# Supplementary Information

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**Table 1. Characteristics of the salt challenge study participants**

| | Mean (SD) |
|---|---|
| Men (*n*) | 12 |
| Age (years) | 33 (6) |
| Height (m) | 1.82 (0.04) |
| Weight (kg) | 79 (7) |
| BMI (kg/m$^2$) | 23.9 (2.1) |
| Waist circumference (cm) | 85 (5) |
| Hip circumference (cm) | 91 (5) |
| Waist-to-hip ratio (WHR) | 0.93 (0.04) |
| Systolic blood pressure (mmHg) | 121 (10) |
| Diastolic blood pressure (mmHg) | 78 (9) |

Screening data, given as means (SD). BMI, body mass index

## Full shotgun metagenomic taxonomic analysis of the human dataset

Based on SpecI taxonomic quantification of the human sub-study metagenomes, we assessed the composition of each such gut microbiome on the level of bacterial phyla, genera and species (for details see Supplementary Data File). For each such taxon, samples were tested for whether, on the whole, overall enrichment or depletion occurred during the intervention (Wilcoxon signed-rank test of relative abundances at baseline and post-intervention, adjusting for multiple testing within each taxonomic level using Benjamini-Hochberg correction). Paired comparison effect sizes were assessed using the nonparametric Cliff's delta measure as implemented in the orddom R package. Results are shown in the Supplementary Data File. No taxon can be shown to be significantly ($Q<0.1$) enriched or depleted under this test, though the small size of the dataset may mean even moderate effects would remain undetectable in this setup while maintaining stringent FDR adjustment.

## Corroboration of human *Lactobacillus* analysis

To ensure results are robust despite *Lactobacillus* having low abundance in the human gut, we repeated the analysis using complementary methods for taxonomic analysis of metagenomes (the mOTU[1] and MetaPhlAn[2] frameworks), yielding largely the same patterns and with the more rapid loss of *Lactobacillus* species under high salt challenge remaining significant in each setup (Extended Data Fig. 10b, c). Yet additional verification was undertaken using qPCR for those *Lactobacillus* species where specific primers were available, again broadly confirming loss of the respective *Lactobacillus* species after high salt challenge (Extended Data Fig. 10d).

## Human gut *Lactobacillus* survival analysis

We next assessed whether *Lactobacillus* stands out among gut bacteria in its rate of loss over time under HSD. The Kaplan-Meier plot in Extended Data Figure 10f shows, for the human study samples, the survival of detected gut bacterial species (using mOTU taxonomy) under high salt challenge, separating *Lactobacillus* mOTUs from all other mOTUs. There is an overall loss of approximately

30% of all gut mOTUs during the HSD intervention, but this loss is significantly (p<1.62e-8) larger for *Lactobacillus* species.

Given the relatively high overall loss of gut mOTUs under HSD, we then tested the same including also the normal salt control samples. The Kaplan-Meier plots in Extended Data Figure 10e reveal several relevant trends. First, importantly, gut *Lactobacillus* in general is lost significantly (p<2e-12) more often than non-*Lactobacillus* mOTUs, which might reflect generally low abundance, special sensitivity or both (Extended Data Fig. 10e). Second, also non-*Lactobacillus* mOTUs are lost significantly (p<1.56e-11) faster under high salt challenge than under normal salt (Extended Data Fig. 10e). Thus taken together, the severe loss of *Lactobacillus* under high salt challenge reflects both a taxon more prone to loss over time, and an environmental factor – high salt – which generally promotes loss (and/or gain) of taxa in human gut microbiomes.

## Supplementary Information References

1 Sunagawa, S. *et al.* Metagenomic species profiling using universal phylogenetic marker genes. *Nature methods* **10**, 1196-1199, doi:10.1038/nmeth.2693 (2013).

2 Segata, N. *et al.* Metagenomic microbial community profiling using unique clade-specific marker genes. *Nature methods* **9**, 811-814, doi:10.1038/nmeth.2066 (2012).