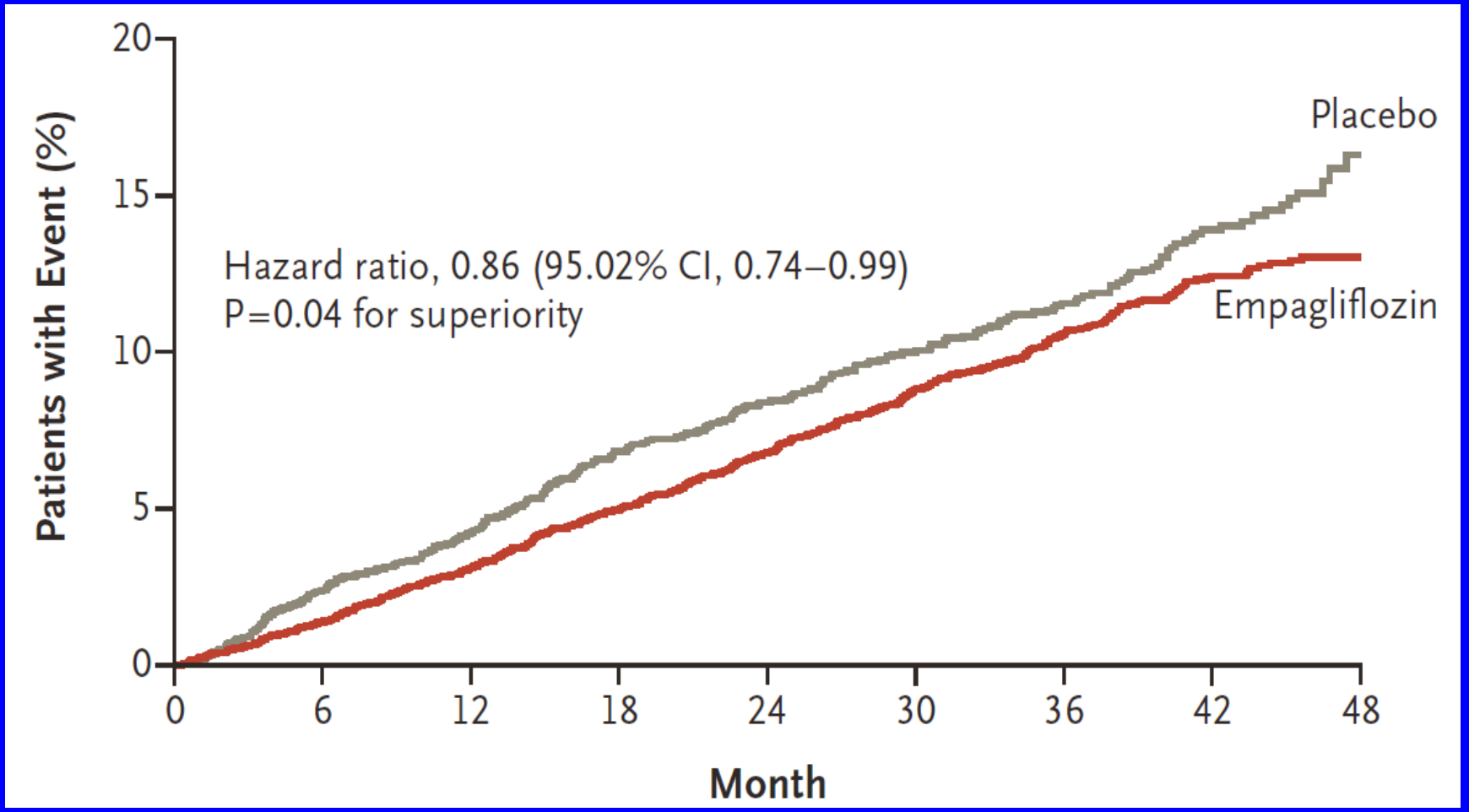


EMPA-REG Trial with Empagliflozin

- Primary end point
  - Three major adverse cardiovascular events (MACE):
    1. primary outcome of first occurrence of cardiovascular death
    2. nonfatal myocardial infarction
    3. nonfatal stroke
- Trial met criteria for both non-inferiority and superiority reduction of major adverse cardiovascular events derived from all three components of the endpoint

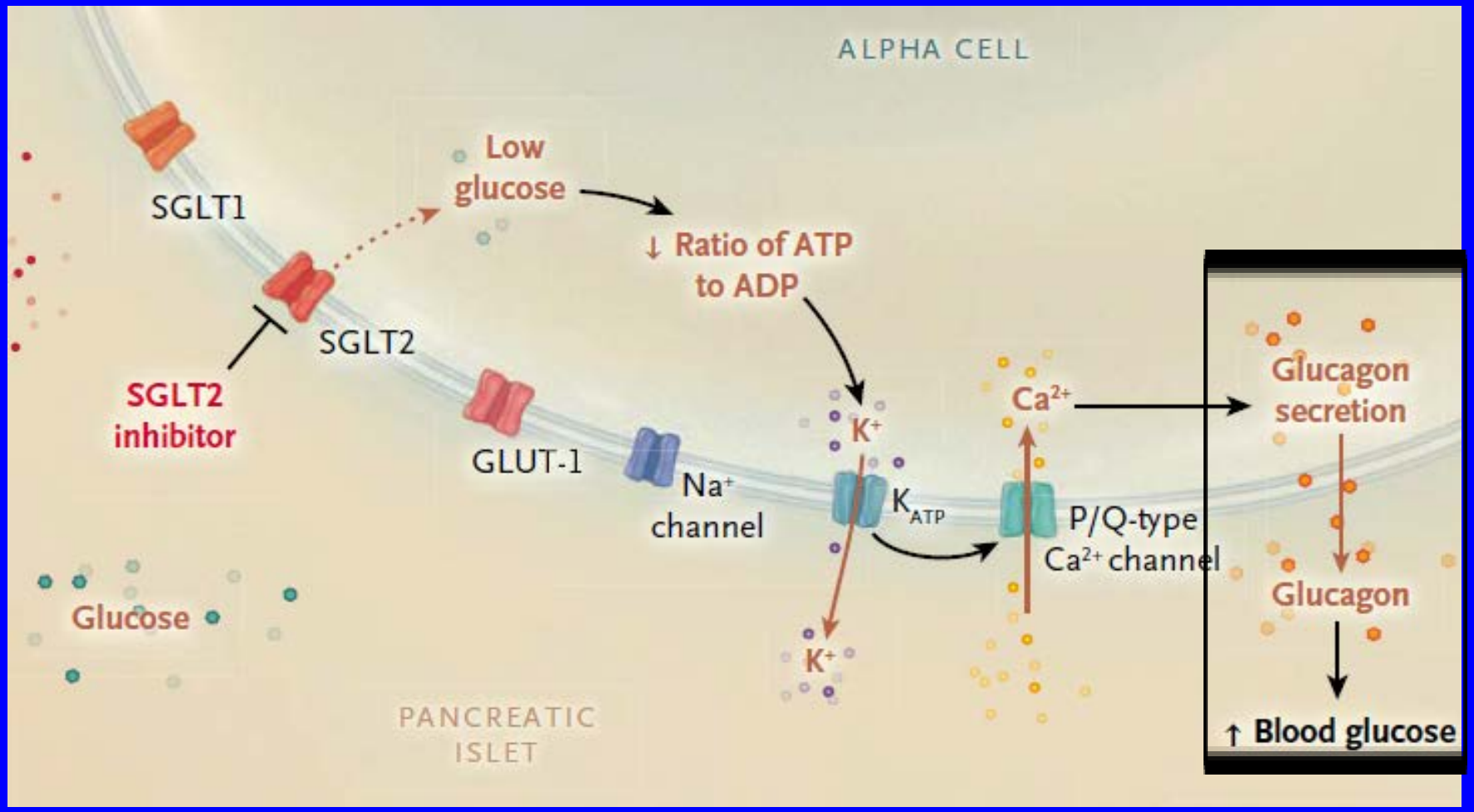
N Engl J Med 2015;373:2117-2128.

EMPA-REG Trial: Primary Outcome Empagliflozin Superiority vs. Placebo



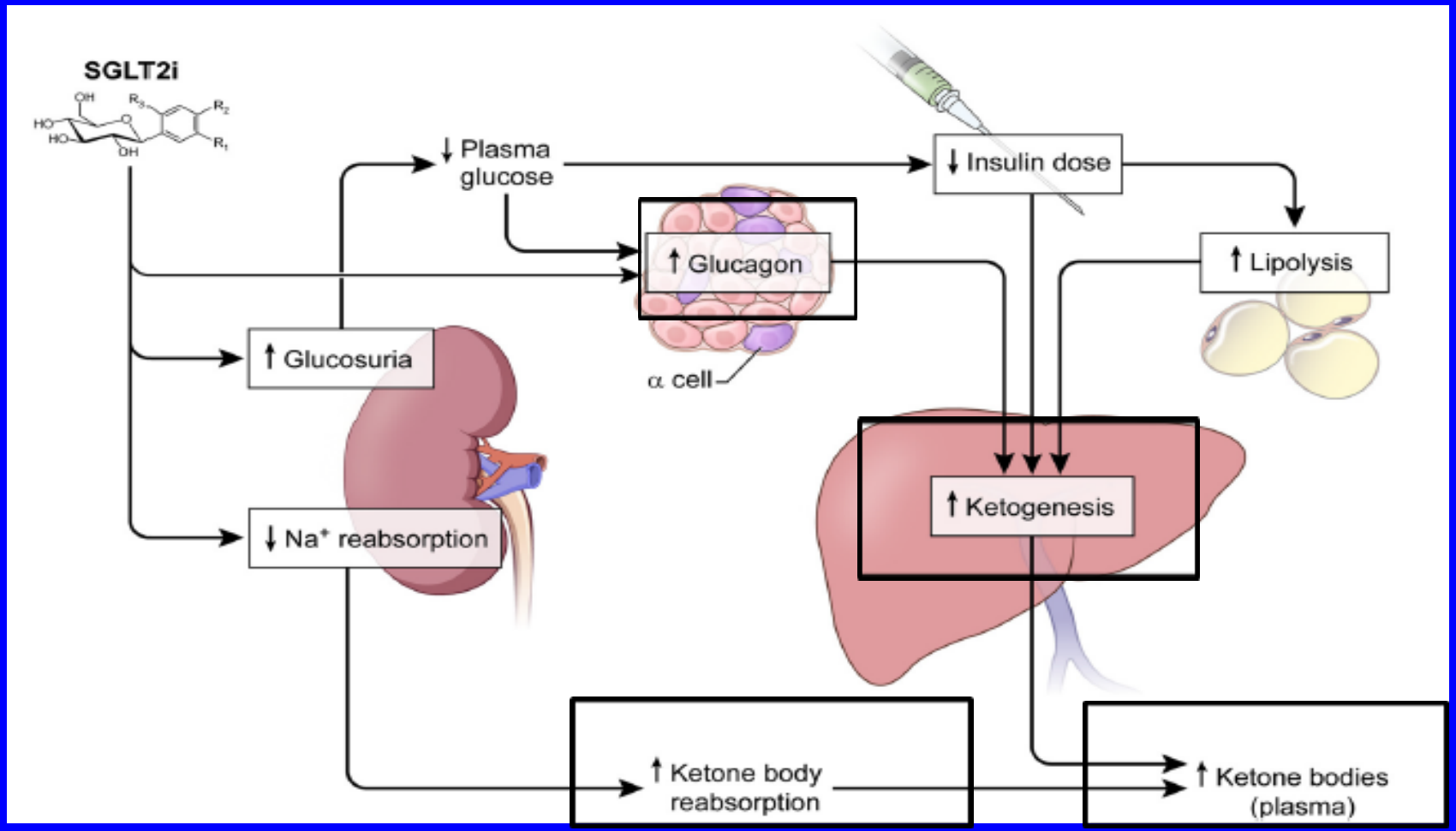
N Engl J Med 2015;373:2117-2128.

$SGLT_2$ Inhibition Increases Glucagon Secretion



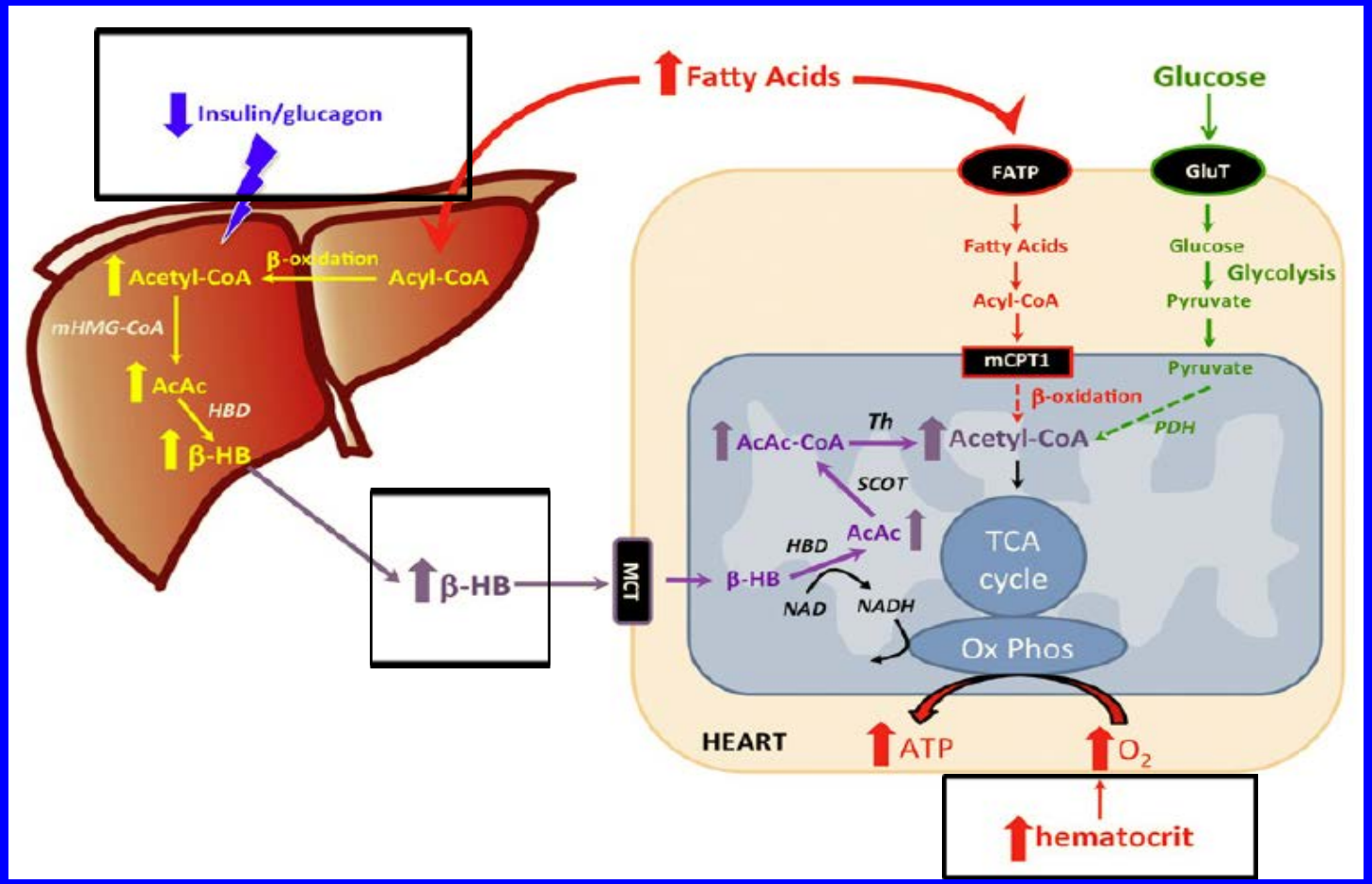
N Engl J Med 2015;373:974-976

$SGLT_2$ Inhibitors Increase Glucagon which ↑ Ketogenesis and ↑ Plasma Ketone Bodies



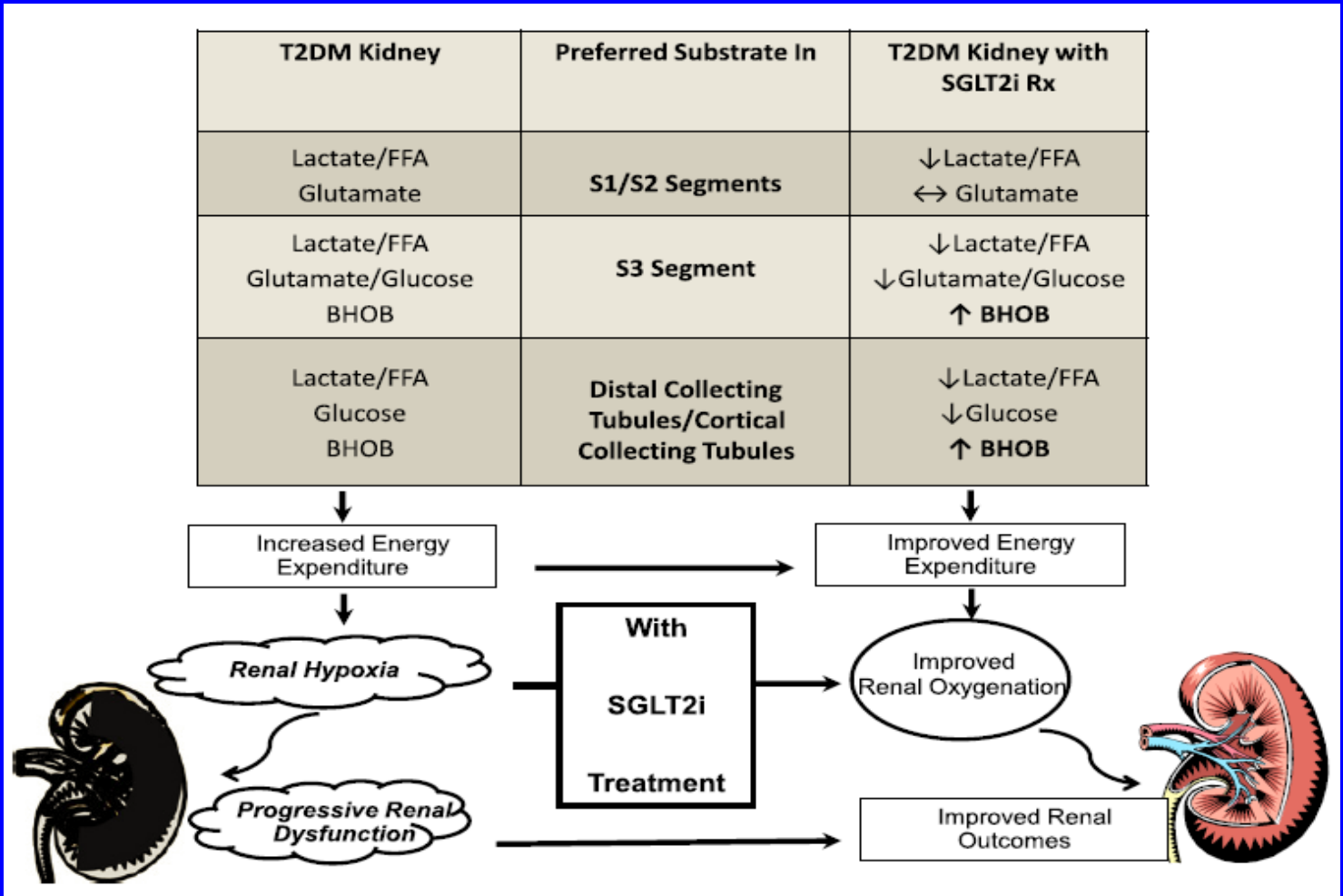
J Clin Endocrinol Metab 2015;100:2849-2852

$SGLT_2$ Inhibitors ↓ the Insulin/Glucagon Ratio -> ↑ β-Hydroxybutyrate -> A "Thrifty Substrate" Hypothesis



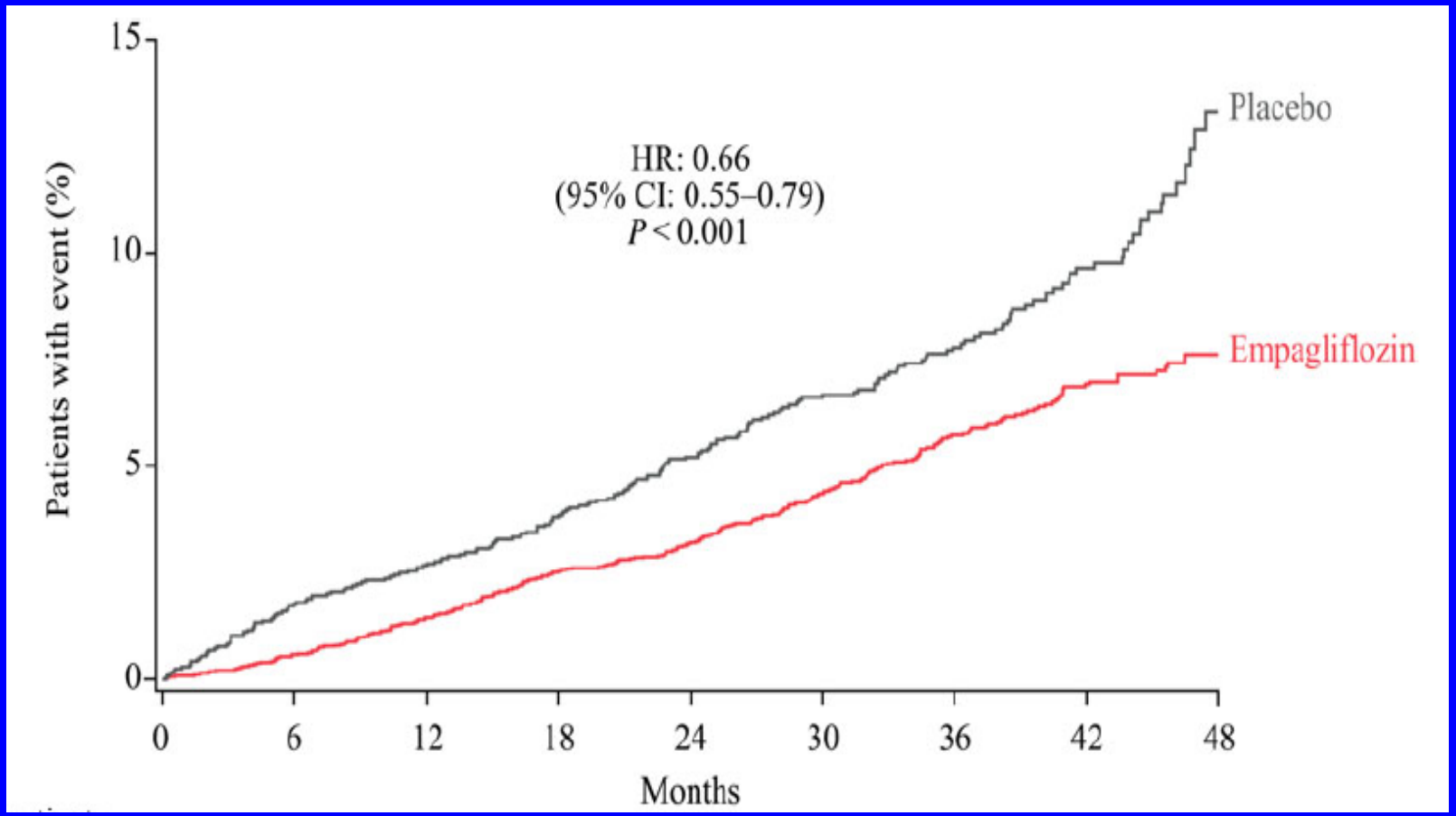
Diabetes Care 2016;39:1115-1122

$SGLT_2$ Inhibitor Therapy Improves Renal Oxygenation -> Improved Renal Outcomes



Diabetes Care 2016;39:1115-1122

Empagliflozin Associated with Slower Progression of Kidney Disease and Lower Rates of Clinically Relevant Renal Events



N Engl J Med 2016;375:323-334

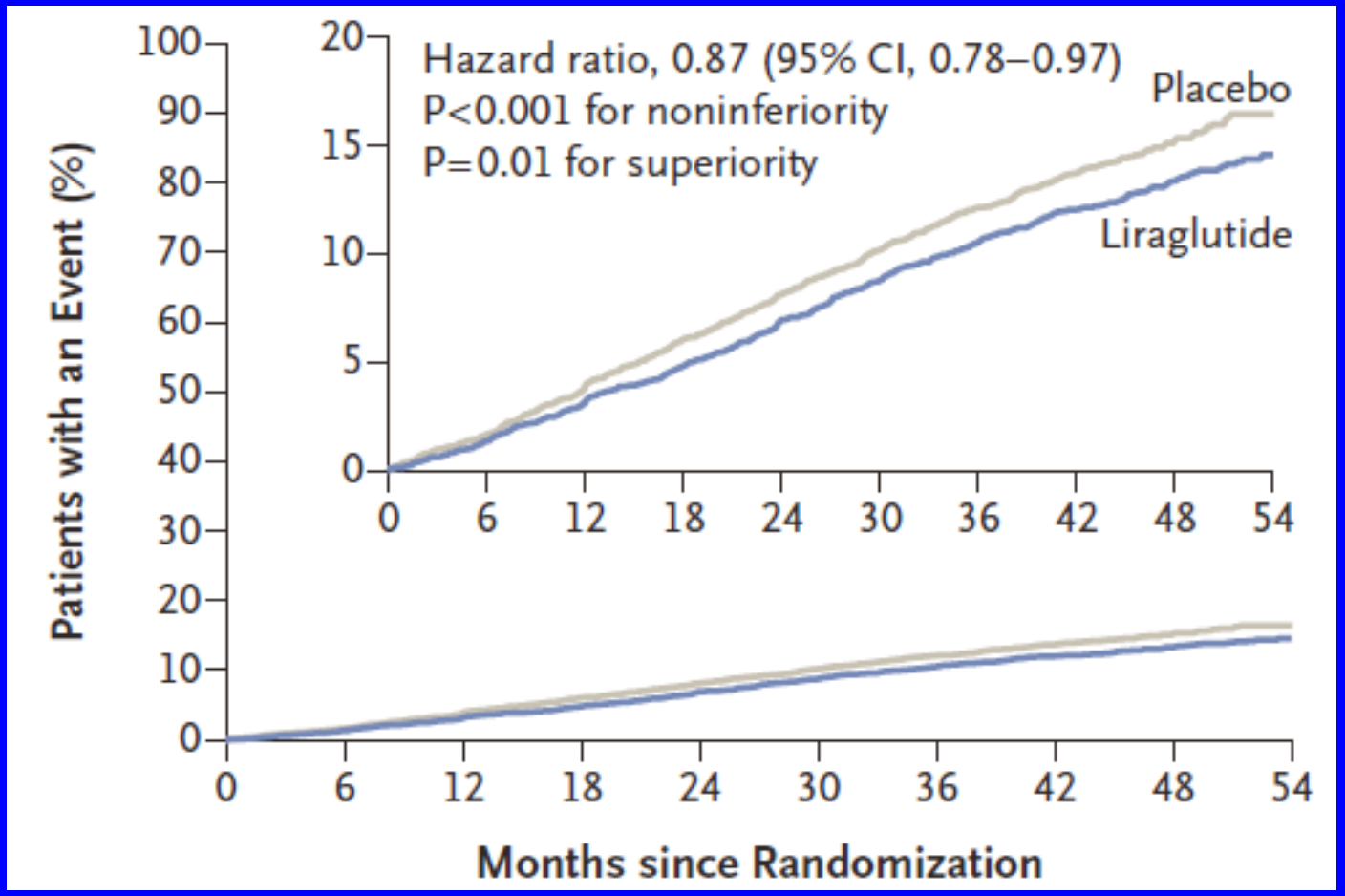
LEADER Trial: Liraglutide Effect and Action in Diabetes-Evaluation of Cardiovascular Outcome Results



- Primary end point
  - Three major adverse cardiovascular events (MACE):
    1. primary outcome of first occurrence of cardiovascular death
    2. nonfatal myocardial infarction
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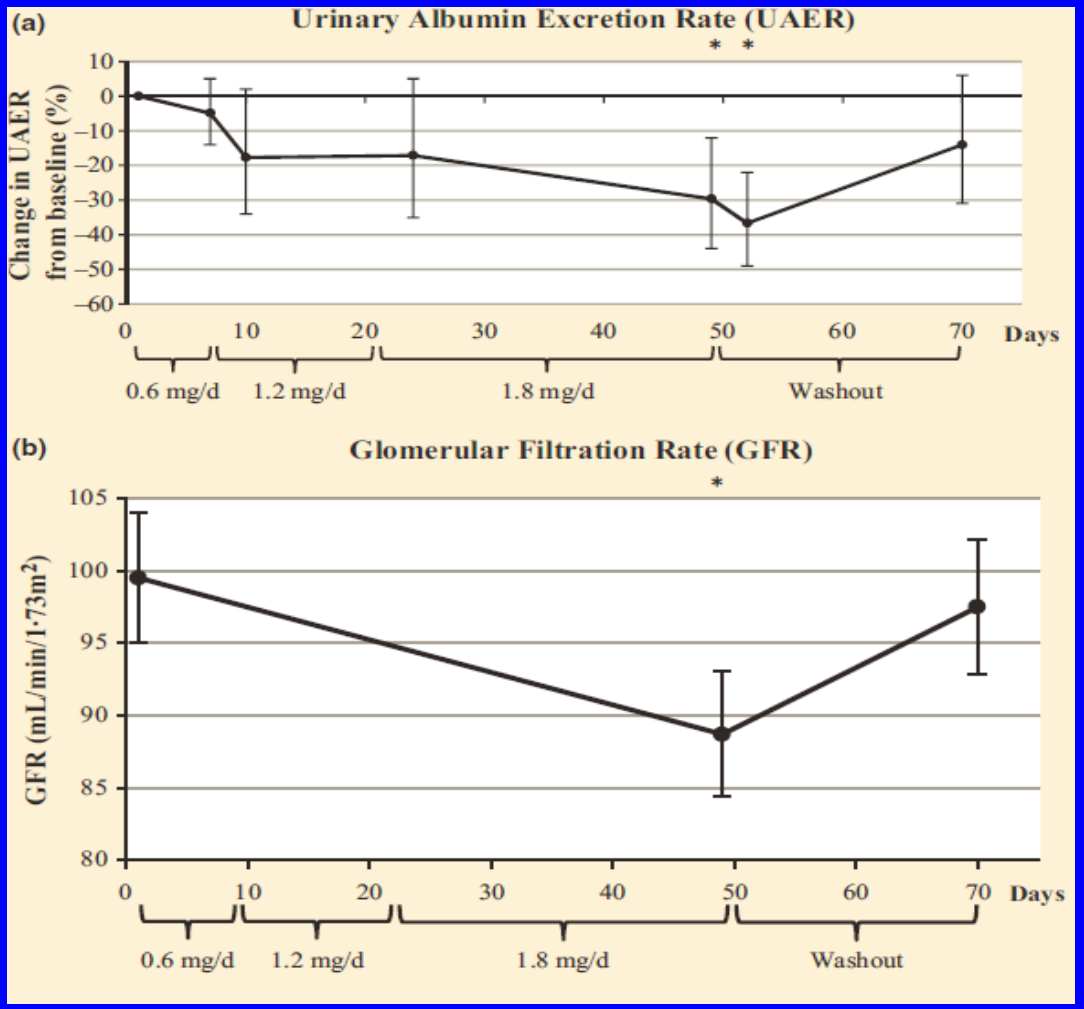
N Engl J Med 2016;375:311-322

LEADER Trial: Primary Outcome Liraglutide Superiority vs. Placebo



N Engl J Med 2016;375:311-322

Liraglutide Treatment ↓ Albuminuria and ↓ Hyperfiltration in Type 2 DM

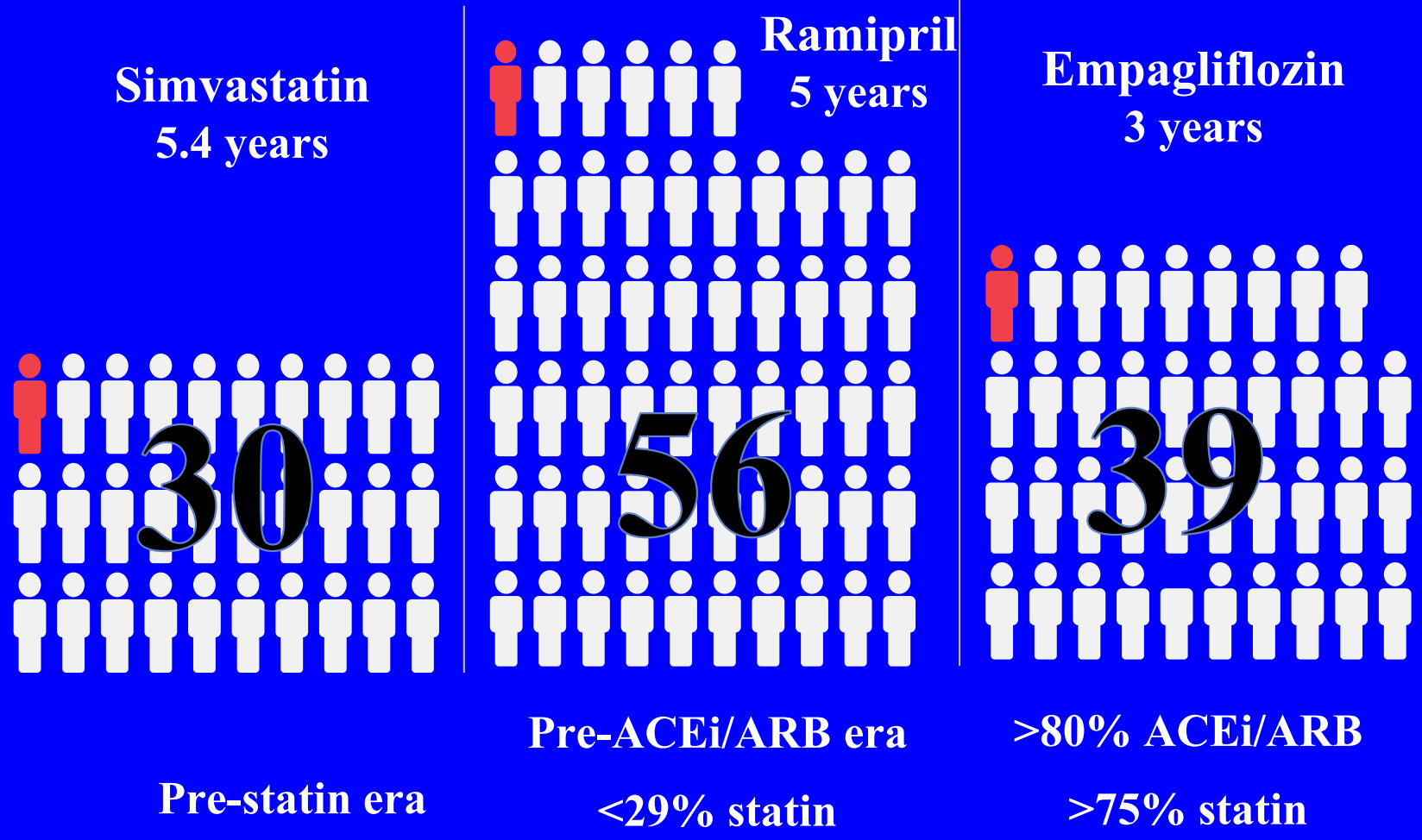


Baseline
UACR mg/g CR
32.7 (10.4-61.4)

Baseline
GFR (ml/min/1.73 m2)
99.5 (95-106)

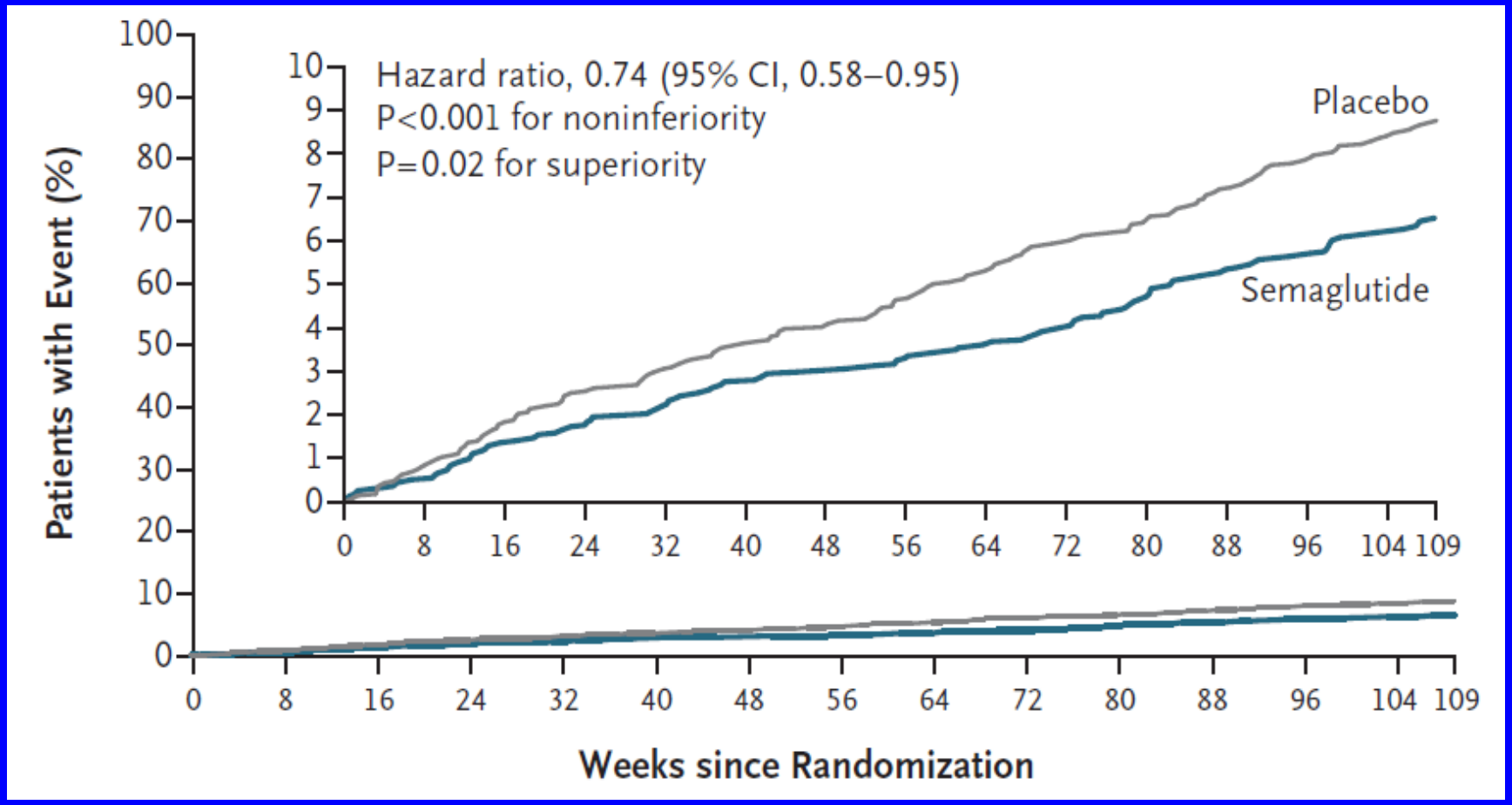
Diabet Med 2015;32:343-352

Number Needed to Treat (NNT) to Prevent ONE Death Across Landmark Trials in Patients with High Cardiovascular Risk



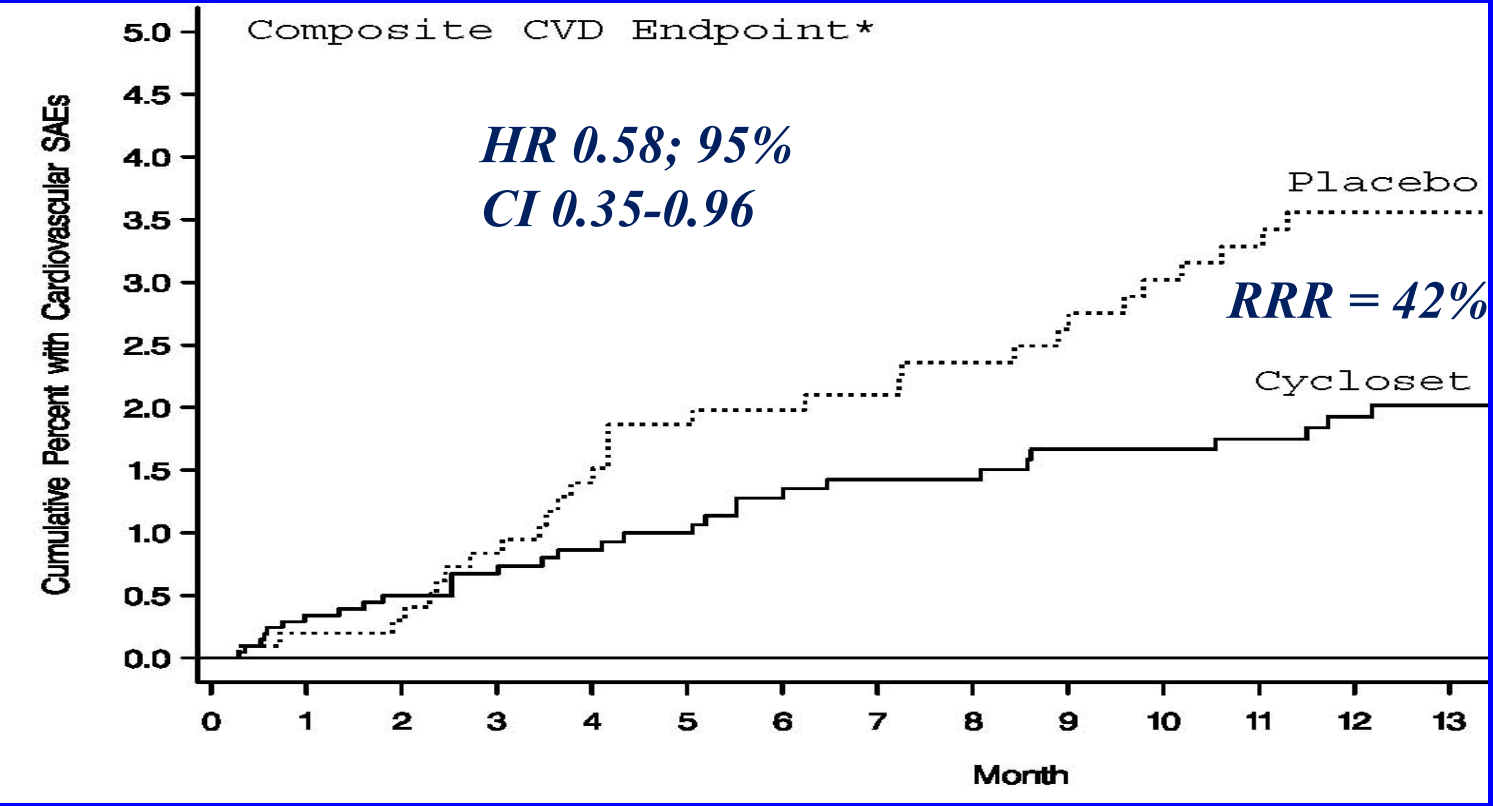
LEADER Trial with Liraglutide-NNT to prevent one death was 98

SUSTAIN-6 Trial: Primary Outcome Semaglutide Superiority vs. Placebo



N Engl J Med 2016; DOI:10.1056/NEJMoa1603827

Cycloset Demonstrated Cardiovascular Safety Profile



*MI, Stroke, hospitalization unstable angina, hospitalization CHF, or coronary revascularization

Diabetes Care 2010;33:1503-1508

Four Different Diabetes Drugs Superiority vs. Placebo in Reducing CV Events

