Lessons Learned
MDCRC 6200: SR/MA

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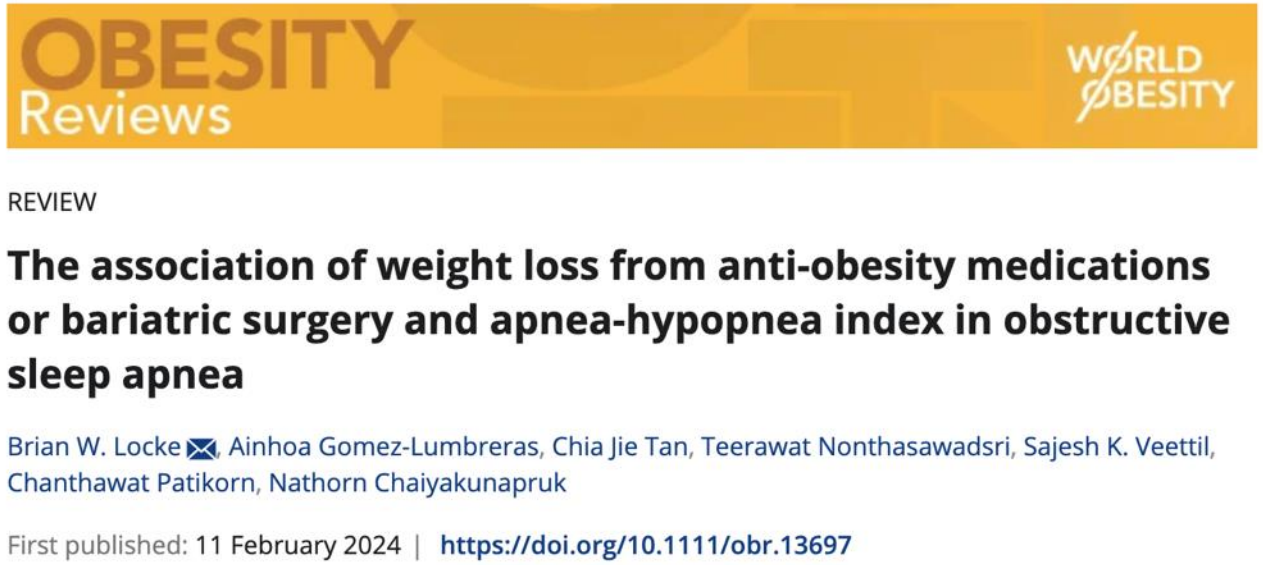
Objectives

- Walk through the timeline of our project (MDCRC 6200 ‘22)
- Discuss considerations for topic choice
- Discuss some things that went well (& not) with our team
- Highlight pitfalls
- Open discussion/brainstorm

Aim to publish your stuff!

- It's bad [science] to abandon partly completed SRMAs
- Get [career] credit for the time you spend
- You'll learn the most by making the project 'publication quality'
- There are venues for all types of project – **just scope it correctly**

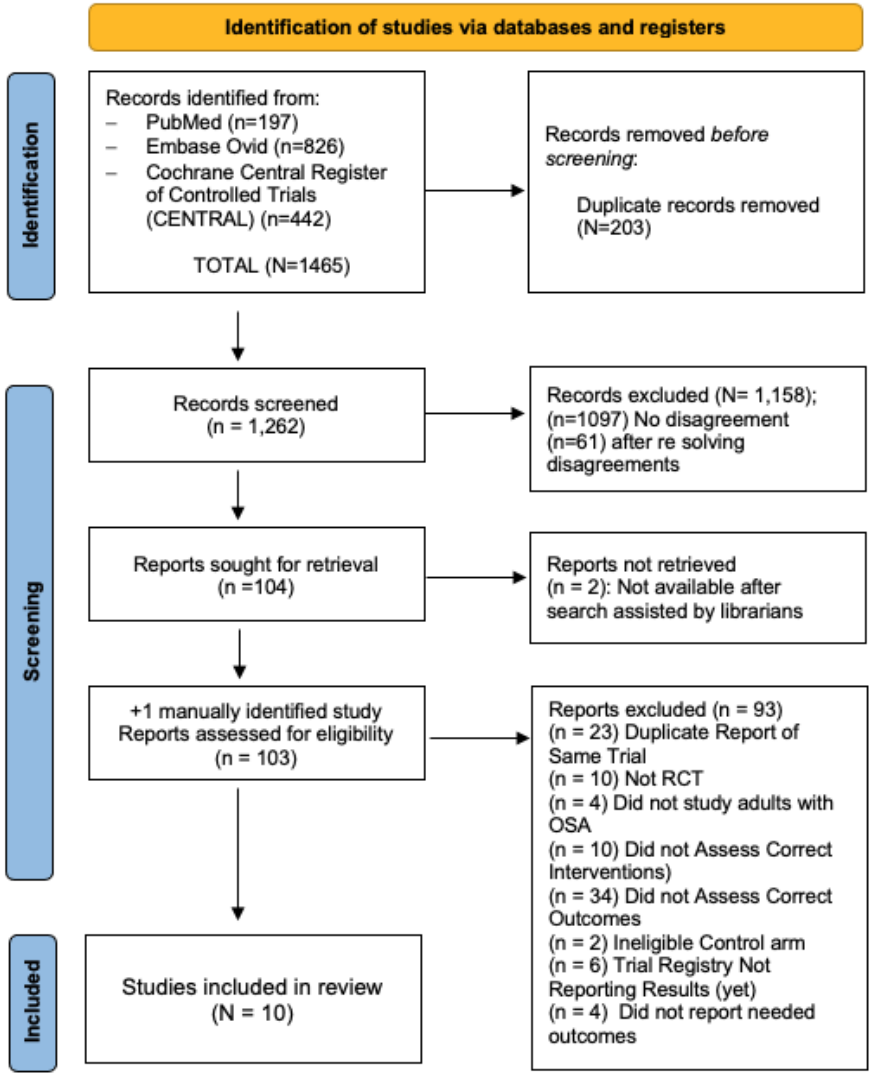


Group of 3 (Tee, Ainhoa, Myself) – rest of TA's contributed, especially CJ after course completed.

Topic Choices

- ~~Hypercapnia & Weight~~ 1 study
  - Limited by the literature
- ~~Prevalence of OSA in ICU~~ boring
  - Need group enthusiasm
- OSA & Weight Loss?
  - GLP-1RAs → Meds → Meds & Surg
  - Initially, only found 3 studies
  - Ultimately found 10 (trial registers!)

→ **Gap:** little direct evidence on new weight management options **(GLP-1s)** & OSA



Our PICO(T): RCTs involving…

- Patients: *adults with overweight or obesity and who have OSA*
- Intervention: *either an anti-obesity medication (FDA approved or not) or bariatric surgery.*
- Comparison: *placebo, no treatment, or usual care (including CPAP or lifestyle modification).*
- Outcome: change in Apnea Hypopnea Index (AHI)
- (Time): at least 4 weeks duration

- Question: How much heterogeneity in AHI change is explained *percentage weight change between randomization and last follow-up*

The real (50 million * $3,000/yr =) $150 billion question: Will tirzepatide treat OSA?

Strengths of our Topic:

- Emerging field (**GLP-1 RA's!**) with a knowledge gap
- Able to quantitatively analyze
  - meta-analysis and meta-regression
  - 3→10 RCTs (started borderline low, ended borderline high)
- Similar analyses existed, but never our question & we had new studies

OBESITY Reviews
WORLD OBESITY

OBESITY COMORBIDITY/TREATMENT | Full Access

Weight loss and lifestyle interventions for obstructive sleep apnoea in adults: Systematic review and meta-analysis

Almudena Carneiro-Barrera, Amparo Díaz-Román, Alejandro Guillén-Riquelme, Gualberto Buela-Casal

First published: 04 January 2019 | https://doi-org.ezproxy.lib.utah.edu/10.1111/obr.12824 |
Citations: 78

Systematic review registration number: PROSPERO 2018 CRD42018102740

JOURNAL ARTICLE

Effectiveness of Lifestyle Interventions on Obstructive Sleep Apnea (OSA): Systematic Review and Meta-Analysis FREE

Marzieh Hosseini Araghi, BSc, MPH, Yen-Fu Chen, PhD, Alison Jagielski, BSc, MSc, Sopna Choudhury, BSc, Dev Banerjee, BSc, MBChB, MD, FRCP, Shakir Hussain, PhD, G. Neil Thomas, PhD, Shahrad Taheri, MBBS, PhD, FRCP

Sleep, Volume 36, Issue 10, 1 October 2013, Pages 1553–1562, https://doi.org/10.5665/sleep.3056
Published: 01 October 2013 **Article history**

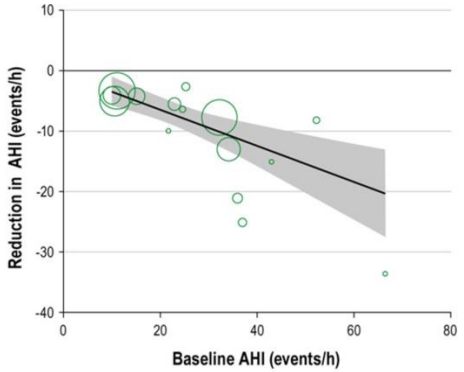


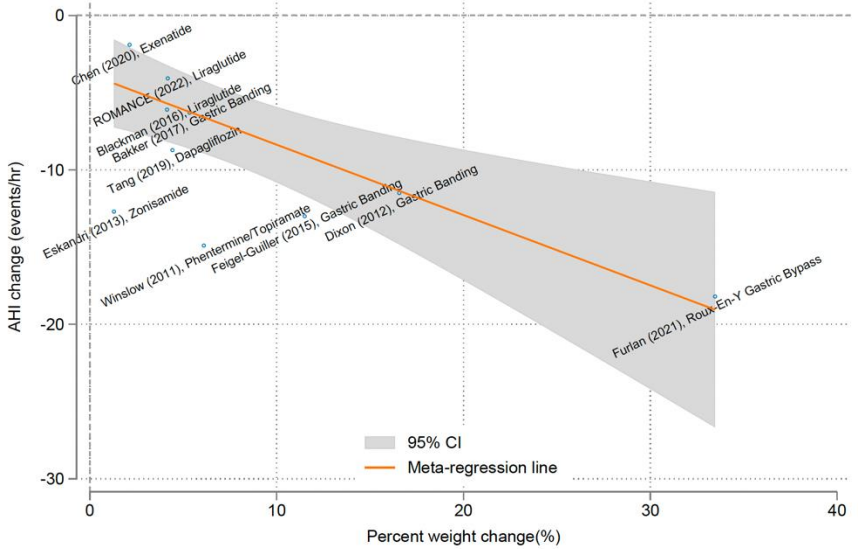
Figure 7 Meta-regression of baseline AHI against reduction AHI (the shaded area represents the 95% confidence intervals).

Weaknesses of our topic

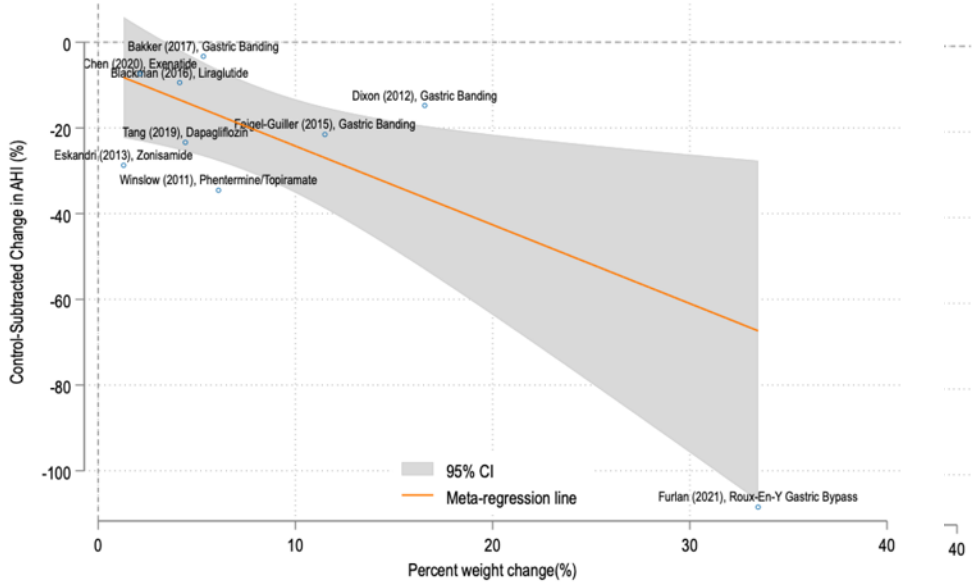
- Many ongoing trials
  - Short window before needing to redo
  - Pressure with other SRMA groups

  (also, indicates of a good topic)
- Meta-regression: more nuanced*
  - **Be careful with complex analyses**
  - Expertise, reviewers, etc.

  (but, enabled addressing a gap)

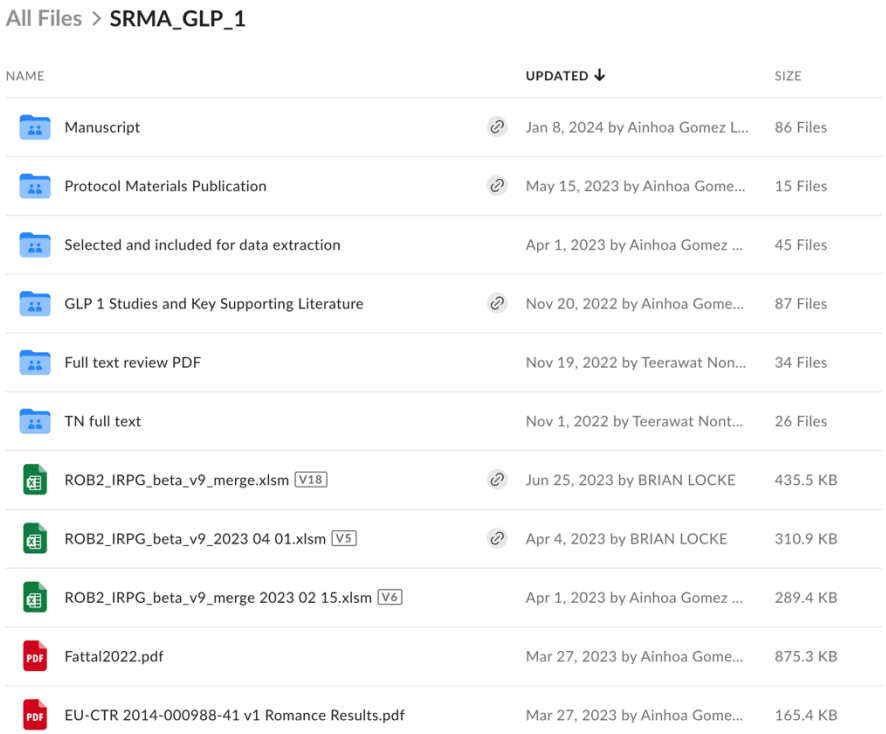


12.3 Meta-regression of AHI relative change vs % weight loss



Strengths / Weaknesses of our team

- Mix of interests and strengths
  - Defined roles: methods & subject matter, metabolic research, systematic review expert, etc.
  - Organization:
    - we used a shared box **(discuss conventions)**
    - ultimately github for the code: https://github.com/reblocke/AOM-and-Bari-Surg-for-OSA-SRMA



Timeline

- The class deadlines come fast
  - Sessions are more useful the more you've done.
  - Polished > Rough >> Nothing
  - Objectives build on each other
    - Don't fall behind early!

Date	Topics
Week 3 09/03	Ignite #1 – Research proposal presentation
Week 6 09/24	Ignite #2 – Search/screening presentations
Week 10 10/29	Ignite #3 – Data extraction, study characteristics, and prelim results
Week 13 11/19	Ignite #4 – Prelim Findings & Abstract

Progress will be **MUCH** slower once the class finishes.

TABLE 1 Characteristics of included studies. *N* refers to the number randomized. %Female and age are presented as intervention: control. ROMANCE trial is presented as a name given that the trial publication has not yet been released. Compared to PSG, HSAT results in a lower AHI due to the inability to capture arousals and the use of recording time as a surrogate for total sleep time.[48] AASM 1999 = 10s duration; 50% airflow decrease from baseline or both 30% decrease and a 3% desaturation or arousal. AASM 2007 = 1999, but hypopneas must result in 4% desaturation or arousal; AASM 2012 = 1999, but hypopneas must result in a 3% oxygen desaturation or arousal. The distinction is relevant because the 1999 criteria scores more events than the 2012 criteria, which scores more events than the 2007 criteria.[49] In the study by Yiangou and colleagues, patients were assigned to a bariatric surgery pathway, where Roux-en-Y gastric bypass, gastric sleeve, or gastric banding could be performed after shared decision-making between patient and surgeon. N/A = not applicable, as the formal report from the ROMANCE trial is not yet published, and results are taken from the clinical trial registration.

1st author	Year	Country	Num of sites	Intervention	*N*	Comparison	N	% Female by arm	Age by arm	Follow-up (months)	Hypopnea definition	Sleep test	Overall risk of bias
Surgery													
Bakker[37]	2017	USA	2	LGB	28	CPAP	21	43:43	50.7 ± 9.2:46.3 ± 10.5	18	AASM 1999	PSG	Some concerns
Dixon[40]	2012	AUS	7	LAGB	30	Conventional Weight Loss Program	30	43:40	47.4 ± 8.8:50.0 ± 8.2	24	Not specified, but required to be the same on reassessment	PSG	Some concerns
Feigel-Guiller[39]	2015	FRA	1	LAGB	33	Intensive Nutritional Care	33	47:25	46.9 ± 8.6:50.1 ± 7.4	36	French Guidelines (as of 1999)	PSG	High risk
Furlan[38]	2021	BRA	1	Roux-en-Y Bypass	29	Usual Care	19	92:69	40[36–49]:48 [39–53]	36	AASM 2012	HSAT	High risk
Pharmacologic													
Blackman[41]	2016	USA & CAN	40	Liraglutide 3 mg	180	Placebo	179	28:28	48.6 ± 9.9:48.4 ± 9.5	8	AASM 2007	PSG	Low risk
Chen[46]	2020	CHN	1	Exenatide	22	Insulin	21	55:52	51.14 ± 15.25:55.35 ± 11.83	3	Not Reported	PSG	Some concerns
Eskandari[42]	2013	SWE	1	Zonisamide	16	Placebo	16	0:13	55 ± 10:53 ± 14	1	AASM 2007	HSAT	Low risk
ROMANCE[43,47]	N/A	UK	1	Liraglutide 3 mg ± CPAP	66	Placebo ±CPAP	66	58:52	54.5[45–61]:53.5 [49–57]	26	AASM 2007	HSAT	Some concerns
Tang[44]	2019	CHN	2	Dapagliflozin and Metformin	18	Glimepiride and Metformin	18	45:35	56.1 ± 7.2:57.9 ± 10	6	Chinese Medical Society	HSAT	Some concerns
Winslow[45]	2010	USA	1	Phentermine-ER/ Topiramate	22	Placebo	23	59:35	53.4 ± 7.0:51.4 ± 5.7	7	Not Reported	PSG	Low risk

Abbreviations: CPAP, continuous positive airway pressure; HSAT, home sleep apnea testing; LAGB, laparoscopic adjustable gastric banding; LGB, laparoscopic gastric banding; PSG, in-lab polysomnography; ER Extended Release; AUS, Australia; BRA, Brazil; CAN, Canada; CHN, China; FRA, France; SWE, Sweden; UK, United Kingdom; USA, United States of America.

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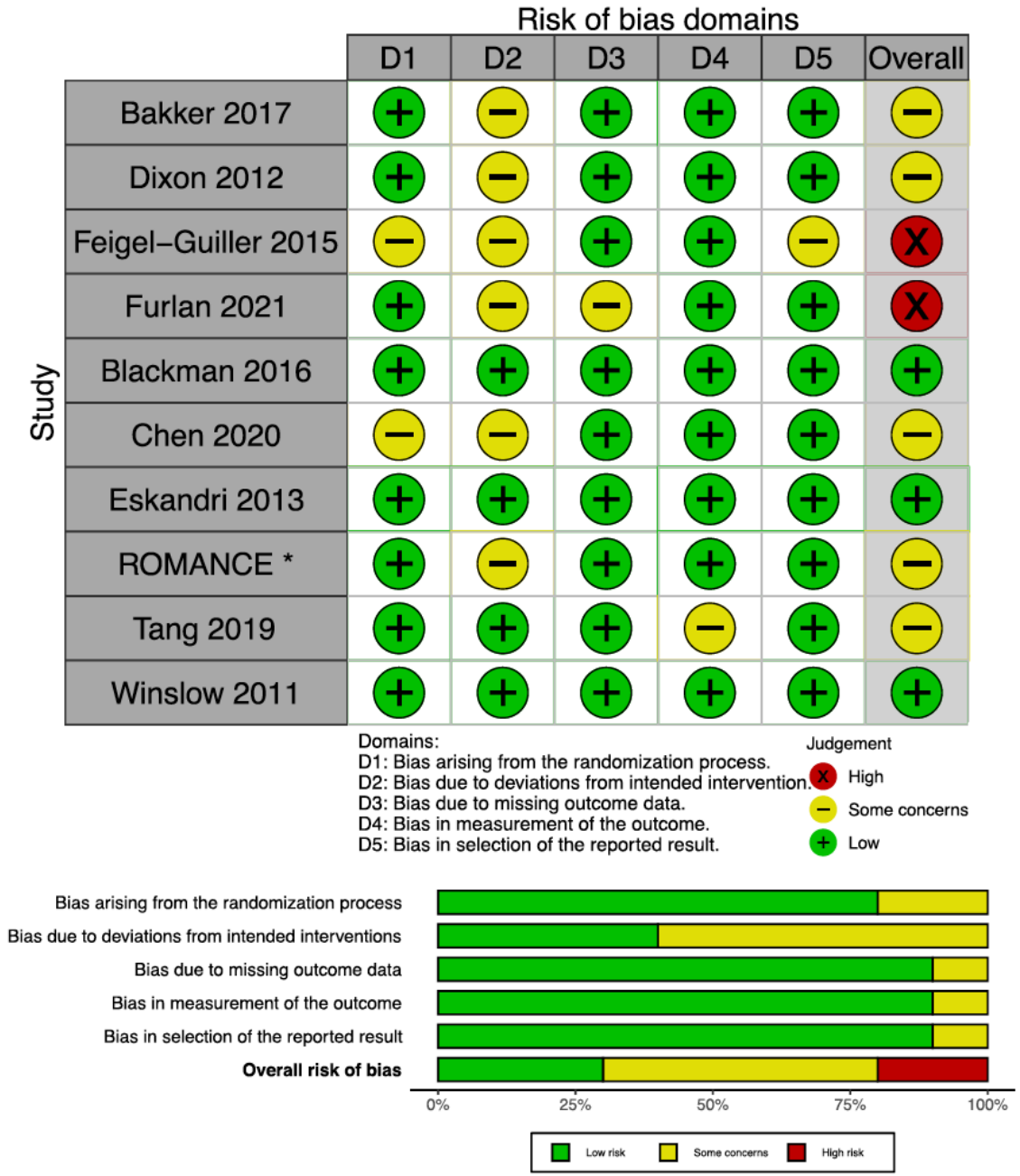

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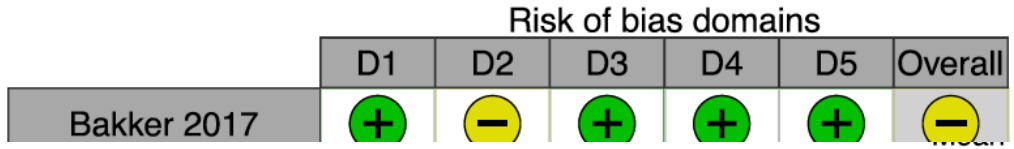
Sleep test	Overall risk of bias
PSG	Some concerns
PSG	Some concerns
PSG	High risk
HSAT	High risk
PSG	Low risk
PSG	Some concerns
HSAT	Low risk
HSAT	Some concerns
HSAT	Some concerns
PSG	Low risk

lab polysomnography; ER

FIGURE 2 Risk of bias of included studies. Generated using robvis package.[50] Risk of bias was assessed in five domains: randomization (D1), deviation from intended intervention (D2), missing outcome data (D3), outcome measurement (D4), and selection of reported results (D5).



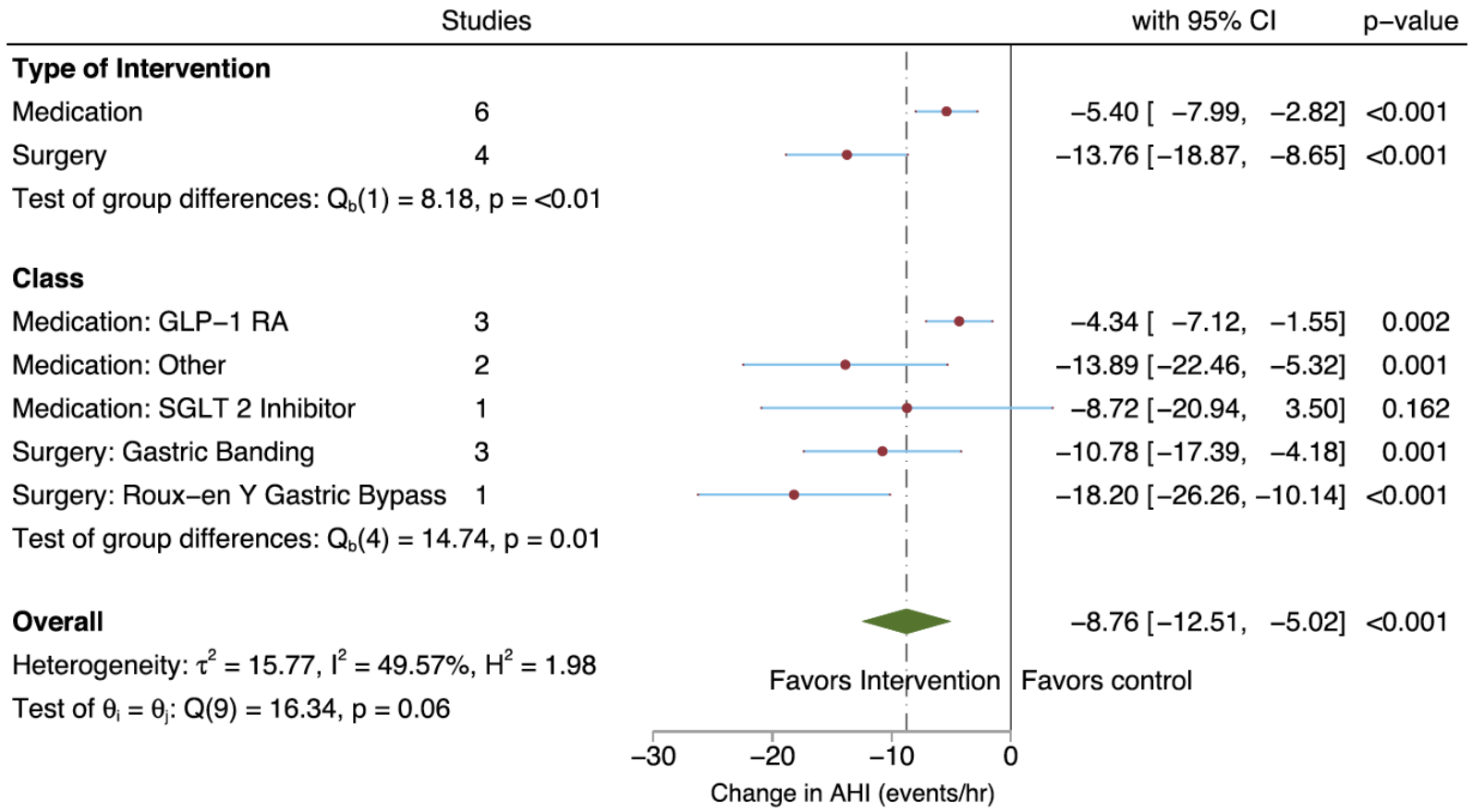
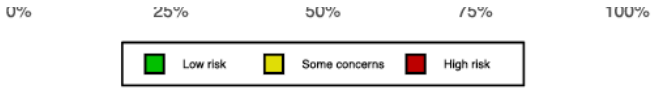


FIGURE 3 AHI change caused by weight loss interventions, grouped by type of intervention and intervention class. Random effects metanalysis. "Other" medication class includes phentermine/topiramate (stimulant and carbonic anhydrase inhibitor) and zonisamide (carbonic anhydrase inhibitor).



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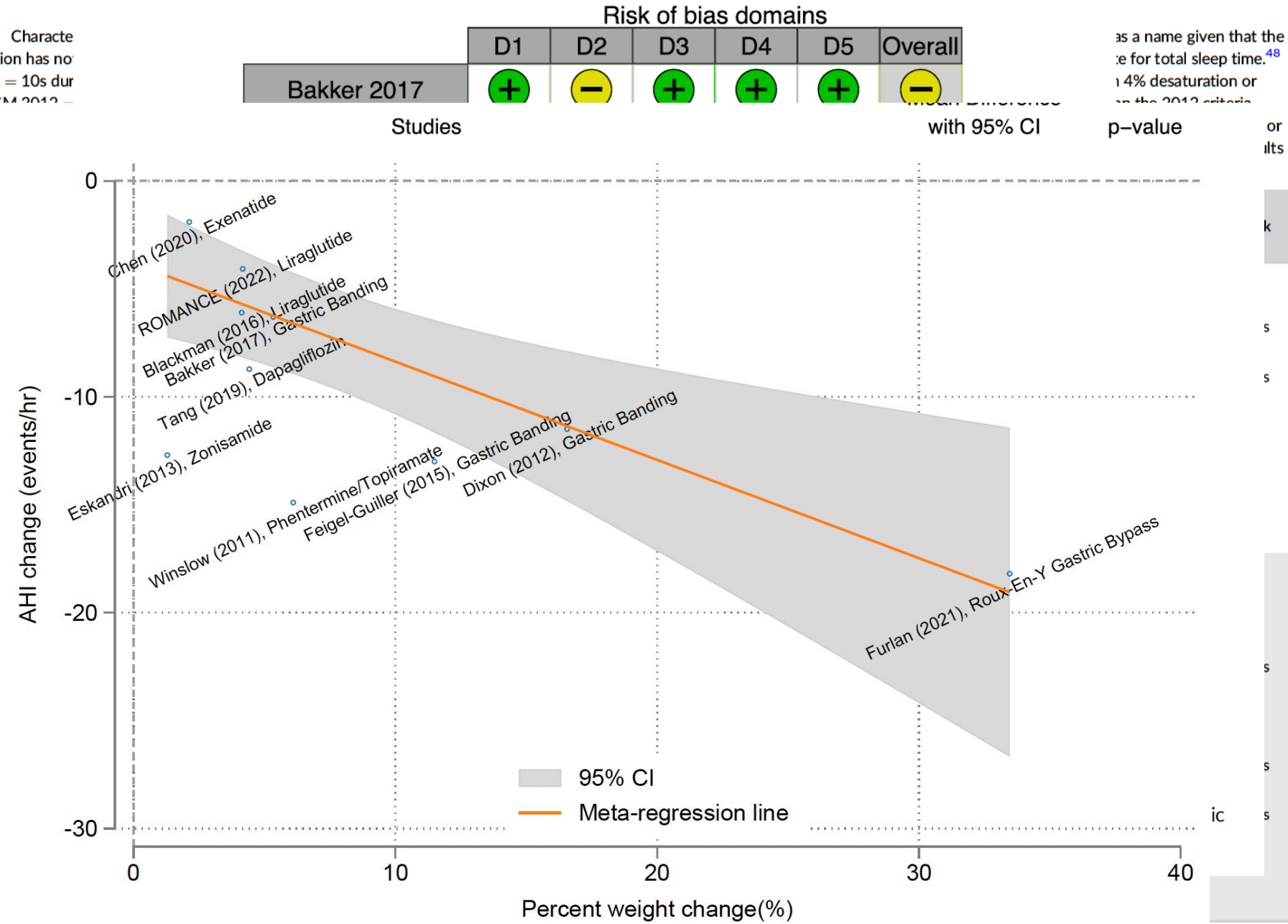

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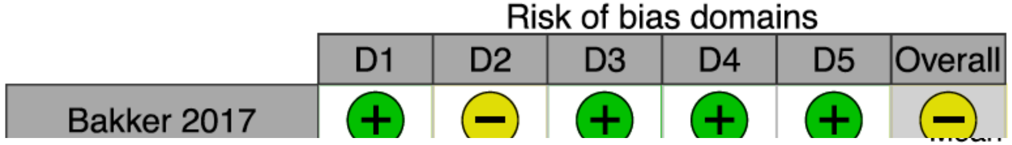


Studies | with 95% CI | p–value

AHI change (events/hr)

0

-10

-20

-30

Table of Contents

Meta-regression line

0 10 20 30 40

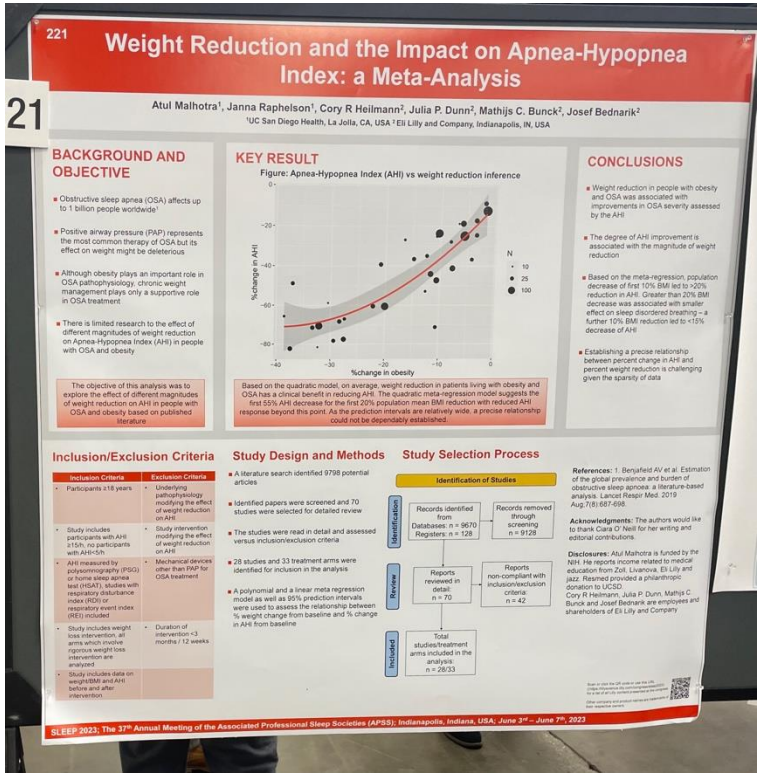
Percent weight change(%)

Abbreviations: CPAP, co ... lab polysomnography; ER Extended Release; AUS,

FIGURE 2 Risk of bias of included studies. Generated using robvis package.[50] Risk of bias was assessed in five domains: randomization (D1), deviation from intended intervention (D2), missing outcome data (D3), outcome measurement (D4), and selection of reported results (D5).

Our Progress:

- Completed draft Dec 2022
- Fine-tuned methods/figures & **back-and-forth data requests from borderline includable studies*** until June 2023
- Submitted ➞ Reject from JAMA Network Open June 2023
- Submitted to Obesity Review – July 2023
- Revisions – Sept to Oct 2023
- Accepted Dec 2023
- Published Feb 2024



Our Progress:

- Completed draft Dec 2022
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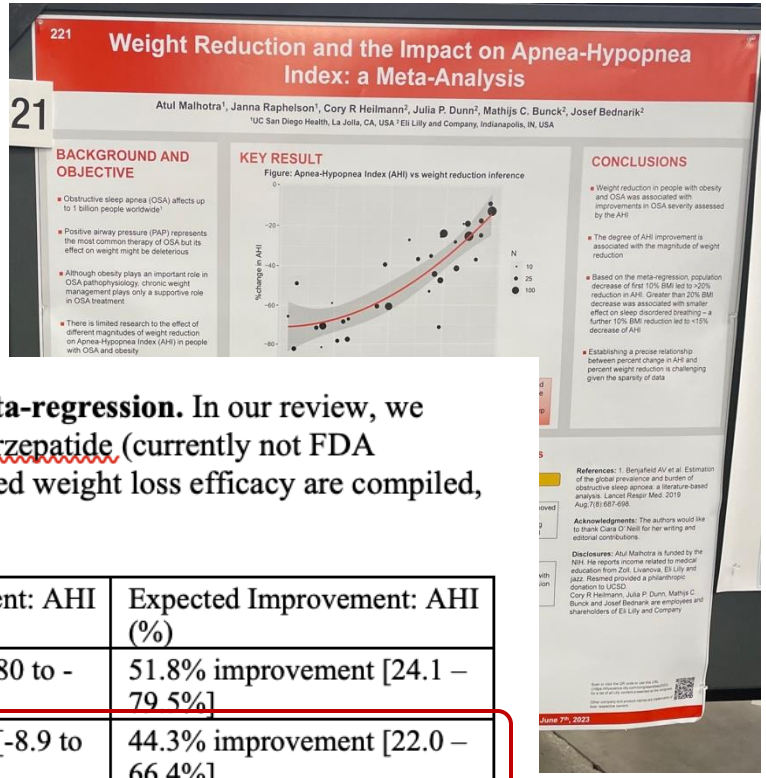

S7: Estimates of the weight loss effect of other commonly used interventions based on our study's meta-regression. In our review, we identified no studies evaluating several commonly used weight loss interventions, including semaglutide, tirzepatide (currently not FDA approved), and gastric sleeve surgery. Estimates for the expected average AHI change based on the published weight loss efficacy are compiled, assuming that they follow the same weight loss–AHI change relationship identified in our review.

Intervention	Estimated Weight Loss	Source	Expected Improvement: AHI (events/hr)	Expected Improvement: AHI (%)
Vertical sleeve gastrectomy	25%	Heymsfield and Wadden 2017 NEJM Review[22]	AHI -15.2 (95 CI -9.80 to -20.61 events/hr)	51.8% improvement [24.1 – 79.5%]
Tirzepatide	20.9%	SURPASS Trial[23]	AHI -13.3 events/hr [-8.9 to -17.7]	44.3% improvement [22.0 – 66.4%]
Semaglutide	10.8%	AGA 2022 guideline[24]	-8.74 events/hr (95 CI -6.22 to -11.2 events/hr)	25.7% improvement [14.4 – 37.0%]
Naltrexone-Bupropion	3.0%	AGA 2022 guideline[24]	-5.20 events/hr (95 CI -2.6 events/hr to -7.77 events/hr)	11.4% improvement [-1.1 – 23.9%]
Orlistat	2.0%	AGA 2022 guideline[24]	-4.7 events/hr (-2.0 to 7.45 events/hr)	9.5% improvement [-3.9 – 22.9%
Galesis-100	2.0%	AGA 2022 guideline[24]	-4.7 events/hr (-2.0 to 7.45 events/hr)	9.5% improvement [-3.9 – 22.9%

Eli Lilly to Ask FDA to Approve Weight Loss Drug for Sleep Apnea

ITER PUBLICATIONS

ve Sleep

D., Ronald R. Grunstein, M.D., Ph.D., Ingo Fietze, M.D., Terri E. Weaver, Ph.D., Susan Redline, in, Ph.D., Scott A. Sands, Ph.D., +5, for the SURMOUNT-OSA Investigators* Author Info &

DOI: 10.1056/NEJMoa2404881

Takeaways:

- Choose a topic where:
  - All group members are excited about the question
  - There is a literature to support the SRMA
  - It's a hot topic
- Project Execution
  - Use box or another shared drive to organize
  - Choose simple, quantitative methods if possible
  - Invest time early to meet deadlines

- brian.locke@imail.org

- Feel free to use my STATA code
  - (will make more sense after the STATA session)

- Other SRMA recommendations:
  - Read related SRMAs to understand structure/framing
  - Keep the STATA template ready to combine studies you read about
    - (MA is fast but takes practice, SR is slow/methodological)