

1 ***Appendix S1: Detailed description of the experimental procedure, the assessment of***  
2 ***parameters, and the laboratory analyses***

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4 *Assessment of vascular function: arterial stiffness, retinal vessel diameters*

5 Before and after the intervention period, participants were admitted to the Department of  
6 Sport, Exercise and Health of the University of Basel to assess arterial stiffness and retinal  
7 vessel diameters. To prepare for the measurements, participants were instructed to abstain  
8 from caffeine, alcohol and heavy physical activity, and to fast at least four hours.

9 Arterial stiffness was measured oscillometrically using a VaSera VS-1500 vascular screening  
10 system (Fukuda Denshi Co. Ltd, Tokyo, Japan). Triple measurements were taken in a supine  
11 position after resting for at least 10 minutes and 5 minutes between the measurements in a  
12 quiet room with a controlled temperature between 22-24 °C. Standard blood pressure cuffs  
13 were placed at each upper arm and above each ankle. Electrocardiogram leads were attached  
14 at each wrist, and a phonocardiogram was placed on the sternal border in the second  
15 intercostal space. The heart-ankle pulse wave velocity (PWV) was measured based on the  
16 vessel length between the heart valve and the ankle artery divided by the time taken for the  
17 pulse wave to propagate from the aortic valve to the ankle. ARCSolver algorithm was applied  
18 to pulse wave signals acquired at the left upper arm to estimate central PWV (1). The average  
19 of the three PWV-measurements was taken for statistical analysis.

20 A fundus camera (Topcon TRC NW) and the analyzing software Visualis (Visualis 2.80,  
21 Imedos Systems UG) were used for retinal image acquisition. Three crisp images of each eye  
22 were taken at an angle of 45 degrees with the optic disc at the center. All arterioles and  
23 venules 0.5–1 disk diameter away from the optic disk margin were marked. Retinal arteriolar  
24 and venular diameter segments were semi-automatically marked using an analysis software  
25 (Vesselmap 2®; IMEDOS Systems GmbH, Jena, Germany). Arteriolar and venular diameters

26 from the three images of each eye were averaged to Central Retinal Arteriolar Diameter  
27 Equivalents (CRAE) and Central Retinal Venular Diameter Equivalents (CRVE) by use of the  
28 Parr–Hubbard formula (2). The arteriolar-to-venular diameter ratio (AVR) was calculated  
29 from the CRAE and CRVE. The values of each eye were again averaged. To guarantee  
30 optimal standardization, the same vessel segments were chosen at both time points using the  
31 pre-intervention assessment as a reference.

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### 33 *Assessment of abdominal fat: quantification and distribution*

34 Before and after the intervention period, participants were admitted to the Department of  
35 Radiology and Nuclear Medicine of the University Hospital of Basel for an abdominal MRI.  
36 Data for the evaluation of percentage liver fat (%-LF), total liver volume (TLV), visceral  
37 adipose tissue (VAT), and subcutaneous adipose tissue (SAT) were acquired using a  
38 MAGNETOM Prisma 3T scanner (Siemens Healthineers, Erlangen, Germany). A transversal  
39 T2\*-IDEAL (3D spoiled gradient echo with 6 echoes) sequence was used for the liver fat  
40 measurement, and a two-point Dixon (3D spoiled gradient echo with two echoes) sequence in  
41 coronal orientation for the SAT and VAT quantification. Both scans were performed in breath  
42 holding (up to 20 seconds each). Details on data acquisition and evaluation are described  
43 elsewhere (3). In short, the T2\*-IDEAL scan covered the whole liver. Those images were  
44 segmented manually to derive %-LF and TLV. The two-point Dixon scan was used for the  
45 automatic SAT and VAT volume segmentation which was subsequently manually corrected,  
46 and spatially confined to the upper end of the femoral head and the lower end of the ninth  
47 thoracic vertebra.

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### 49 *Assessment of glucose tolerance, blood lipids, uric acid, hepatic enzymes, and creatinine*

50 Before and after the intervention period, participants were admitted to the St. Clara Research

51 Ltd. in the morning after an overnight fast for an oral glucose tolerance test (OGTT). For this  
52 purpose, they were instructed to abstain from heavy physical activity within the two days  
53 before the test, to eat meals containing carbohydrates, and to come on an empty stomach, i.e.,  
54 not eat or drink (water allowed until two hours before the test) nor consume alcohol within ten  
55 hours before the test.

56 An antecubital catheter was inserted into a forearm vein for blood collection. After taking a  
57 fasting blood sample (t = -15 min) for assessment of fasting glucose and insulin  
58 concentrations (ethylenediaminetetraacetic acid (EDTA) tubes), blood lipids, uric acid,  
59 hepatic enzymes, creatinine concentrations (lithium heparin tubes), participants received a  
60 standardized solution containing 75 g of glucose.

61 Blood samples were taken at regular time intervals after administration of the solution (t = 30,  
62 60, 90, and 120 min) for assessment of glucose and insulin concentrations. The samples were  
63 collected on ice into tubes (EDTA, 6 µmol/L blood). After centrifugation (4 °C at 3000 rpm  
64 for 10 min), plasma samples were immediately processed into different aliquots and stored at  
65 -80 °C until analysis.

66

#### 67 *Assessment of gastrointestinal tolerance and dietary patterns*

68 Gastrointestinal tolerance was assessed using the Gastrointestinal Symptom Rating Scale  
69 (GSRS) (4) before and during the second and fourth week of intervention. The 15 items of  
70 this scale combine into five symptom clusters: reflux, abdominal pain, indigestion, diarrhea  
71 and constipation.

72 To assess changes in dietary patterns, participants completed dietary records seven days  
73 before the intervention and during the second and the fourth week of the intervention. The  
74 dietary records were analyzed qualitatively by categorizing the foods into 11 different groups  
75 (vegetables, fruits, cereals/bread, other carbohydrates, meat/fish/other protein sources, dairy

76 products, fats/nuts/seeds, beverages with added sugar (e.g., coffee with sugar), beverages with  
77 sweeteners, sugar-sweetened beverages, and sweets) and comparing the number of servings  
78 per food group.

79

#### 80 *Laboratory analysis*

81 Plasma glucose was measured by a glucose oxidase method (Rothen Medizinische  
82 Laboratorien AG, Basel, Switzerland; range of assay, 0.6 to 45.0 mmol/L). Plasma insulin  
83 was quantified using an electro-chemiluminescent immunoassay (Rothen Medizinische  
84 Laboratorien AG, Basel, Switzerland; range of assay, 4.0 to 1000.0 mIU/L; intra- and inter-  
85 assay variability below 4.3% and 5.3%).

86 The laboratory of the St. Clara Hospital in Basel assessed fasting blood lipids, uric acid,  
87 hepatic enzymes, and creatinine. Serum blood lipids (serum triglyceride, cholesterol, and high  
88 density lipoprotein (HDL)) were measured with enzymatic colorimetric tests. The intra- and  
89 inter-assay variability are below 2.1% and 2.3% (triglyceride), 2.1% and 7.4% (cholesterol),  
90 and 1.1% and 1.5% (HDL). Low density lipoprotein (LDL) was calculated with the  
91 Friedewald-Formula (5). Serum uric acid was measured with an enzymatic colorimetric test  
92 with an intra- and inter-assay variability below 1.7% and 2.0%. Hepatic enzymes alanine  
93 aminotransferase (ALAT) and aspartate aminotransferase (ASAT) were measured with  
94 enzymatic colorimetric tests. The intra- and inter-assay variability are below 1.8% and 1.8%  
95 (ALAT), and 1.6% and 1.8% (ASAT). Creatinine was assessed with a kinetic colorimetric test  
96 based on the Jaffe method (6) with an intra- and inter-assay variability below 2.9% and 3.4%.

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98 **References**

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