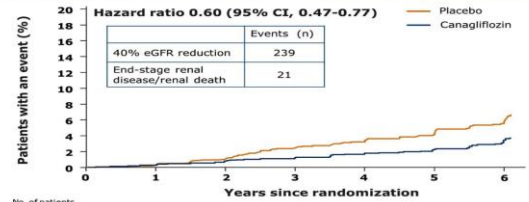
## Renal outcomes in EMPA-REG



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## Renal outcomes in CANVAS

### Composite of 40% Reduction in eGFR, End-stage Renal Disease, or Renal Death



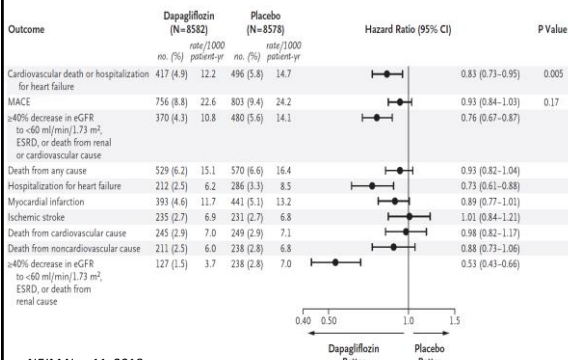
No. of patients	Placebo	Canagliflozin
4227	5664	3029
1274	2654	1229
1173	2495	1173
919	1781	919

Presented at the 72nd Scientific Sessions of the American Diabetes Association, June 12, 2017, San Diego, CA.

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CANVAS Program

## Renal outcomes in DECLARE



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