Modulation of gut microbiota through intermittent fasting; a potential approach to ameliorate metabolic diseases

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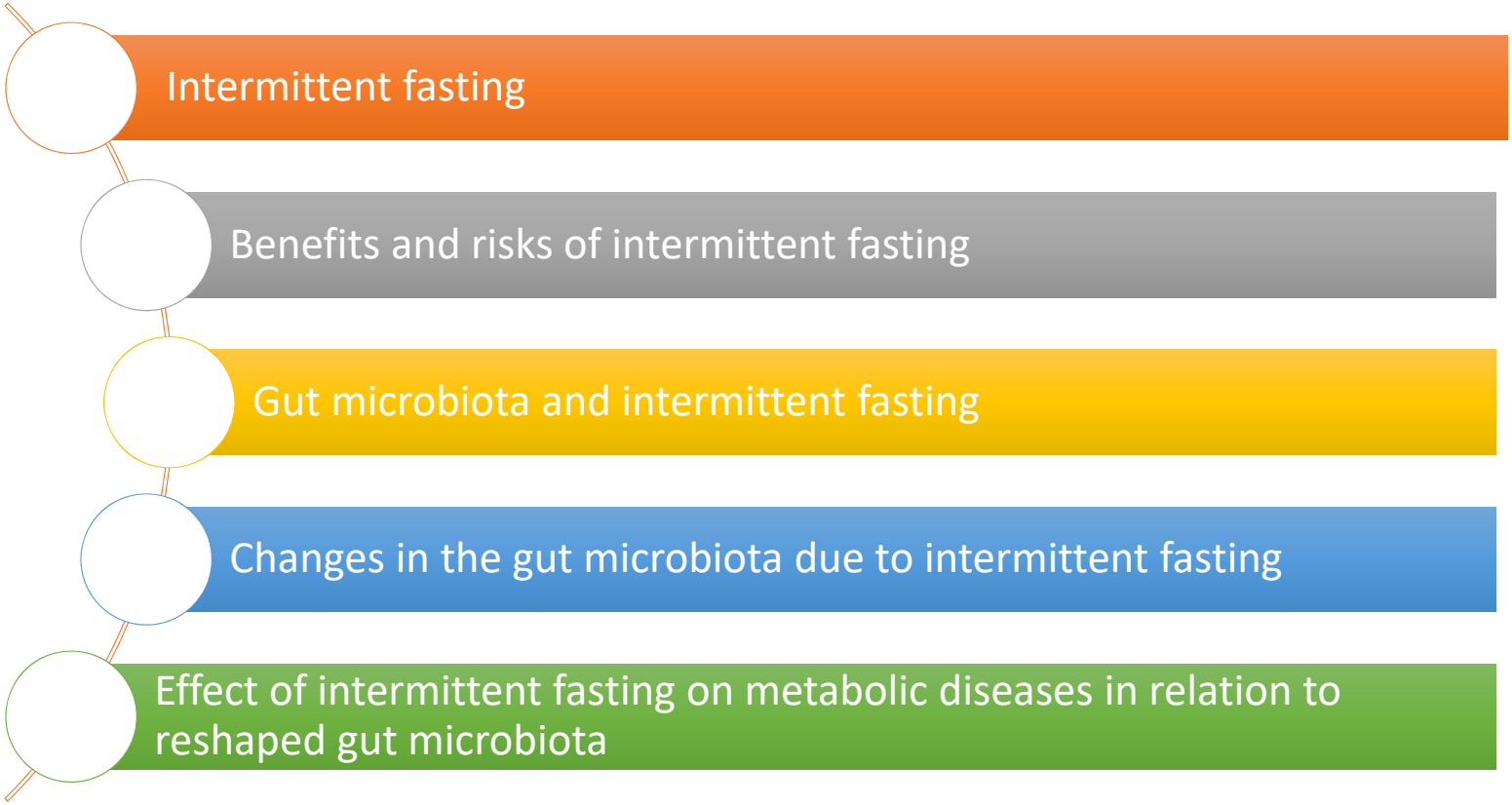
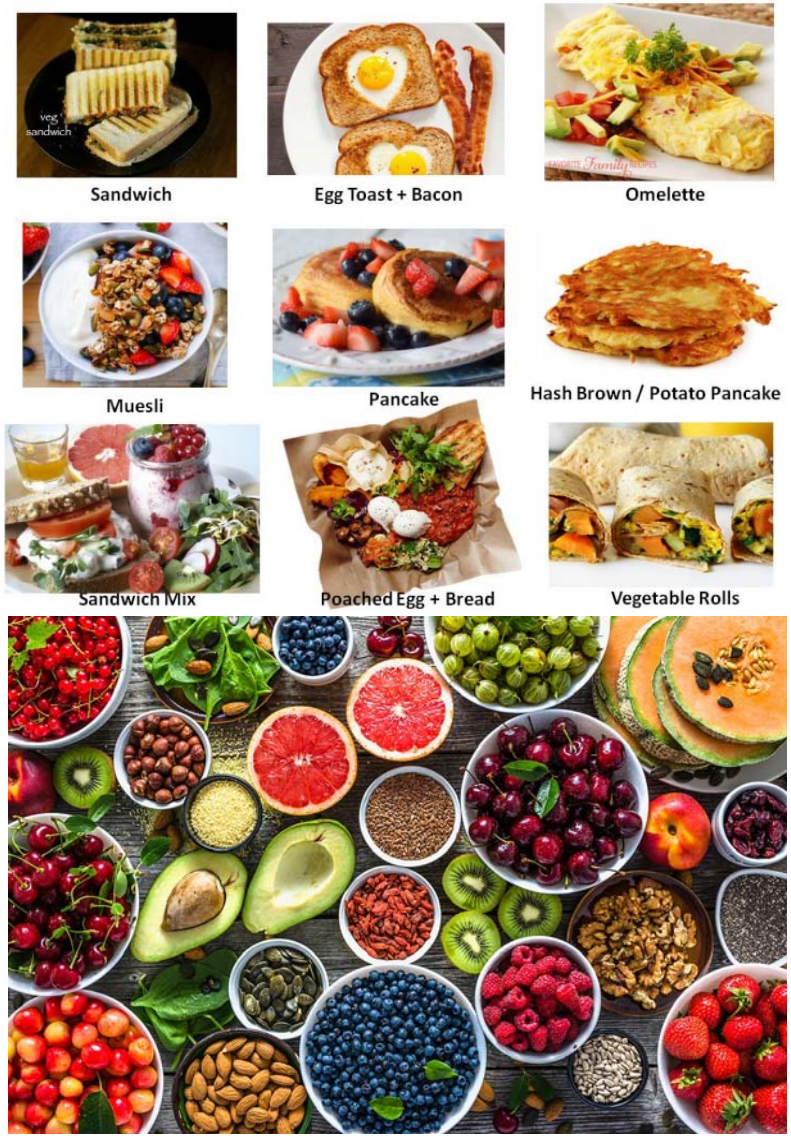
Outline


Intermittent fasting
Benefits and risks of intermittent fasting
Gut microbiota and intermittent fasting
Changes in the gut microbiota due to intermittent fasting
Effect of intermittent fasting on metabolic diseases in relation to reshaped gut microbiota

- What to eat……
- When to eat……

Intermittent fasting

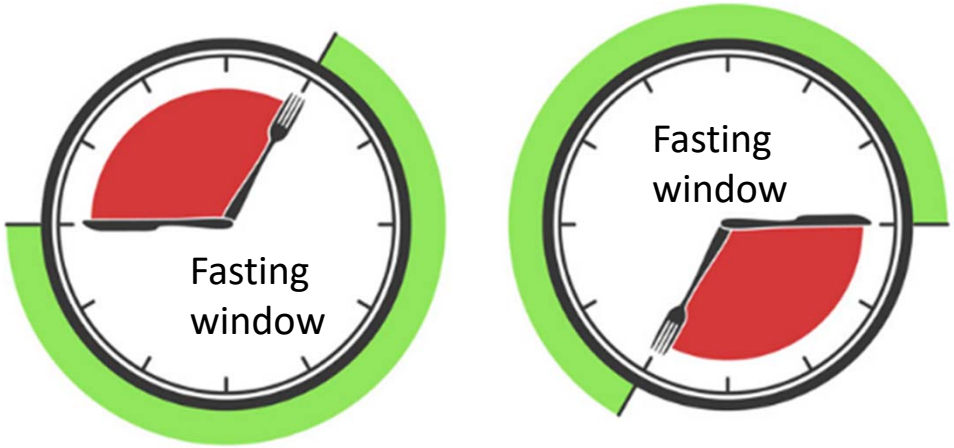


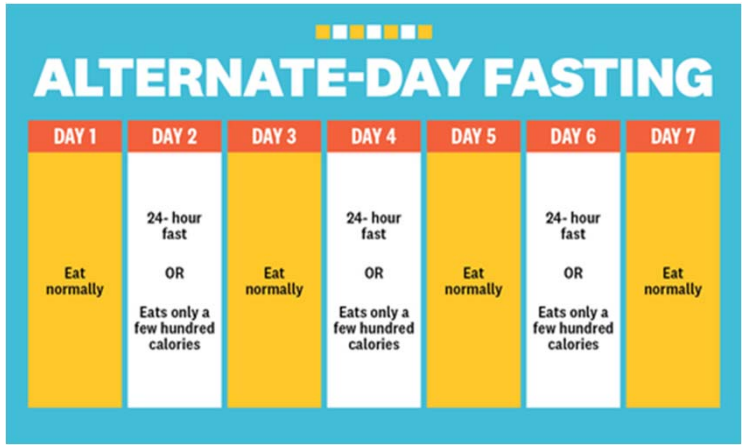
Intermittent fasting

- A term describing several regimens of periods of voluntary abstinence from food and drink
- An eating plan that switches between fasting and eating on a regular schedule.
- A metabolic shift that occurred due to changing dietary habit
- A way to manage your weight and prevent or even reverse some forms of diseases

Types of Intermittent fasting

- Alternate day fasting
- 5:2 intermittent fasting (2 days in a week)
- Daily time restricted fasting (i.e., 16:8 or 1 meal in 24 hour)





Benefits of Intermittent fasting

- Intermittent fasting elicits conserved, adaptive cellular responses that
  - improves glucose regulation,
  - Reduce Insulin resistance,
  - increases stress resistance, and
  - suppresses inflammation.
- Activate pathways that enhance intrinsic defenses against oxidative and metabolic stress
  - Remove or repair damaged molecules
  - Helps to reduce weight and fat
  - Improve cardio metabolic health

Risk of Intermittent fasting

- ⚠ Hunger and cravings
- ⚠ Headache (due to low blood sugar and remove of caffeine)
- ⚠ Digestive issues (constipation, diarrhea, nausea, and bloating)
- ⚠ Irritability and mood changes
- ⚠ Bad breath
- ⚠ Sleep disturbances
- ⚠ Dehydration

Who should avoid

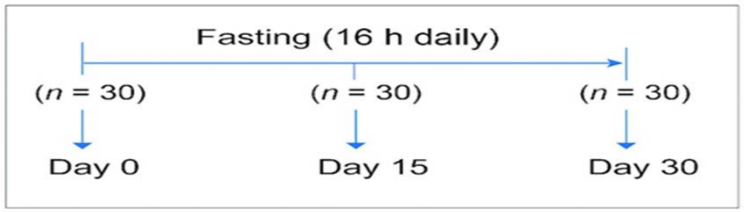
- People who are pregnant or breastfeeding
- young children
- older adults who experience weakness
- people with immunodeficiencies
- people with current or past eating disorders
- people with dementia
- traumatic brain injury or post concussive syndrome

Gut microbiota and Intermittent fasting

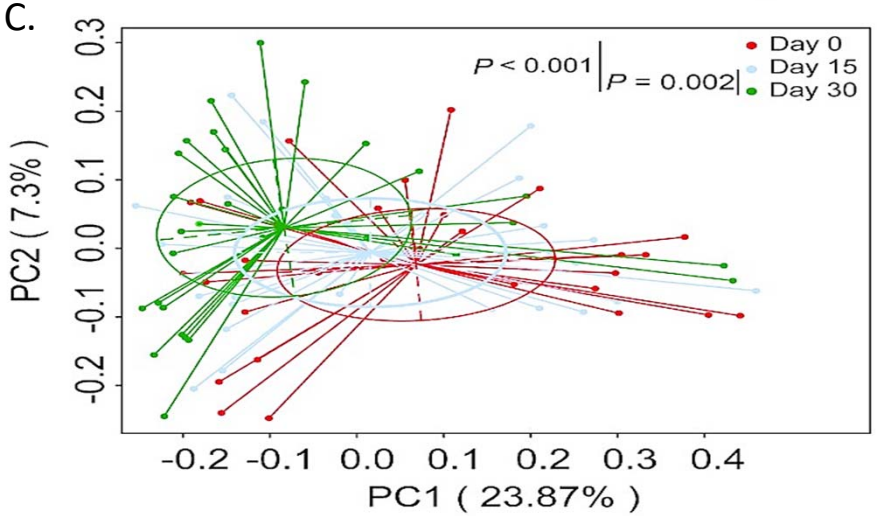
- Gut microbiota is a vast and complex microbial community, with >1000 bacterial sp. and trillions of microorganisms.
- Abundant bacterial phyla are Firmicutes and Bacteroidetes.
- Changes in the gut ecosystem accomplishes a range of health effects.
- An emerging body of evidence suggests beneficial effects of IF on the health through
  - increasing the microbial diversity and abundance in the gut,
  - improving the immune function and
  - ameliorating the metabolic status

Changes in the microbial diversity in the gut

A.



C.



B. Table: Alpha diversity in the gut microbiota

Diversity index	Before fasting Day 0 (n=30)	After fasting Day 30 (n=30)	*P* value[2]
Shannon	5.17 ± 0.49	5.40 ± 0.44	0.02
Simpson	0.92 ± 0.04	0.94 ± 0.02	0.001
Chao1	350.9 ± 34.5	372.4 ± 55.5	0.04
ACE	354.4 ± 34.9	378.6 ± 56.4	0.01
Goods coverage	0.99 ± 0.0002	0.99 ± 0.0002	1

[1]Data presented as mean ± SD.
[2]Wilcoxon signed-rank test performed to compare groups.

(A) Study design of the cohort (*n* = 30). (B) The diversity of gut microbiota was assessed by calculating the different index. (C) A principal coordinates analysis was generated based on the Bray – Curtis distance. Each point corresponds to a community from a single individual.

Su et al., 2021

Changes in the bacterial taxa due to intermittent fasting

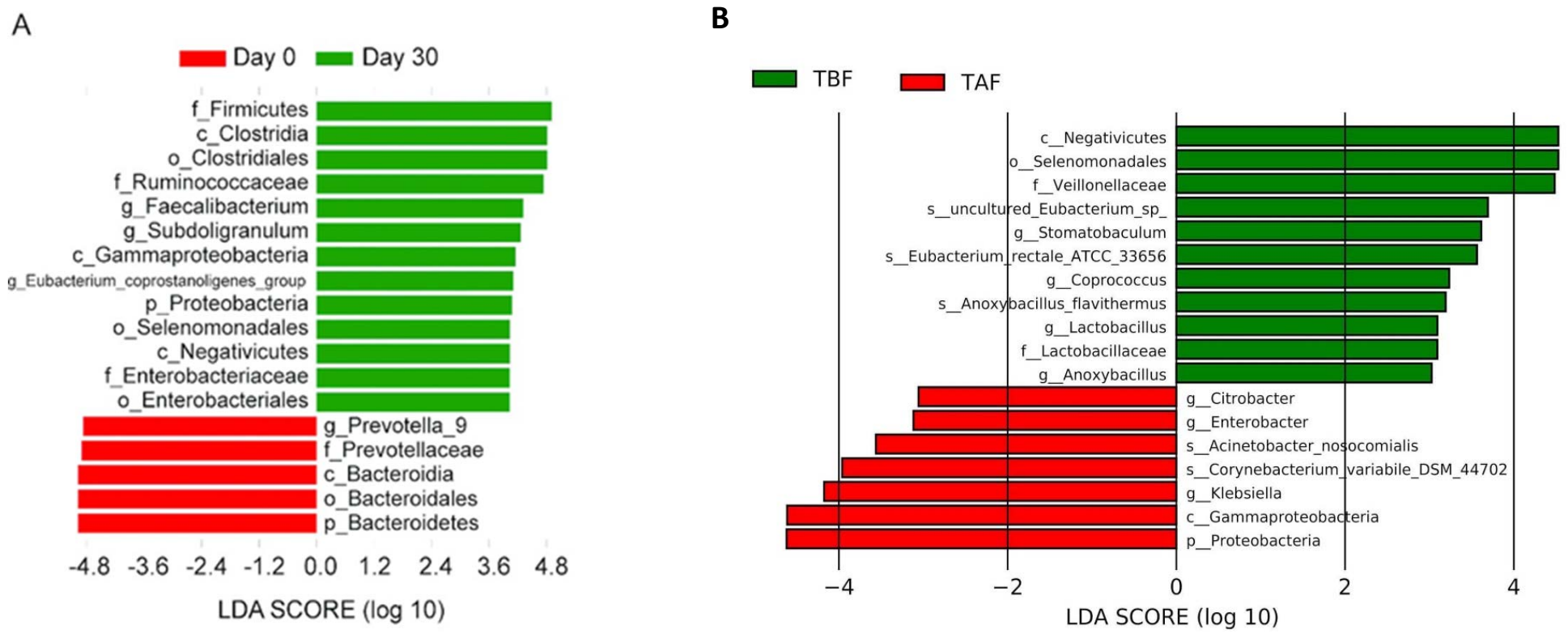


Figure: Intermittent fasting–provoked changes of bacterial taxa. (A) and (B) Taxa that show alternative abundance before and after fasting. Taxa with a log linear discriminant analysis (LDA) score above 4.00 as determined by using linear discriminant analysis coupled with effect size measurements (LEfSe). Data shown are the 10Log LDA scores following LEfSe analyses;

Sui et al,. 2021

Ali et al., 2021

Relative abundance of bacterial phyla

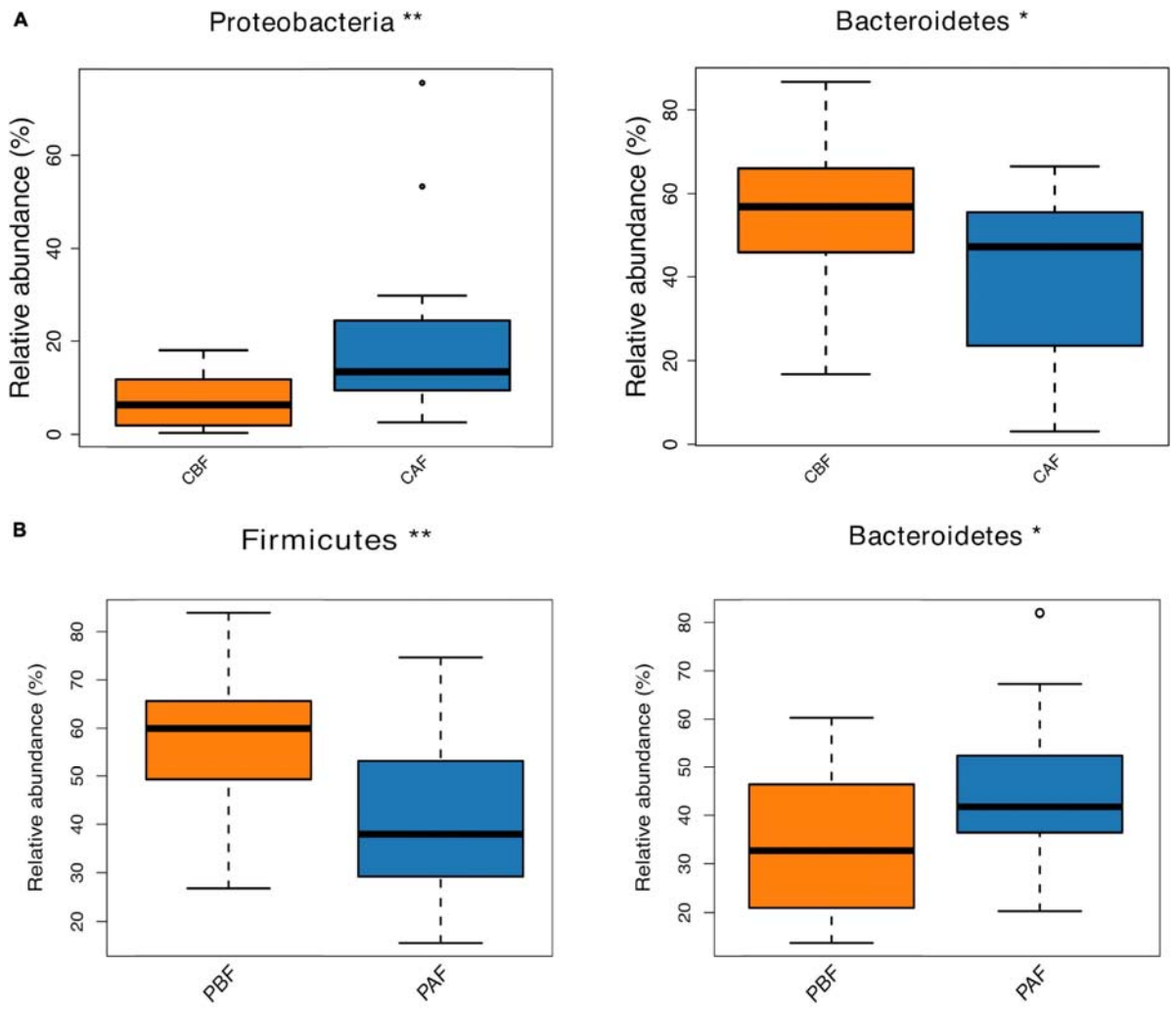


Figure: Relative abundances of bacterial phyla was varied among each group at phylum level. **(A)** Chinese before fasting vs. Chinese after fasting, **(B)** Pakistani before fasting vs. Pakistani after fasting; $*P < 0.05$, $**P < 0.01$.

Ali et al., 2021

Relative abundances of bacterial taxa among each group at genus level

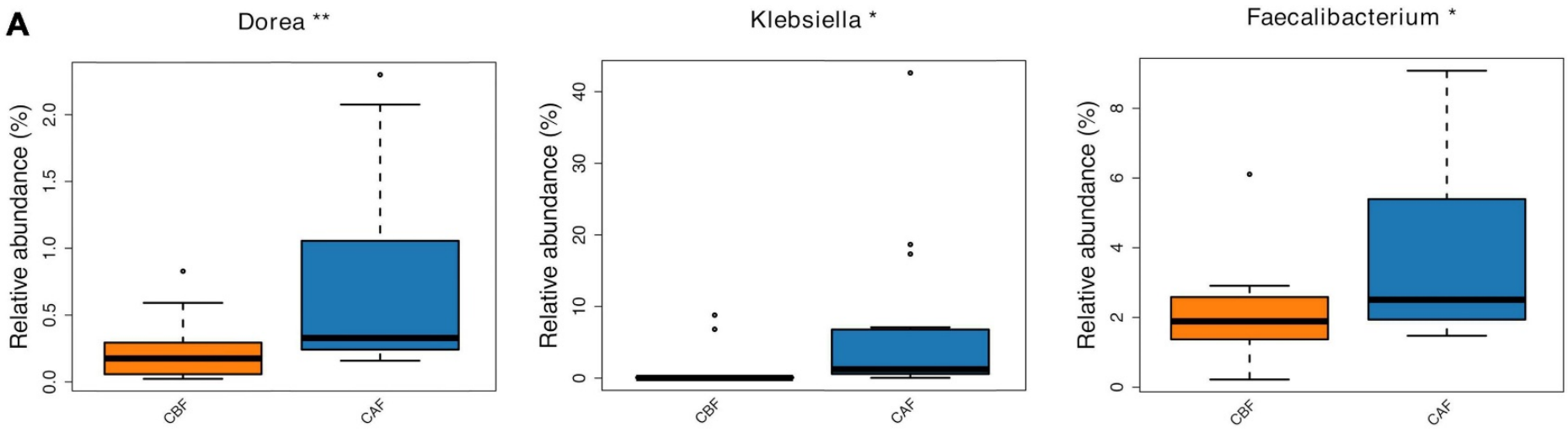


Figure. Relative abundances of bacterial taxa analyzed by using a metastats test was varied among each group at genus level. **(A)** Chinese before fasting vs. Chinese after fasting *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$.

Ali et al., 2021

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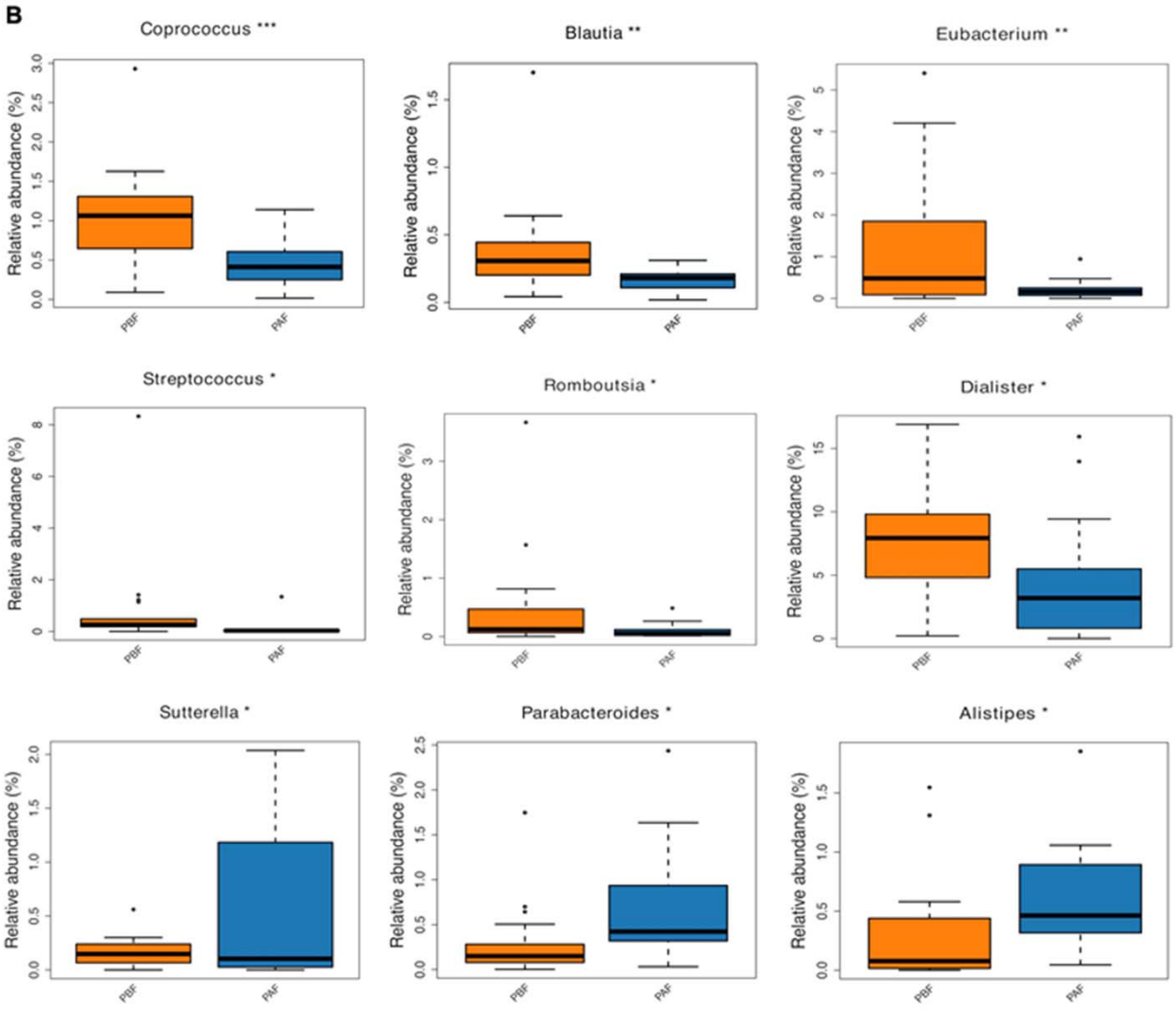


Figure. Relative abundances of bacterial taxa was varied among each group at genus level. **(B)** Pakistani before fasting vs. Pakistani after fasting, $*P < 0.05$, $**P < 0.01$, $***P < 0.001$.

Ali et al., 2021

Venn diagram of unique and shared OTUs in fasting groups

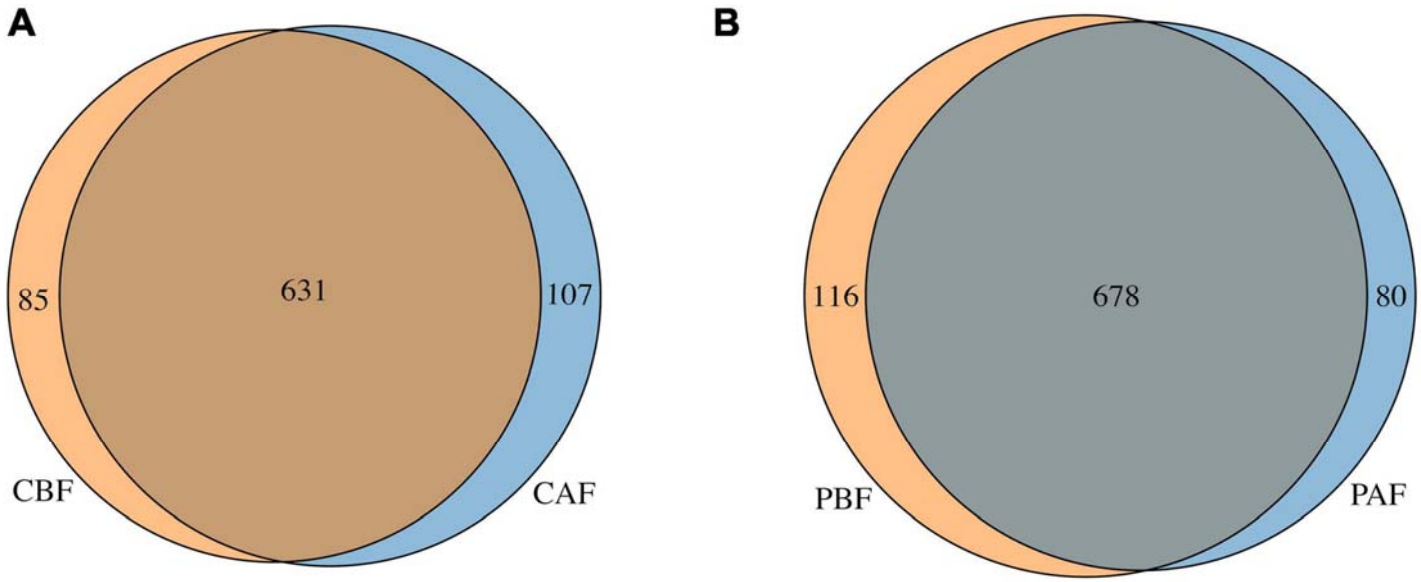


Figure. Venn diagram of unique and shared OTUs (operational taxonomic units) in different fasting groups. **(A)** Chinese before fasting vs. Chinese after fasting, **(B)** Pakistani before fasting vs. Pakistani after fasting. The overlaps represent the common taxa between groups, and the non-overlapping portions represent unique taxa in each group

Ali et al., 2021

Changes in the microbial composition

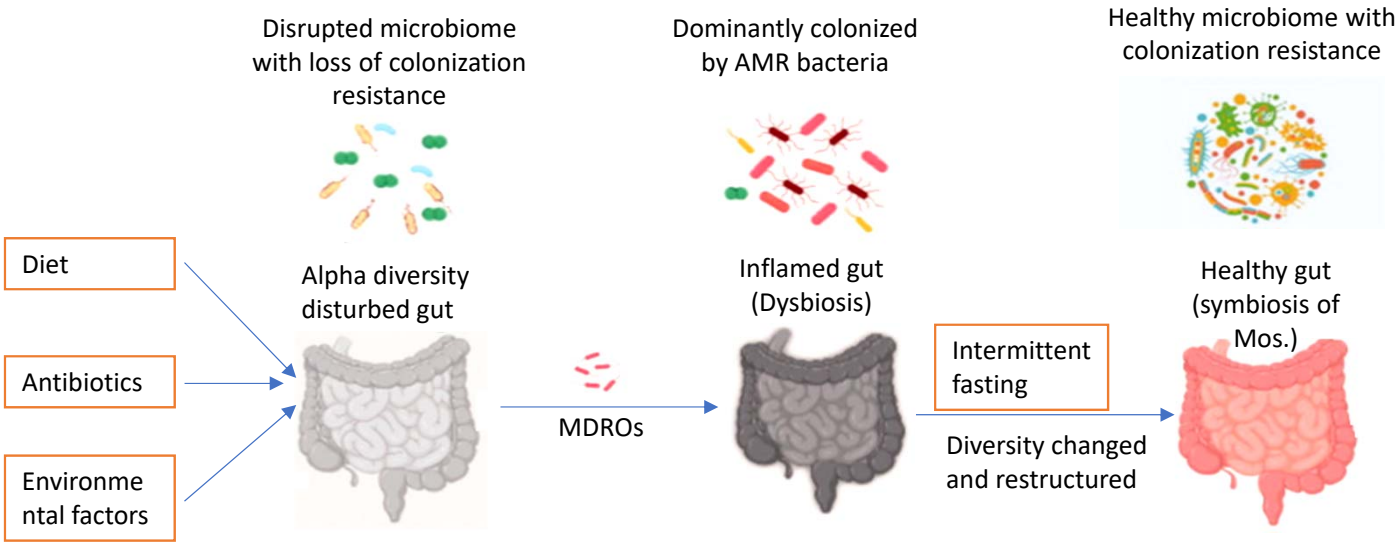
Reference	Participants (n)	Duration and type of fasting	Comparison group	Change in microbial Composition
He et al. (2019) [8]	Healthy adults aged 18–40 years ($n = 16$)	1 week: water-only fasting ($n = 6$)	1 week: juice fasting ($n = 10$)	↓ *Fusobacterium* water-only fasting ↔ *Akkermansia* water-only fasting ↔ juice fasting
Remely et al. (2015) [41]	Overweight ($n = 13$)	CR and PF/TRF (non-traditional fasting regimen) (600–800 kcal)	None	↑ *Lactobacillus* ↑ *Enterobacteria* ↑ *Akkermansia*
Cignarella et al. (2018) [42]	Adults with MS ($n = 16$)	15 days: ADF	15 days: ad libitum	↑ *Bacteroides* ↑ *Lactobacillus* ↑ *Prevotella* (fasting group)
Özkul et al. (2019) [43]	Healthy adults aged 31–56 years ($n = 9$)	29 days: Ramadan fasting /TRF	None	↑ *Bacteroides* ↑ *Akkermansia*
Gabel et al. (2020) [44]	Obese adults ($n = 14$)	12 weeks: TRF	None	↔
Özkul et al. (2020) [45]	Healthy adults ($n = 9$)	29 days: Ramadan fasting /TRF	None	↑ *Bacteroides* ↑ *Butyricicoccus* ↑ *Faecalibacterium* ↑ *Roseburia* ↑ *Allobaculum* ↑ *Eubacterium* ↑ *Dialister* ↑ *Erysipelotrichi*

Abbreviations: ADF, alternate-day fasting; CR, calorie restriction; MS, multiple sclerosis; PF, periodic fasting; TRF, time-restricted feeding; ↑, statistically significant increase ($p < 0.05$); ↔, no change.

Llewellyn-Waters and Abdullah, 2021

Effect of Intermittent fasting on metabolic diseases in relation to altered gut

- Disruption or changes in the gut microbiota contributes to development of metabolic diseases including
  - Hypertension,
  - Obesity,
  - Type 2 diabetes etc.



de Cabo and Mattson, 2019; Dharmaratne et al., 2021

Intermittent fasting on overweight or obesity

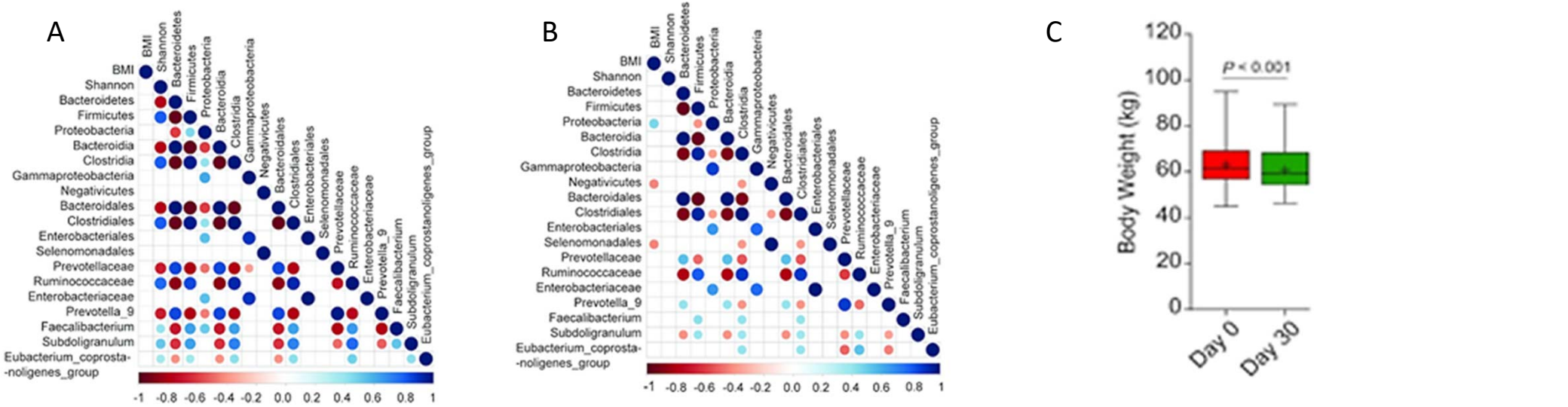
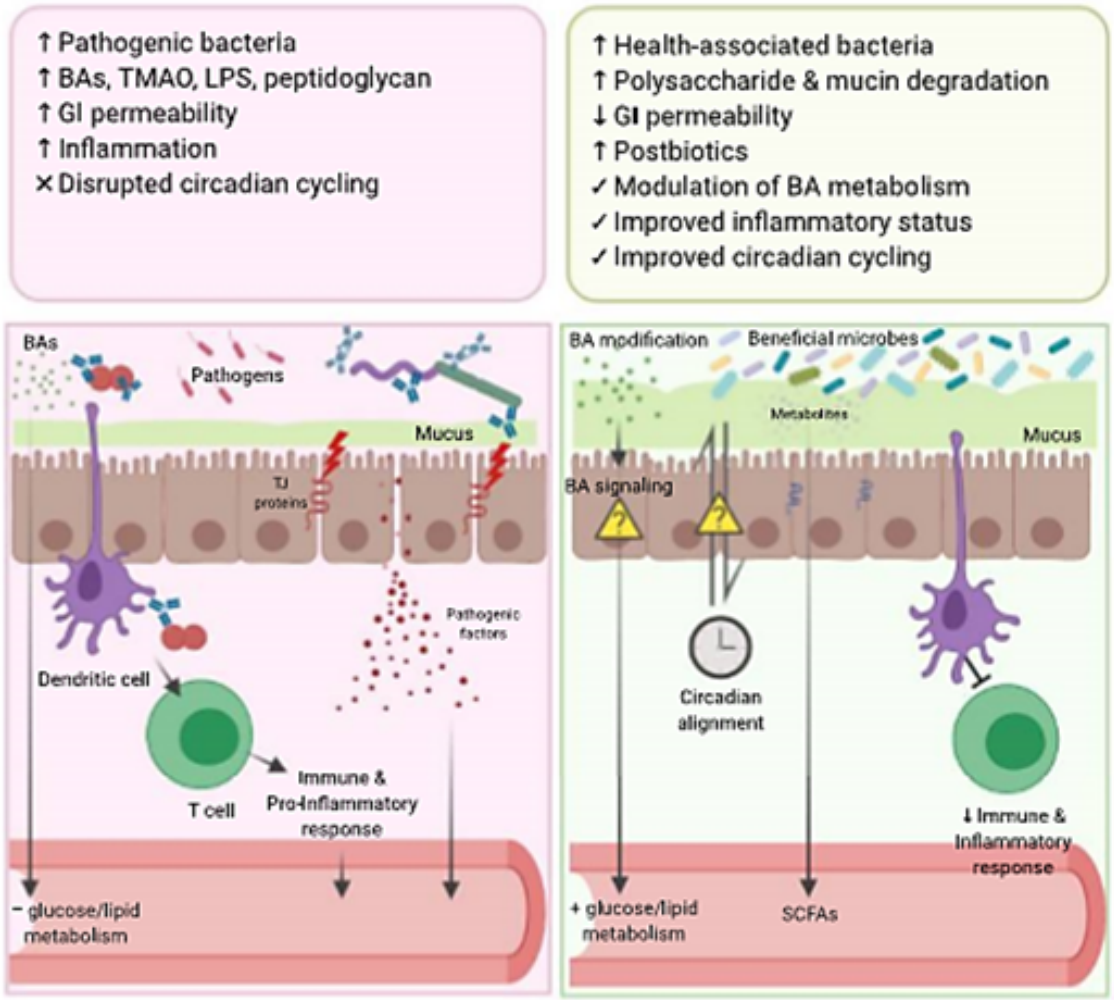


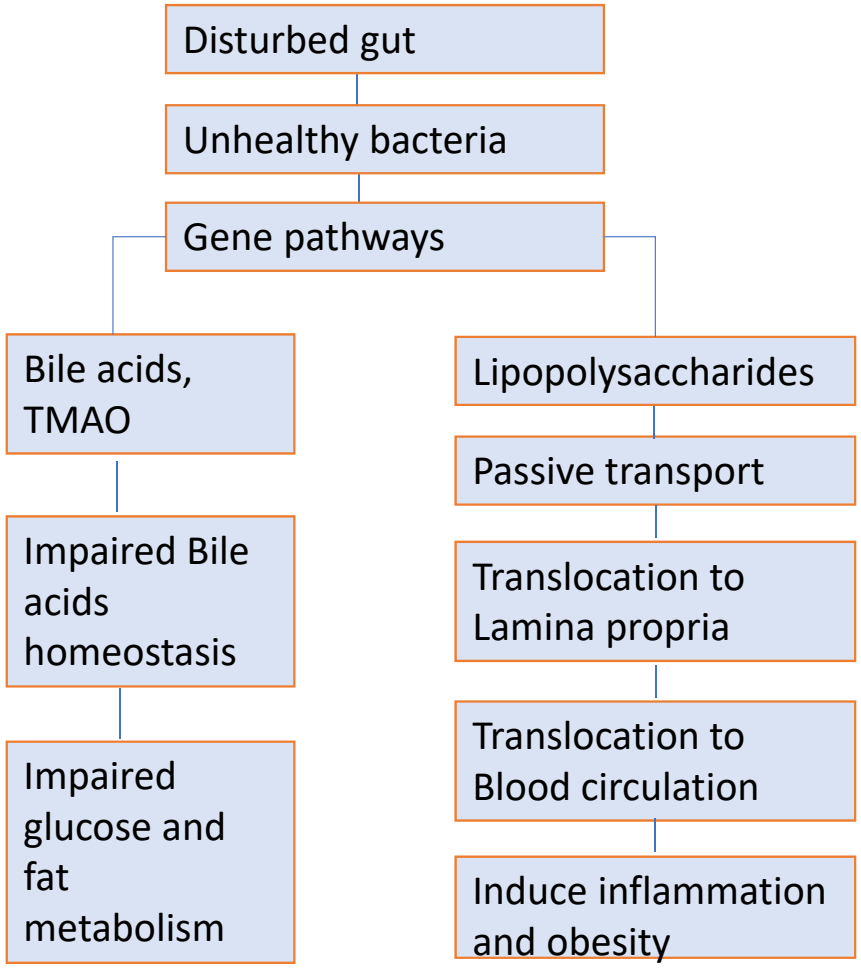
Figure: (A) correlation matrix between microbiota and BMI before fasting (B) At the end of fasting. Positive correlations are displayed in blue and negative correlations in red. Color density is proportional to the correlation coefficients (bottom score). All the correlations shown are statistically significant (Spearman correlation, $P < 0.05$). The size of the dots is inversely proportional to the P value. Only correlations with a P value less than 0.05 are shown. (C) Boxplot for body weight before and after fasting.

Sui et al,. 2021

Effects of fasting on the gut microbiome and Intestinal interface

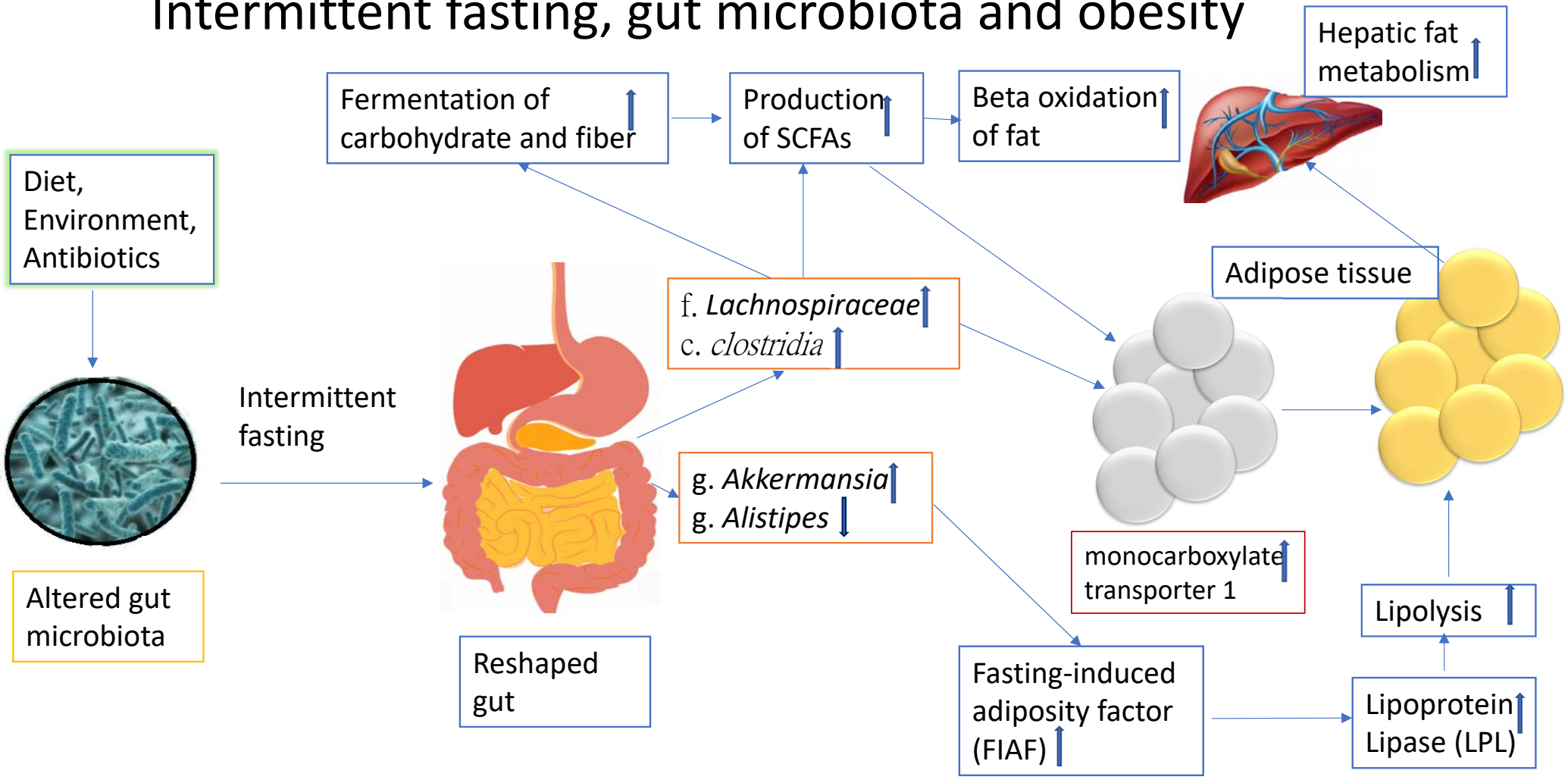


Before fasting **After fasting**



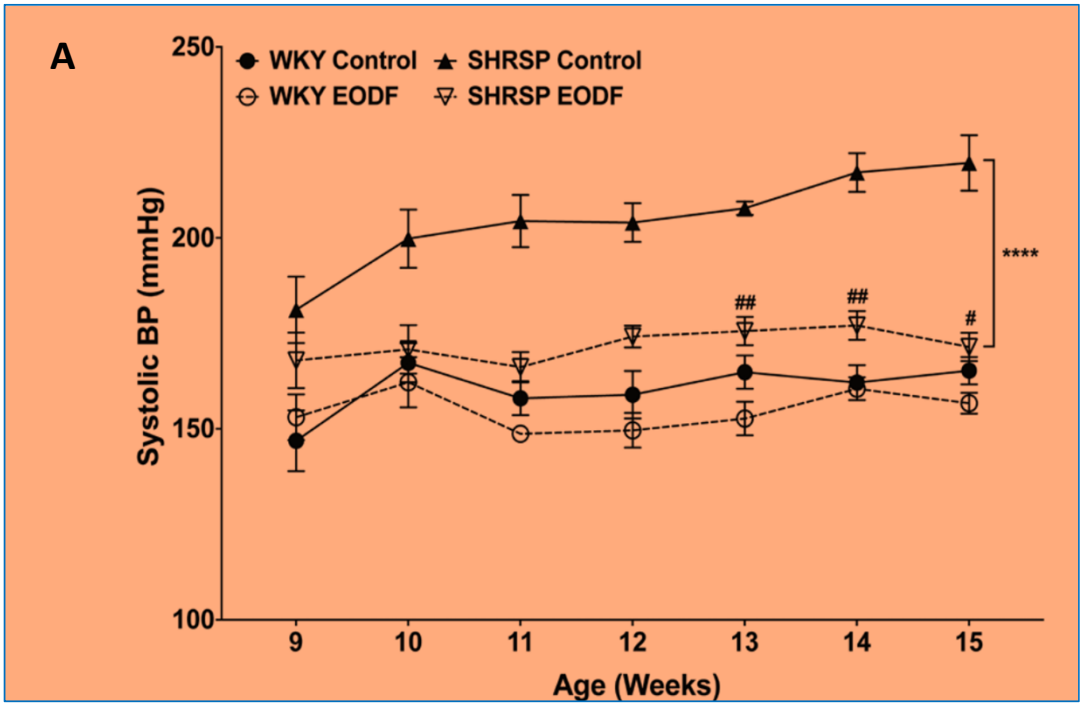
Mohr et al., 2021

Intermittent fasting, gut microbiota and obesity



Li et al., 2020; Mohr et al., 2021

Intermittent fasting and Hypertensive disorder



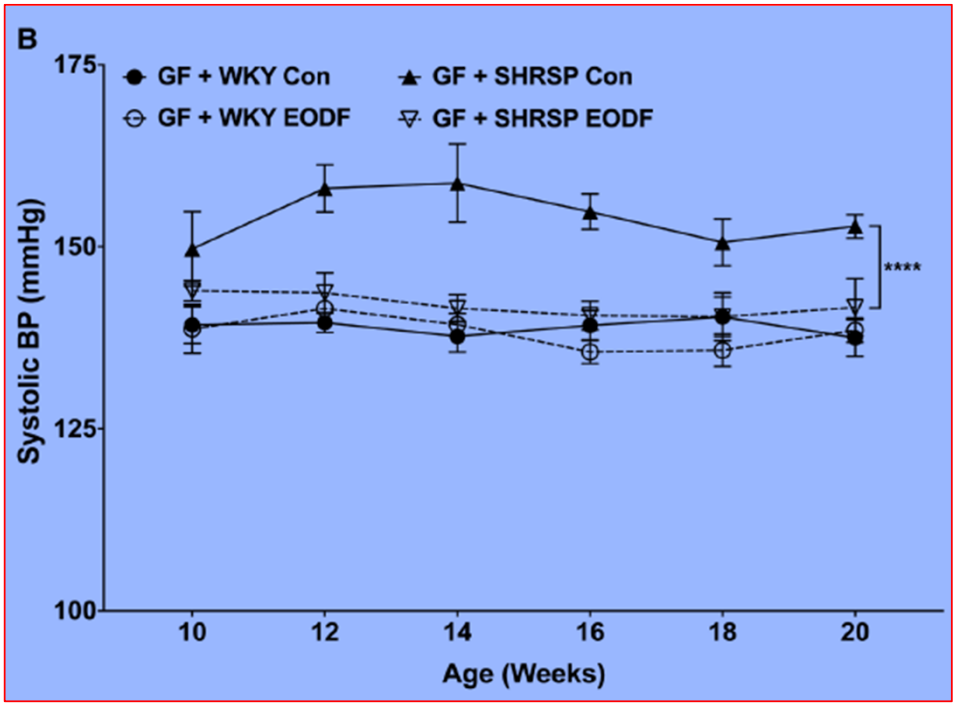
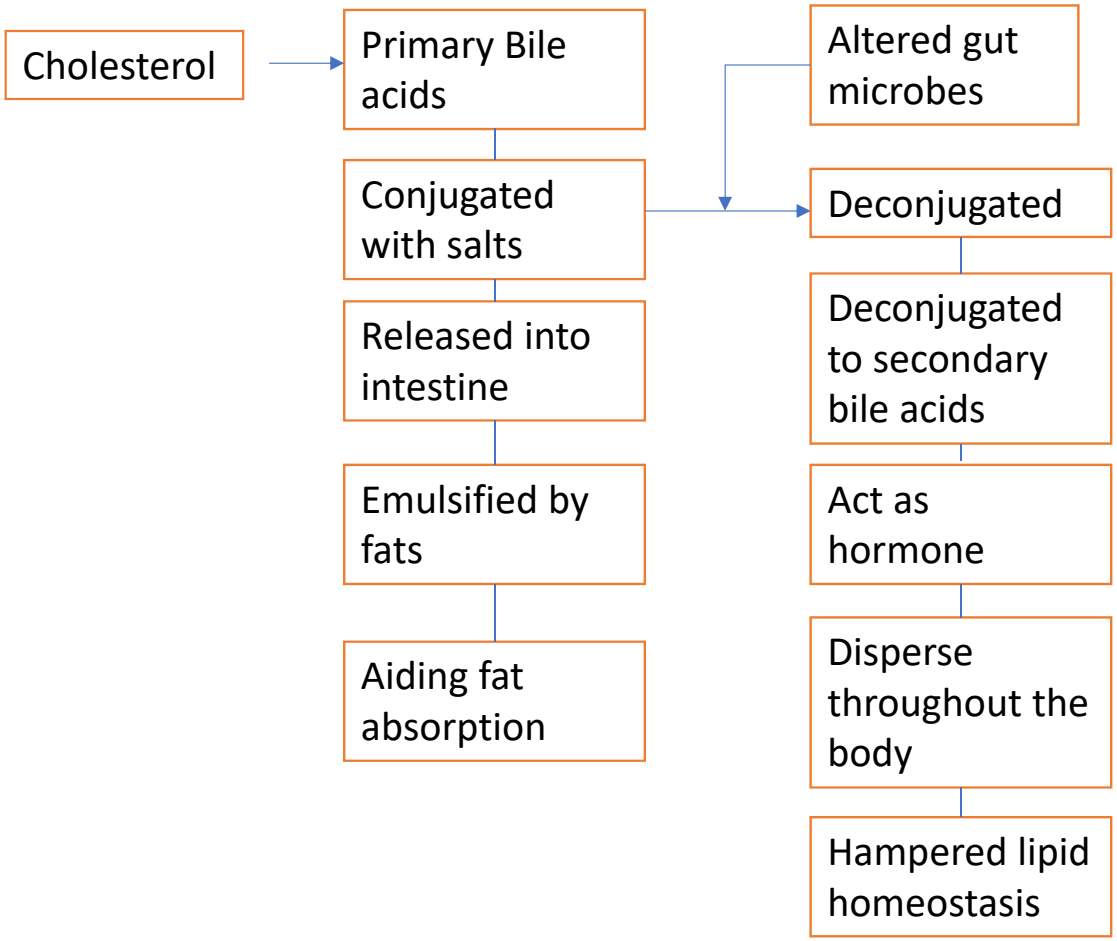


Figure: (A) Every other day fasting (EODF) prevents elevated systolic blood pressure (SBP) in spontaneously hypertensive stroke prone (SHRSPs) and (B) (EODF) prevents SBP in SHRSPs through manipulation of the gut microbiota. ****P≤0.0001.

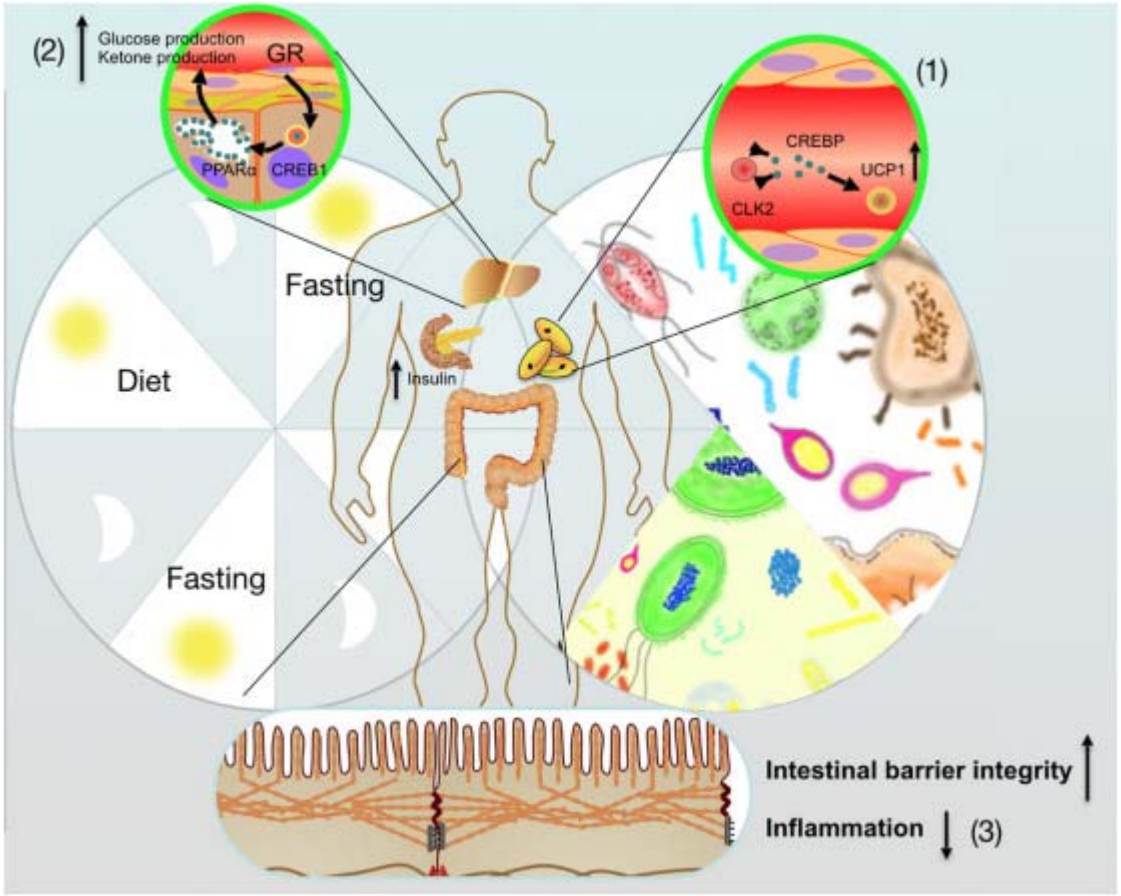
Shi et al., 2021

Intermittent fasting, Hypertensive disorder and gut microbiota

- Yet to be revealed
- Mainly metabolites produced by gut microbes are responsible
- Bile acids, amino acids, Nitric oxides, Acetate, propionates etc.
- Tryptophan metabolism in the gut and its downstream metabolites, including serotonin and indole play important roles in BP regulation
- L-histidine has anti hypertensive effects via central histamine H3 receptors



Intermittent fasting on host energy metabolism regulated by gut microbiota



- By improving gut microbial ecosystem, IF promotes WAT beiging.
- Gut microbiota increase hepatic ketone production
- Optimized microbial community by IF is responsible for the protection of host intestinal barrier.

GR = glucocorticoid receptor; CREB1 = cyclic AMP response element binding protein 1;
PPARα = peroxisome proliferators-activated receptor α;

Fig. Summary of IF-mediated positive effects by which gut microbiota regulates host energy metabolism

Rong et al., 2021

Conclusion and Future Research

- Intermittent fasting could ameliorate metabolic diseases through positive change of gut microbiota
- Any types of fasting could have benefits on human health
- Need to conduct more research on whether the change is short lived
- Need more research to explore the benefits on other diseases such as neurodegenerative diseases, aging, cancer etc.

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