**Supplementary Methods -** a systematic review of the fasting literature

What is currently known, and to what degree of certainty, regarding the influence of different forms of fasting on the composition of the gut microbiota? To this end, a semisystematic review was conducted in February 2022. Primary articles in MEDLINE matching a search for “fasting” and “microbiome” were identified and further augmented with tools for “similar articles” searches as well as additional listings of work citing or cited by previous review articles on this topic. Studies involving human subjects where interventions involved either periodic or intermittent fasting or calory restriction, and where gut microbiome analysis from stool samples was undertaken, were retained. This search identified N=15 primary articles meeting these criteria, as listed in **Table 1**, with this literature described in further detail below. As analysis protocols diverge substantially across this body of literature, a truly comprehensive meta-analysis would require reprocessing raw data while accounting for differences in laboratory and sampling methodology as well as study design, but in searching for consensus findings, a survey of the reported results alone reveals relevant associations. Studies involving both a fasting intervention and a refeeding/maintenance follow-up are here represented with these stages treated separately, following terminology in Maifeld et al. 2021 (“fasting”, “refeeding”, “study effect”), and separate subcohorts similarly treated separately (including if pooled in the source study).

For comparison, the focus is placed on gut microbiome alterations at the level of taxonomic genus, with entities judged to correspond to the same such taxon across studies treated as same, following again the comparison within Maifeld et al., 2021 [2] with the results of Mesnage et al., 2020 [147] (and with the results from each used in that comparison also reused here to represent the two studies and their respective substudies). Only taxa reported as significantly altered in abundance, with direction (enrichment/depletion) reported, following correction for multiple testing if undertaken, are included. In a few cases, the direction of genus-level change can be inferred from the reported direction of change at the level of OTU or species signals. Taxa not reported as altered in abundance under these criteria are considered for purposes of this consensus analysis to not have been altered in abundance. In cases where taxa are reported elevated at a one-time point, the transition to that time point is considered to involve a significant enrichment of that taxon. Only taxa altered in more than one study is reported, and for a semisystematic summary of reported literature, only the direction (depleted/enriched) of a change is tracked, rather than its amplitude. Multivariate composition change findings (beta diversity) and changes in (any form of) alpha diversity metrics are also reported and listed. The full resulting set of reported findings by us and others is shown in **Supplementary Table S1** and represented in **Figure 2**.

While this collection of evidence represents most human data applicable and available, it is clear the majority of studies have low sample numbers and accordingly low power. Several report findings from using doubtful statistical methodologies (i.e. in several cases for example basing results on LEfSe scores with no correction for multiple testing) that accordingly do not replicate in our comparison. Comparing reported results further suffers from inconsistencies in reference databases and bioinformatic workflows. Accordingly, a fuller picture warrants a proper reanalysis of the available data, reprocessing all sequences from the currently published studies using a single framework, as we did compare the two largest -omics studies of Buchinger fasting and refeeding to date in our recent work [2].

This overview explicitly does not consider results from animal models. We recognize such work is irreplaceable in mechanistic validation, and that there exists a substantial body of knowledge resulting from it. However, with even the variability between human studies reported here being high, differences between models and setups (reflecting both differences in biology between species and effects of living conditions and morbidities, and the design of each intervention itself) are likely to impact even further, raising always the question on whether a particular animal finding truly translates to a human setting useful in practice. As such, we consider the present overview a first step in collecting the human evidence to use as a scaffold for interpreting animal intervention results in subsequent literature overviews and targeted experiments.