The PCORnet Bariatric Study: Preliminary Results from a Large PCORnet Demonstration Project

NIH HCS Collaboratory and PCORnet Grand Rounds, August 17, 2018

Neely Williams, Mdiv; David Arterburn, MD MPH; Kathleen McTigue, MD MPH; and Laura Rasmussen-Torvik, PhD MPH

on behalf of the PCORnet Bariatric Study Collaborative

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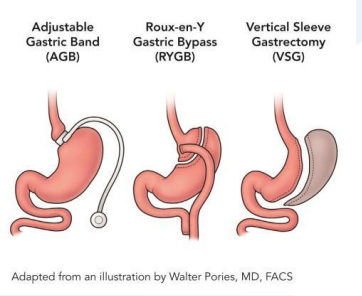
A bit about the PCORnet Bariatric Study…

- Studying the three most commonly used weight-loss procedures in the US
  - Adjustable gastric band (AGB) – lap band or band
  - Roux-en-Y gastric bypass (RYGB) – bypass
  - Sleeve gastrectomy (SG) - sleeve



- We are looking at how each procedure compares to the other two for:
  - Weight loss and regain; Improvement in diabetes risk; Adverse events over a 1, 3, and 5 year interim

- Why is this topic important?
  - Use of bariatric surgery has expanded considerably
  - Sleeve gastrectomy procedure has been used increasingly over past decade – despite a lack of data comparing its effectiveness to other procedures

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A bit about me….

- As stated I am, Neely Williams, one of the co-PI of this study
- Patient/Non-Scientist
- I had Bariatric Surgery in 2011 – 7 years ago
- I am a widow, mother and great grandmother
- I also work as a community engagement strategist, and minister
- My experiences led me to PCORnet – a Network dedicated to placing patients central in the research process

My road map to becoming a Patient PI in the bariatric study

- As a PI, I worked to develop solutions and contributed to decision making
- I am a minister, a community advocate, and a community organizer
  - Case management for diverse populations
  - Coalition building for different initiatives
- I have served in numerous capacities in the Greater Nashville Community
- I served on the PCORnet Obesity Task Force (2014)
  - Task Force members: patients, surgeons, researchers

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Major Successes (January 2016 – Aug 2018)

- **7 Common Data Model (CDM) queries successfully executed**
  - Study Specific Data Characterization (n=2)
  - Scientific Queries
    - Weight loss (n=2), individual-level & distributed
      - 41 data contributing sites from 11 CDRNs
    - Diabetes risk (n=2), individual-level & distributed
      - 34 data contributing sites from 11 CDRNs
    - Adverse Events (n=1), individual level
      - 10 data contributing sites from 5 CDRNs

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Major Successes (January 2016 – Aug 2018)

- Major dissemination activities:
  - Published papers:
    - Cohort Description, JMIR Research Protocols
    - Adolescent weight loss, Surgery for Obesity & Related Diseases
  - Papers in progress:
    - Adult weight loss, revised & resubmitted twice, Annals of Internal Medicine
    - Comparison of weight loss/regain in individual-level vs. distributed queries, in review, Clinical Epidemiology
    - 3 other manuscripts in production
  - 5 abstracts accepted by three conferences

- Tremendous amount of work to collect & analyze data in ~18 months
  - Coordinating Center work: programming, beta-testing & distributing queries
  - Site teams of data collection: running queries, troubleshooting data
  - Scientific Core team: leading data cleaning & analyses

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Aim 1: Weight Loss Outcomes

- 46,510 adults from 41 health systems
- Procedure distribution
  - 24,982 RYGB (53%)
  - 18,961 SG (41%)
  - 2,567 AGB (6%)

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- 60% HTN; 49% Dyslipidemia; 49% OSA; 40% GERD; 37% T2DM; 30% Depression; 21% Anxiety
- RYGB patients had higher BMI & more comorbidity

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Availability of follow-up weight measures, adults

	1-year	3-year	5-year
	N (% of eligible)		
All procedures	44,978 (84%)	20,783 (68%)	7,159 (69%)

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	N (% of eligible)		
All procedures	**44,978 (84%)**	**20,783 (68%)**	**7,159 (69%)**
RYGB	24,061 (86%)	12,429 (67%)	5,257 (67%)
Sleeve	18,550 (84%)	6,847 (73%)	1,293 (76%)
AGB	2,367 (76%)	1,507 (60%)	609 (55%)

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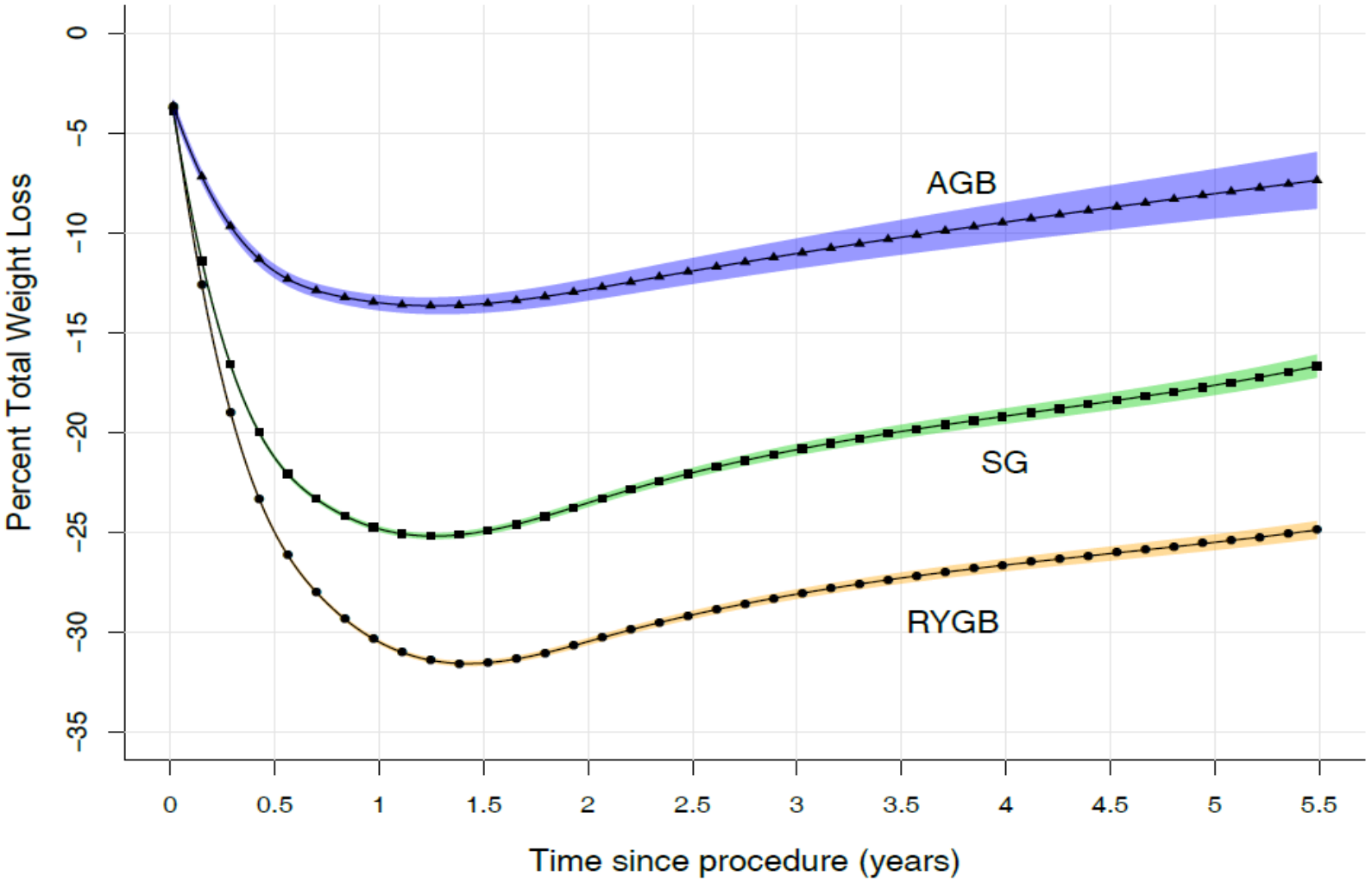
Percent Total Weight Loss in Adults



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Preliminary results. Do not cite without permission from authors.

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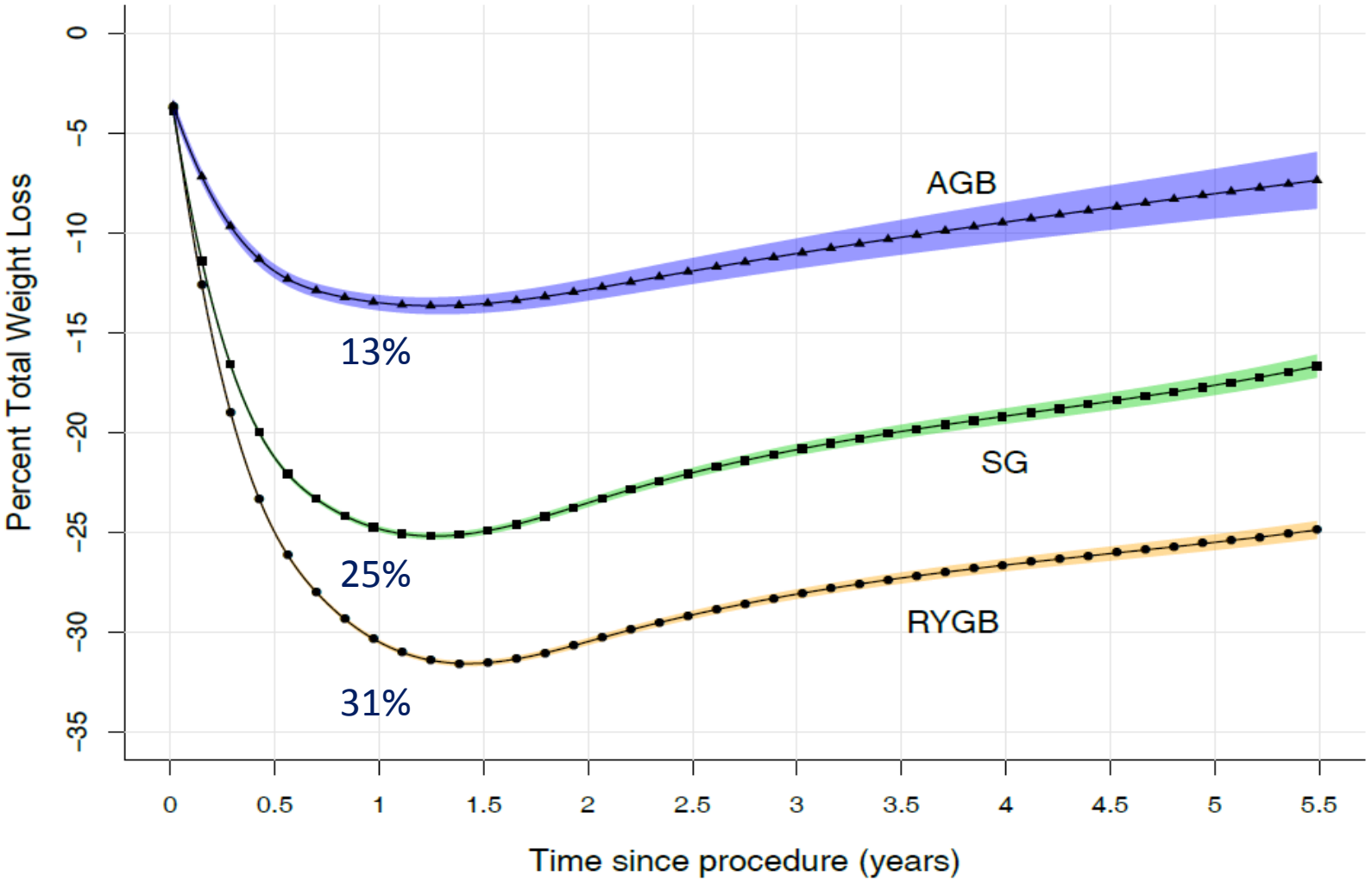

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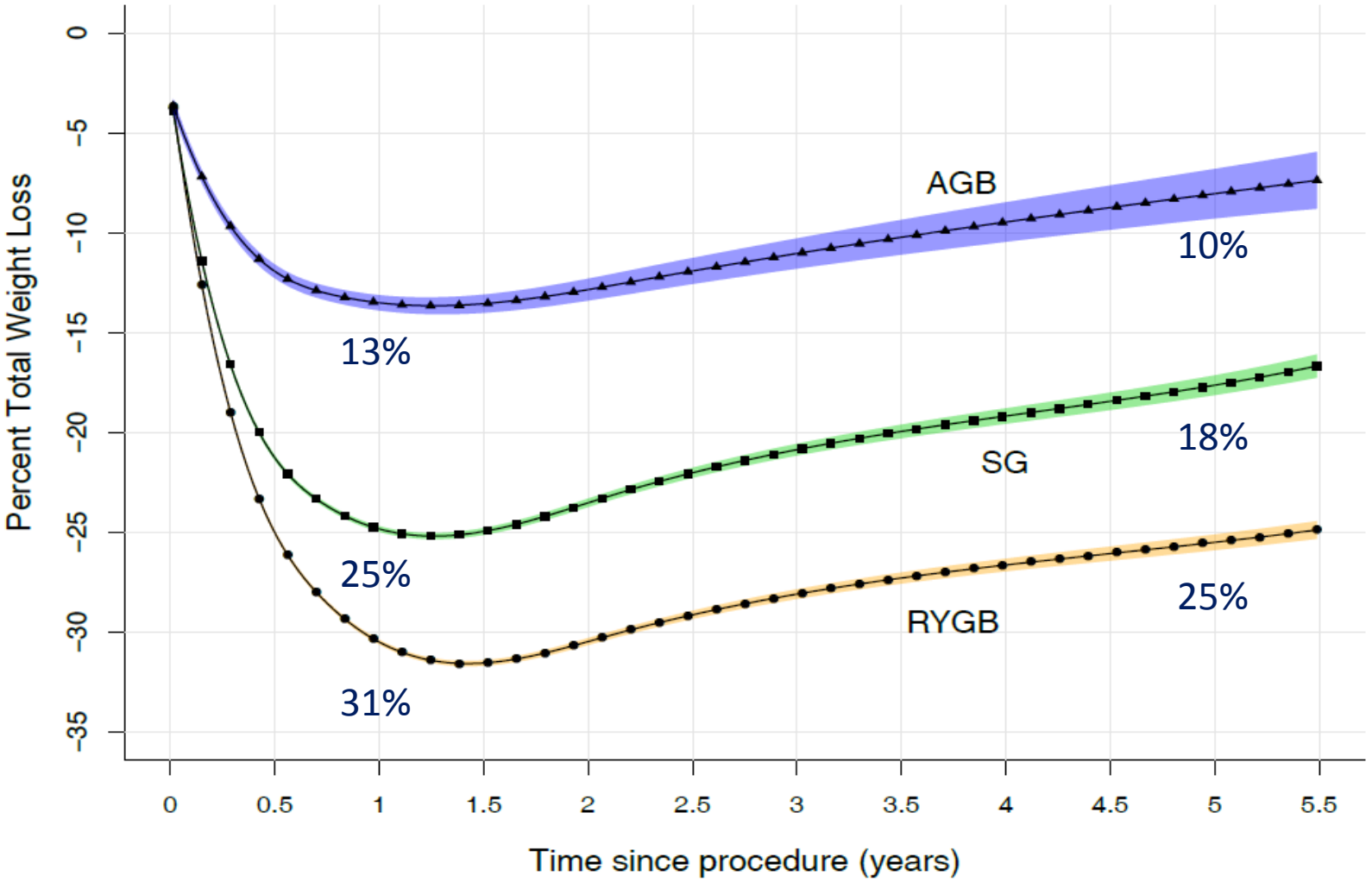

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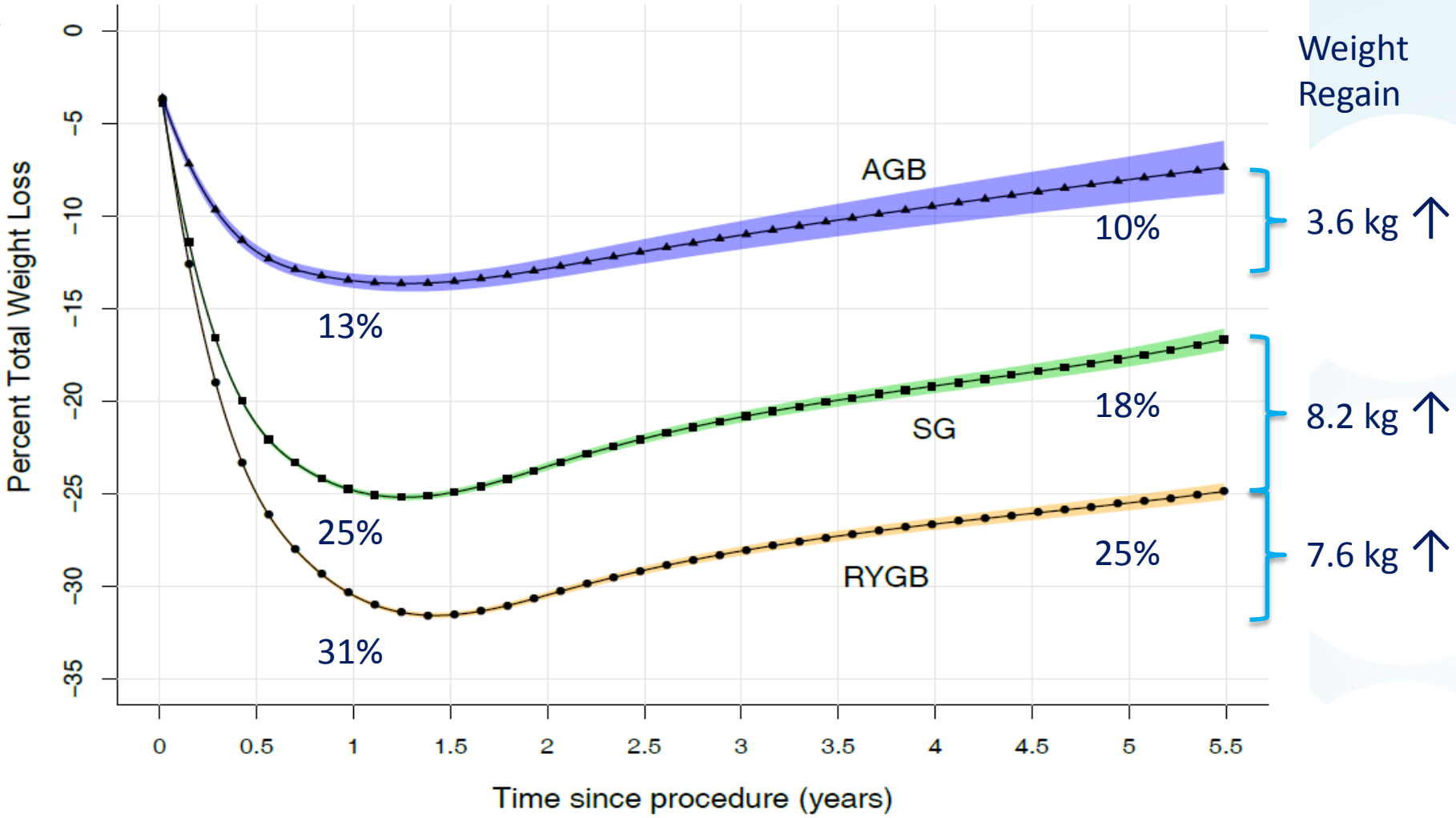

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Subgroups who lost less weight with bariatric surgery

- Older patients (>65 years)
- Patients with diabetes
- African American & Hispanic patients
- Patients with pre-operative BMI <50 kg/m^2
- **Differences were generally <3% TWL**

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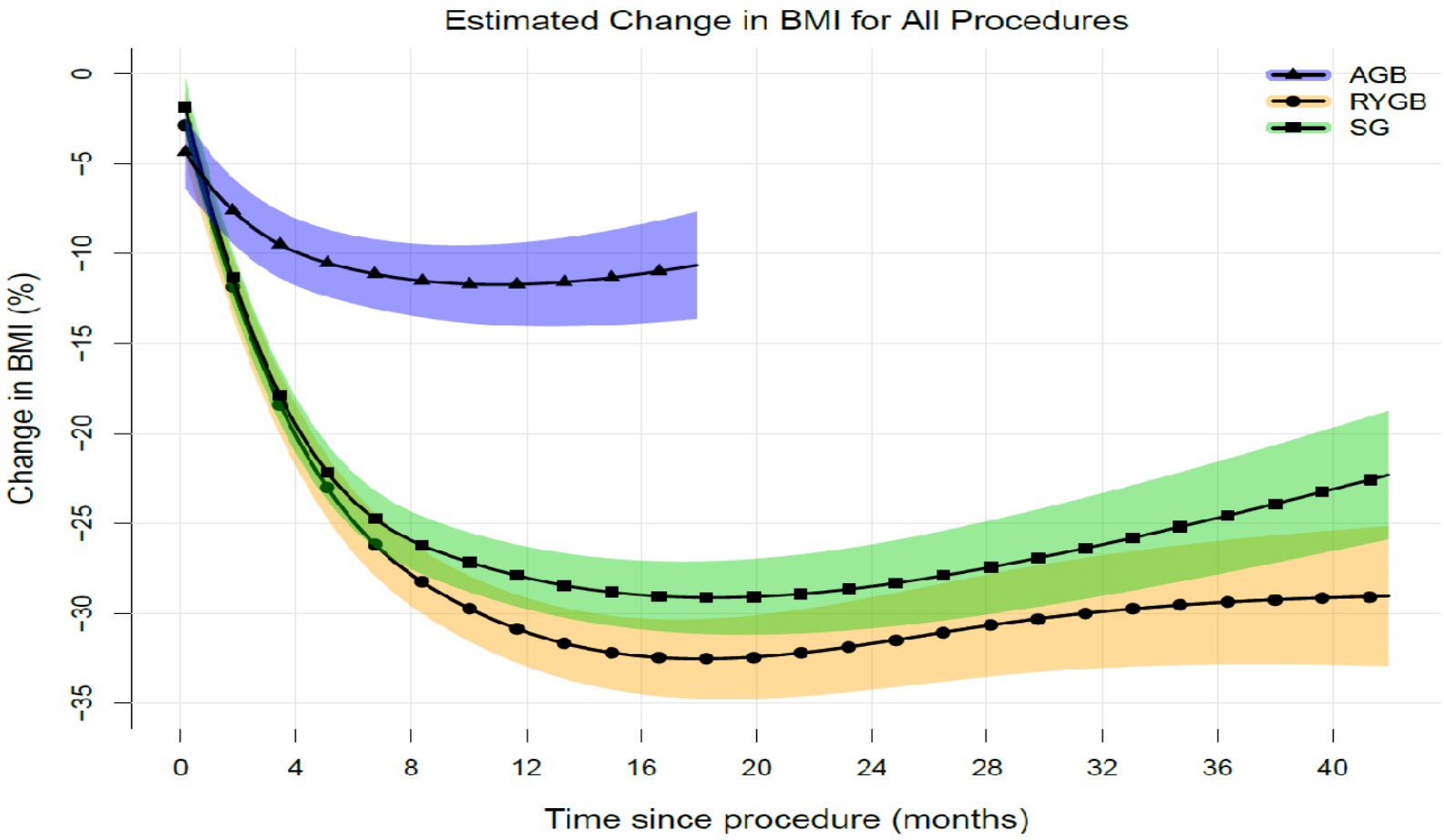
A similar weight loss pattern was seen in 544 adolescents from 27 health systems, but less follow-up data



Inge T, et al for the PBS Collaborative. Surg Obes Relat Dis. 2018 (in press)

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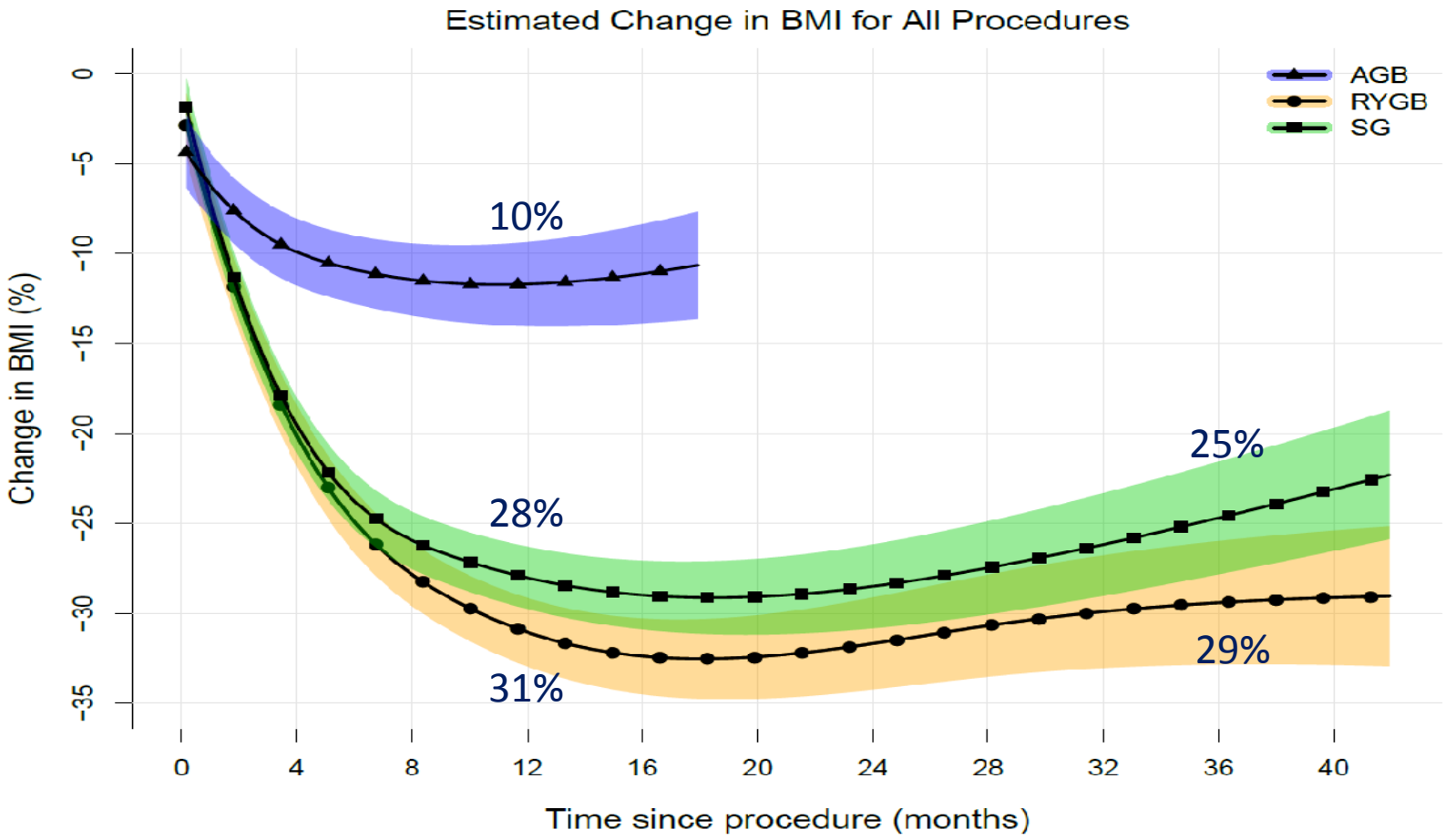

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Aim 2: Diabetes Outcomes

- **Primary Outcome:**
  - **Diabetes Remission:** defined as HbA1c <6.5% after 6 months without any prescription order for a diabetes medication
- **Secondary Outcomes:**
  - **DM Relapse:** defined as HbA1c ≥6.5% or the occurrence of any prescription order for a diabetes medication

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Among 10,019 PBS patients with active diabetes…

- 50% of patients had a HbA1c <7;
  22% had HbA1c ≥8

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Among 10,019 PBS patients with active diabetes…

- 50% of patients had a HbA1c <7; 22% had HbA1c ≥8
- On average, patients used 1.7 DM prescription medications
  - 0 DM meds: 19%
  - 1 DM med: 22%
  - ≥3 DM meds: 20%
- Most common DM drugs: Biguanides (e.g., metformin; 65%), Insulins (48%) & Sulfonylureas (32%)

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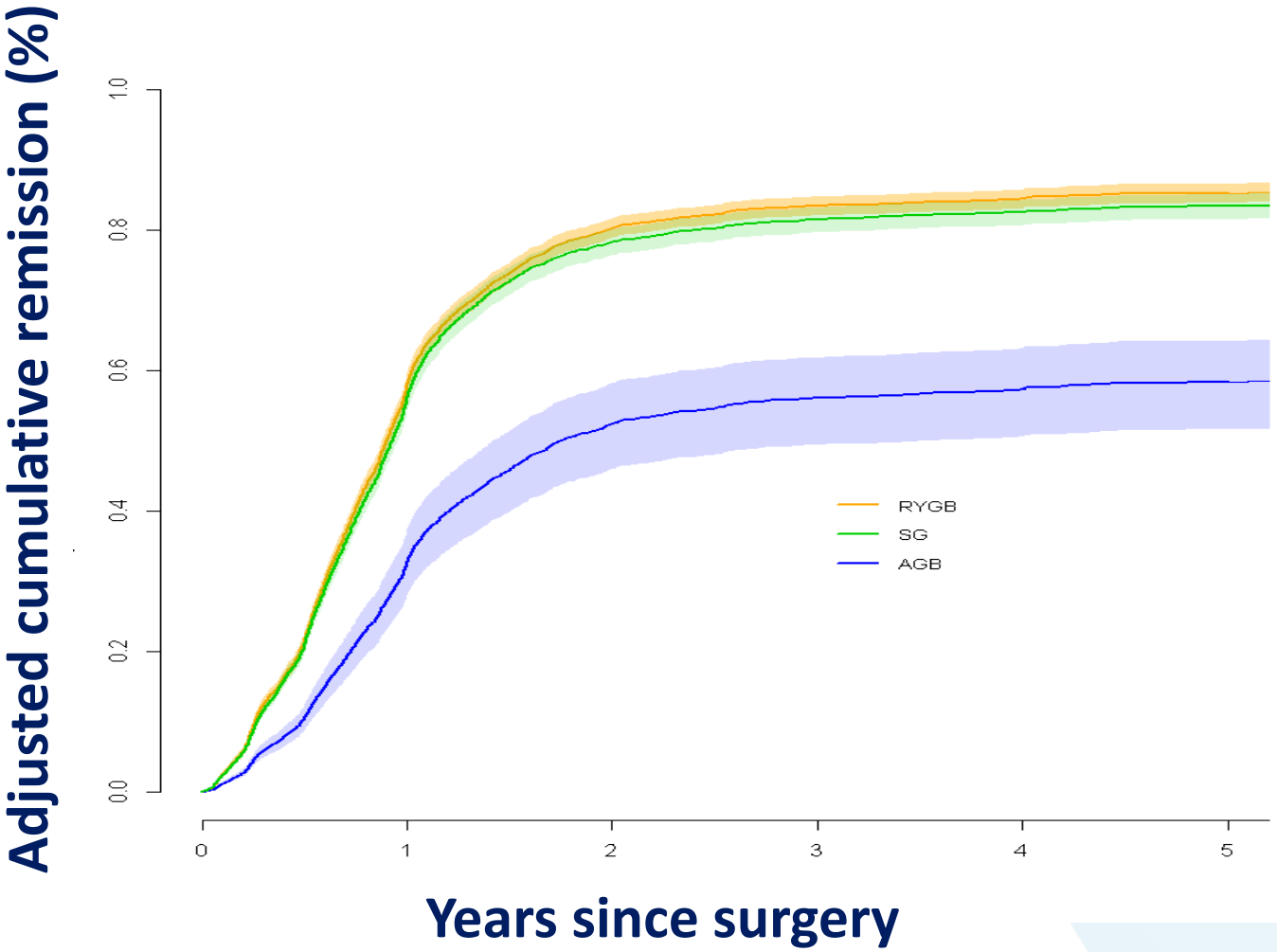
Cumulative incidence of DM remission



RYGB
SG
AGB

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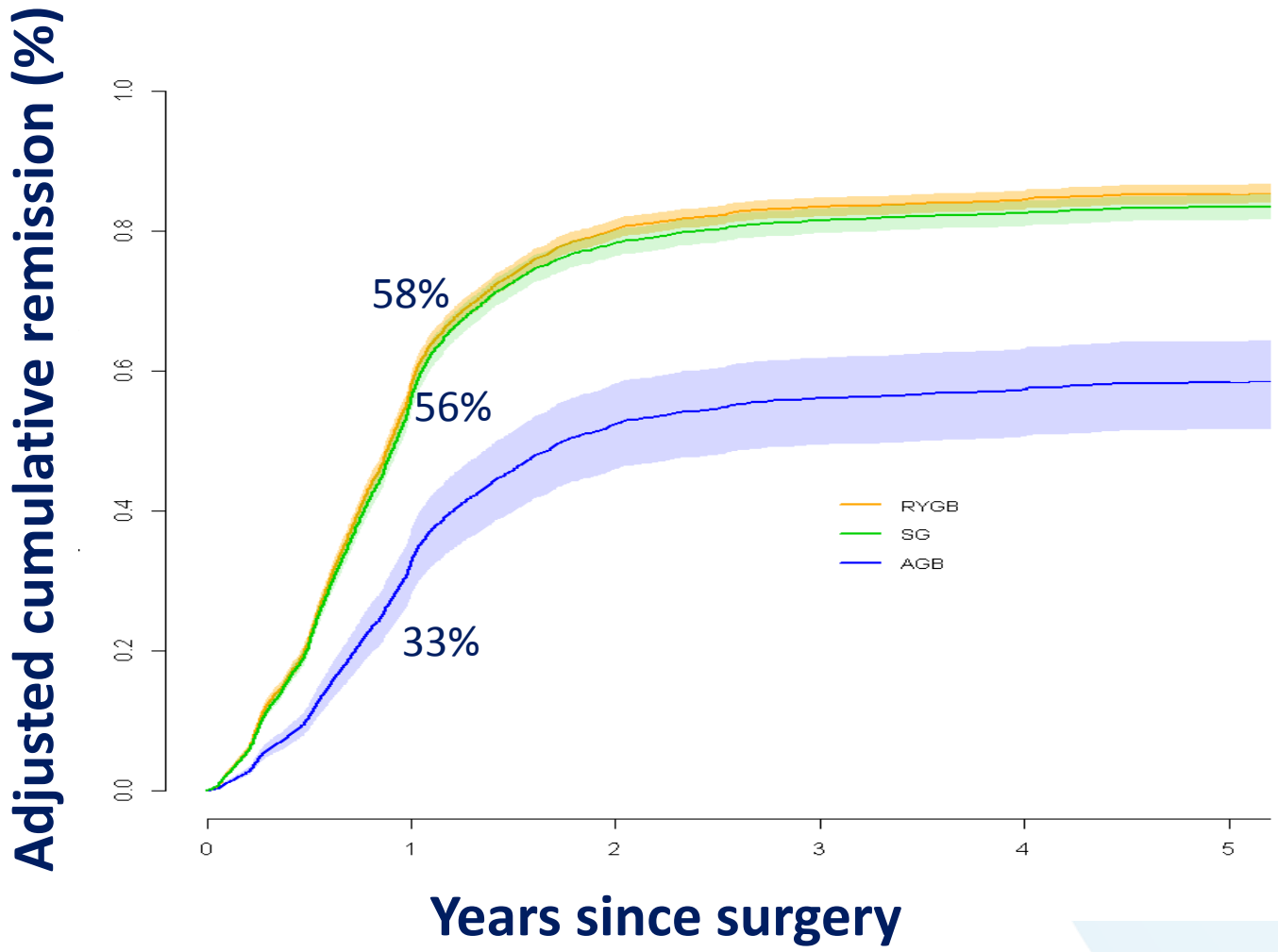

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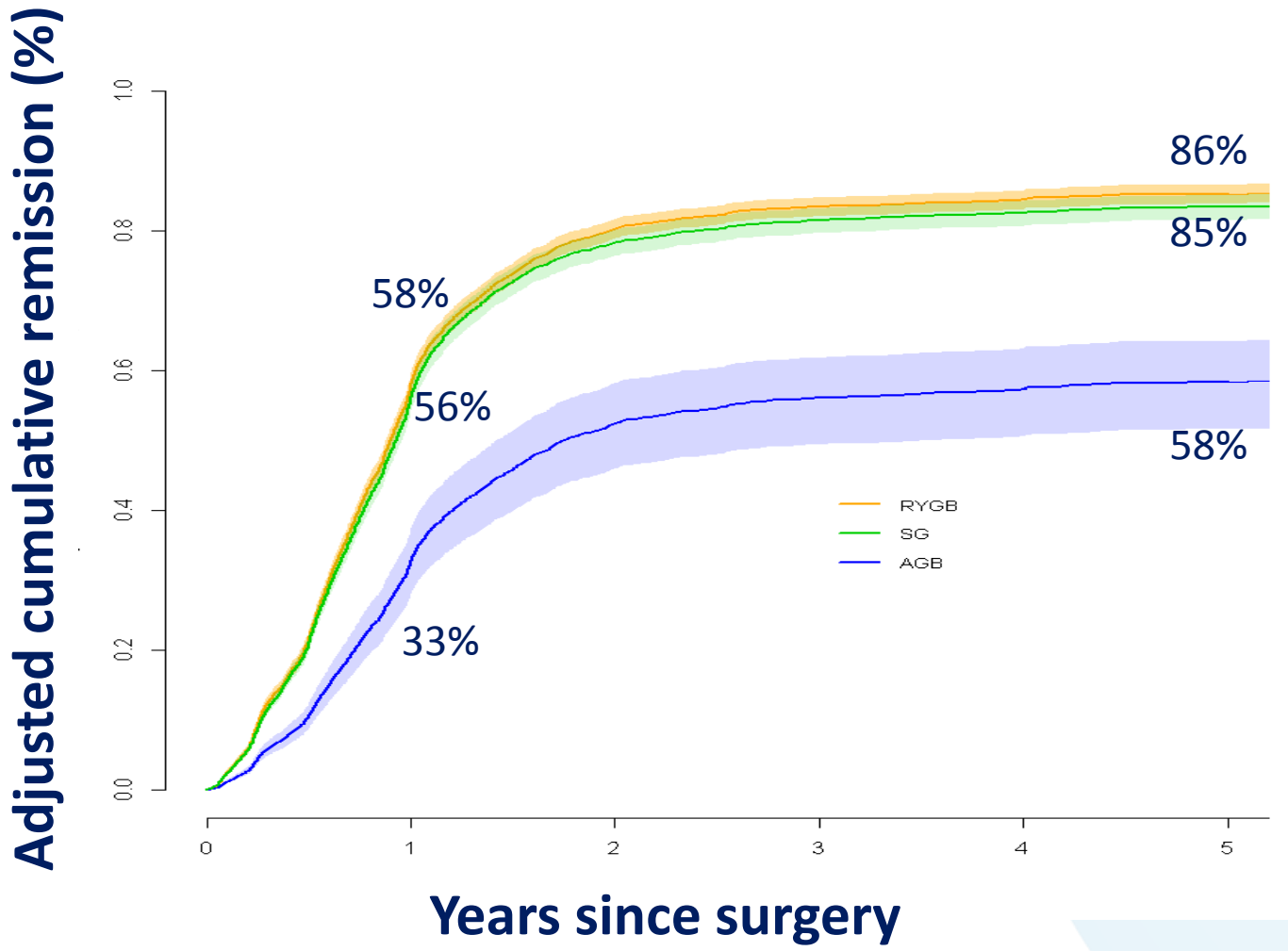

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Adjusted HRs for diabetes remission

Diabetes Remission	Adjusted HR (95% CI)	P-Value
RYGB vs SG	1.10 (1.04, 1.16)	0.007
RYGB vs AGB	2.19 (1.89, 2.53)	<0.0001
SG vs AGB	1.85 (1.53, 2.25)	<0.0001

Rate of remission was:

- **10% higher for RYGB vs. SG patients**
- **~twice as high for RYGB vs. AGB patients**

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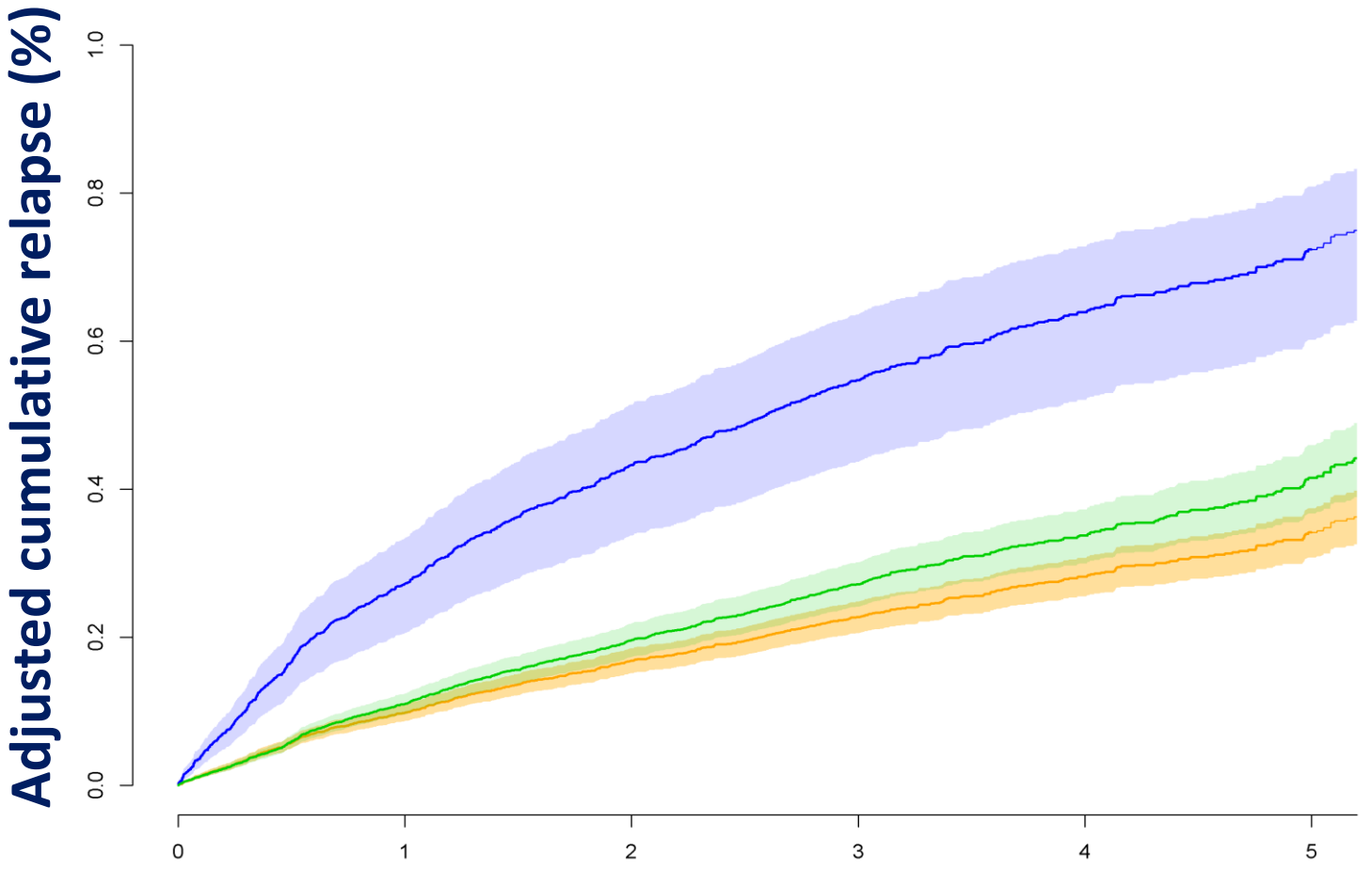
Cumulative incidence of diabetes relapse



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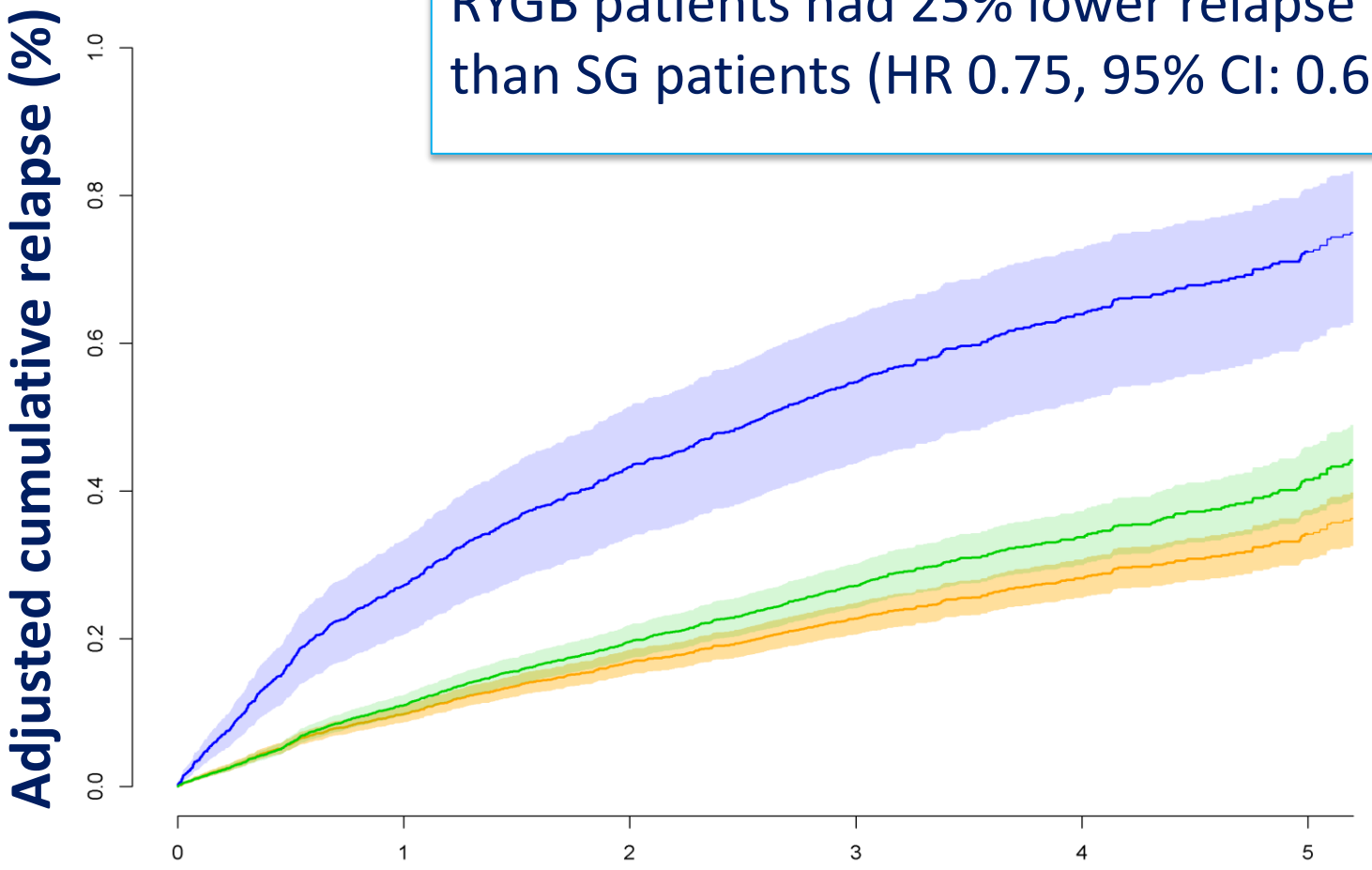
Cumulative incidence of diabetes relapse

RYGB patients had 25% lower relapse rate than SG patients (HR 0.75, 95% CI: 0.67-0.84)



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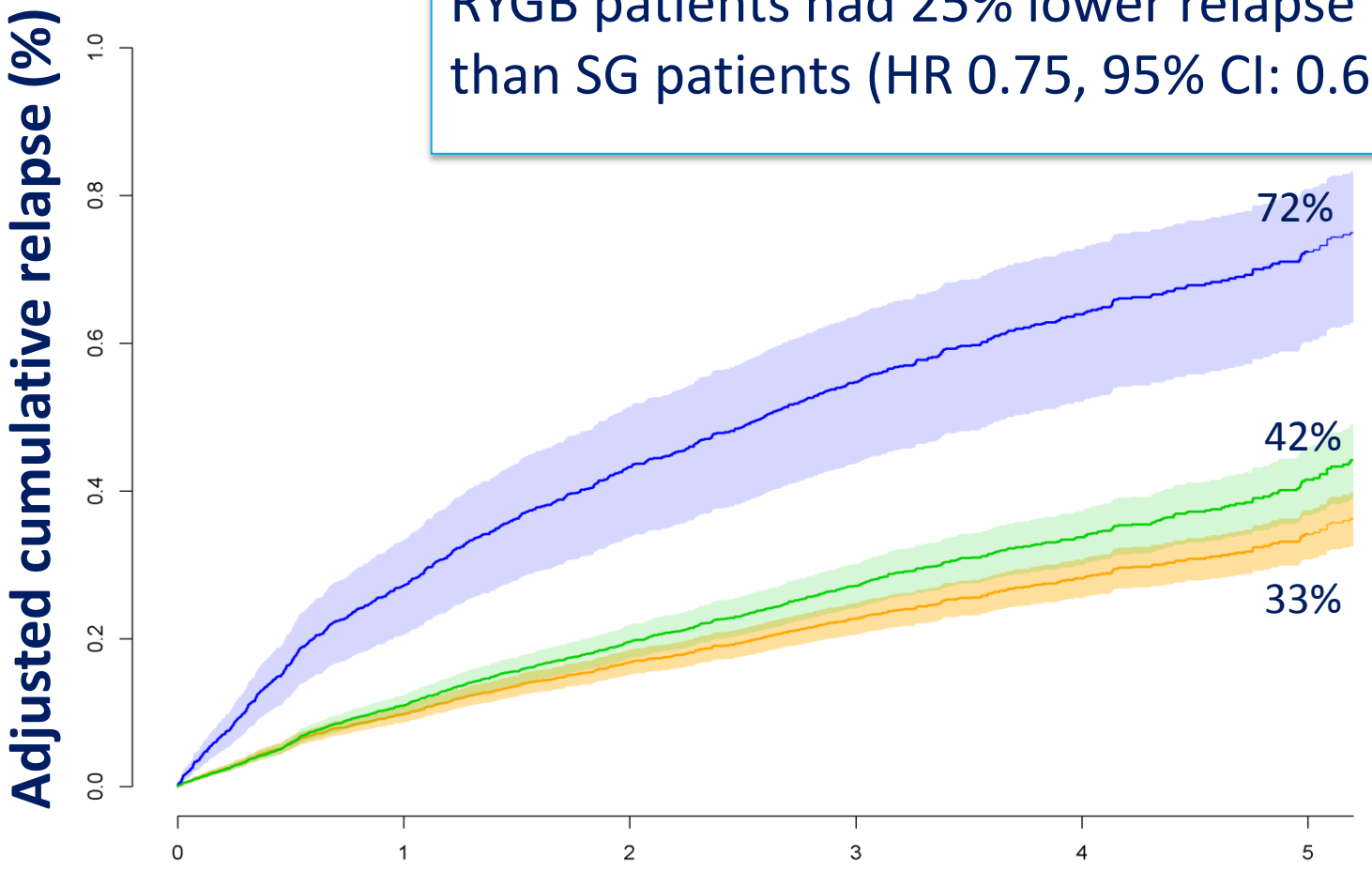

Subgroups with lower rates of remission

- Patients who were prescribed insulin
  - Those who had RYGB had higher rates of DM remission than those who had SG
- Patients with poorly controlled diabetes (HbA1c $\geq$ 7)
  - Those who had RYGB had higher rates of DM remission than those who had SG

Racial/ethnic background & starting BMI (<50 vs $\geq$50) did not impact DM remission rates

Aim 3 –Adverse Events

- Data collection restricted to those health systems that had existing linkages to insurance claims and death data **or** sites with sufficient samples and ability to link to claims and death data
- 34,089 adults from 10 sites in 5 CDRNs
- 1, 3, and 5-year Adverse Event Outcomes:
  - Reoperation
  - Reoperation with endoscopy
  - Rehospitalization
  - Mortality
- 30-day rate of Major Adverse Events

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Adjusted 5-year Adverse Events

	SG (n=15504)	RYGB (n=18056)	AGB (n=1154)
Any reoperation	18%	20%	28%
Any reoperation or endoscopy	23%	30%	31%
Rehospitalization (all cause)	33%	38%	42%
Death (all cause)	0.84%	0.89%	1.08%

Adjusted Hazard Ratios
Comparisons Between Procedures

	SG vs RYGB	AGB vs RYGB	AGB vs. SG
30-day Major Adverse Event	0.74*	0.46*	0.62*
Reoperation	0.89*	1.45*	1.62*
Reoperation or endoscopy	0.72*	1.02	1.42*
Rehospitalization (all cause)	0.82*	1.14*	1.39*
Mortality (all cause)	0.94	1.22	1.29

*P<0.05

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Preliminary results. Do not cite without permission from authors.

Limitations

- Observational data; confounding that may have persisted despite covariate & propensity score adjustment
- Missing BMI, HbA1c data may introduce bias
  - Sensitivity analyses suggest missing data were unlikely to change the interpretation of our main results
- Comorbid health conditions identified from ICD-9 may underestimate prevalence, can be inaccurately coded, & do not account for severity
- AGB procedure under-represented as often carried out in small ambulatory surgical centers
- DM medication use is estimated from prescribing data, not dispensing, & does not account for adherence
- Within a calendar year, unable to differentiate loss to follow-up due to administrative reasons vs. health care utilization

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How did stakeholders contribute to the *research idea*?

- **PCORnet Obesity Task Force (2014)** – Generated obesity research topic ideas. Ideas were prioritized, resulting in a PCORI funding announcement for two topics (weight loss surgery; effects of antibiotics on weight in children)

- At PBS kick-off meeting, requested two major changes to science:
  - Do three pair-wise comparisons of bariatric procedures, as opposed to two pair-wise comparisons
  - Interview bariatric surgeons as part of qualitative aim – not just conduct patient focus groups

These activities were carried out, with stakeholder input on data collection and interpretation.

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How did our stakeholders help us *develop and execute our scientific aims*?

- Reviewed plans to identify cohort.
  - Includes reviewing diabetes medication lists, bariatric surgery procedure codes.
- Using the same process as investigators, prioritized our HTE analyses. Final rankings were decided by investigators and stakeholders.
- Actively participated in development of focus group and surgeon interview templates.

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My perspective of Lessons Learned as a Patient PI

- How to Create a collaborative environment where all stakeholders are empowered to share their prospective and expertise - including patients/non-scientists.

- Enhanced understanding and appreciation for the **LIVED EXPERIENCE** in the research process.

- Intentional planning – remember the issues and needs of patients are different than researchers who are funded to carryout this & similar work. Patients need:
  - Funding for dissemination travel
  - Increased time to understand scientific documents
    - Setting time aside to review these w/ partners is invaluable
  - Capacity to securely receive study sensitive data (when it is part of project's output)

- Increased training for patient/non-scientist in the overall research process

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Participating in a PCORI demonstration project: *A network lead PI perspective*

Laura Rasmussen-Torvik, PhD, MPH, FAHA
Assistant Professor
Department of Preventive Medicine
Northwestern University Feinberg School of Medicine

CAPriCORN Network Lead Investigator and Northwestern University Site Investigator for the Bariatric Surgery Demonstration Project

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Health Systems Participating (Contributing Data) in the PCORnet Bariatric Study

CaPriCORN
- Northwestern
- Loyola University
- University of Chicago
- University of Illinois

GPC
- U of Wisconsin - Madison
- Kansas University
- U of Iowa Health Care
- Medical College of Wisconsin
- Marshfield Clinic
- UT Southwestern

PaTH
- Johns Hopkins
- University of Pittsburgh
- Temple University
- University of Utah
- Penn State and Hershey
- Geisinger
- University of Utah

NYC - CDRN
- NYU
- Mount Sinai
- Montefiore/ Einstein
- Weill Cornell

PORTAL
- KP – Southern California
- Health Partners
- KP - Colorado
- KP - Northwest
- KP - Washington
- KP – Mid Atlantic

SCHILHS
- Partners Healthcare
- Boston HealthNet
- Wake Forest Baptist
- Beth Israel Deaconess

PEDSnet
- Cincinnati Children's
- Nemours
- Nationwide

pSCANNER
- UC - Irvine
- UCLA

OneFlorida
- UF Health
- Orlando Health
- Tallahassee Memorial Health System

Mid-South
- Vanderbilt
- Greenway
- UNC

REACHnet
- Tulane
- Baylor Scott & White
- Ochsner

Systems are organized into Clinical Data Research Networks. See pcornet.org for more info.

Critical EARLY education of a (*network lead*) PI

- Working with the PCORI CDM
- The collaborative and administrative nature of a CDRN project

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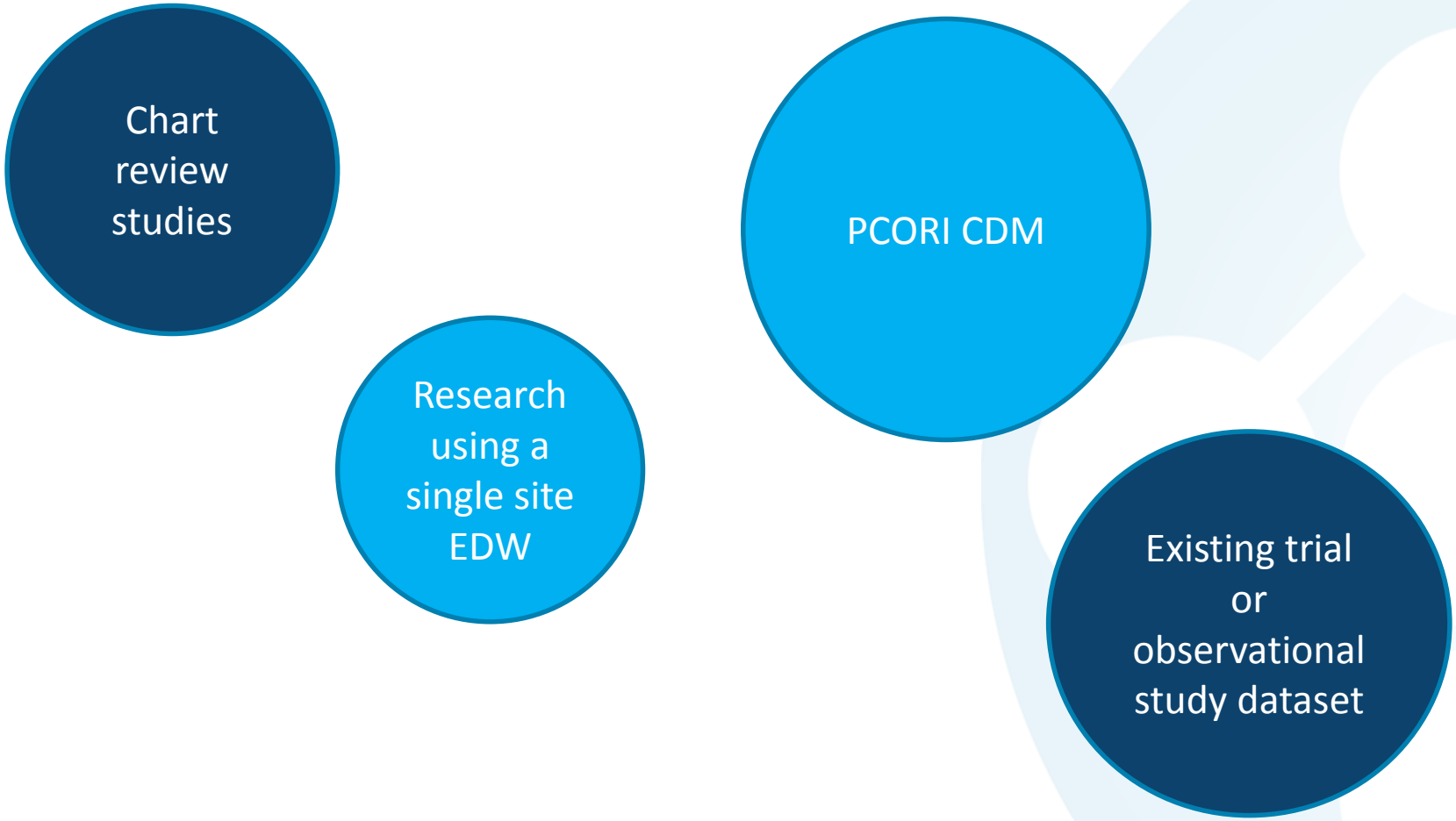
Data sources—bariatric surgery research



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Network lead PI responsibilities

- IRB approval at all node sites
- Budgeting at all node sites
- Monitoring query completion at all node sites
- Stakeholder identification
- Authorship for the network at all node sites
  - *A well-organized central project team is required for all of the above to succeed*
- **Participation on research team**
  - design, analysis and interpretation decisions

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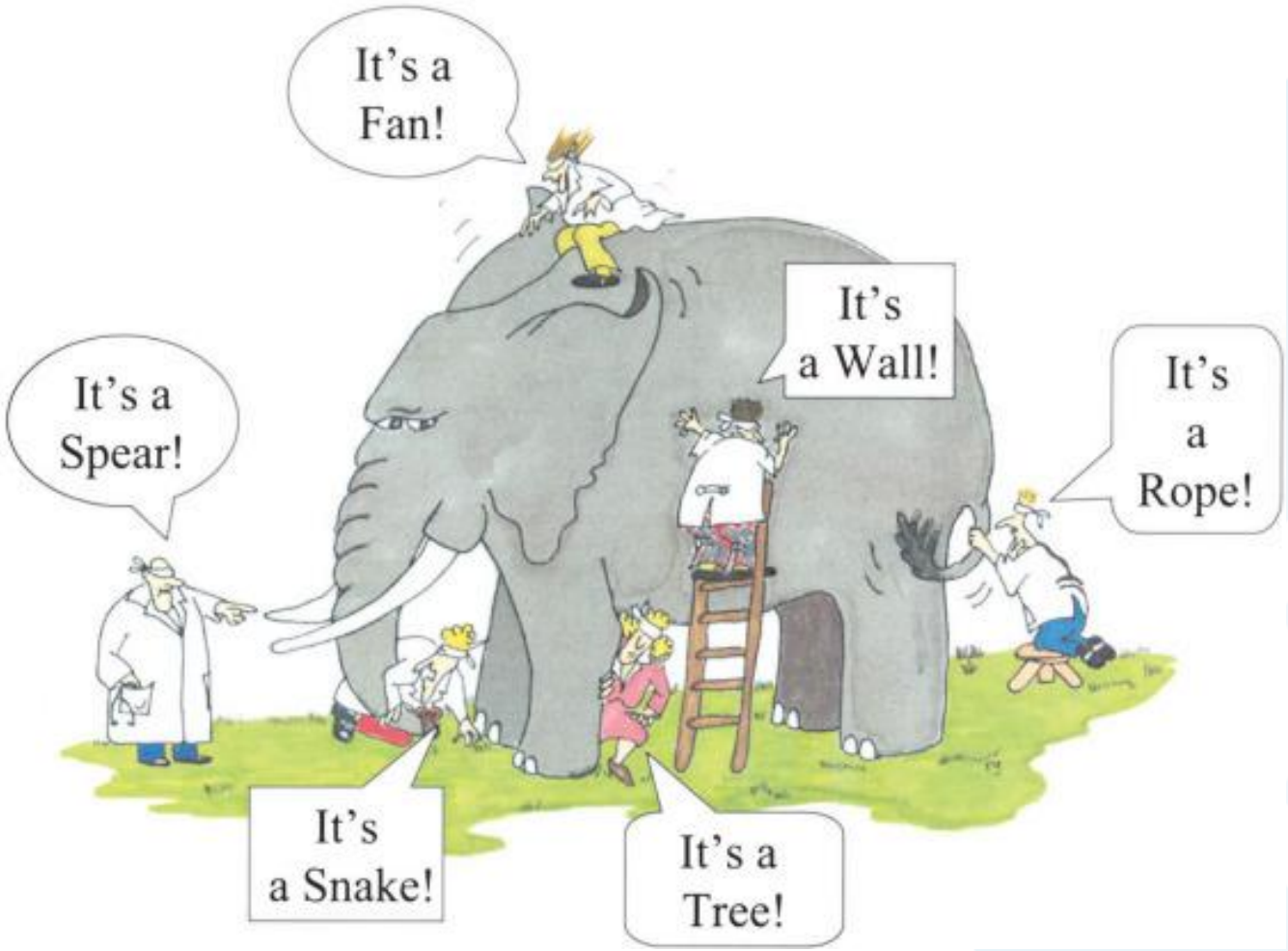
Understanding node site data



The elephant in uremia: Oxidant stress as a unifying concept of cardiovascular disease in uremia Jonathan Himmelfarb, Peter Stenvinkel, T. Alp Ikizler, Raymond M. Hakim Kidney International Volume 62, Issue 5, Pages 1524-1538 (November 2002) DOI: 10.1046/j.1523-1755.2002.00600.x

Critical contributors from each node (*data contributing*) site

- Clinical expert with awareness of local practice patterns
- Informatics expert with understanding of conversion of EHR to CDM
- Topical experts in various aspects of bariatric surgery research

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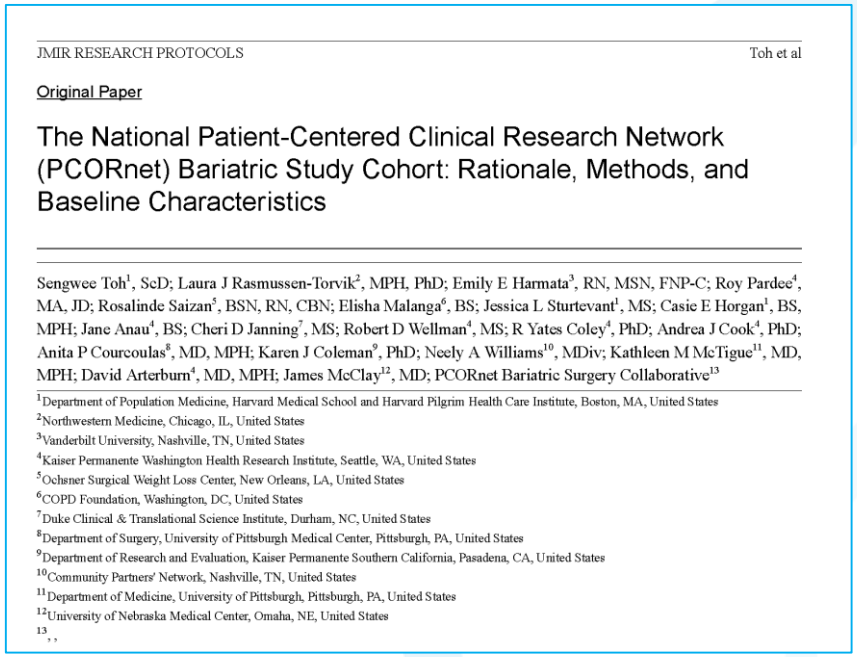
Authorship

- PIs, Scientific Core
- PCORnet CC
- Stakeholders
- Node site
  - Clinical
  - Informatics
  - Topical experts
- Requires central organization
  - Early opportunity for feedback on results
  - Multiple rounds of review before dissemination to a large group
  - *CDRN-level contact with contributors*
  - PCORI guidelines provide framework



JMIR RESEARCH PROTOCOLS Toh et al

Original Paper

The National Patient-Centered Clinical Research Network (PCORnet) Bariatric Study Cohort: Rationale, Methods, and Baseline Characteristics

Sengwee Toh[1], ScD; Laura J Rasmussen-Torvik[2], MPH, PhD; Emily E Harmata[3], RN, MSN, FNP-C; Roy Pardee[4], MA, JD; Rosalinde Saizan[5], BSN, RN, CBN; Elisha Malanga[6], BS; Jessica L Sturtevant[1], MS; Casie E Horgan[1], BS, MPH; Jane Anau[4], BS; Cheri D Janning[7], MS; Robert D Wellman[4], MS; R Yates Coley[4], PhD; Andrea J Cook[4], PhD; Anita P Courcoulas[8], MD, MPH; Karen J Coleman[9], PhD; Neely A Williams[10], MDiv; Kathleen M McTigue[11], MD, MPH; David Arterburn[4], MD, MPH; James McClay[12], MD; PCORnet Bariatric Surgery Collaborative[13]

[1]Department of Population Medicine, Harvard Medical School and Harvard Pilgrim Health Care Institute, Boston, MA, United States
[2]Northwestern Medicine, Chicago, IL, United States
[3]Vanderbilt University, Nashville, TN, United States
[4]Kaiser Permanente Washington Health Research Institute, Seattle, WA, United States
[5]Ochsner Surgical Weight Loss Center, New Orleans, LA, United States
[6]COPD Foundation, Washington, DC, United States
[7]Duke Clinical & Translational Science Institute, Durham, NC, United States
[8]Department of Surgery, University of Pittsburgh Medical Center, Pittsburgh, PA, United States
[9]Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA, United States
[10]Community Partners' Network, Nashville, TN, United States
[11]Department of Medicine, University of Pittsburgh, Pittsburgh, PA, United States
[12]University of Nebraska Medical Center, Omaha, NE, United States
[13], , ,

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Questions?

For more information -

- pcornetbariatricstudy.org
- https://clinicaltrials.gov/ct2/show/NCT02741674
- A description of the study cohort –
  - The National Patient-Centered Clinical Research Network (PCORnet) Bariatric Study Cohort: Rationale, Methods, and Baseline Characteristics. *JMIR Research Protocols*. 2017 Dec 5;6(12):e222.
- Results: Weight loss and regain in adolescents –
  - PCORnet Bariatric Study Collaborative. Comparative effectiveness of bariatric procedures among adolescents: the PCORnet bariatric study. Surg Obes Relat Dis. 2018 Apr 17. [Epub ahead of print]

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