Aims/hypothesis: Individuals with type 2 diabetes have aberrant intestinal microbiota. However, recent studies suggest that metformin alters the composition and functional potential of gut microbiota, thereby interfering with the diabetes-related microbial signatures. We tested whether specific gut microbiota profiles are associated with prediabetes (defined as fasting plasma glucose of 6.1–7.0 mmol/l or HbA1c of 42–48 mmol/mol [6.0–6.5%]) and a range of clinical biomarkers of poor metabolic health. Methods: In the present case–control study, we analysed the gut microbiota of 134 Danish adults with prediabetes, overweight, insulin resistance, dyslipidaemia and low-grade inflammation and 134 age- and sex-matched individuals with normal glucose regulation. Results: We found that five bacterial genera and 36 operational taxonomic units (OTUs) were differentially abundant between individuals with prediabetes and those with normal glucose regulation. At the genus level, the abundance of Clostridium was decreased (mean log_2 fold change −0.64 (SEM 0.23), p_{adj} = 0.0497), whereas the abundances of Dorea, [Ruminococcus], Sutterella and Streptococcus were increased (mean log_2 fold change 0.51 (SEM 0.12), p_{adj} = 5 × 10^{-4}; 0.51 (SEM 0.11), p_{adj} = 1 × 10^{-4}; 0.60 (SEM 0.21), p_{adj} = 0.0497; and 0.92 (SEM 0.21), p_{adj} = 4 × 10^{-4}, respectively). The two OTUs that differed the most were a member of the order Clostridiales (OTU 146564) and Akkermansia muciniphila, which both displayed lower abundance among individuals with prediabetes (mean log_2 fold change −1.74 (SEM 0.41), p_{adj} = 2 × 10^{-3} and −1.65 (SEM 0.34), p_{adj} = 4 × 10^{-4}, respectively). Faecal transfer from donors with prediabetes or screen-detected, drug-naive type 2 diabetes to germfree Swiss Webster or conventional C57BL/6 J mice did not induce impaired glucose regulation in recipient mice.

Conclusions/interpretation: Collectively, our data show that individuals with prediabetes have aberrant intestinal microbiota characterised by a decreased abundance of the genus Clostridium and the mucin-degrading bacterium A. muciniphila. Our findings are comparable to observations in overt chronic diseases characterised by low-grade inflammation.

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