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
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
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
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
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
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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- Mean BMI: 49 kg/m² with 38% BMI 50+ kg/m²
- 60% HTN; 49% Dyslipidemia; 49% OSA; 40% GERD; 37% T2DM; 30% Depression; 21% Anxiety
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RYGB patients had higher BMI & more comorbidity
Availability of follow-up weight measures, adults

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<td>RYGB</td>
<td>24,061 (86%)</td>
<td>12,429 (67%)</td>
<td>5,257 (67%)</td>
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<tr>
<td>Sleeve</td>
<td>18,550 (84%)</td>
<td>6,847 (73%)</td>
<td>1,293 (76%)</td>
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<td>AGB</td>
<td>2,367 (76%)</td>
<td>1,507 (60%)</td>
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Percent Total Weight Loss in Adults

Preliminary results. Do not cite without permission from authors.
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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 $<50 \text{ kg/m}^2$
- Differences were generally $<3\%$ TWL
A similar weight loss pattern was seen in 544 adolescents from 27 health systems, but less follow-up data.
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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
Among 10,019 PBS patients with active diabetes...

- 50% of patients had a HbA1c < 7;
- 22% had HbA1c ≥ 8
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%)
Cumulative incidence of DM remission

Adjusted cumulative remission (%)

Years since surgery

Preliminary results. Do not cite without permission from authors.
Cumulative incidence of DM remission

Years since surgery

Adjusted cumulative remission (%)

RYGB
SG
AGB

58%
56%
33%

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Cumulative incidence of DM remission

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Adjusted HRs for diabetes remission

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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

Adjusted cumulative relapse (%)

Years since initial DM remission

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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)

Years since initial DM remission

Adjusted cumulative relapse (%)

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Cumulative incidence of diabetes relapse

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Adjusted cumulative relapse (%)

Years since initial DM remission

Preliminary results. Do not cite without permission from authors.
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 ≥ 7)
  - Those who had RYGB had higher rates of DM remission than those who had SG

*Racial/ethnic background & starting BMI (<50 vs ≥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
## Adjusted 5-year Adverse Events

<table>
<thead>
<tr>
<th>Event</th>
<th>SG (n=15504)</th>
<th>RYGB (n=18056)</th>
<th>AGB (n=1154)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any reoperation</td>
<td>18%</td>
<td>20%</td>
<td>28%</td>
</tr>
<tr>
<td>Any reoperation or endoscopy</td>
<td>23%</td>
<td>30%</td>
<td>31%</td>
</tr>
<tr>
<td>Rehospitalization (all cause)</td>
<td>33%</td>
<td>38%</td>
<td>42%</td>
</tr>
<tr>
<td>Death (all cause)</td>
<td>0.84%</td>
<td>0.89%</td>
<td>1.08%</td>
</tr>
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## Adjusted Hazard Ratios
### Comparisons Between Procedures

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

*P<0.05

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

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
Data sources—bariatric surgery research

Chart review studies

Research using a single site EDW

PCORI CDM

Existing trial or observational study dataset
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

Terms and Conditions
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
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
Questions?

For more information -

- pcornetbariatricstudy.org
- https://clinicaltrials.gov/ct2/show/NCT02741674
- A description of the study cohort –
- Results: Weight loss and regain in adolescents –