Evidence Gaps in Metabolic Surgery

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Presenter Disclosure

Philip R. Schauer MD

Board Member/Advisory Panel – GI Dynamics; Persona; Keyron, Mediflix
Consultant – Ethicon, Medtronic, Keyron, Novo Nordisk, Lilly, Heron
Research Support – Ethicon, NIH, Medtronic, Pacira;
Stock/Shareholder - SEHQC, LLC

Clinical Trials (Last 2 Years):

STAMPEDE
MS-MACE
ARMMS
SPLENDOR-NASH
SPLENDID-Cancer

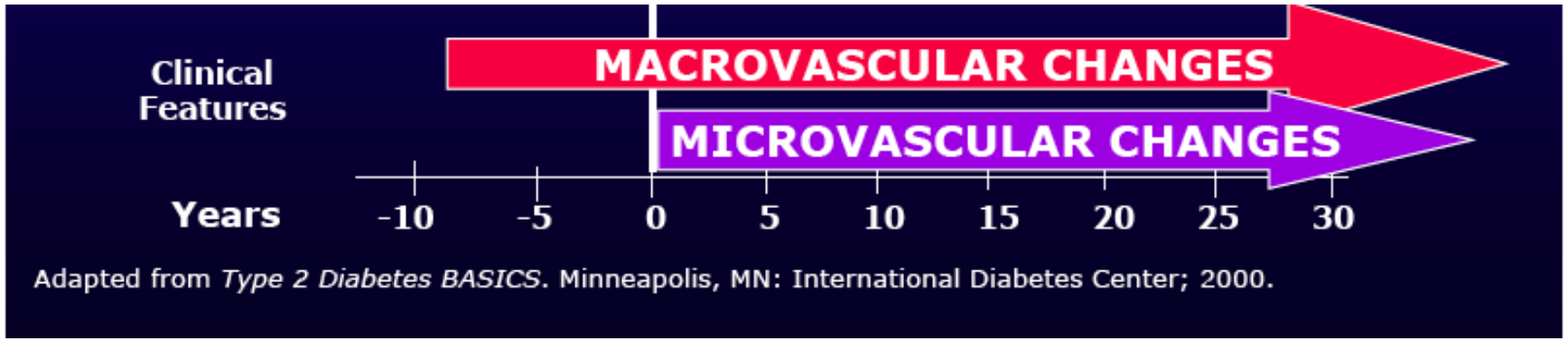
Results of 12 RCT's for Bariatric Surgery to Treat Obesity and Diabetes

PENNINGTON BIOMEDICAL RESEARCH CENTER LSU

STUDY	Pts w/BMI <35 kg/m²	Study design	No. pts	Follow-up (months)	Remission criteria	Remission or change in HbA1c (%)[a]	P value
Dixon	22%	LAGB vs control	60	24	HbA1c < 6.2%	73 vs 13	< 0.001
Schauer	36%	RYGB vs SG vs control	150	60	HbA1c ≤ 6.0%	22 vs 15 vs 0	< 0.05
Mingrone	0%	RYGB vs BPD vs control	60	60	HbA1c ≤ 6.5%	42 vs 68 vs 0	0.003
Ikramuddin	59%	RYGB vs control	120	60	HbA1c < 6.0%	7 vs 0	0.02
Liang	100%	RYGB vs control	101	12	HbA1c < 6.5%	90 vs 0 vs 0	< 0.0001
Halperin	34%	RYGB vs control	38	12	HbA1c < 6.5%	58 vs 16	0.03
Courcoulus	43%	RYGB vs LAGB vs control	69	36	HbA1c < 6.5%	40 vs 29 vs 0	0.004
Wentworth	100%	LAGB vs control	51	24	FBG < 7.0 mmol/L	52 vs 8	0.001
Parikh	100%	(RYGB/LAGB/SG) vs control	57	6	HbA1c < 6.5%	65 vs 0	0.0001
Ding	34%	LAGB vs control	45	12	HbA1c < 6.5%	33 vs 23	0.46
Cummings	25%	RYGB vs control	43	12	HbA1c < 6.0%	60 vs 5.9	0.002
Shah	85%	RYGB vs control	80	24	HbA1c < 6.5%	60 vs 2.5	<0.001

Annu. Rev. Med. 2020. 71:1-15

What about the effect of surgery on Long-term Morbidity/ Mortality



28 Observational Studies:
6 JAMA, 2 NEJM,
1 Lancet,
2 Diabetes Care,
1 Gastroenterology

All show mortality benefit for surgery

Risk reduction
30-89%, Avg 45%

**Cleveland Clinic Study

Table 1—Association of metabolic and bariatric surgery with risk of all-cause mortality in 28 comparative observational studies

First author (journal)	Publication year	Reduction in risk of death (%)
MacDonald KG (J Gastrointest Surg)	1997	68
Christou NV (Ann Surg)	2004	89
Flum DR (J Am Coll Surg)	2004	33
Adams TD (N Engl J Med)	2007	40
Busetto L (Surg Obes Relat Dis)	2007	60
Peeters A (Ann Surg)	2007	72
Sjöström L (N Engl J Med)	2007	29
Sowemimo OA (Surg Obes Relat Dis)	2007	82
Perry CD (Ann Surg)	2008	50
Marsk R (Br J Surg)	2010	30
Maciejewski MK (JAMA)*	2011	36
Johnson RJ (Am Surg)	2012	40
Scott JD (Surg Obes Relat Dis)	2013	55
Arterburn DE (JAMA)**	2015	53
Eliasson B (Lancet Diabetes Endocrinol)	2015	58
Guidry CA (Am J Surg)	2015	52
Davidson LE (JAMA Surg)	2016	40
Flanagan E (Am Surg)	2016	68
Lent MR (Diabetes Care)	2017	56
Pontiroli AE (Cardiovasc Diabetol)	2018	48
Reges O (JAMA)	2018	50
Fisher DP (JAMA)	2018	67
Mousa OM (Ann Surg)	2019	51
Kauppila JH (Gastroenterology)	2019	37
Ceriani V (Int J Obes)	2019	36
Aminian A (JAMA)	2019	41
Singh P (Br J Surg)	2020	30
Liakopoulos V (Diabetes Care)	2020	42

Wiggins T et al. Plos Medicine, July 2020

Meta-analysis of Bariatric Surgery and All Cause Mortality

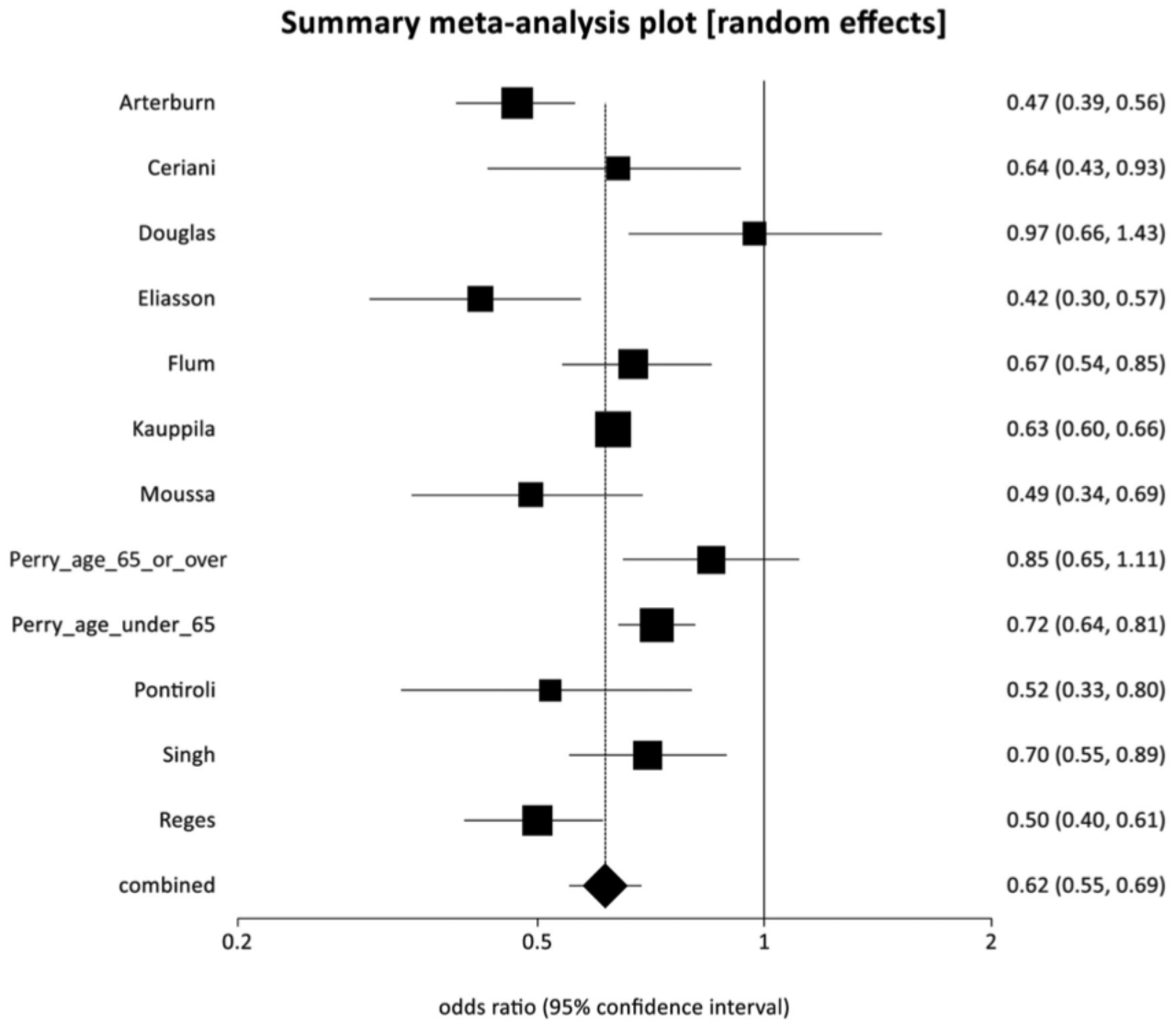


Fig 2. Forest plot of all-cause mortality (pooled odds ratio 0.62, 95% CI 0.55 to 0.69, $p < 0.001$).

JAMA | Original Investigation

Association of Metabolic Surgery With Major Adverse Cardiovascular Outcomes in Patients With Type 2 Diabetes and Obesity

Ali Aminian, MD; Alexander Zajichek, MS; David E. Arterburn, MD, MPH; Kathy E. Wolski, MPH; Stacy A. Brethauer, MD; Philip R. Schauer, MD; Michael W. Kattan, PhD; Steven E. Nissen, MD

IMPORTANCE Although metabolic surgery (defined as procedures that influence metabolism by inducing weight loss and altering gastrointestinal physiology) significantly improves cardiometabolic risk factors, the effect on cardiovascular outcomes has been less well characterized.

OBJECTIVE To investigate the relationship between metabolic surgery and incident major adverse cardiovascular events (MACE) in patients with type 2 diabetes and obesity.

DESIGN, SETTING, AND PARTICIPANTS Of 287 438 adult patients with diabetes in the Cleveland Clinic Health System in the United States between 1998 and 2017, 2287 patients underwent metabolic surgery. In this retrospective cohort study, these patients were matched 1:5 to nonsurgical patients with diabetes and obesity (body mass index [BMI] ≥30), resulting in 11 435 control patients, with follow-up through December 2018.

EXPOSURES Metabolic gastrointestinal surgical procedures vs usual care for type 2 diabetes and obesity.

Editorial page 1

Supplemental content

2,287 Metabolic Surgery
Vs.
11,435 Medical RX

Aminian A, et al. *JAMA*. 2019 Sep 2. doi: 10.1001/jama.2019.14231. [Epub ahead of print]

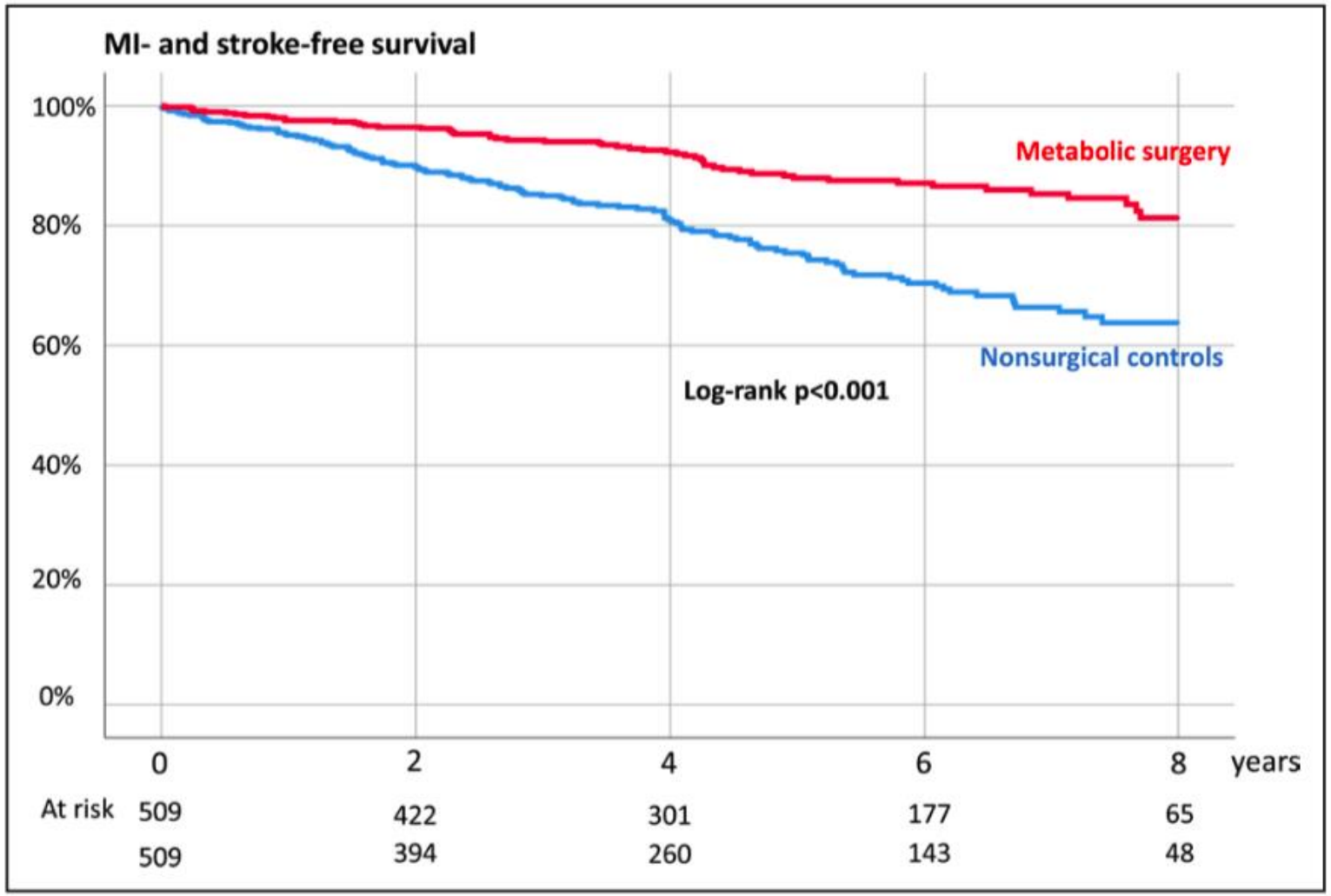
SUMMARY: Metabolic Surgery

- 41% ↓ in death
- 62% ↓ in heart failure
- 31% ↓ in heart disease
- 33% ↓ in stroke
- 60% ↓ in kidney failure
- 22% ↓ in atrial fibrillation

By operating on 13 patients: one life can be saved

Aminian A, et al. *JAMA*. 2019 Sep 2. doi: 10.1001/jama.2019.14231. [Epub ahead of print]

Association of Metabolic Surgery With Major Adverse Cardiovascular Outcomes in Patients With Previous Myocardial Infarction and Severe Obesity



Circulation. 2020;142:00–00. DOI: 10.1161/CIRCULATIONAHA.120.048585

Success (but Unfinished) Story of Metabolic Surgery

Ali Aminian[1] and Steven E. Nissen[2]

Diabetes Care 2020;43:1175–1177 | https://doi.org/10.2337/dci20-0006

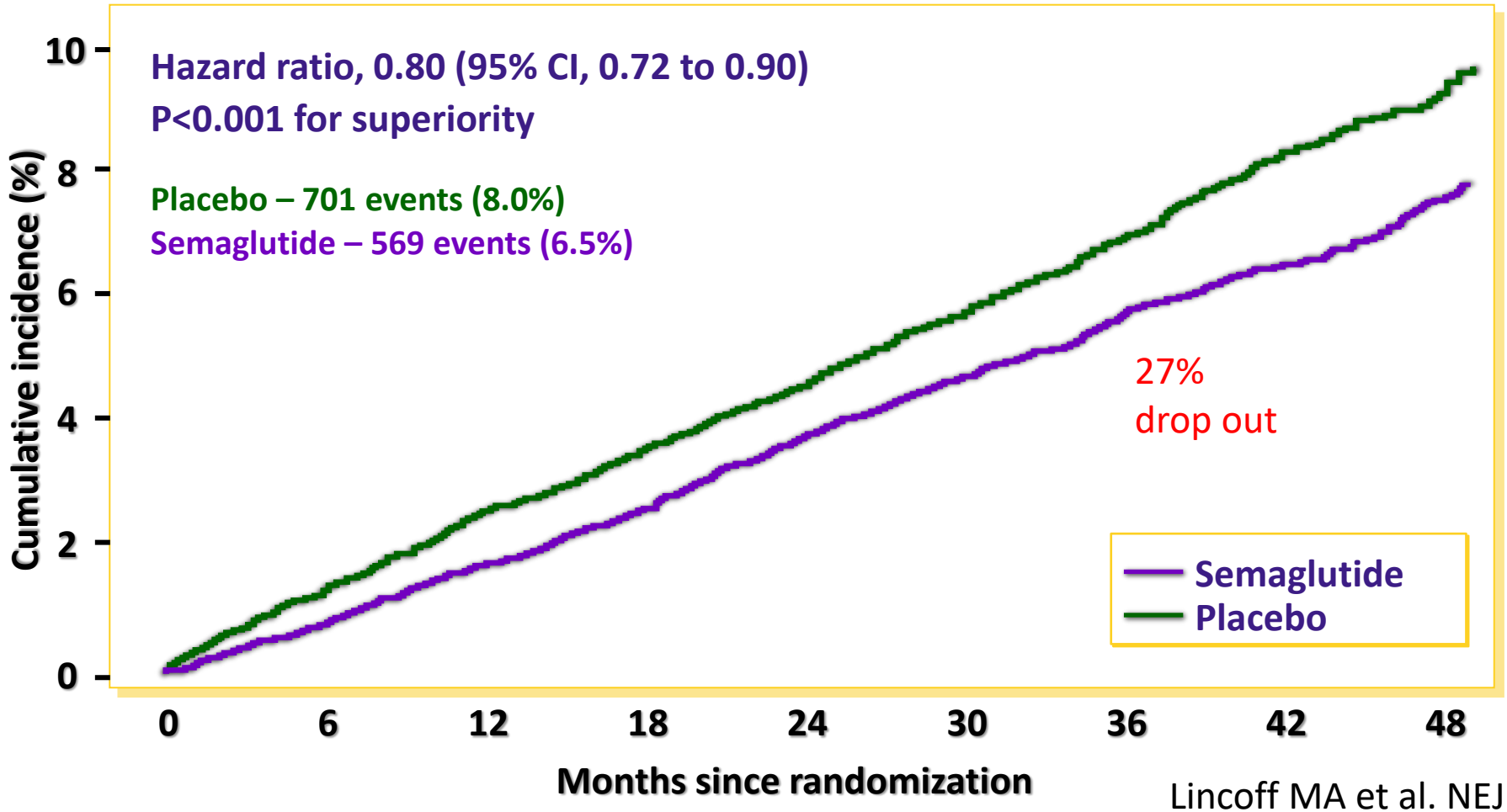
" A large well-designed RCT is essential to definitively evaluate the effectiveness of metabolic surgery in reducing CV morbidity and mortality in patients with obesity and T2D. "

SELECT Trial – Cardiovascular Efficacy

Secondary Prevention

CV Death, Nonfatal MI, or Nonfatal Stroke

Primary Cardiovascular Composite Endpoint

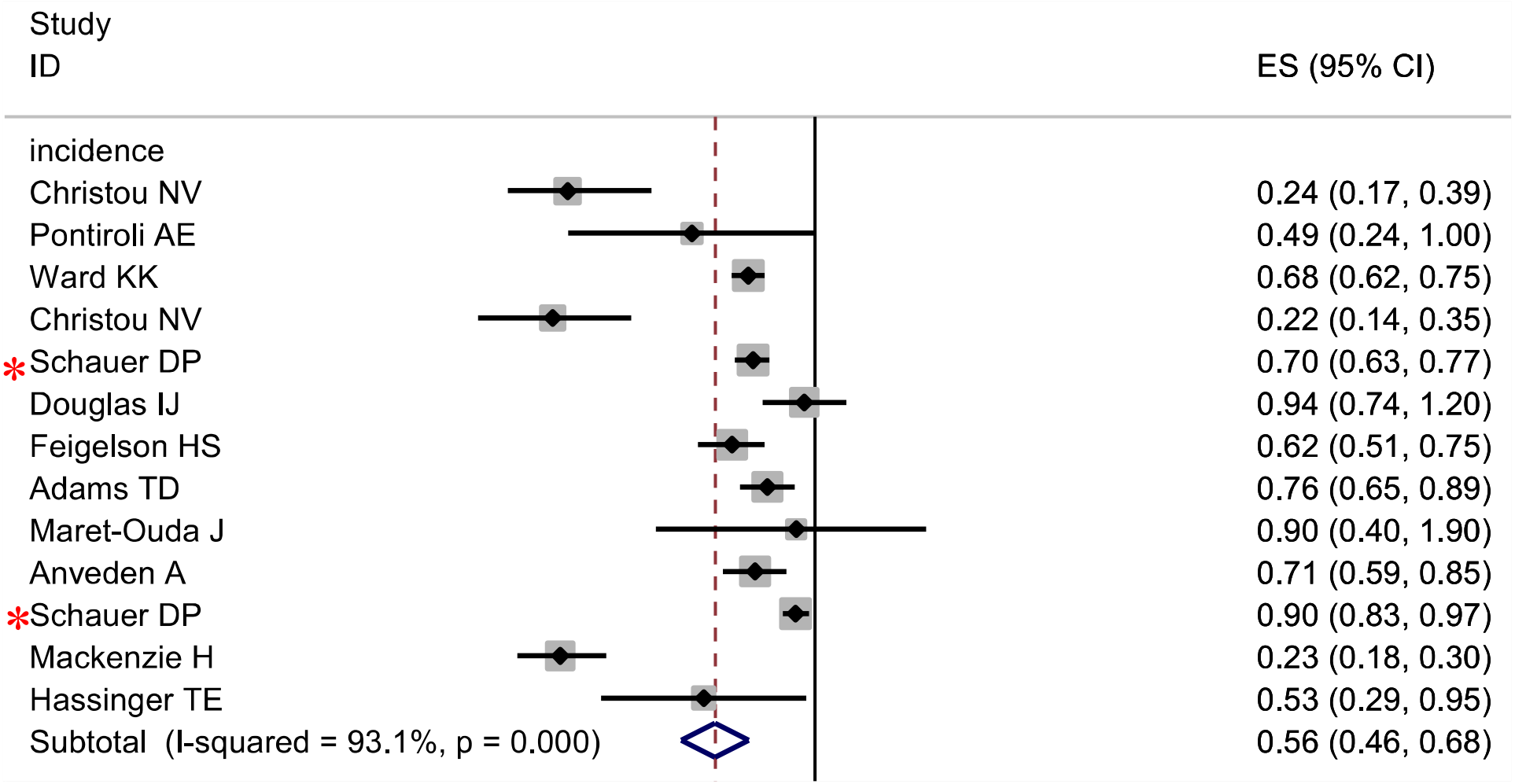


Semaglutide
20% Risk Reduction
NNT = 67

Metabolic Surgery
>50% Risk Reduction
NNT = 13

Lincoff MA et al. NEJM November 2023

Metabolic Surgery Associated with Lower Cancer Risk (Observational Data)



Zhang, *et al. Obes Surg.* 2020;30(4):1265-1272.

Future Directions

We need a Multicenter RCT for Metabolic Surgery

DREAMMS Study Design

Key Inclusion Criteria
Obesity
Type 2 Diabetes
+/-CVD

What’s the “Take Home?”

- Metabolic Surgery is more effective than medical RX for glycemic control and weight loss, AND improves HTN and nephropathy
- Risk of surgery = cholecystectomy, hysterectomy
- Observational studies show reduced morbidity and mortality for Metabolic Surgery
- We need a Multi-center RCT