UT Southwestern
Medical Center

Diabetes Recurrence

with and without recurrent weight gain

Ildiko Lingvay, MD, MPH, MSCS
Professor, Endocrinology
University of Texas Southwestern Medical Center
Dallas, Texas, USA

Dr. Ildiko Lingvay

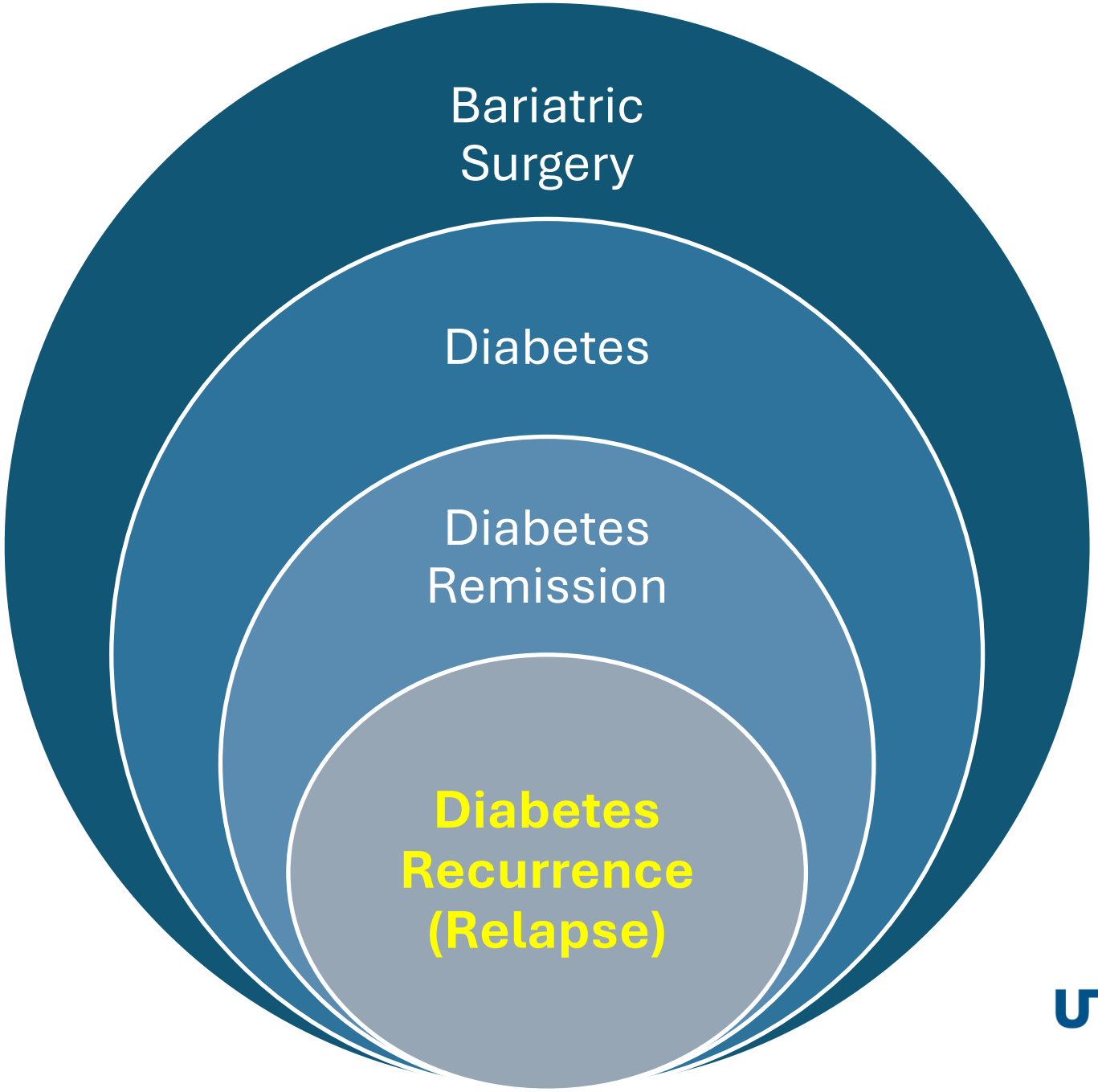
- Received research funding (paid to institution) from NovoNordisk, Sanofi, Boehringer-Ingelheim
- Received research related consulting fees (paid to institution) from NovoNordisk
- Received advisory/consulting fees and/or other support from: Abbvie, Altimmune, Astra Zeneca, Bayer, Betagenon AB, Bioio Inc., Biomea, Boehringer-Ingelheim, Carmot, Cytoki Pharma, Eli Lilly, Intercept, Janssen/J&J, Juvena, Keros Therapeutic, Inc, Mediflix, Merck, Metsera, Novo Nordisk, Pharmaventures, Pfizer, Regeneron, Sanofi, Shionogi, Structure Therapeutics, TARGET RWE, TERNS Pharma, The Comm Group, WebMD, and Zealand Pharma.

What I will Cover:

- ***Definitions***
- ***Prevalence***
- ***Predictors***
- ***Treatment***
- ***Big Picture***

What I will Cover:

- ***Definitions***
- ***Prevalence***
- ***Predictors***
- ***Treatment***
- ***Big Picture***



UT Southwestern Medical Center

Remission of Diabetes – ADA Consensus

- The term used to describe a sustained metabolic improvement in T2D to nearly normal levels should be ***remission of diabetes***.
- Remission should be defined as:
  - a return of ***HbA1c to <6.5%*** (<48 mmol/mol) that occurs spontaneously or following an intervention
    - when HbA1c is determined to be an unreliable marker of chronic glycemic control, FPG <126 mg/dL (<7.0 mmol/L) or eA1C <6.5% calculated from CGM values can be used as alternate criteria
  - ***persists for at least 3 months*** in the ***absence of usual glucose-lowering pharmacotherapy***

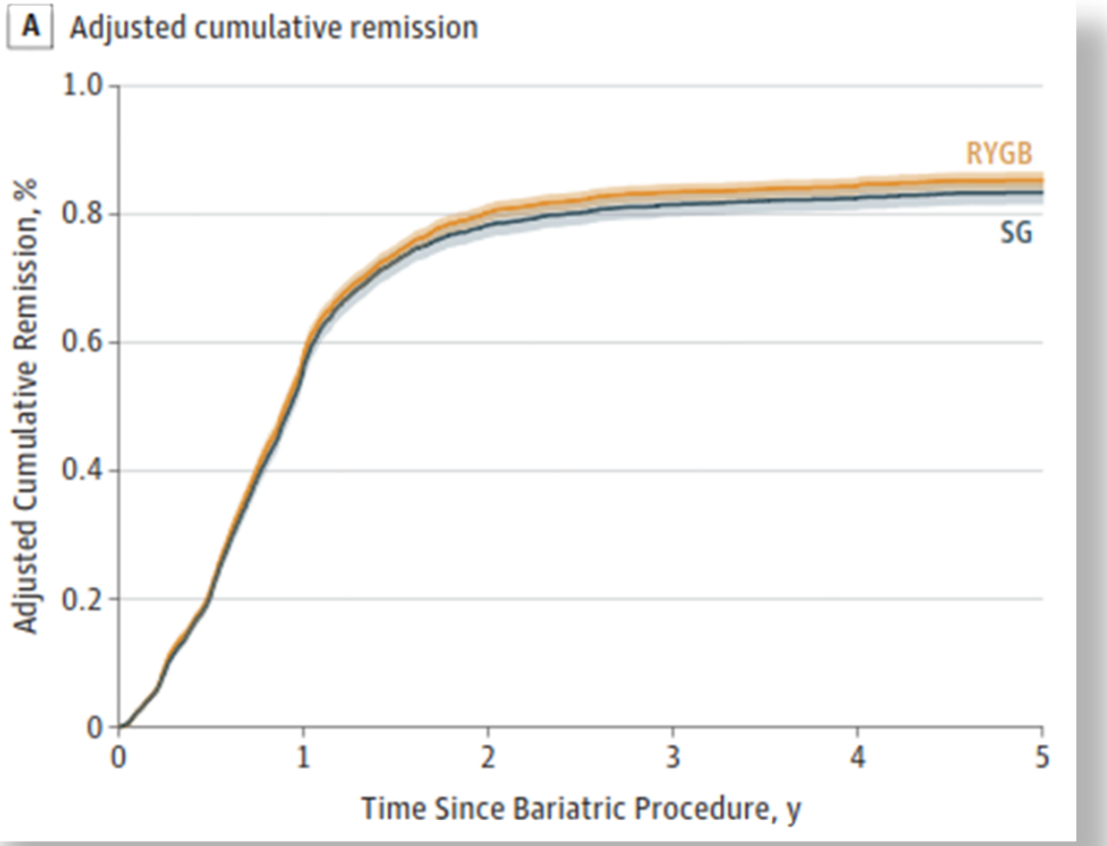
What I will Cover:

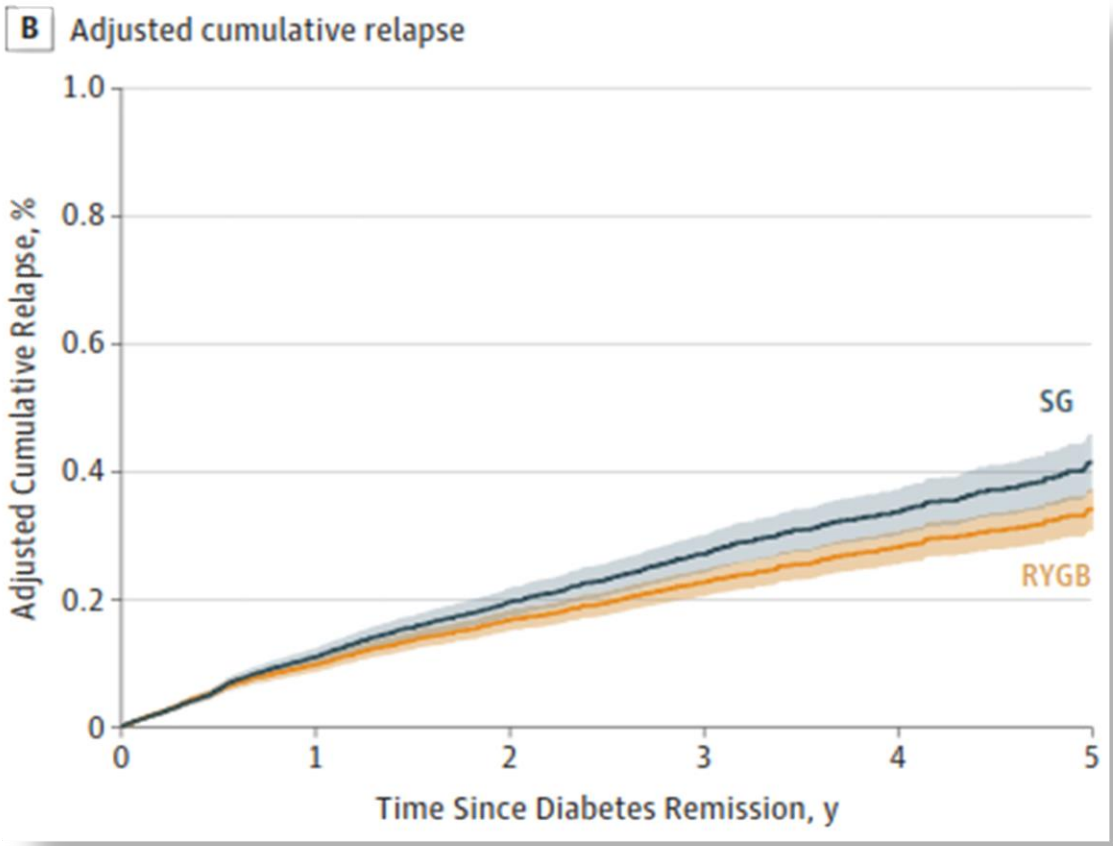
- ***Definitions***
- ***Prevalence***
- ***Predictors***
- ***Treatment***
- ***Big Picture***

Cumulative Incidence of Remission & Relapse

DM remission: A1c<6.5% + no DM meds x 6 mo

DM relapse: A1c>6.5% AND/OR DM meds after remission





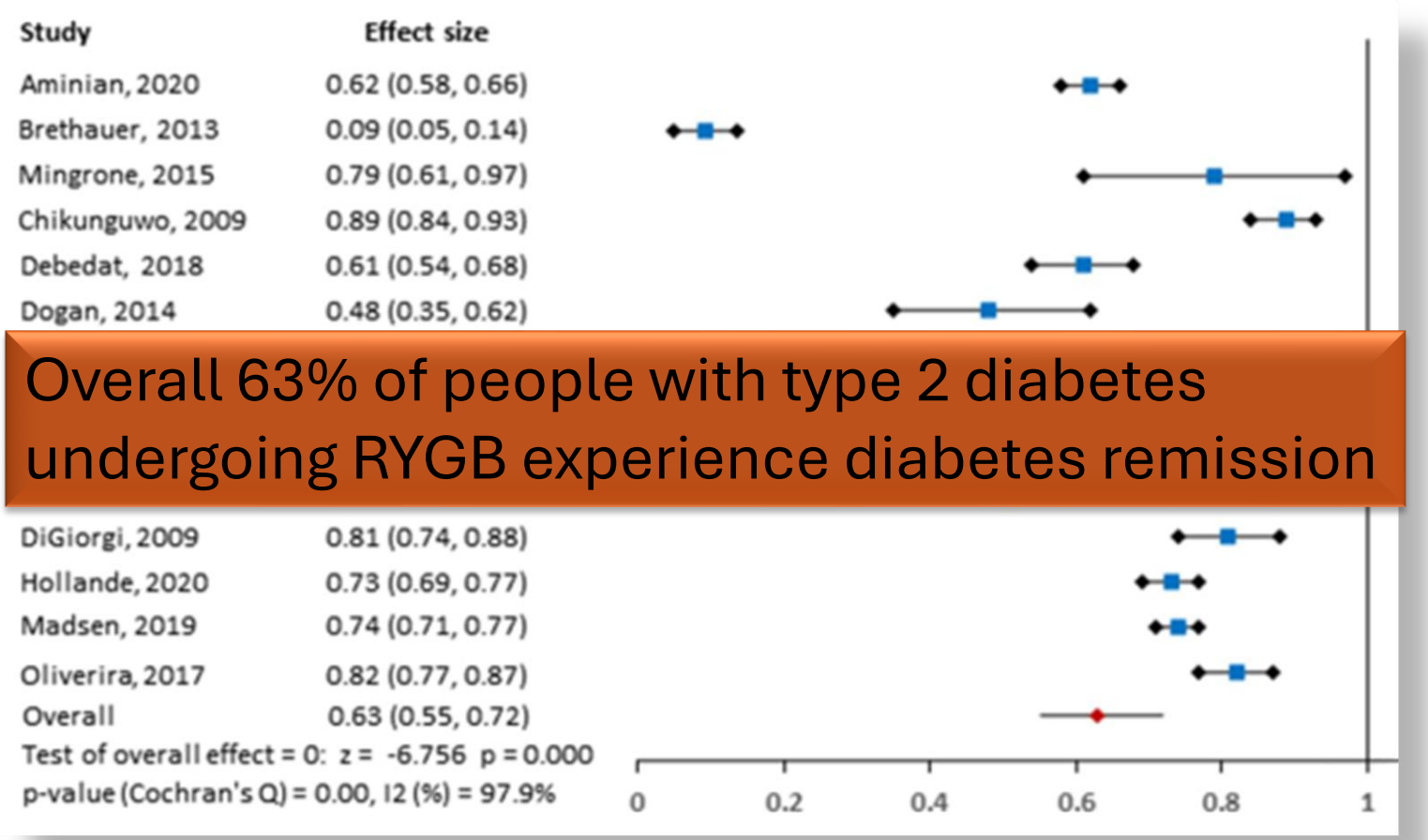
- Unmatched surgical cohort with N=6233 (64.2%) RYGB, N=3477 (35.8%) SG
- Baseline A1c 7.2% and 1.66 glucose lowering medications

McTIgue KM. JAMA Surg. 2020;155(5):e200087

UT Southwestern Medical Center

Meta-analysis: Prevalence of Remission

Analysis included RYGB only

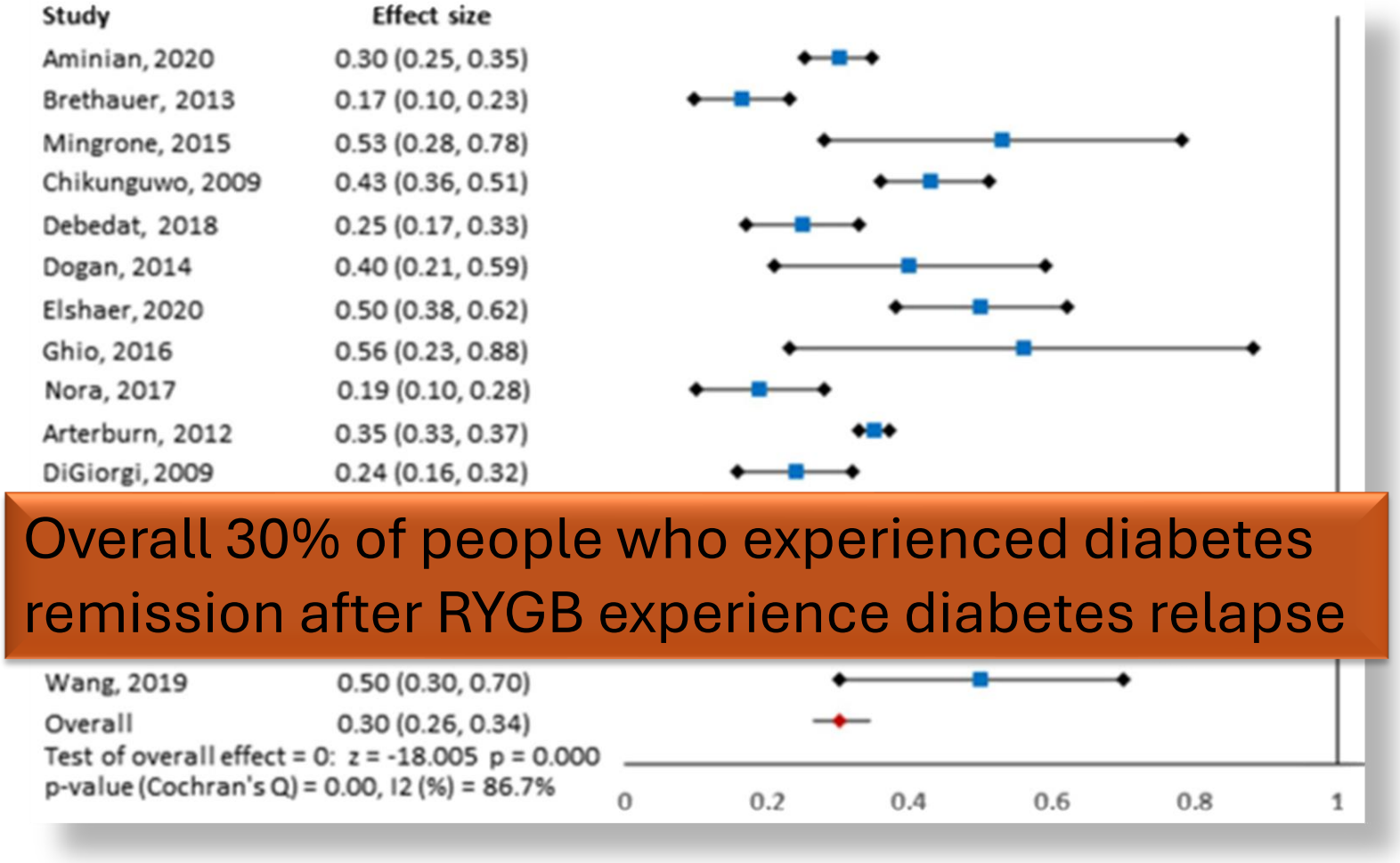


Yu Z et al. Obesity Surgery (2021) 31:5034–5043

UT Southwestern Medical Center

Meta-analysis: Prevalence of Relapse

Analysis included RYGB only



Overall 30% of people who experienced diabetes remission after RYGB experience diabetes relapse

Yu Z et al. Obesity Surgery (2021) 31:5034–5043

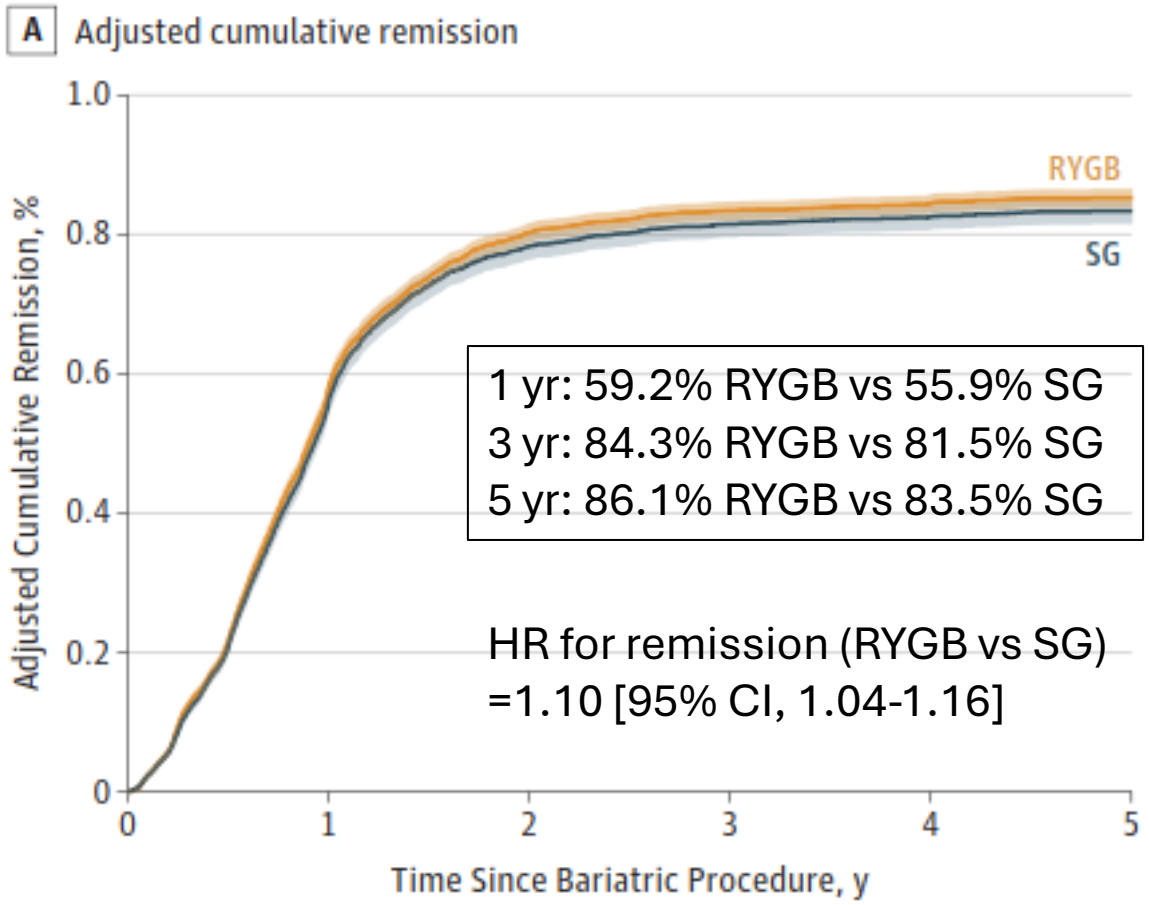
UT Southwestern Medical Center

What I will Cover:

- ***Definitions***
- ***Prevalence***
- ***Predictors***
- ***Treatment***
- ***Big Picture***

Remission & Relapse with RYGB vs SG

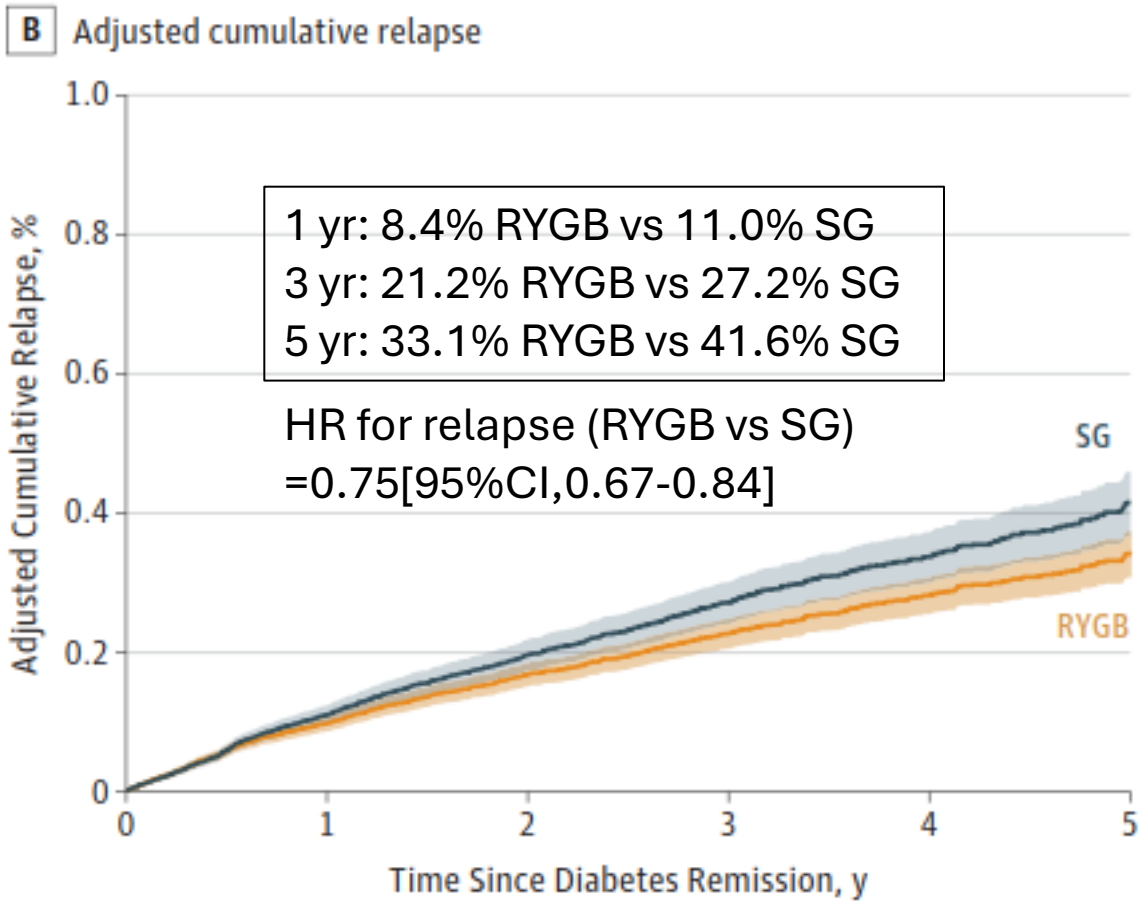
DM remission: A1c<6.5% + no DM meds x 6 mo



1 yr: 59.2% RYGB vs 55.9% SG
3 yr: 84.3% RYGB vs 81.5% SG
5 yr: 86.1% RYGB vs 83.5% SG

HR for remission (RYGB vs SG)
=1.10 [95% CI, 1.04-1.16]

DM relapse: A1c>6.5% AND/OR DM meds after remission



1 yr: 8.4% RYGB vs 11.0% SG
3 yr: 21.2% RYGB vs 27.2% SG
5 yr: 33.1% RYGB vs 41.6% SG

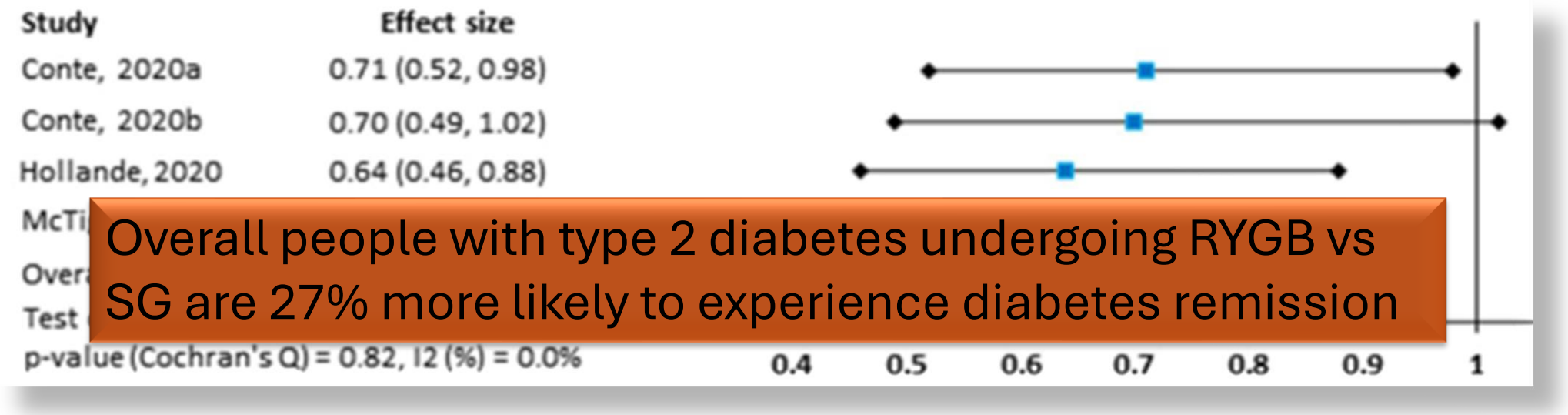
HR for relapse (RYGB vs SG)
=0.75[95%CI,0.67-0.84]

- Unmatched surgical cohort with N=6233 (64.2%) RYGB, N=3477 (35.8%) SG
- Baseline A1c 7.2% and 1.66 glucose lowering medications

McTIgue KM. JAMA Surg. 2020;155(5):e200087

UT Southwestern Medical Center

Meta-analysis: Remission of Diabetes with RYGB vs SG



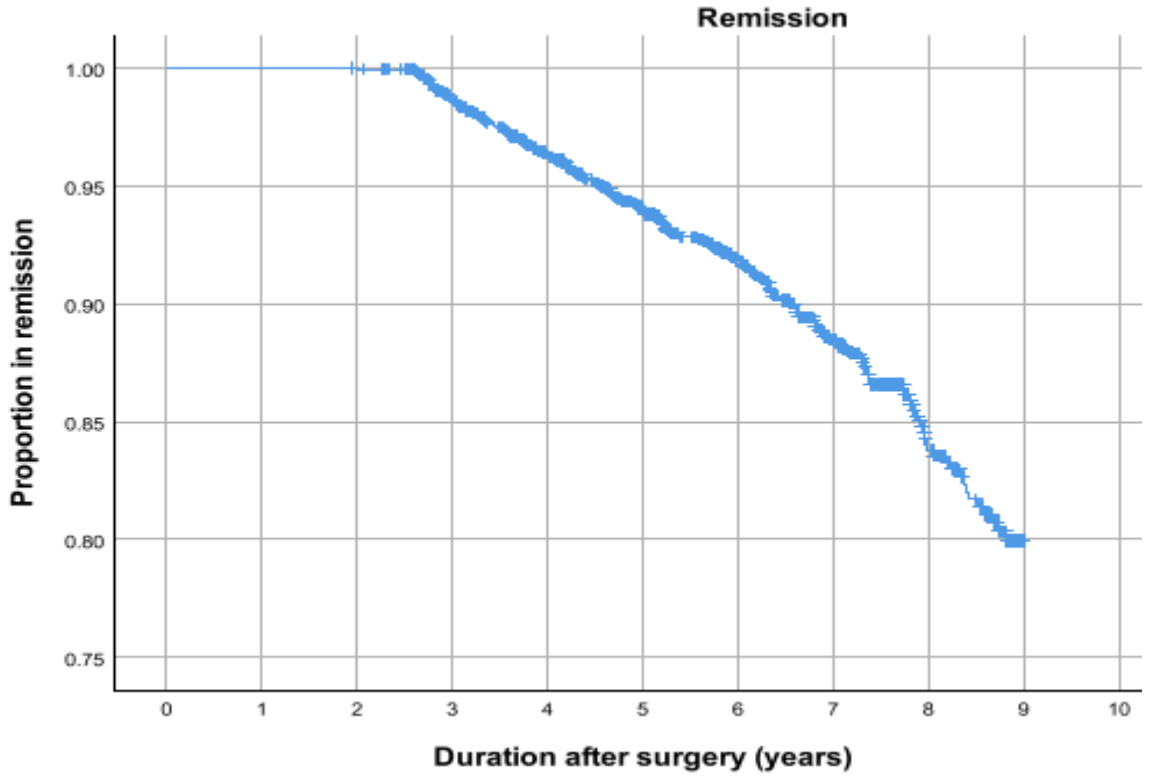
Overall people with type 2 diabetes undergoing RYGB vs SG are 27% more likely to experience diabetes remission

Yu Z et al. Obesity Surgery (2021) 31:5034–5043

UT Southwestern Medical Center

Swedish Registry: Diabetes Relapse

- RYGB or SG with diabetes remission at 2 years (N=2090)
- Median follow-up 5.9 yrs (from surgery)
- Cumulative relapse 20.1%



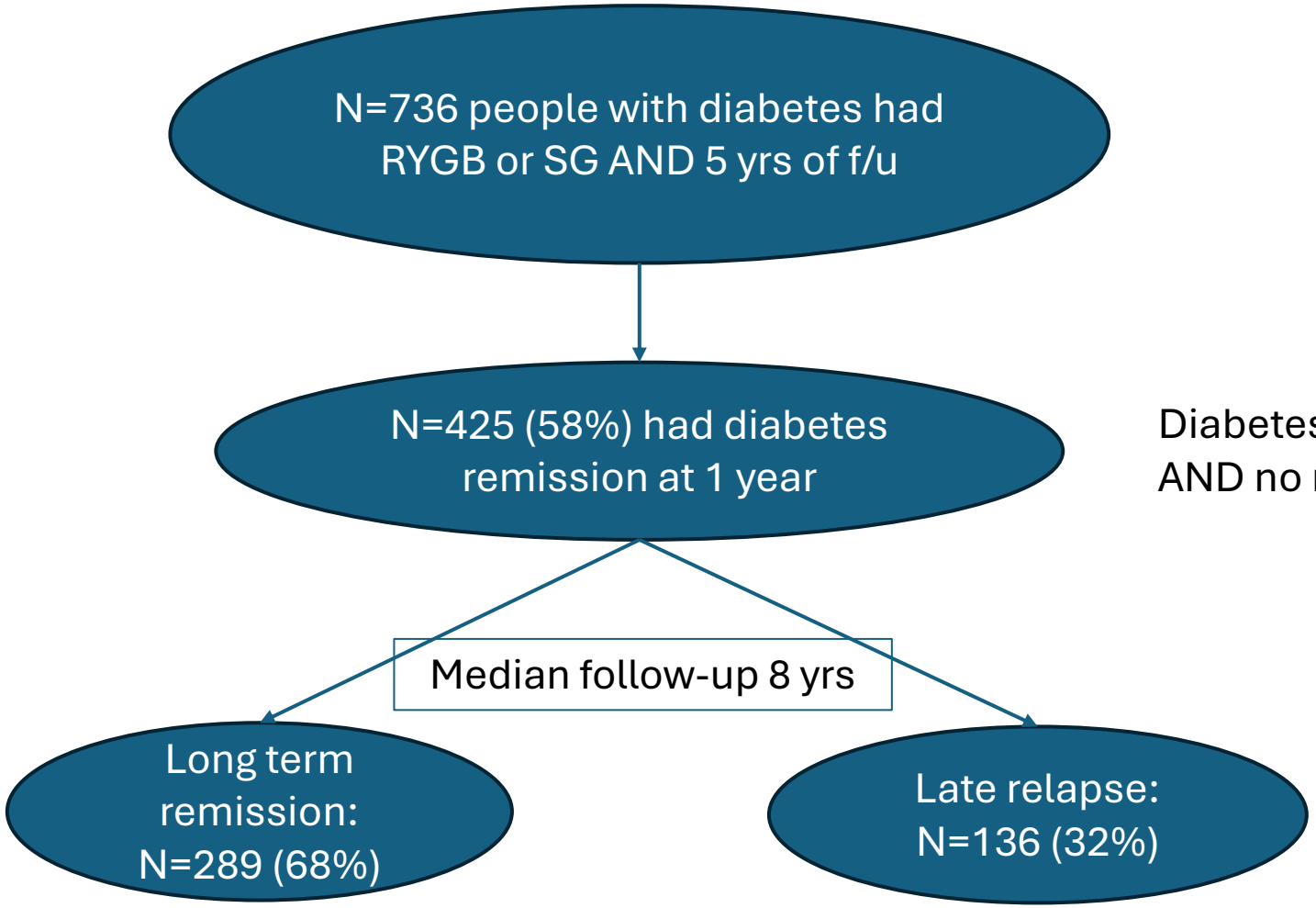
Jans A et al. Surgery for Obesity and Related Diseases 18 (2022) 305–313

UT Southwestern Medical Center

Characteristic	Unadjusted HR (95% CI)	Adjusted HR (95% CI)*	Adjusted *P* value*
Diabetes duration (years prior to surgery)	1.11 (1.07–1.14)	1.09 (1.05–1.14)	<.001
Glycosylated hemoglobin A1C (HbA1C) prior to surgery	1.02 (1.01–1.02)	1.01 (1.00–1.02)	.013
Insulin treatment prior to surgery	3.53 (2.63–4.73)	2.67 (1.84–3.90)	<.001
Percentage total weight loss 1 yr after surgery	.94 (.92–.96)	.93 (.91–.96)	<.001
Age	.99 (.98–1.00)	.98 (.97–1.00)	.050
BMI	.96 (.94–.99)	.98 (.95–1.01)	.219
Sex			
Female	Reference	Reference	Reference
Male	.96 (.72–1.29)	.65 (.46–.91)	.012
Education			
Primary education ≤9 yr	.91 (.62–1.35)	.83 (.54–1.27)	.388
Secondary education 10–12 yr	Reference	Reference	Reference
Higher education ≤3 yr	1.16 (.75–1.78)	1.33 (.84–2.10)	.226
Higher education >3yr	.85 (.53–1.38)	.96 (.57–1.60)	.870
Surgical method			
Roux-en-Y gastric bypass	Reference	Reference	Reference
Sleeve gastrectomy	2.42 (.89–6.61)	2.67 (.96–7.43)	.061

HR = hazard ratio; CI = confidence interval; BMI = body mass index.
* Multivariable Cox regression including all factors listed in the table.

Cleveland Clinic Long-Term Retrospective Study



Diabetes remission: HbA1c <6.5% AND no meds

Aminian A. et al. Diabetes Care 2020;43:534–540

UT Southwestern Medical Center

Table 3—Independent predictors of late relapse of diabetes after bariatric surgery in multivariable analyses

	Main model*			Second model*		
Predictors	OR	95% CI	*P*	OR	95% CI	*P*
Preoperative number of diabetes medications	2.04	(1.54, 2.71)	<0.001	2.13	(1.58, 2.87)	<0.001
Preoperative duration of diabetes (years)	1.08	(1.02, 1.14)	0.005	1.10	(1.03, 1.16)	0.002
Type of surgery (SG vs. RYGB)	2.21	(1.22, 4.01)	0.009	—	—	—
Weight loss at 1 year (%)	—	—	—	0.92	(0.89, 0.95)	<0.001
Late weight regain#	—	—	—	3.69	(2.18, 6.24)	<0.001

	Main model*	Second model*
Multiple logistic regression equation^	L = −2.4917 + (0.0789 × preoperative duration of diabetes) + (0.714 × preoperative number of diabetes medications) + (0.7929 × [1, for SG, or 0, for RYGB])	L = −0.729 + (0.0919 × preoperative duration of diabetes) + (0.7565 × preoperative number of diabetes medications) − (0.0877 × short-term weight loss) + (1.3059 × [1, for late weight regain, or 0, for no weight regain])

*Main model to be used before surgery to predict late diabetes relapse based on preoperative characteristics; second model to be used 1 year after bariatric surgery to predict late relapse based on preoperative characteristics and weight changes. #Categorical variable defined as >5% weight regain from the weight recorded 1 year after bariatric surgery. ^Estimated probability of late relapse of diabetes after initial remission for a given patient (100%) = EXP [L]/(1 + EXP [L]). The notation EXP is equivalent to ex, where "e" is the base of the ln (2.718).

Aminian A. et al. Diabetes Care 2020;43:534–540

Table 3—Independent predictors of late relapse of diabetes after bariatric surgery in multivariable analyses

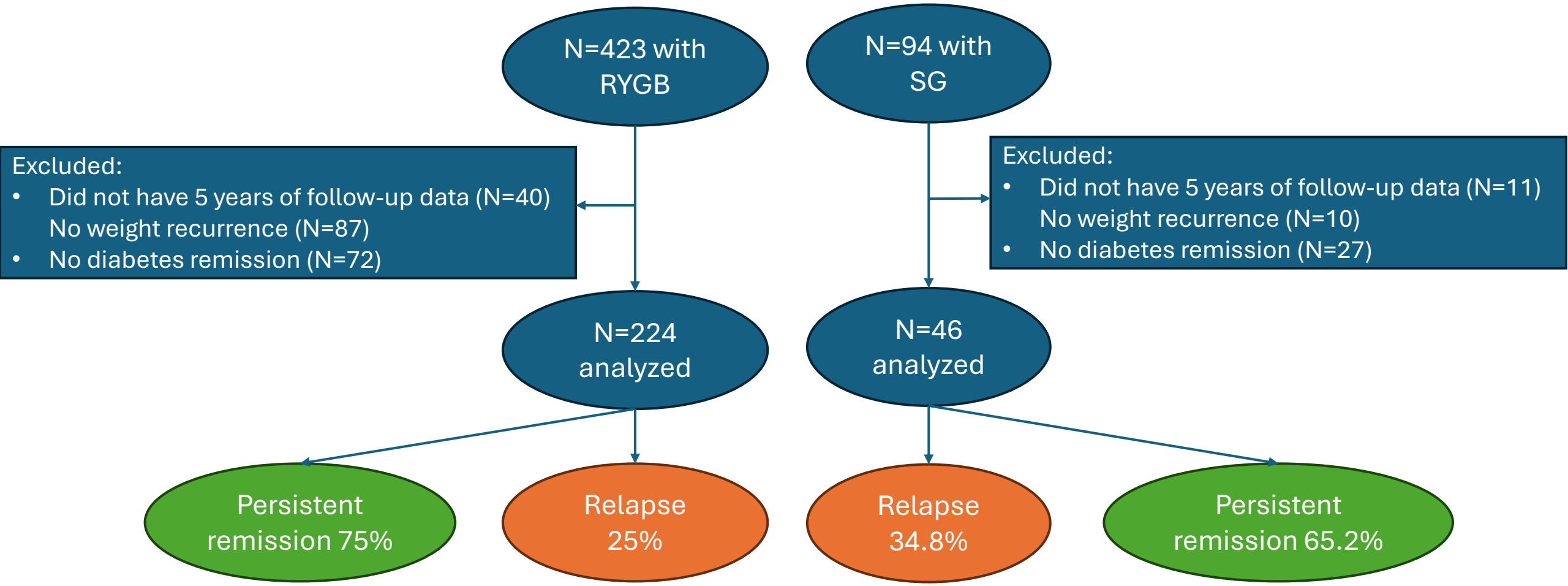
	Main model*			Second model*		
Predictors	OR	95% CI	*P*	OR	95% CI	*P*
Preoperative number of diabetes medications	2.04	(1.54, 2.71)	<0.001	2.13	(1.58, 2.87)	<0.001
Preoperative duration of diabetes (years)	1.08	(1.02, 1.14)	0.005	1.10	(1.03, 1.16)	0.002
Type of surgery (SG vs. RYGB)	2.21	(1.22, 4.01)	0.009	—	—	—
Weight loss at 1 year (%)	—	—	—	0.92	(0.89, 0.95)	<0.001
Late weight regain#	—	—	—	3.69	(2.18, 6.24)	<0.001

	Main model*	Second model*
Multiple logistic regression equation^	L = −2.4917 + (0.0789 × preoperative duration of diabetes) + (0.714 × preoperative number of diabetes medications) + (0.7929 × [1, for SG, or 0, for RYGB])	L = −0.729 + (0.0919 × preoperative duration of diabetes) + (0.7565 × preoperative number of diabetes medications) − (0.0877 × short-term weight loss) + (1.3059 × [1, for late weight regain, or 0, for no weight regain])

*Main model to be used before surgery to predict late diabetes relapse based on preoperative characteristics; second model to be used 1 year after bariatric surgery to predict late relapse based on preoperative characteristics and weight changes. #Categorical variable defined as >5% weight regain from the weight recorded 1 year after bariatric surgery. ^Estimated probability of late relapse of diabetes after initial remission for a given patient (100%) = EXP [L]/(1 + EXP [L]). The notation EXP is equivalent to ex, where "e" is the base of the ln (2.718).

Aminian A. et al. Diabetes Care 2020;43:534–540

Mayo Clinic Retrospective Study (wt regain)



Definition of diabetes remission: HbA1c<6.5% AND no meds x 3 mo

Ghanem, OM. J Am Coll Surg 2024;238:862–871.

UT Southwestern Medical Center

Mayo Clinic Retrospective Study (wt regain)

RYGB only

Variable	Weight recurrence				
	<25%, Mild	25%–49.9%, Moderate	50%–74.9%, Severe	≥75%, Complete	p Value
No. of patients	55	82	57	30	
Continued diabetes remission	47_{a} (85.5)	$67_{a,b}$ (81.7)	36_{b} (63.2)	18_{b} (60)	0.005*

Nonoverlapping subscripts represent statistically significant differences intragroup according to Bonferroni's adjustment.
*Pearson chi-square with Bonferroni's adjustment.

Variable	Adjusted odds ratio	95% CI		p Value
		Lower	Upper	
Age at surgery, y, (increasing)	0.97	0.94	1.01	0.13
Sex (ref = f)	1.15	0.53	2.48	0.73
Preoperative BMI, kg/m^2, (increasing)	0.97	0.92	1.02	0.24
Preoperative type 2 diabetes mellitus duration, y	1.06	1.02	1.10	0.04*
Preoperative HbA1c, %, (increasing)	1.50	1.10	2.06	0.01*
Preoperative fasting glucose, mg/dL, (increasing)	1.00	0.99	1.01	0.18
Insulin use at baseline (ref = no)	2.63	1.17	5.91	0.02*
Weight recurrence, %, (increasing)	1.03	0.99	1.07	0.06

*Statistically significant.
ref, Reference.

Ghanem, OM. J Am Coll Surg 2024;238:862–871.

UT Southwestern Medical Center

Summary of Predictors

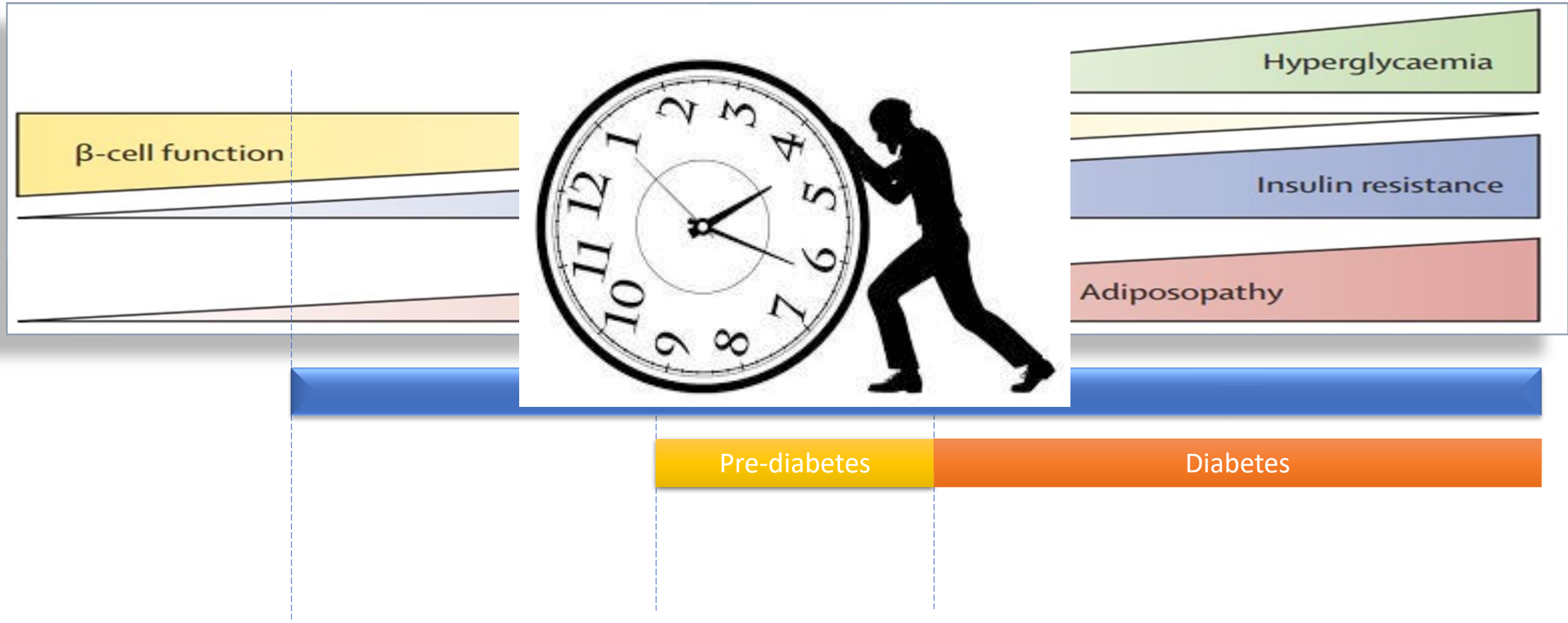
Remission

- Baseline:
  - Shorter DM duration
  - No Insulin use
  - Lower A1c
  - Fewer glucose lowering meds
- Procedure:
  - RYGB (vs SG)
- Post-procedure:
  - Weight loss during 1 year postop

Relapse

- Baseline:
  - Longer DM duration
  - Insulin use
  - Higher A1c
  - Higher # of DM meds
- Procedure:
  - SG (vs RYGB)
- Post-procedure:
  - Less weight loss during 1 year postop
  - Weight regain after nadir

The Metabolic Disease Continuum



Lingvay et al.
Lancet 2022

The Metabolic Disease Continuum

Diabetes Remission

Hyperglycaemia

β-cell function

Insulin resistance

Predictor #1: Disease severity (starting point)

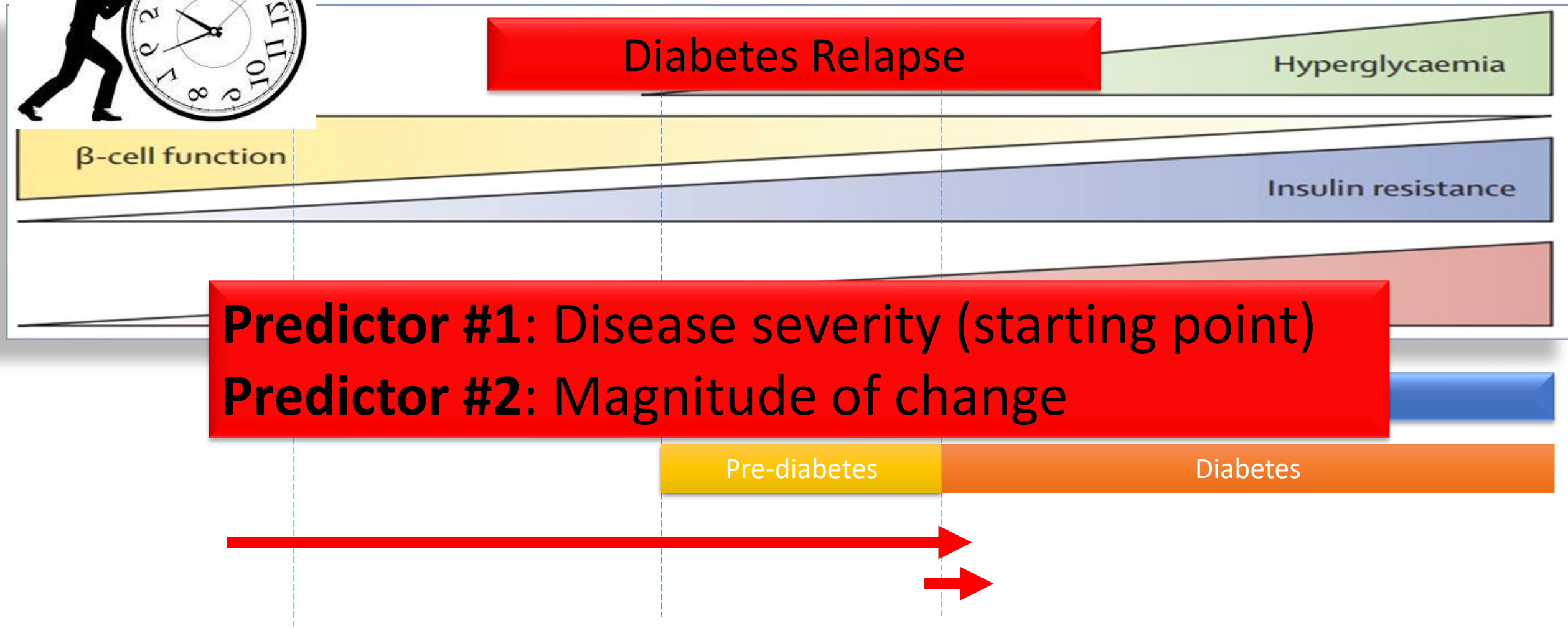
Predictor #2: Magnitude of change

Pre-diabetes

Diabetes

Lingvay et al.
Lancet 2022

The Metabolic Disease Continuum



Lingvay et al.
Lancet 2022

Summary of Predictors

Remission

- Baseline:
  - Shorter DM duration
  - No Insulin use
  - Lower A1c
  - Fewer glucose lowering meds
- Procedure:
  - RYGB (vs SG)
- Post-procedure:
  - Weight loss during 1 year postop

Predictor #1: Disease severity *(starting point)*

Predictor #2: Magnitude of change

Summary of Predictors

Predictor #1: Disease severity
(starting point)

Predictor #2: Magnitude of change

Relapse

- Baseline:
  - Longer DM duration
  - Insulin use
  - Higher A1c
  - Higher IMS score
  - Higher # of DM meds
- Procedure:
  - SG (vs RYGB)
- Post-procedure:
  - Less weight loss during 1 year postop
  - Weight regain after nadir

What I will Cover:

- ***Definitions***
- ***Prevalence***
- ***Predictors***
- ***Treatment***
- ***Big Picture***

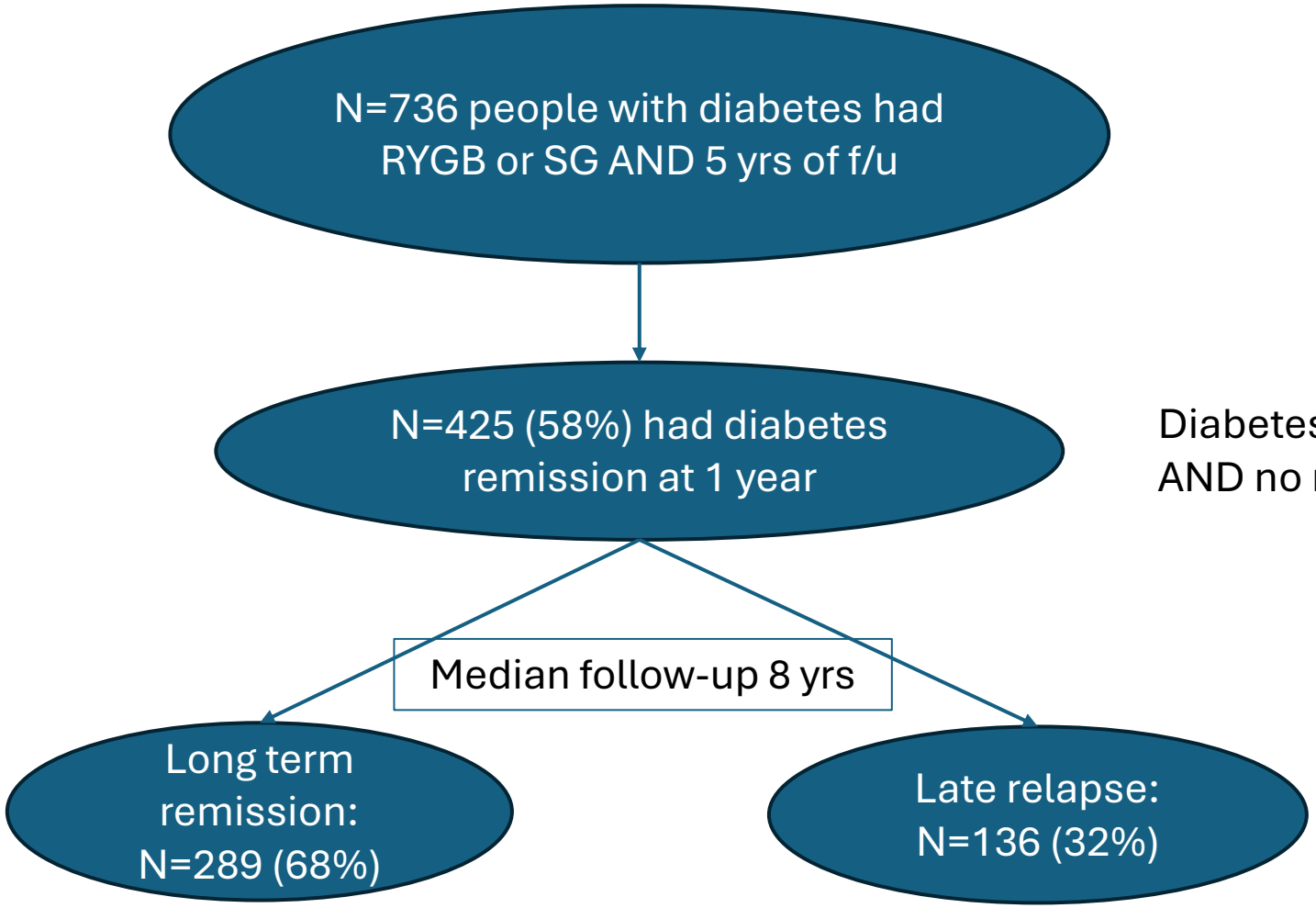
Management of Diabetes Relapse

1. Prevent:
   - Treat weight regain early
2. Treat:
   - Use glucose lowering agents with weight benefit (or at least weight neutral), avoid agents with associated weight gain
   - Manage associated cardiovascular risk factors (lipids, blood pressure, inflammation, coags)
   - Manage weight regain

What I will Cover:

- ***Definitions***
- ***Prevalence***
- ***Predictors***
- ***Treatment***
- ***Big Picture***

Cleveland Clinic Long-Term Retrospective Study



Diabetes remission: HbA1c <6.5% AND no meds

Aminian A. et al. Diabetes Care 2020;43:534–540

UT Southwestern Medical Center

Long-Term Outcomes with Diabetes Relapse

Table 1—Long-term metabolic profile of post–bariatric surgery patients with late relapse of diabetes following initial remission (n = 136)

Variable	Baseline	Long-term	P
HbA_{1c} (%)	7.2 (6.3–8.7)	6.4 (6.0–6.8)	<0.001
HbA_{1c} (mmol/mol)	55 (45–72)	46 (42–51)	<0.001
Diastolic BP (mmHg)	77.3 ± 10.7	73.9 ± 9.5	0.004
Number of diabetes drugs	2 (1–3)	1 (1–1)	<0.001
On insulin therapy	40 (29.4)	16 (11.8)	<0.001

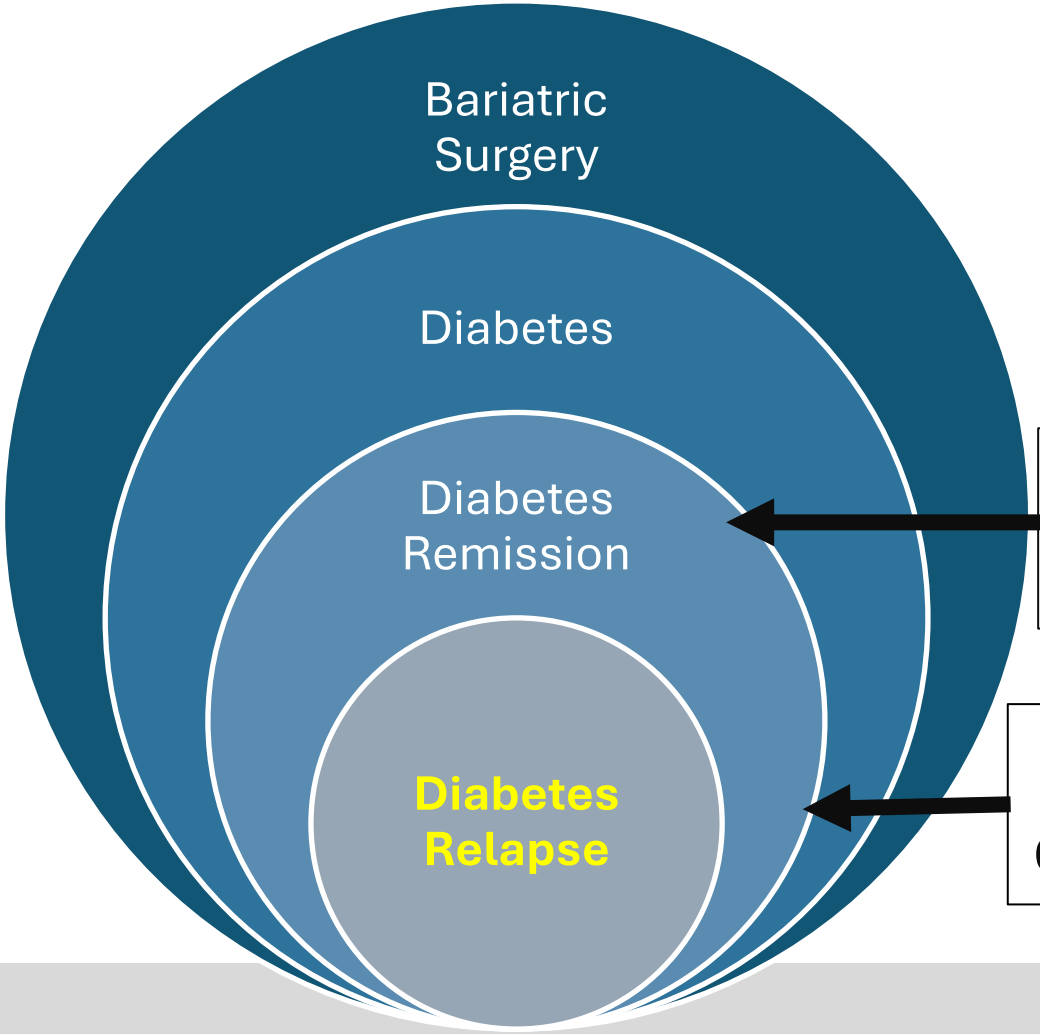
Data are median (IQR), mean ± SD, or n (%). BP, blood pressure. *Defined as HbA_{1c} <7% (53 mmol/mol), irrespective of diabetes medications.

- Improvement in glycemic control
- Lower number of diabetes medications including insulin use
- Improved blood pressure
- Improved lipid profile

Aminian A. et al. Diabetes Care 2020;43:534–540

UT Southwestern Medical Center

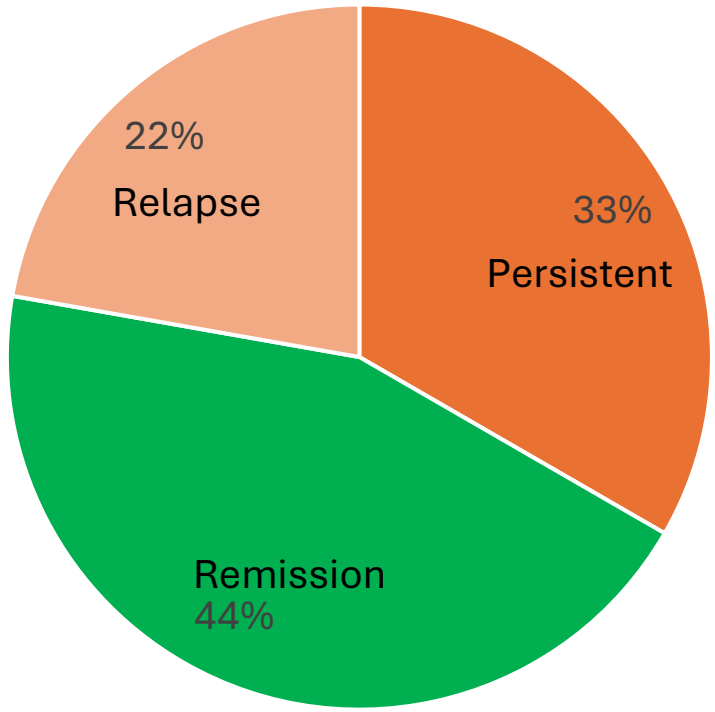
Conclusions



~2/3 of those with diabetes

~1/3 of those with diabetes remission

Long term diabetes status after bariatric surgery



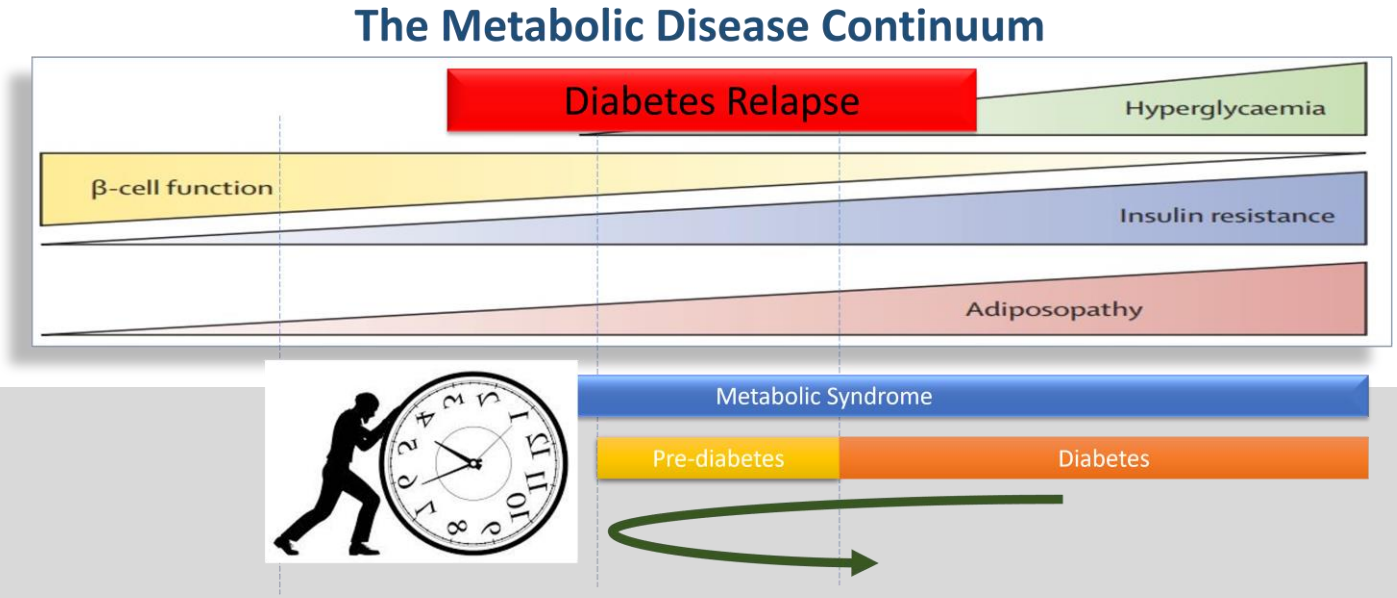
UT Southwestern Medical Center

Conclusions

- Predictors of remission and relapse are similar
  - Person's disease state

Diabetes Relapse ≠ Failure

- Big picture – still better than where they started
  - Burden of treatment
  - Disease control
  - CV risk factor and events
  - QoL




TEAMWORK
MAKES
THE DREAM
WORK


THANKS
FOR THE
TEAMWORK!