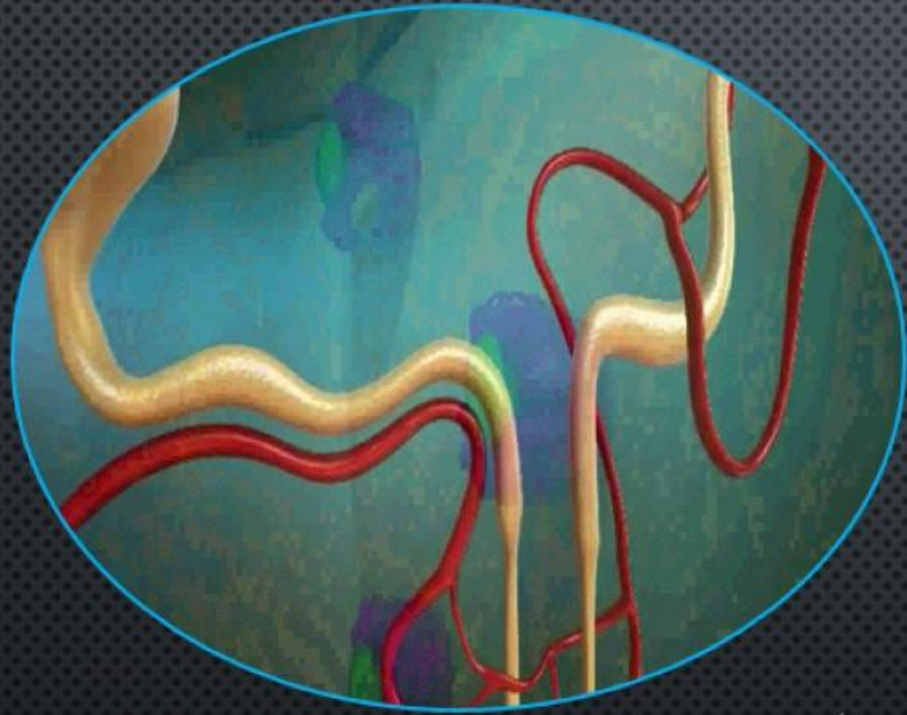


SGLT2 INHIBITORS AND CV SAFETY



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San Antonio, Texas
Associate program director interventional cardiology
Director catheterization lab UT / clinical proteomics



CONFLICTS:

**BALANCED BETWEEN ALL COMPANIES RELATED TO
SGLT2 INHIBITORS**



OBJECTIVES

- UNDERSTAND OFF TARGET EFFECTS OF SGLT2 INHIBITORS
- UNDERSTAND BENEFITS OF SGLT2 INHIBITORS ON CV DISEASE
- BENEFITS OF KIDNEY PROTECTION
- GUIDELINES: ONLY APPROVED FOR TYPE 2 DIABETES PATIENTS



SAFETY

Hypotension

Lactic acidosis

Renal

Amputations

UTI

Bone fractures

Fournier gangrene



WHAT IS THE INCIDENCE OF **FOURNIER
GANGRENE PER 100,000 PATIENTS?**

1. <1%
2. 1-3%
3. 4-5%
4. 6-10%

Answer 1-3%



Fournier gangrene (flesh eating infection): fatigue/fever/swelling/skin redness

Necrotizing fasciitis of the perineal soft tissue (external genitals/anus)

Death

Incidence FDA adverse reporting site (2017)

Canaflozin-21 patients

Dapagliflozin-16 patients

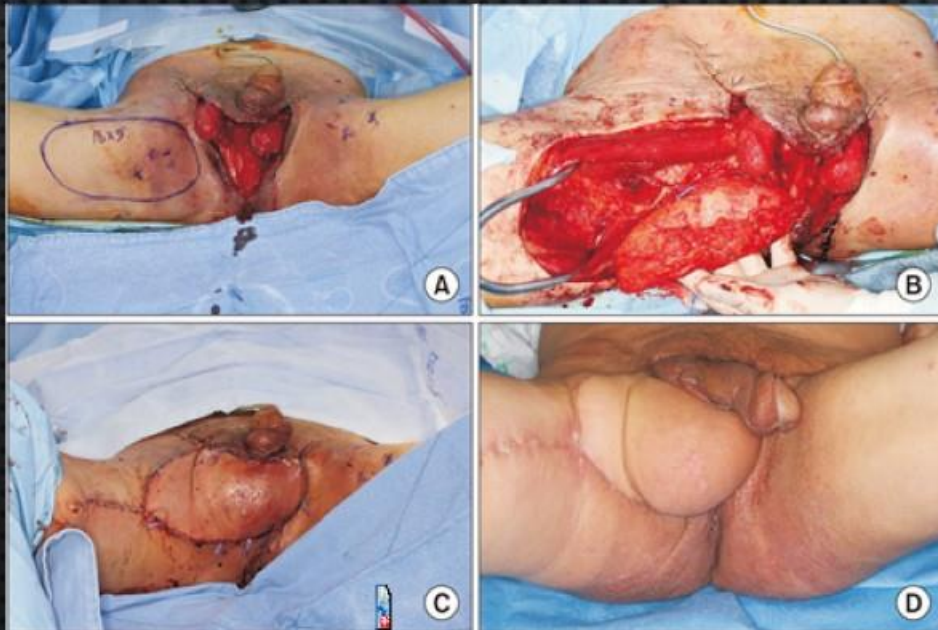
Empagliflozin-18 patients

Incidence: 1.6 – 3.0 men in every 100,000

More common in men

Treatment: antibiotics / surgery

Possibly: streptococcus and Escherichia coli being most common organisms



J Cutan Aesthet Surg 2012;5:273-6

Ann Surg Treat Res. 2018 Dec;95(6):324-332



SAFETY

Hypotension

Lactic acidosis

Renal

Amputations

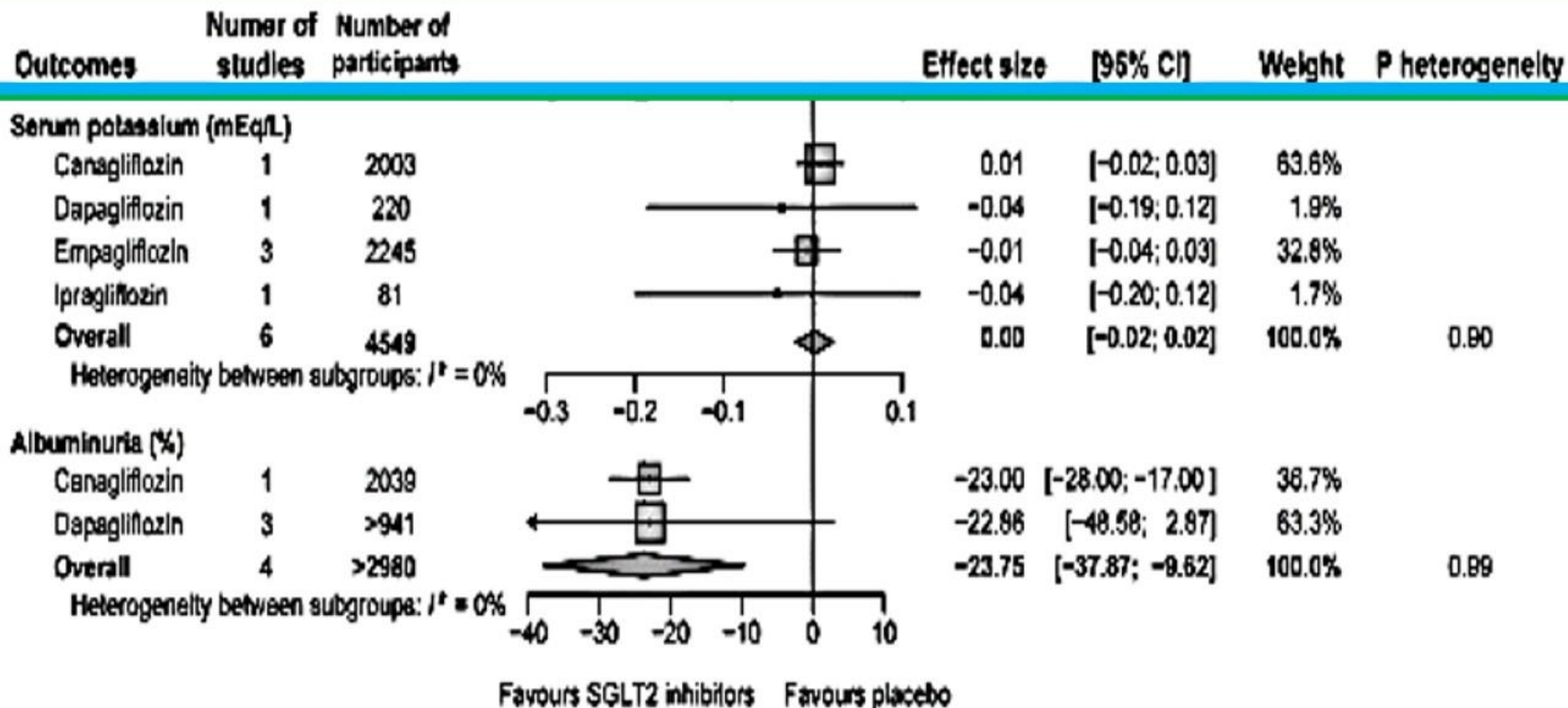
UTI

Bone fractures

Fournier gangrene



Patients with diabetes and chronic renal disease (<60 cc/min)



WHAT IS THE % RELATIVE RISK REDUCTION WITH SGLT2 INHIBITORS FOR ACUTE KIDNEY INJURY

1. 10%
2. 25%
3. 45%
4. NO BENEFIT

Answer 25%



WHAT IS THE % RELATIVE RISK REDUCTION WITH SGLT2 INHIBITORS FOR END STAGE RENAL DISEASE

1. 15%
2. 35%
3. 45%
4. NO BENEFIT

Answer 35%



SGLT2 inhibitors **protect** kidney

38 723 participants

>252 required dialysis or transplantation or died of kidney disease

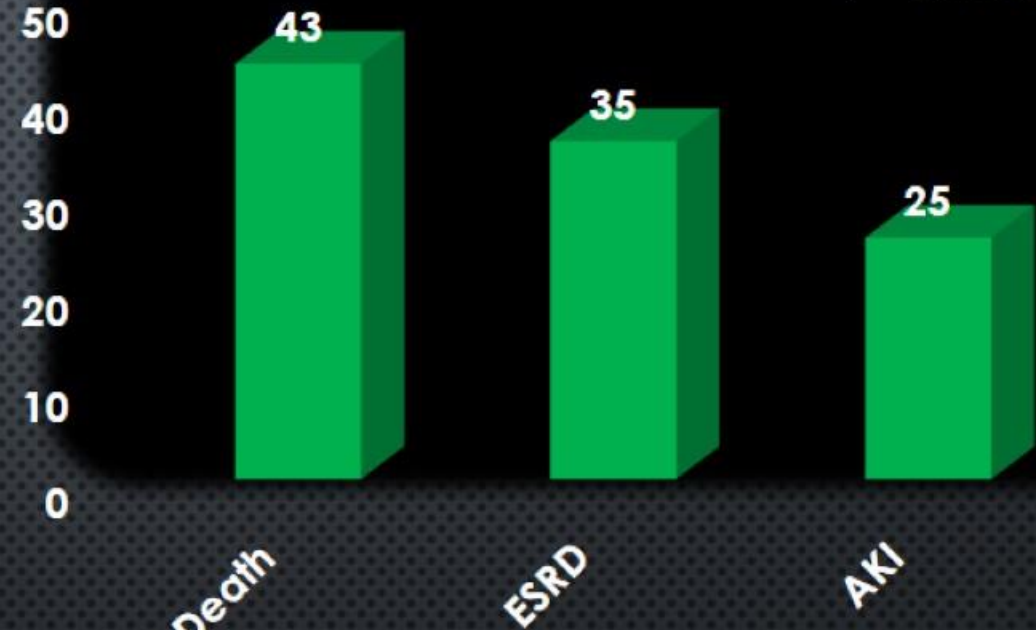
>335 developed end-stage kidney disease

>943 had acute kidney injury

43% reduction in the risk of dialysis, transplantation, or death due to kidney disease (RR 0.57, 95% CI 0.52–0.86, p=0.0019)

% REDUCTION with SGLT2 inhibitors

P<0.0001



Dialysis-Transplant-Death

ESRD

AKI

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SGLT2 inhibitors for the prevention of kidney failure in patients with type 2 diabetes: a systematic review and meta-analysis

Abstract: Niu, Yanyan; Wang, Xiang; Li, Hongbin; Ren, Xue; Zhao, Fuxun; Li, Jun; Li, Jun; Research, W. Medicine; David, J. Clayton, David C. Wheeler; Clive A. Evans; Srinivas Sampath; Adnan L. Khan; Vijay J. Jandev

Summary
Background The effects of sodium glucose co-transporter 2 (SGLT2) inhibitors on kidney failure, particularly the need for dialysis or transplantation or death due to kidney disease, is uncertain. Additionally, previous studies have been underpowered to reliably assess heterogeneity of effects on kidney outcomes by different levels of estimated glomerular filtration rate (eGFR) and albuminuria. We aimed to do a systematic review and meta-analysis to assess the effects of SGLT2 inhibitors on major kidney outcomes in patients with type 2 diabetes and to determine the consistency of effect size across trials and different levels of eGFR and albuminuria.

Lancet Diabetes Endocrinol 2019, 7, 463-74
Published Online November 5, 2019
http://dx.doi.org/10.1016/S2213-8588(19)30264-8
See Comment page 470

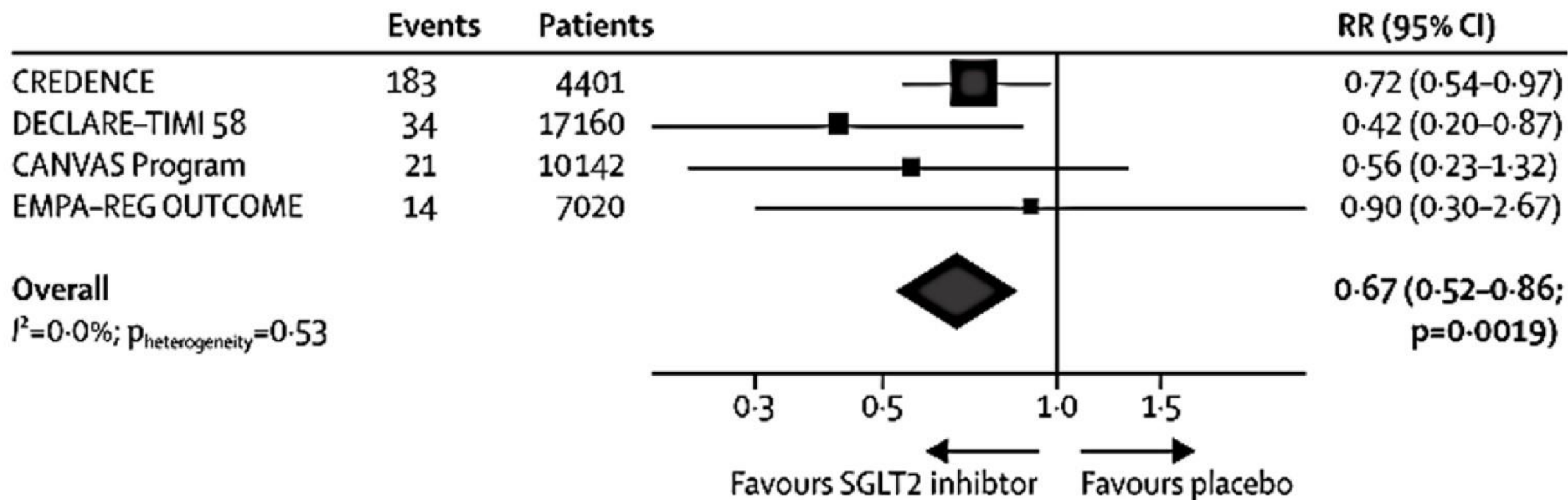
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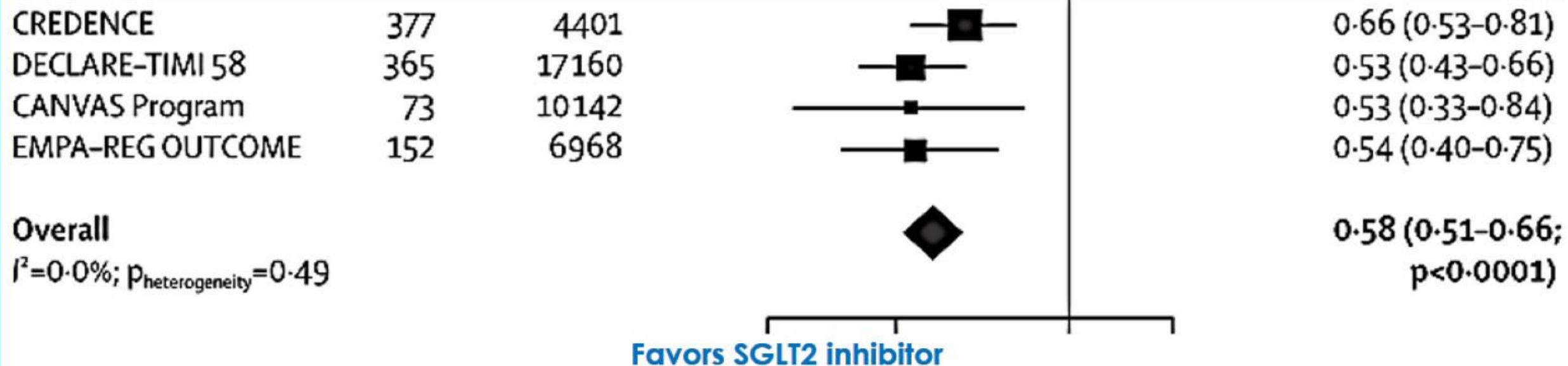
Effect of SGLT2 inhibitors on dialysis, transplantation, or death due to kidney disease



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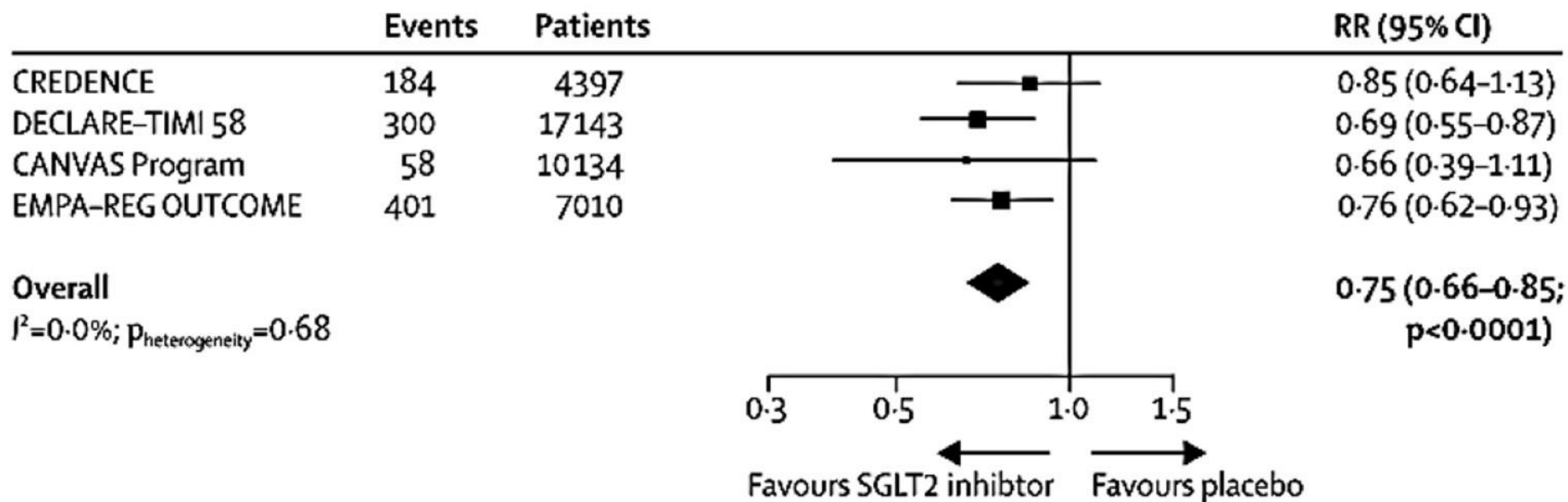
B Substantial loss of kidney function, ESKD, or death due to kidney disease



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Beneficial effect of SGLT2 inhibitors on acute kidney injury

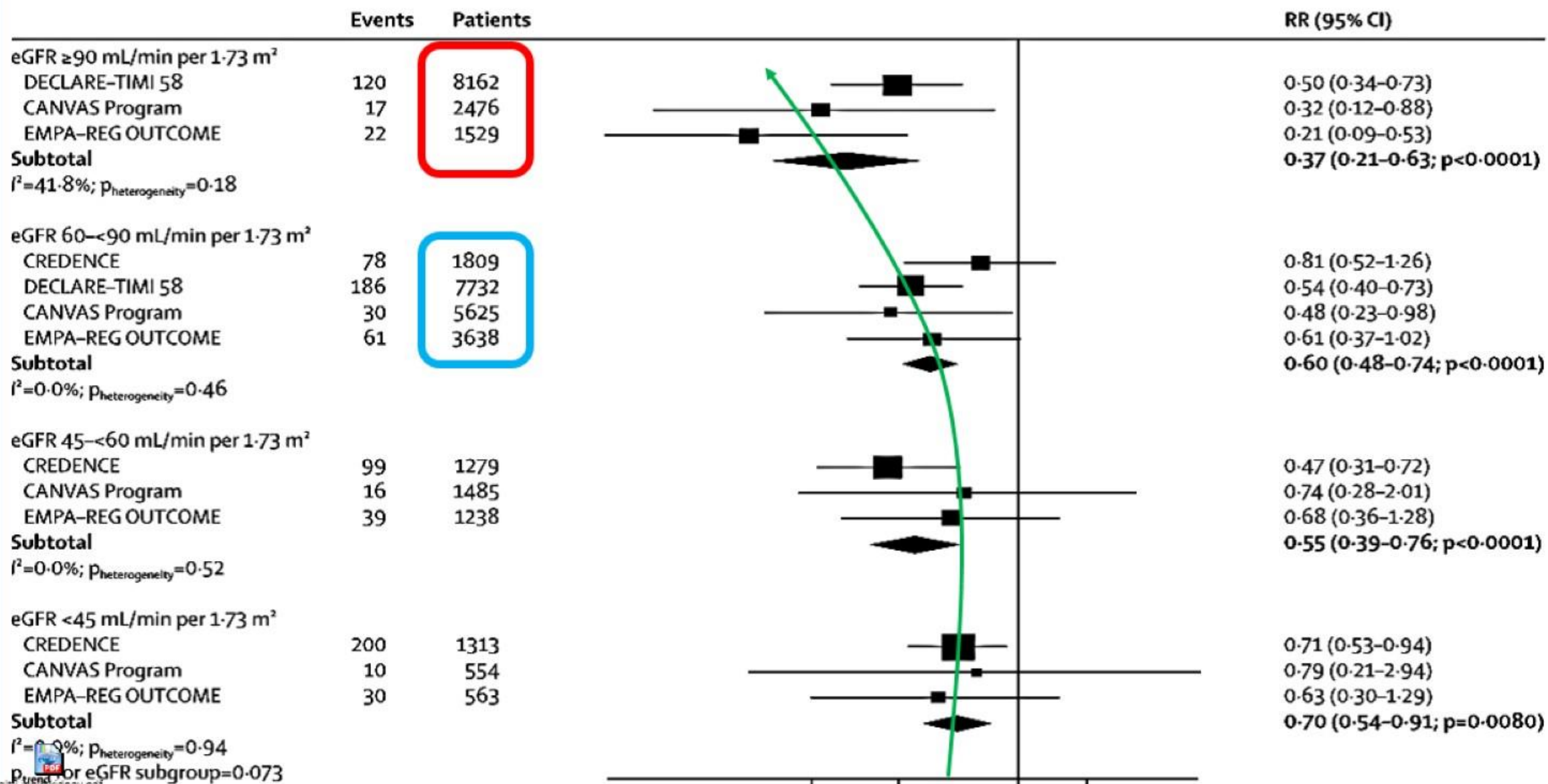


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More benefit seen in high GFR patients

A



RAS inhibition patients appear to do better with SGLT2 inhibitors

RAS blockade*

CREDESCENCE	377	4401
DECLARE-TIMI 58	317	13950
CANVAS Program†	209	8113
EMPA-REG OUTCOME	125	5627

Subtotal

$I^2=8.7\%$; $p_{\text{heterogeneity}}=0.35$

No RAS blockade

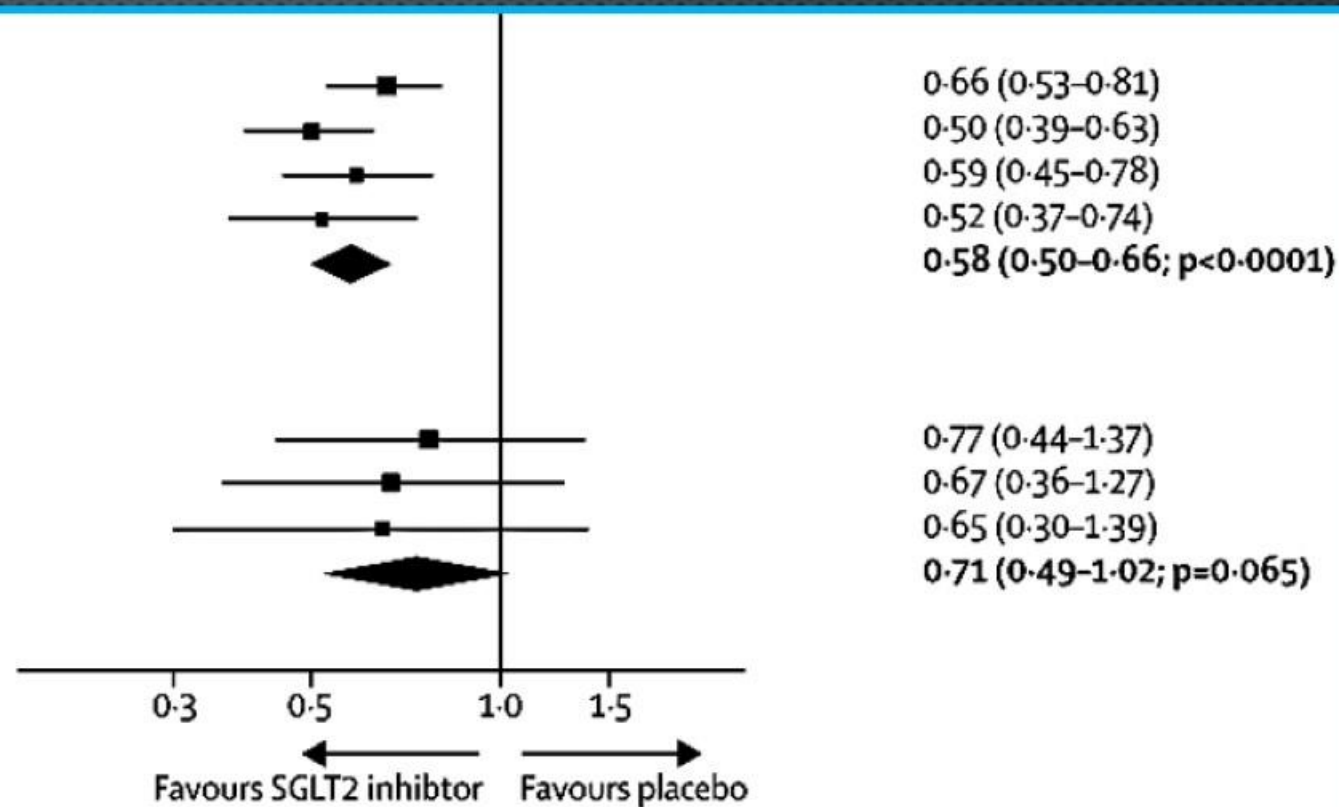
DECLARE-TIMI 58	48	3210
CANVAS Program†	40	2021
EMPA-REG OUTCOME	27	1341

Subtotal

$I^2=0.0\%$; $p_{\text{heterogeneity}}=0.92$

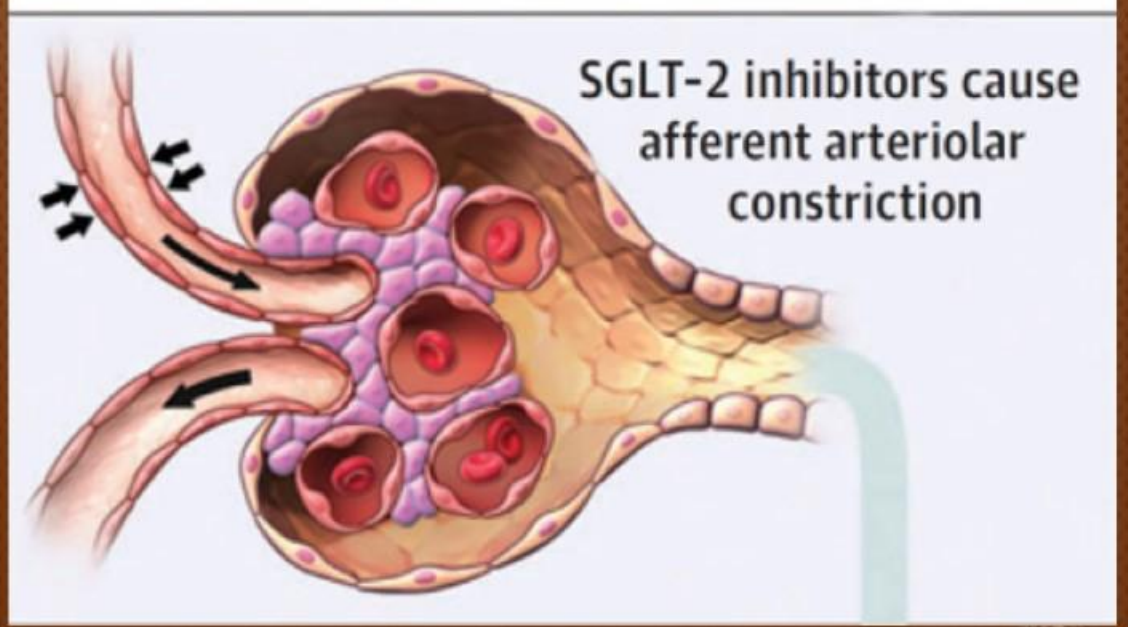
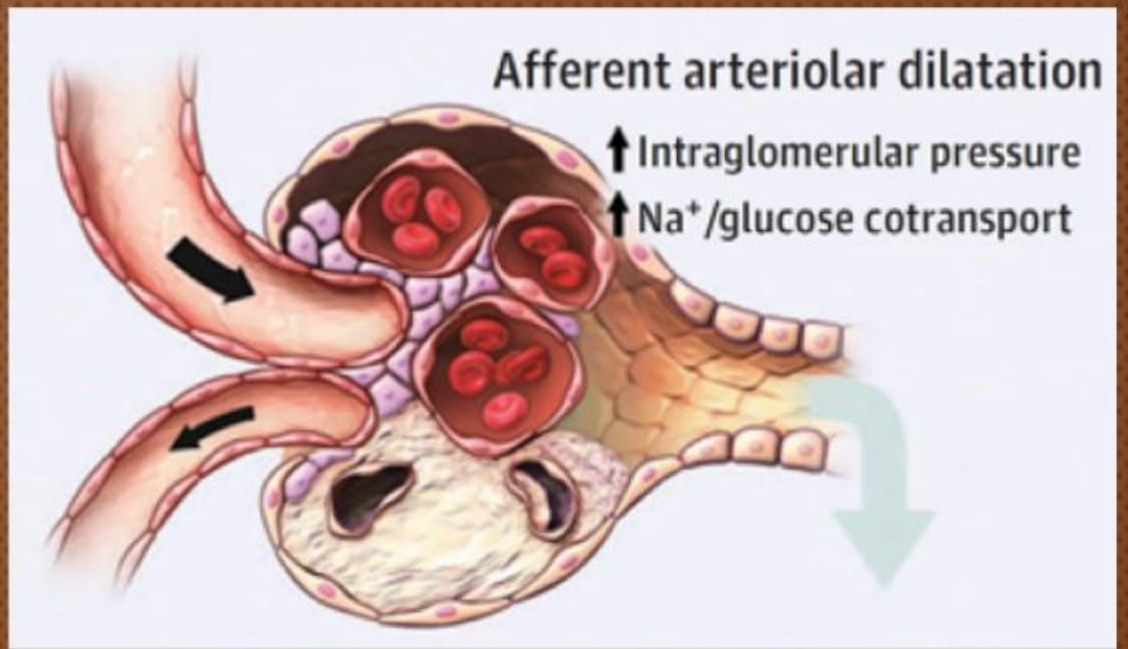
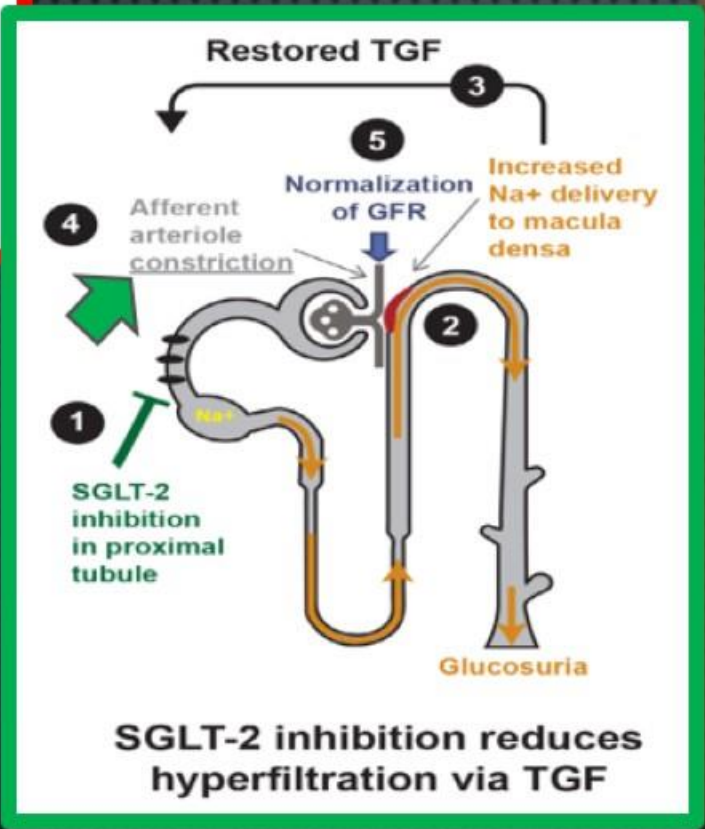
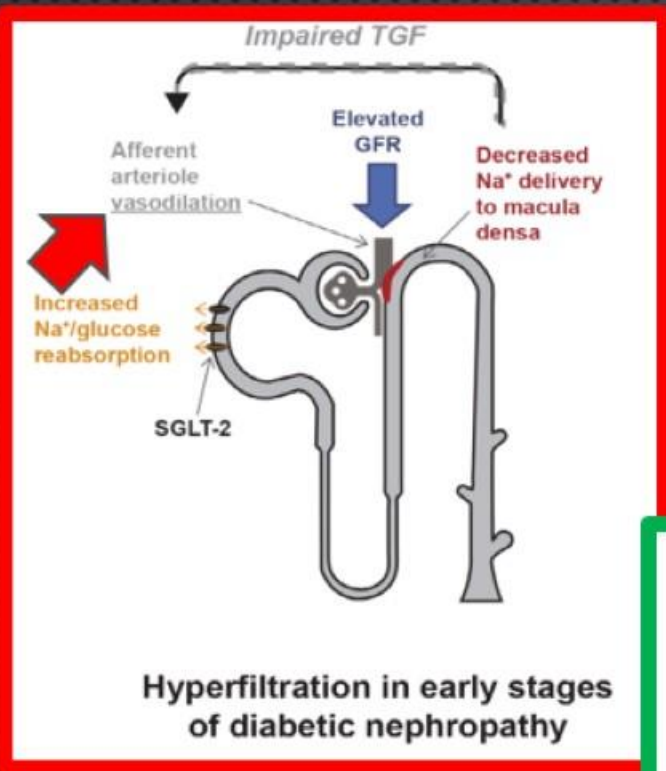
$p_{\text{heterogeneity}}$ for use of RAS inhibition=0.31

Numbers are lower

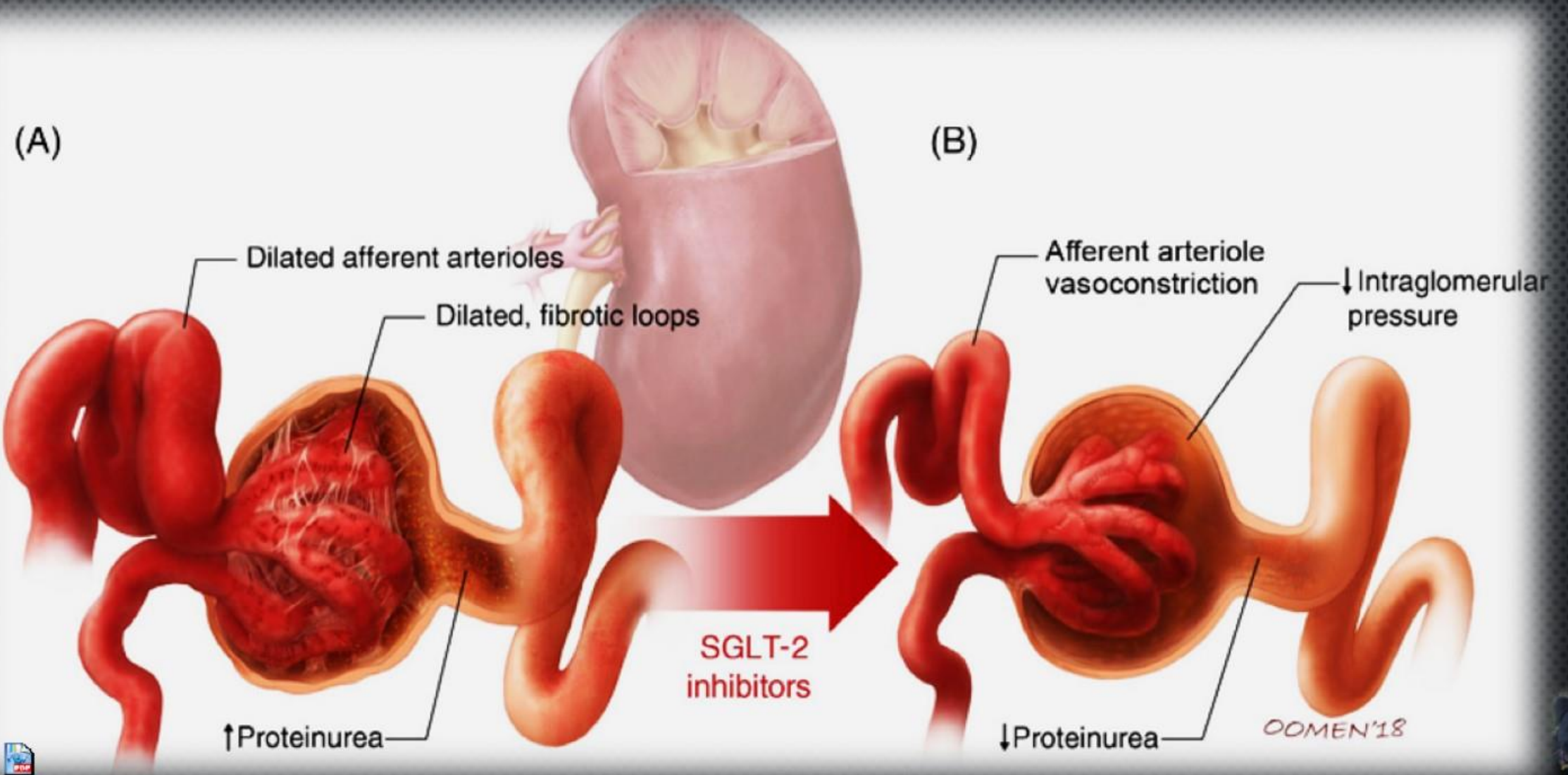


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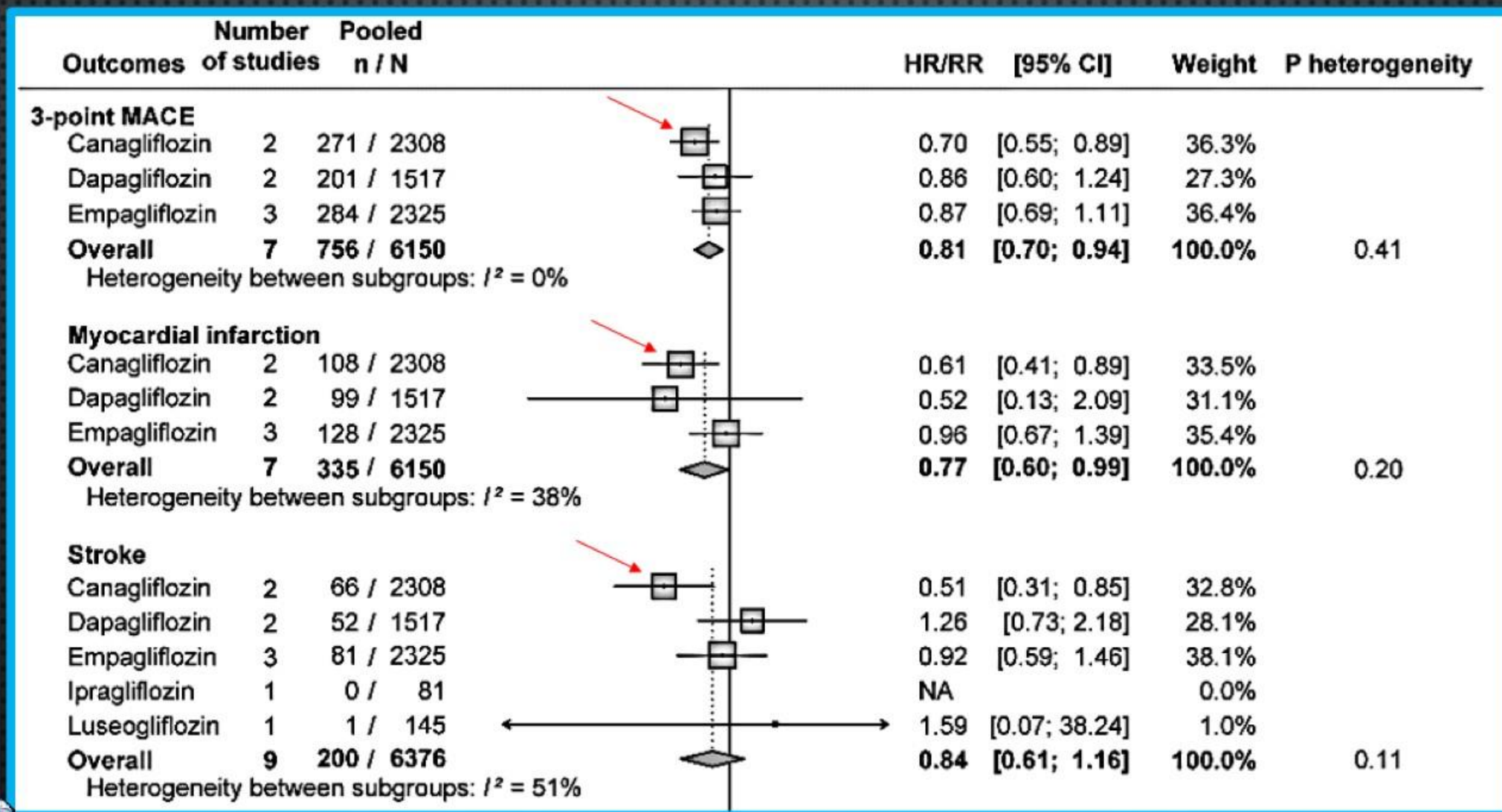




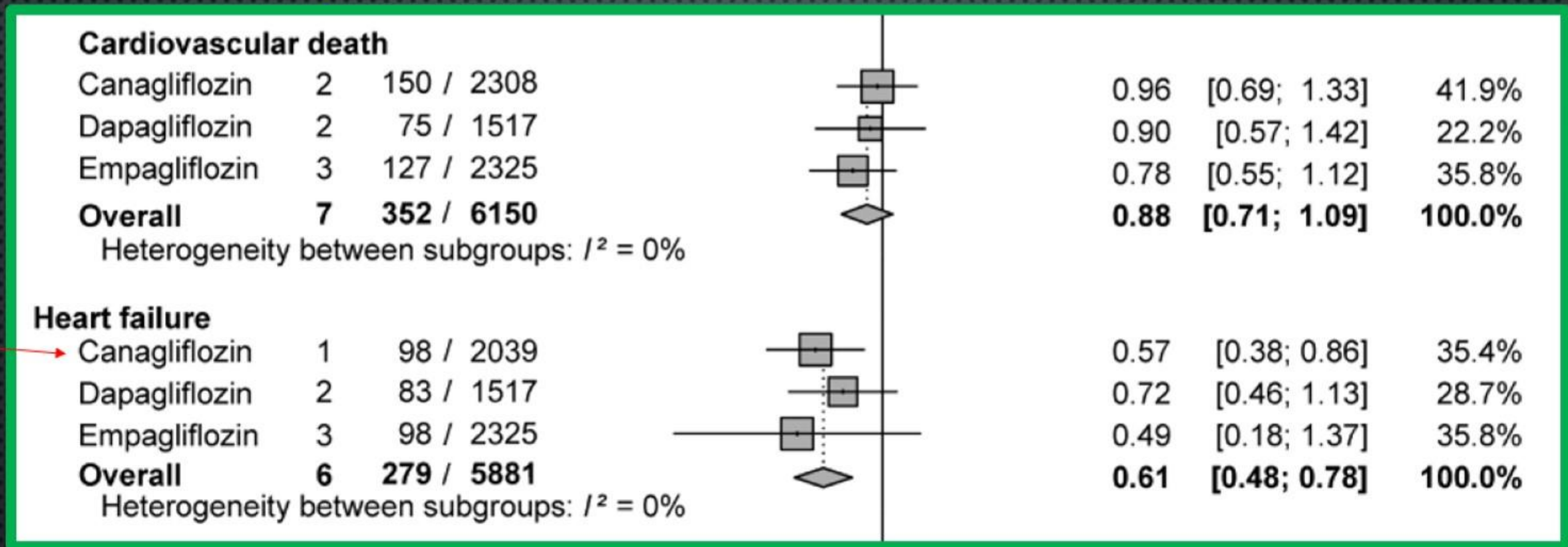
Summary of kidney protection with SGLT2 inhibitors



SGLT2 inhibitors on CV outcomes and all-cause mortality in type 2 diabetes and **chronic kidney disease** GFR < 60 mL/min/1.73



SGLT2 inhibitors on CV death and heart failure in type 2 diabetes and chronic kidney disease GFR < 60 mL/min/1.73



Favors SGLT2 inhibitors



SAFETY

Hypotension

Lactic acidosis

Renal

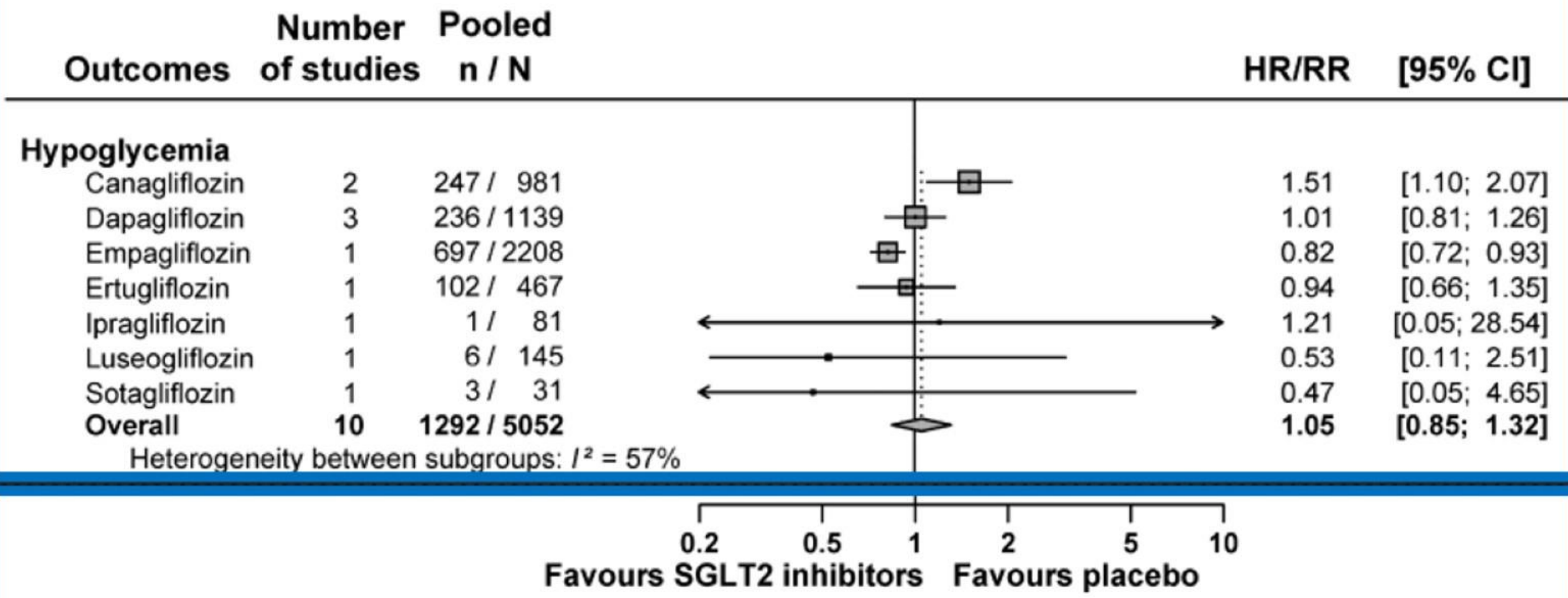
Amputations

UTI

Bone fractures

Fournier gangrene

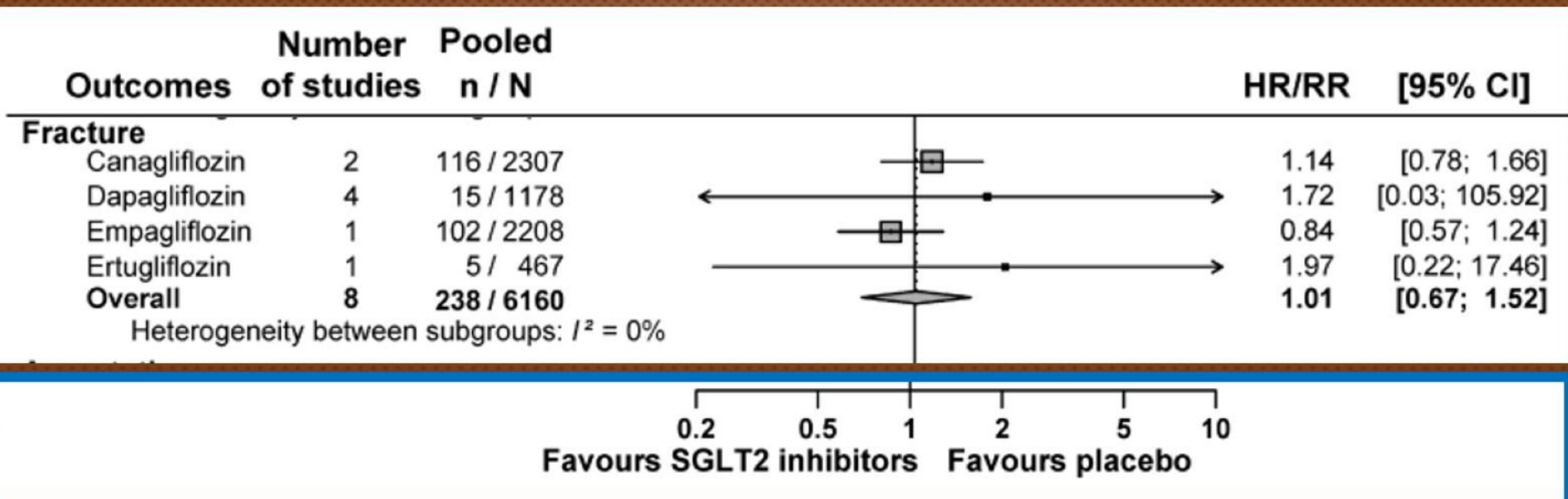




Diabetes Obes Metab. 2019;21:1237 – 1250



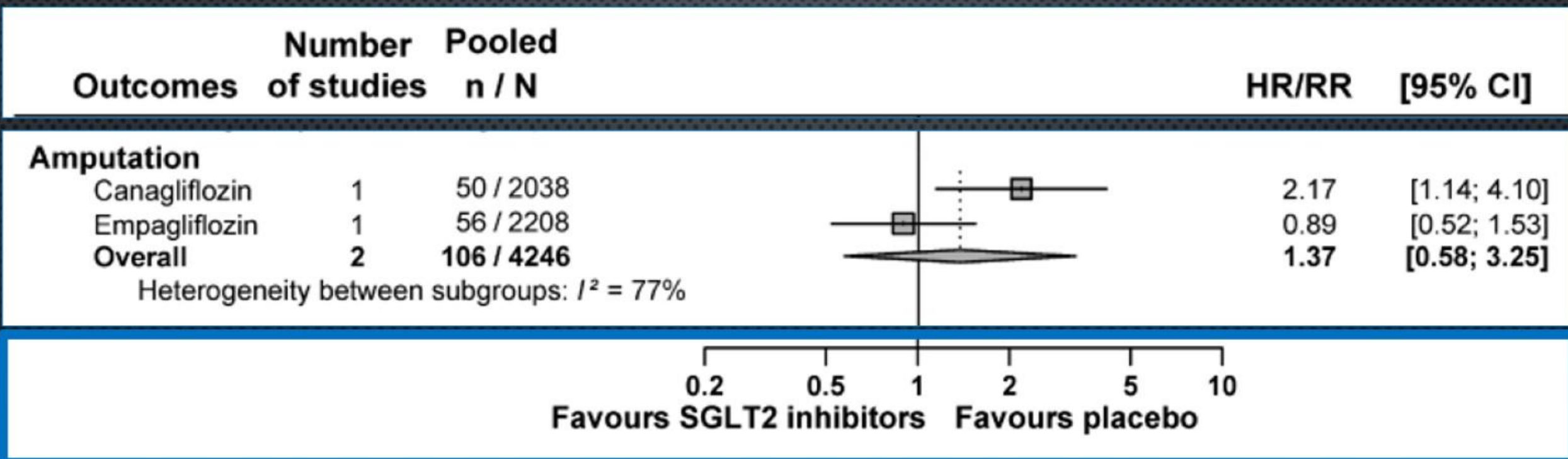
No safety problem seen



Diabetes Obes Metab. 2019;21:1237 – 1250



No apparent safety problem seen after dapa and crediance

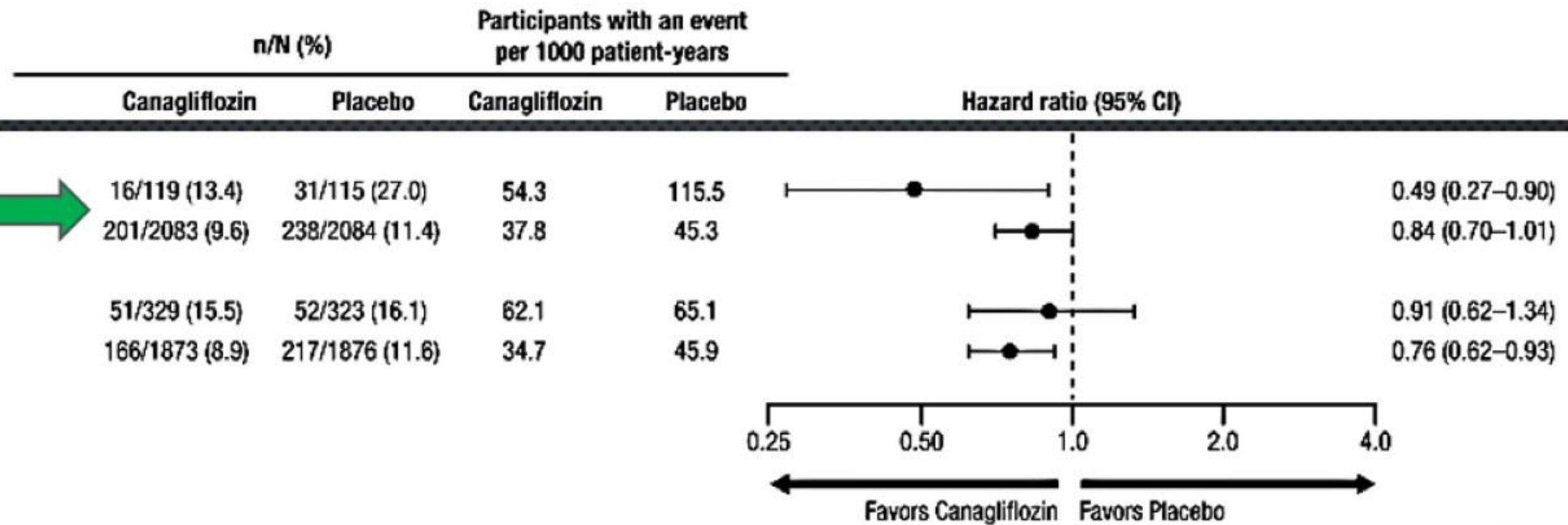


Diabetes Obes Metab. 2019;21:1237 – 1250





Canagliflozin and Cardiovascular and Renal Outcomes in Type 2 Diabetes Mellitus and Chronic Kidney Disease in Primary and Secondary Cardiovascular Prevention Groups
Results From the Randomized CREDENCE Trial



WHAT IS THE % INCREASE IN URINARY TRACK INFECTIONS WITH SGLT2 INHIBITORS

1. 10%
2. 25%
3. 45%
4. NO INCREASE

Answer no increase

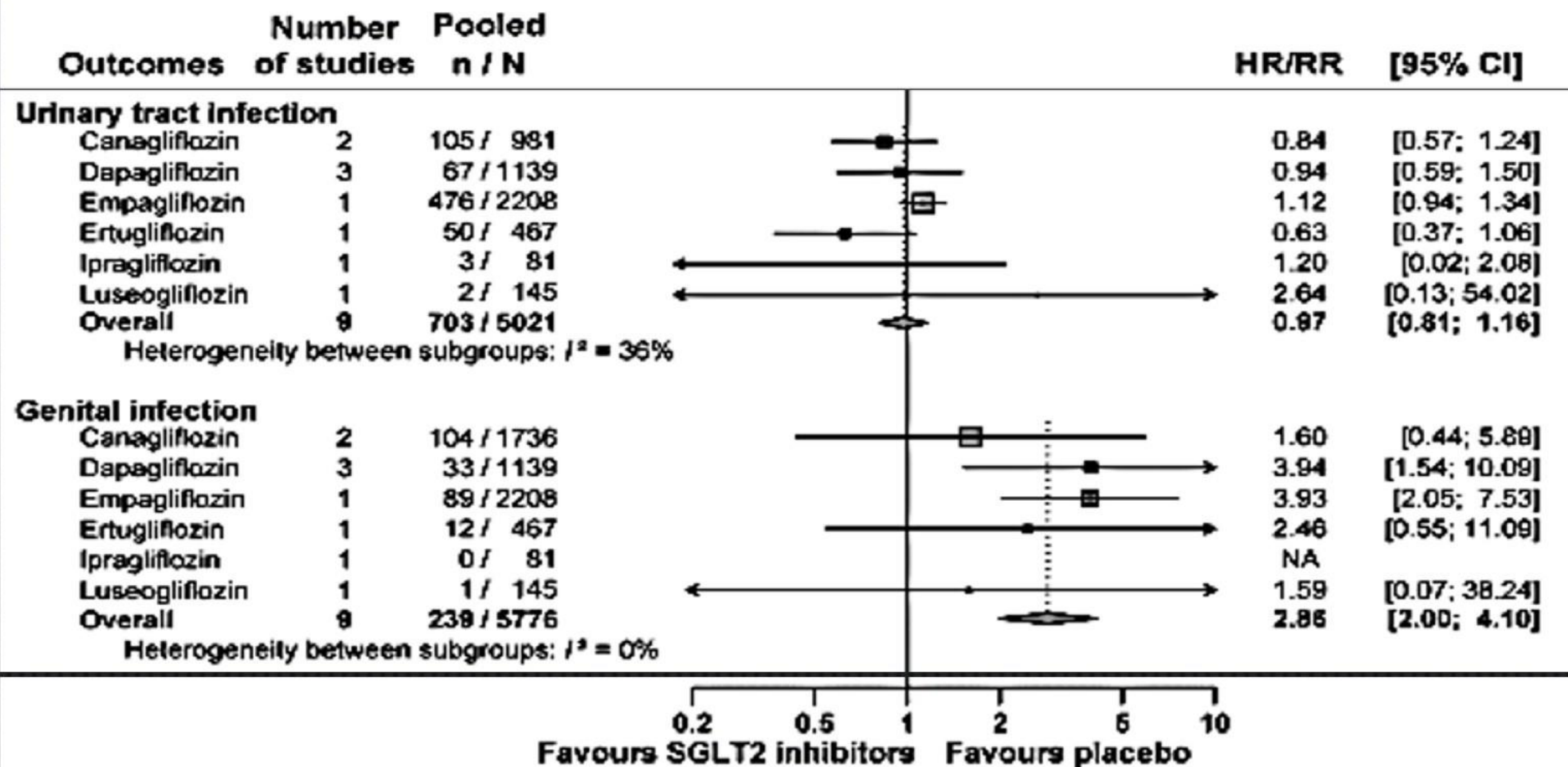


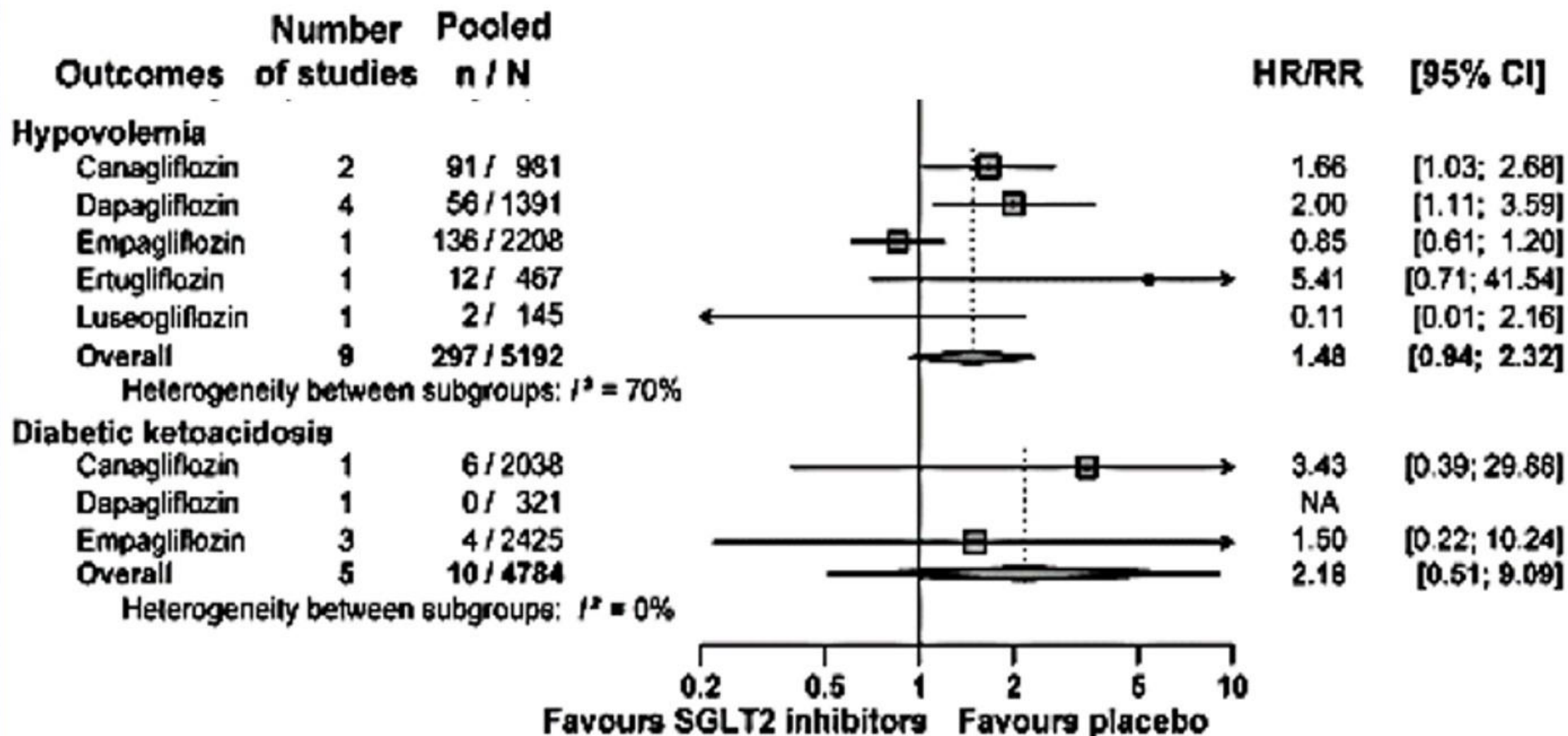
IS THERE A SIGNIFICANT INCREASE IN GENITAL INFECTIONS WITH SGLT2 INHIBITORS

1. TRUE
2. FALSE

Answer True







CLOSING HIGHLIGHTS

- **FOURNIER GANGRENE-WATCH CAREFULLY AND WARN PATIENTS ESPECIALLY MEN**
- **SGLT2 INHIBITORS SIGNIFICANTLY PROTECT THE DIABETES KIDNEY**
- **SGLT2 INHIBITORS HAVE NO INCREASE IN URINARY TRACK INFECTIONS**
- **SGLT2 INHIBITORS APPEAR TO NO LONGER HAVE CONCERN WITH AMPUTATIONS ...BUT CAUTION AND CHECK PULSES IN FEET WITH DOCUMENTED ABI ONCE YEARS ON CHART**



