Can the gut microbiome be used as a presurgical biomarker to predict bariatric surgery weight loss outcomes? – A systematic review

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Financial Disclosures/ Conflicts of Interest

- No financial disclosures
- No conflicts of interest to declare

Outline

- Introduction and Rationale
- Methodology
- Results
- Conclusion
- Ongoing/ Future Studies

Introduction – Microbiome and Obesity

PNAS

The gut microbiota as an environmental factor that regulates fat storage

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Contributed by Jeffrey I. Gordon, September 24, 2004

Proc Natl Acad Sci USA. 2004 Nov 2;101(44):15718-23.

Transfer of Intestinal Microbiota From Lean Donors Increases Insulin Sensitivity in Individuals With Metabolic Syndrome

ANNE VRIEZE,* ELS VAN NOOD,* FRITS HOLLEMAN,* JARKKO SALOJÄRVI,‡ RUUD S. KOOTTE,§ JOEP F. W. M. BARTELSMAN,‖ GEESJE M. DALLINGA–THIE,§ MARIETTE T. ACKERMANS,¶ MIREILLE J. SERLIE,# RAISH OOZEER,** MURIEL DERRIEN,** ANNE DRUESNE,** JOHAN E. T. VAN HYLCKAMA VLIEG,** VINCENT W. BLOKS,‡‡ ALBERT K. GROEN,‡‡ HANS G. H. J. HEILIG,§§ ERWIN G. ZOETENDAL,§§ ERIK S. STROES,§ WILLEM M. DE VOS,‡,§§ JOOST B. L. HOEKSTRA,* and MAX NIEUWDORP*,§

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Gastroenterology. 2012 Oct; 143(4): 913-6

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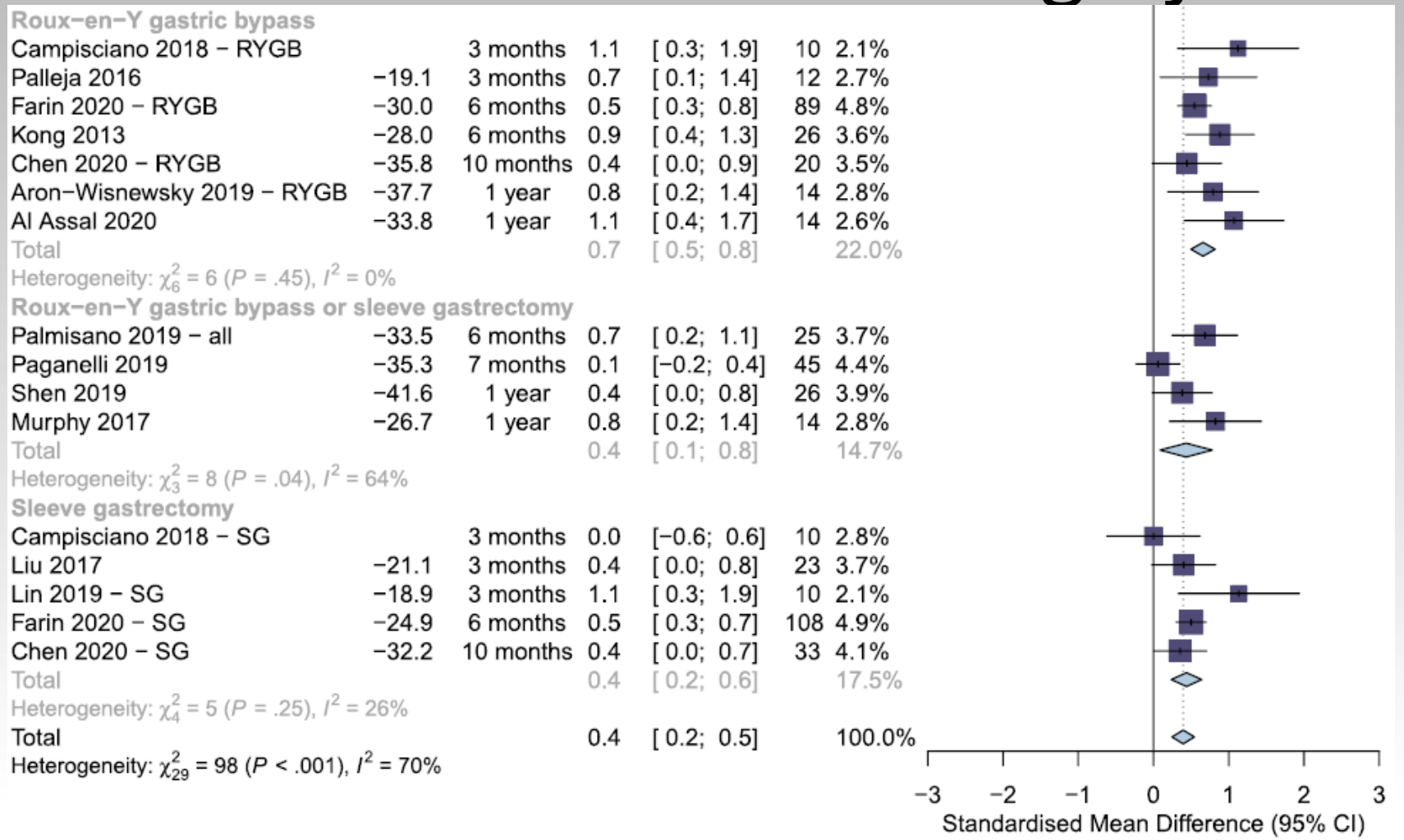
Microbiome and Bariatric Surgery



Gut Microbes. 2022 Jan-Dec;14(1):2020068.

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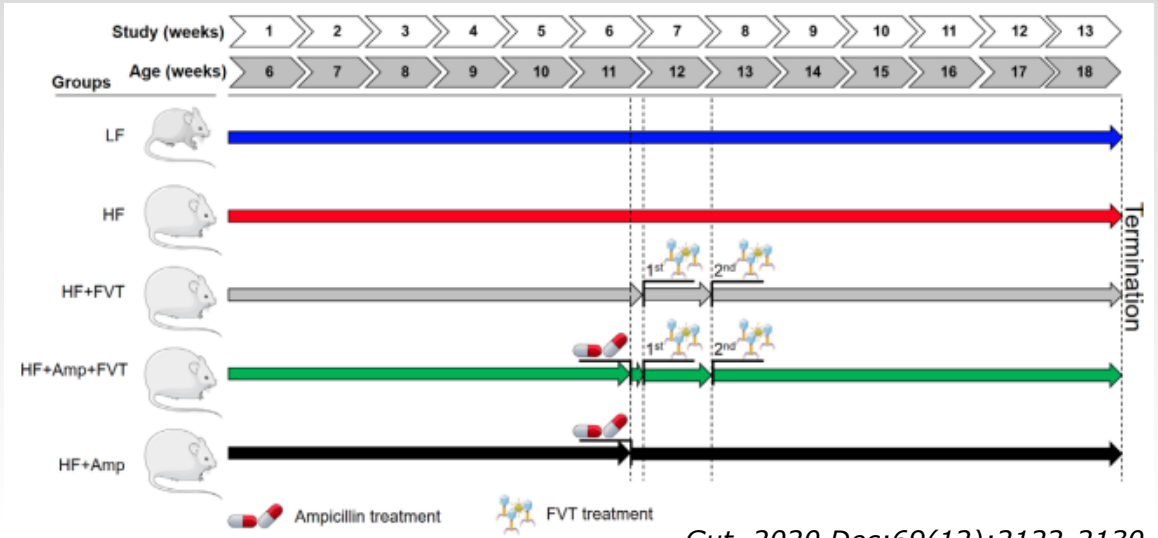
Metagenomics and Bariatric Surgery

ORIGINAL RESEARCH

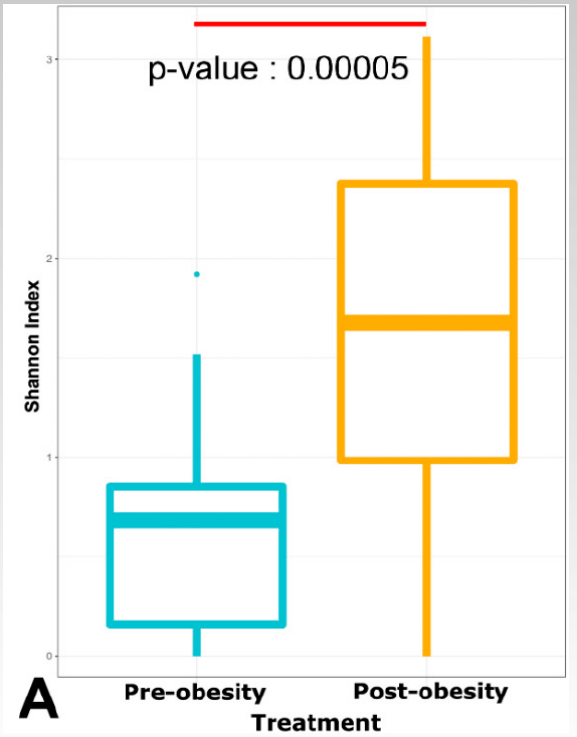
Faecal virome transplantation decreases symptoms of type 2 diabetes and obesity in a murine model

Torben Sølbeck Rasmussen ,[1] Caroline Märta Junker Mentzel,[2] Witold Kot,[3] Josué Leonardo Castro-Mejía,[1] Simone Zuffa,[4] Jonathan Richard Swann,[4] Lars Hestbjerg Hansen,[3] Finn Kvist Vogensen,[1] Axel Kornerup Hansen,[2] Dennis Sandris Nielsen[1]



Gut. 2020 Dec;69(12):2122-2130.

Gut viral alpha diversity after MBS



Appl. Sci. 2021, 11, 10039..

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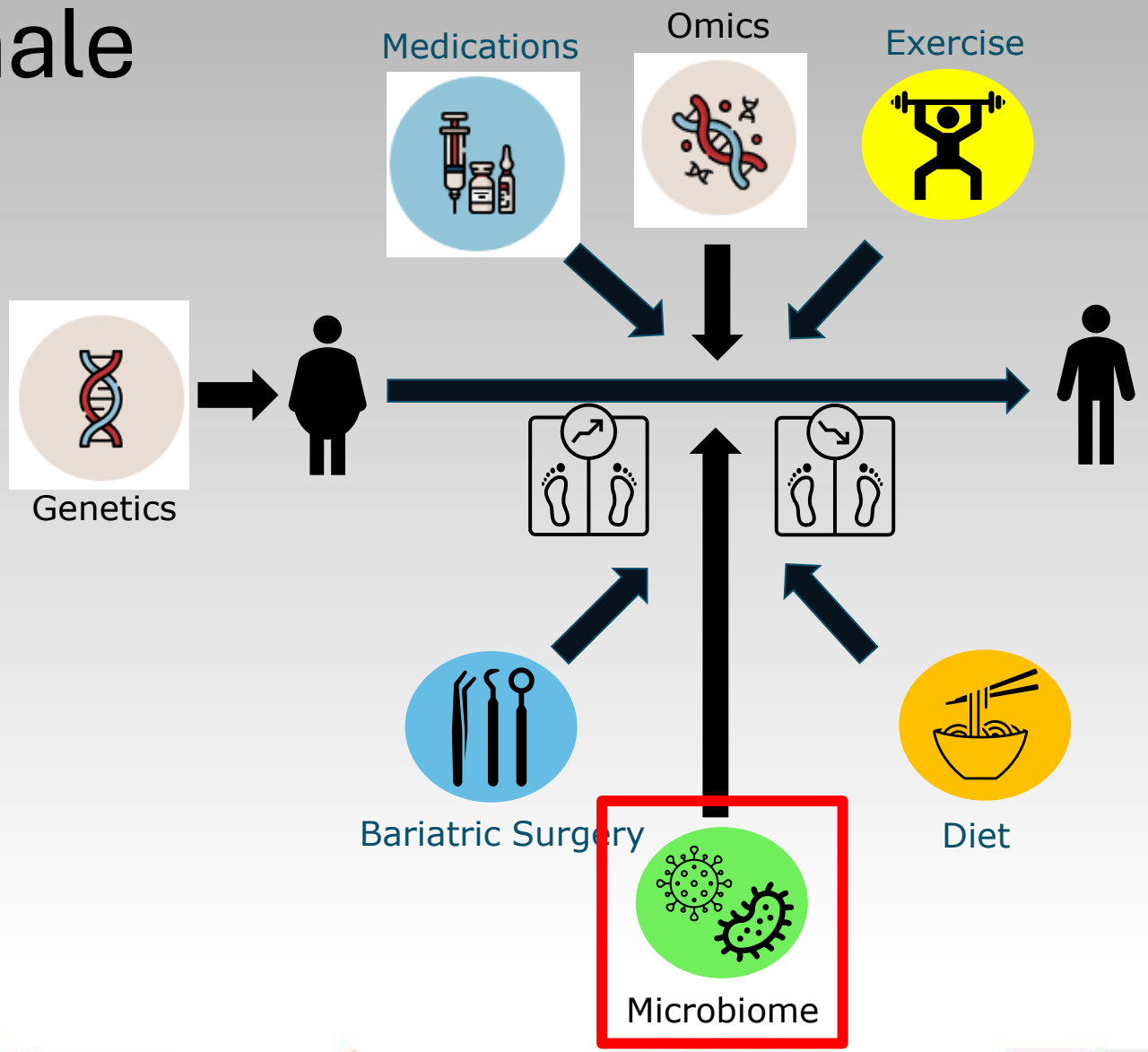
Rationale


Medications
Omics
Exercise
Genetics
Bariatric Surgery
Diet
Microbiome

Rationale – What is known

- Obesity is associated with a microbiota profile that is likely:
  - Less diverse
  - More likely to confer inflammatory phenotypes
  - More likely to lead to increased calorie uptake
- Alpha diversity is increased following weight loss interventions
- Weight loss increased the abundance of genus *Akkermansia*
  - *Akkermansia* supplementation in obese volunteers led to larger weight loss
- Obese individuals have an increased *Firmicutes: Bacteroidetes* ratio
- *Prevotella* predominance within the Bacteroidetes phylum are more likely to lose weight following a high fibre diet
- The microbial profile after bariatric surgery, mimicks lean profile
  - The exact mechanisms that induce microbiome changes after bariatric surgery still unknown.

Rationale – What is unknown?

- Microbial changes after bariatric surgery
  - Result of surgery? Result of caloric intake? Result of weight loss?

- Translational impact of knowledge of microbiome medicine in bariatric surgery
  - ? Role as biomarkers
  - ? Role as adjunctive therapeutics

Aim

- Review of published literature to investigate the

Role of the gut microbiome as **presurgical biomarkers**

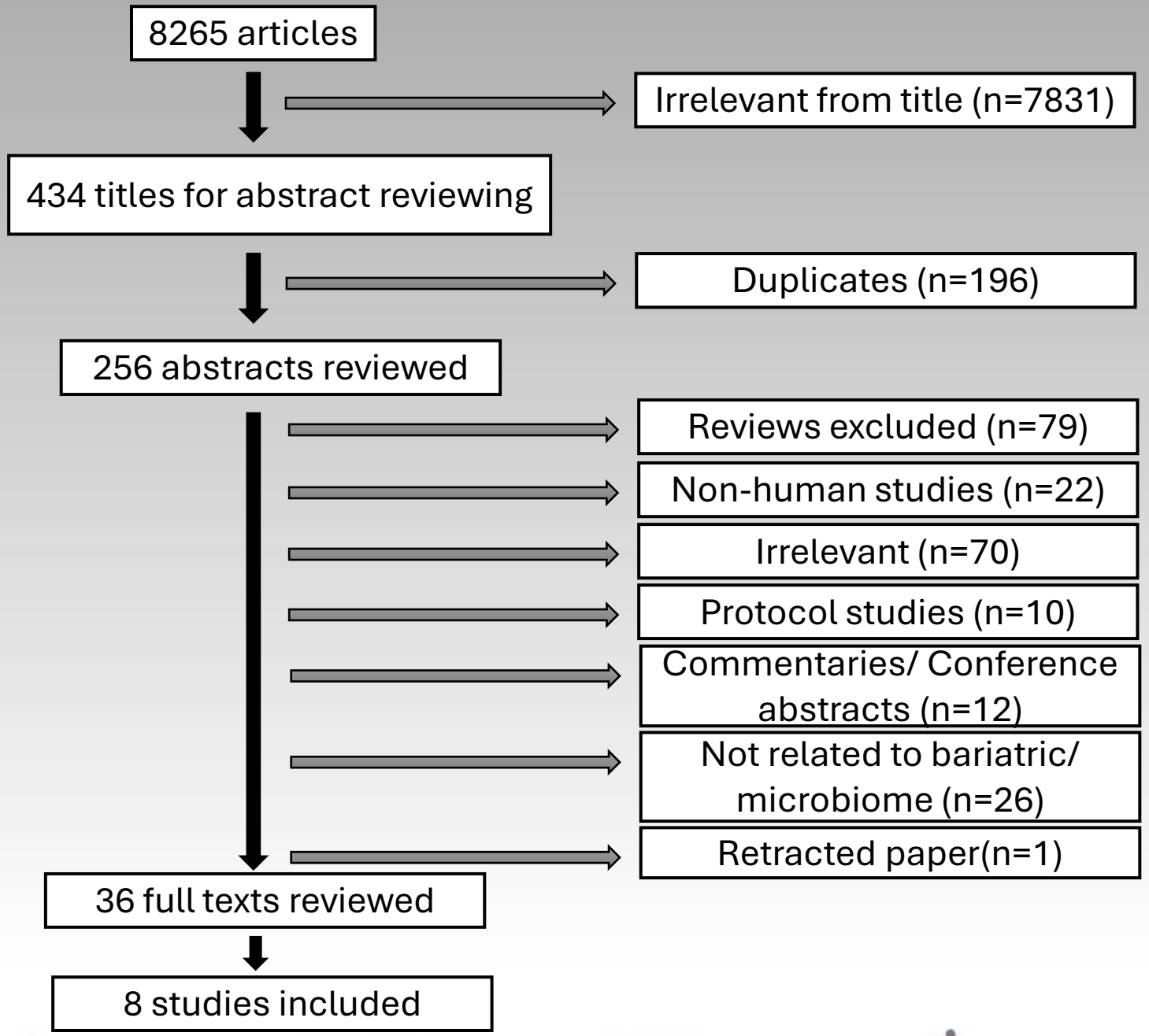
to predict bariatric surgery **weight loss outcomes**

Methodology

- Systematic review
  - P: Adult patients who underwent bariatric surgery
  - I/C: Gut microbial sequencing performed presurgery
  - O: Weight loss/ Weight regain

- 4 databases: Pubmed, Cochrane, EMBASE, Web of Science
- Search terms:
  - Pubmed: (microbiome[MeSH] OR microbiome OR microbio*) AND (bariatric surgery[MeSH] OR bariatric surgery OR bypass, roux en y gastric[MeSH] OR roux en y gastric bypass[MeSH] OR gastrectomy[MeSH] OR sleeve gastrectomy OR RYGB or SG) AND (weight regain OR weight loss OR diet, weight loss[MeSH] OR diets, weight loss [MeSH] OR program, weight loss[MeSH] OR drugs, weight loss[MeSH] OR success* OR sustain*OR insufficient OR inadequate OR outcome*)
  - WoS/ Cochrane/ Embase: (microbiome OR microbio*) AND (bariatric surgery OR bypass, roux en y gastric OR roux en y gastric bypass OR gastrectomy OR sleeve gastrectomy OR RYGB OR SG) AND (weight regain OR weight loss OR diet, weight loss OR diets, weight loss OR program, weight loss OR drugs, weight loss OR success* OR sustain* OR insufficient OR inadequate OR outcome*)
- Inclusion:
  - Last 10 years (2014-2024), End date: 3rd February 2024
  - Full text papers
  - Human studies

Methodology



Results

Study	Study design	Country	Microbial Specimen	Sequencing	Study cohort	Follow-up period	Outcome	Comparative Taxonomy hierarchy analysed
Karami_2020	Prospective cohort	Iran	Stool	RT-PCR for *Firmicutes* & *Bacteroidetes*	LSG (n=18) LRYGB (n=12)	6 months	% EWL correlation with microbiome	Phylum
Stefura_2021	Prospective cohort	Poland	Stool, Oral	16s rRNA	LSG (n=30)	6 months	Optimal vs suboptimal clinical response	Genus
Ben Izhak_2021	Prospective cohort	Israel	Stool	16s rRNA	LSG, LRYGB, OAGB (n=66)	6 months	Correlation analysis	Order
Gutierrez-Repiso_2021	Prospective cohort	Spain	Stool	16s rRNA	LSG (n=76) (40 provided 3-month follow-up)	1 year	Optimal vs suboptimal clinical response	Family
Salazar_2022	Prospective cohort	Spain	Stool	16s rRNA	LSG = 14 LRYGB = 26	3 months	%EWL correlation with microbiome	Genus
Stefura_2022	Prospective cohort	Poland	Stool, Oral	16s rRNA	LRYGB (n=6)	6 months	Optimal vs suboptimal clinical response	Genus

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Results

Study	Study design	Country	Microbial Specimen	Sequencing	Study cohort	Follow-up period	Outcome	Comparative Taxonomy hierarchy analysed
Moran-Ramos_2023	Prospective cohort	Mexico	Stool	16s rRNA	LRYGB (n=20)	1-year	%EWL correlation	Genus
Stefura_2023	Prospective cohort	Poland	Gastric, duodenal, esophageal	16s RNA	LRYGB, LSG (n=32)	1-year	Optimal vs suboptimal clinical response	Genus

Results

- Total of 8 studies, n=300 patients
- Microbiome sequencing method: Majority used 16s (7 studies)
- Majority investigated stool microbiome (n=7)
- Main surgical procedure:
  - LSG (n=138); LRYGB (n=64)
  - 1 study did not give breakdown (Ben Izhak_2021) of LSG, OAGB, LRYGB
  - 1 study investigated duodenal, gastric microbiome (Stefura_2023)

Gut microbial communities

Microorganisms. 2019 Jan 10;7(1): 14.

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Results

- Alpha diversity
  - 3/7 studies reported alpha diversity of samples
  - Baseline alpha diversity was not useful in predicting postoperative weight loss (n=1)
  - Decreased alpha diversity was correlated with postoperative increase in *Veillonella,* which was correlated with poorer weight loss (n=1)

Results

- *Firmicutes: Bacteroidetes* ratio
  - Not useful as a biomarker (n=2 – LRYGB 38; LSG 32)

  - 2 studies investigated differential enrichment of microbial communities in optimal and suboptimal weight loss for LSG
    - Responders: Enriched in certain Firmicutes (ie. *Peptostreptococcaceae* spp., *Peptoniphilaceae* spp, *Tissierellales* spp., *Hathewwaya* spp.)
    - Non-responders: Enriched in certain Bacteroidetes (ie. *Alistipes* spp., *Bacteroides* spp., *Rikenellaceae* spp.)

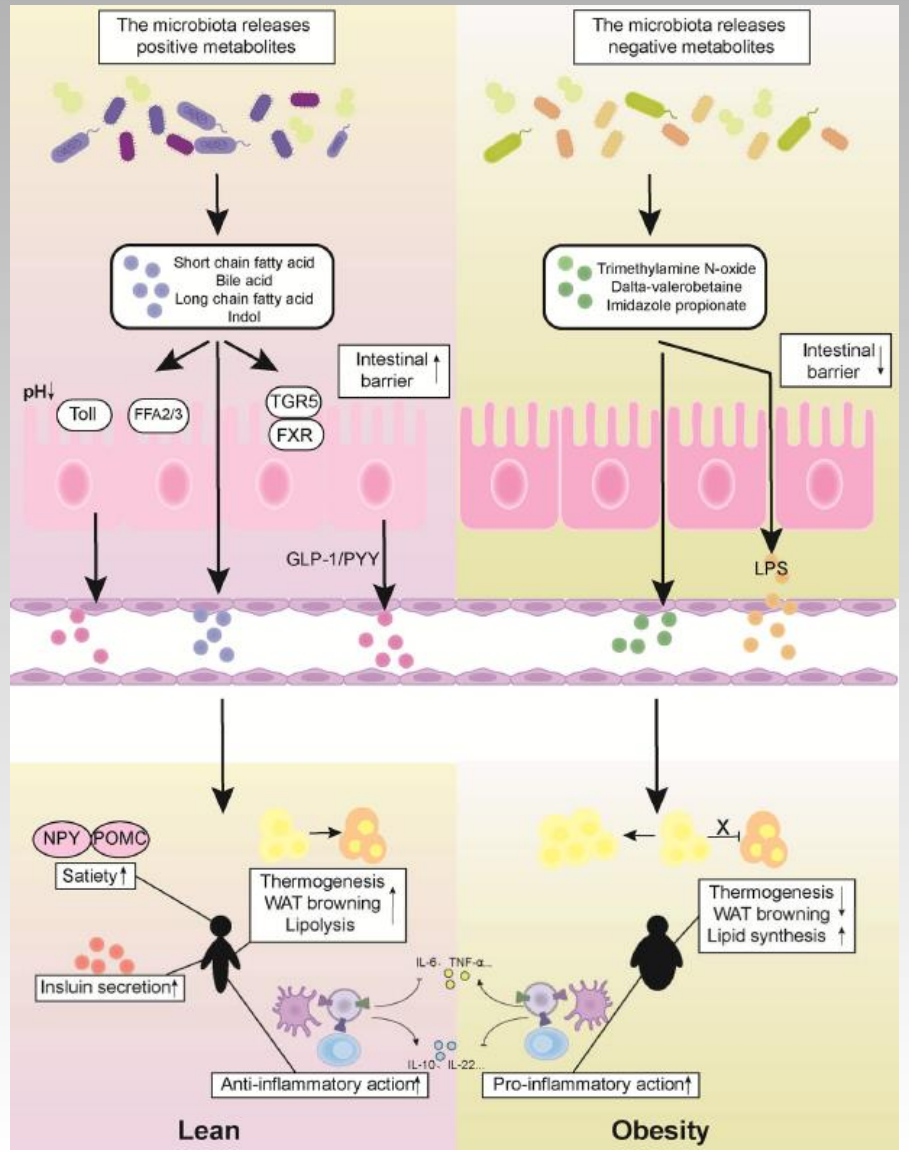
  - Studies investigated microbial differences for LRGYB
    - Only 1 study reported different microbial communities (n=6 LRYGB)
    - Responders: Enriched in Tannerella spp (Bacteroidetes)
    - Non-responders: Enriched in Bernnesiellaceae spp (Bacteroidetes)

Results

- Other Bacterial Phyla
  - Differential enrichment of microbial communities in LSG
  - *Akkermansia* – no correlation
  - *Proteobacteria* phylum of *Campylobactereaceae* was differentially enriched in responders

Results

- Can the enrichment be classified functionally?
- Detrimental metabolites
  - TMAO (Trimethylamine N-oxide) and flora that are TMA (trimethylamine) precursor producers
- Beneficial metabolites
  - Short-chain fatty acids



MedComm. 2022;3:e171.

Results

- TMA producers
  - No significant presurgical signatures were noted

- SCFA producers
  - Propionate producers:
    - *Prevotella & Prevotellaceae* spp enriched in presurgical LSG patients with optimal weight loss
  - Butyrate producers:
    - *Peptoniphilaceae* and *Peptostreptococcus* spp enriched in presurgical LSG patients optimal weight loss

Conclusions

- While the microbial changes after bariatric surgery have been described, the role of presurgical microbial communities as a prognostic marker is not commonly studied

- These studies reporting presurgical microbial biomarkers in bariatric surgery are:
  - Heterogenous
  - Small sample size
  - Differential reporting and analysis techniques

Conclusions

- Based on available literature to date,

- With regards to LSG:
  - Optimal weight responders appeared to have an increased *Firmicutes: Bacteroidetes* ratio, albeit different genus/ species are enriched
  - Optimal weight responders appeared to have enriched SCFA-producers

- With regards to LRYGB:
  - Study sample size small
  - No common conclusive trends observed

Future Work

- Correlation studies are unlikely helpful in providing additional information
  - Limitation of 16s sequencing methods

- Metagenome studies (+ virus, fungi, archaea…)
- Functional analysis
  - Metabolomics
  - Meta-transcriptomics

Future Work

ClinicalTrials.gov

Find Studies | Study Basics | Submit Studies | Data and API | Policy | About | My Saved Studies (0)

Home > Search Results > Study Record

RECRUITING

Pilot Study of the Human Metagenome in Metabolic Diseases

ClinicalTrials.gov ID NCT06363253

Sponsor Sengkang General Hospital

Information provided by Chue Koy Min, Sengkang General Hospital (Responsible Party)

Last Update Posted 2024-04-12







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