

The extent of lifestyle-induced weight loss determines the risk of prediabetes and metabolic syndrome recurrence during a 5-year follow-up

Silke Zimmermann ^{1*}, Mandy Vogel ², Akash Mathew ¹, Thomas Ebert ^{3,4}, Rajiv Rana ¹, Shihai Jiang ¹, Berend Isermann ¹ and Ronald Biemann ^{1*}

¹Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, University of Leipzig, 04103 Leipzig, Germany

²Hospital for Children and Adolescents, Centre for Pediatric Research, Department Woman and Child Health, University of Leipzig, Leipzig, Germany

³Karolinska Institutet, Department of Clinical Science, Intervention and Technology, Division of Renal Medicine, SE-141 86 Stockholm, Sweden

⁴Medical Department III – Endocrinology, Nephrology, Rheumatology, University of Leipzig Medical Center, Leipzig, Germany

*Correspondence: ronald.biemann@medizin.uni-leipzig.de (RB); silke.zimmermann@medizin.uni-leipzig.de (SZ)

Supplementary Materials:

Supplementary Table S1: Clinical parameters of individuals with metabolic syndrome at baseline and after the 6-month lifestyle-induced weight loss intervention period. Data are presented as median (interquartile range). Wilcoxon Signed-Rank Test was used to analyze differences of paired samples between baseline (BL) and lifestyle-induced weight loss in each quartile (Q1-Q4).

Parameters	BL	Q1	<i>p</i>	BL	Q2	<i>p</i>	BL	Q3	<i>p</i>	BL	Q4	<i>p</i>
Age [years]	47.5 ± 9			48 ± 6			49 ± 5			47.5 ± 10.3		
BMI	32.9 ± 6.6	30.9 ± 7.3	<0.01	33.0 ± 5.7	28.8 ± 4.9	<0.01	35.4 ± 3.4	30.0 ± 3.5	<0.01	35.2 ± 3.2	27.5 ± 5.1	<0.01
Weight [kg]	106.2 ± 28	100.1 ± 27.6	<0.01	107 ± 21.8	94.5 ± 18.2	<0.01	108 ± 15.9	93.5 ± 14.5	<0.01	109.8 ± 20	12.7 ± 15.3	<0.01
HDL cholesterol [mmol/L]	1.41 ± 0.7	1.53 ± 0.8	n.s.	1.2 ± 0.4	1.33 ± 0.4	<0.01	1.23 ± 0.4	1.45 ± 0.6	<0.01	1.46 ± 0.4	1.46 ± 0.4	<0.01
TG [mmol/L]	2.19 ± 2.2	2.16 ± 2.8	n.s.	2.0 ± 2.6	1.36 ± 0.8	<0.01	2.03 ± 1.9	1.4 ± 0.8	<0.01	1.83 ± 1.5	0.98 ± 0.4	<0.01
RR _{sys} [mmHg]	140 ± 12	138 ± 16.0	n.s.	138 ± 14.0	122 ± 13.0	<0.01	140 ± 28.5	130 ± 14.0	n.s.	149.0 ± 18.0	130 ± 18.0	0.02
HbA1c [%]	5.6 ± 0.5	5.5 ± 0.4	n.s.	5.6 ± 0.7	5.4 ± 0.3	n.s.	5.4 ± 0.8	5.3 ± 0.7	n.s.	5.6 ± 0.5	5.2 ± 0.6	0.02
Insulin [pmol/L]	88 ± 80	68 ± 28	<0.01	79.5 ± 72.3	45.5 ± 24	<0.01	68 ± 83.3	36 ± 43.3	<0.01	60 ± 52	30 ± 21	<0.01
Glucose [mmol/L]	5.9 ± 0.8	5.8 ± 0.7	n.s.	6.2 ± 1.2	5.7 ± 0.6	0.02	5.9 ± 1.2	5.4 ± 0.6	n.s.	6.2 ± 0.9	5.6 ± 0.7	0.02

Supplementary Table S2. Table showing the number of participants treated with antilipidemic drugs and total numbers of participants in each quartile (Q1-Q4) at each timepoint. Fisher's exact probability test was used to analyze differences in the number of treated versus nontreated participants at different timepoints (only significant values are listed). BL= baseline; LIWL= lifestyle-induced weight loss; FU1-5= years of follow-up

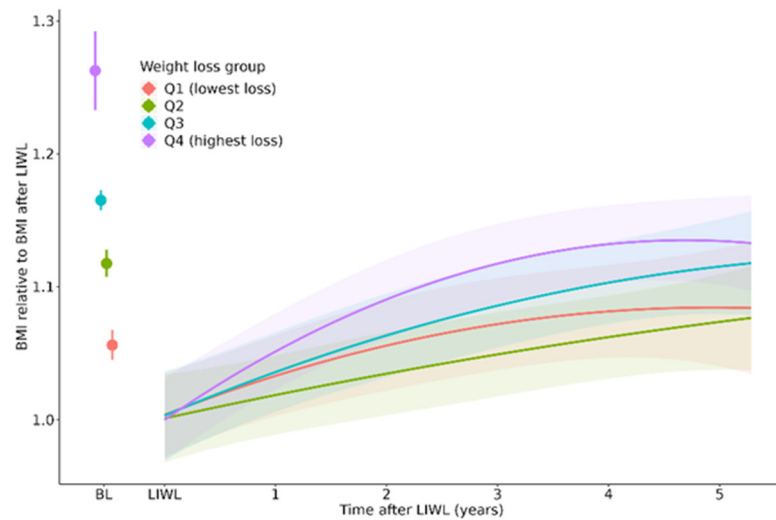
	Q1 antilipidemics/ total	Q2 antilipidemics/ total	Q3 antilipidemics/ total	Q4 antilipidemics/ total	<i>p</i>
BL	4/15	5/14	3/14	3/15	n.s.
FU1	4/11	4/12	4/11	4/14	n.s.
FU2	4/8	4/11	4/11	4/12	n.s.
FU3	4/8	4/8	5/10	4/11	n.s.
FU4	5/6	4/10	4/11	4/12	n.s.
FU5	4/7	4/9	4/11	4/13	n.s.

Supplementary Table S3. Median and interquartile ranges of RR_{dia} levels before and after LIWL and during the 5-year follow-up. The Wilcoxon signed rank test was used to analyze changes between paired samples between BL and subsequent follow-up timepoints (only significant values are listed). BL= baseline; LIWL= lifestyle-induced weight loss; FU1-5= years of follow-up.

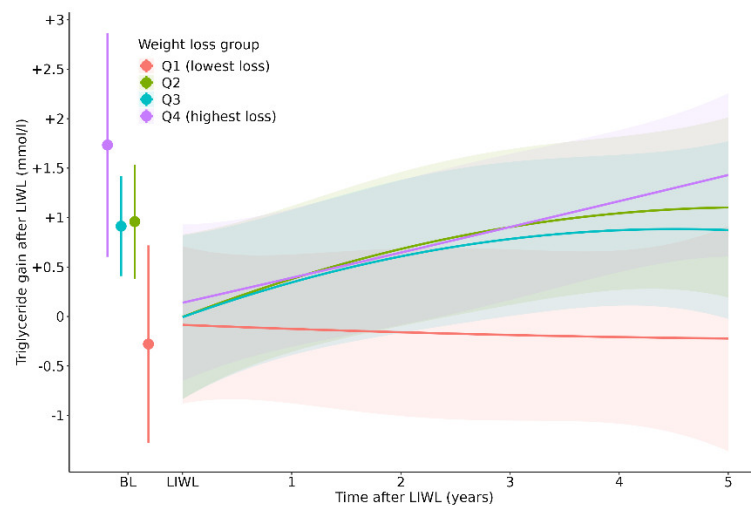
RR _{dia} (mmHg)	BL	Q1	<i>p</i>	BL	Q2	<i>p</i>	BL	Q3	<i>p</i>	BL	Q4	<i>p</i>
LIWL	90 ± 12	90 ± 10	n.s.	84 ± 15	81 ± 7.3	n.s.	85 ± 13	84.5 ± 8	n.s.	91 ± 15.5	84.5 ± 9.5	n.s.
FU1		90 ± 23	n.s.		84 ± 12	n.s.		82 ± 11	n.s.		84 ± 12	n.s.
FU2		99 ± 30.8	n.s.		85 ± 17.3	n.s.		90 ± 13.5	n.s.		82 ± 15.5	n.s.
FU3		88 ± 16	n.s.		88 ± 12	n.s.		85 ± 17.5	n.s.		86 ± 9	n.s.
FU4		88 ± 21	n.s.		85 ± 18	n.s.		90 ± 18.3	n.s.		86 ± 19	n.s.
FU5		85 ± 8	n.s.		89 ± 11.8	n.s.		85 ± 10	n.s.		81 ± 11.8	<0.01

Supplementary Table S4. Table showing the number of participants treated with antihypertensive medication (AHM) and total numbers of participants in each quartile (Q1-Q4) at each timepoint. Fisher's exact probability test was used to analyze differences in the number of treated versus nontreated participants at different timepoints (only significant values are listed). BL= baseline; LIWL= lifestyle-induced weight loss; FU1-5= years of follow-up

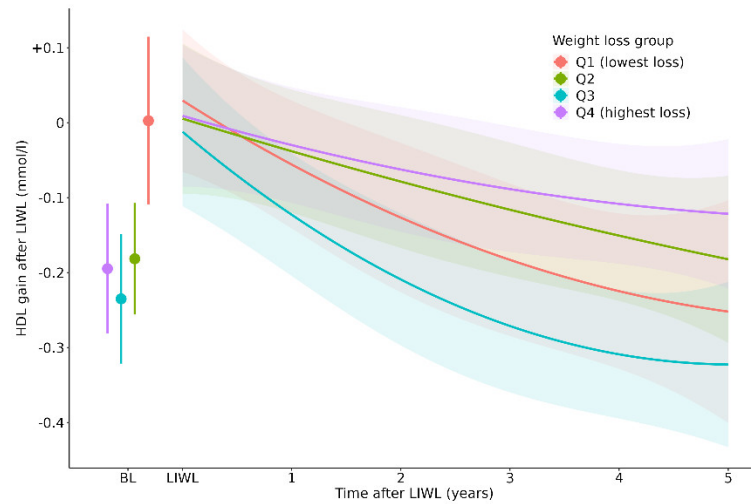
	Q1 AHM/ total	Q2 AHM/ total	Q3 AHM/ total	Q4 AHM/ total	<i>p</i>
BL	11/15	11/14	13/14	12/15	n.s.
FU1	10/11	9/12	7/11	6/14	n.s.
FU2	5/8	10/11	9/11	6/12	n.s.
FU3	8/8	8/8	9/10	6/11	0.02
FU4	5/6	10/10	10/11	8/12	n.s.
FU5	6/7	9/9	10/11	7/13	0.04



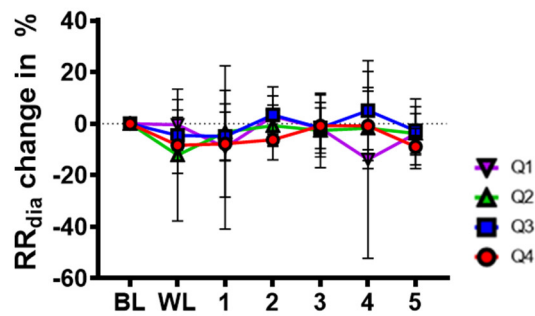
Supplementary Figure S1. BMI trends relative to BMI after lifestyle-induced weight loss in weight loss stratified by quartiles Q1-Q4 in a modeled quadratic dependent on time after LIWL. Data are presented as change in BMI since LIWL. BL= baseline; LIWL= lifestyle-induced weight loss; 1-5= years of follow-up



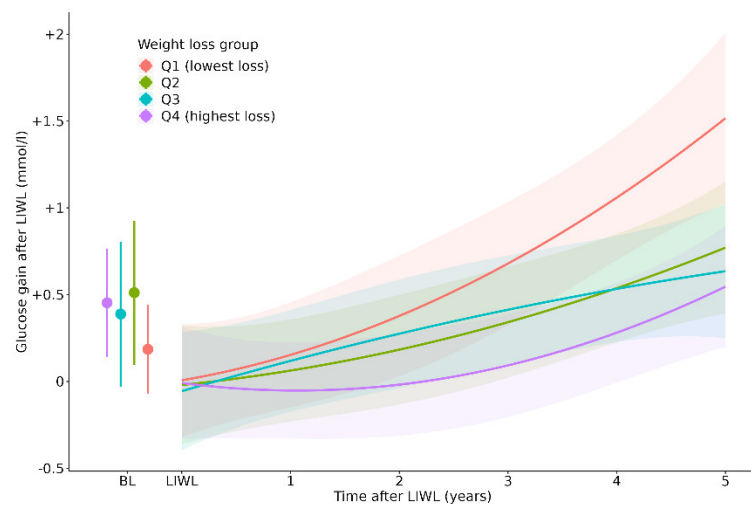
Supplementary Figure S2. Triglyceride level trends relative to triglyceride levels after lifestyle-induced weight loss stratified by weight loss quartiles Q1-Q4 in a modeled quadratic dependent on time after LIWL. Data are presented as change in Triglycerides after LIWL. BL= baseline; LIWL= lifestyle-induced weight loss; 1-5= years of follow-up



Supplementary Figure S3. HDL cholesterol relative to HDL cholesterol after lifestyle-induced weight loss stratified by weight loss quartiles Q1-Q4 in a modeled quadratic dependent on time after LIWL. Data are presented as change in HDL cholesterol after LIWL. BL= baseline; LIWL= lifestyle-induced weight loss; 1-5= years of follow-up



Supplementary Figure S4: Long-term effects of lifestyle-induced weight loss on diastolic blood pressure during the 5-year follow-up. Data are presented as the median (interquartile range). BL= baseline; WL= weight loss; 1-5= years of follow-up.



Supplementary Figure S5. Fasting plasma glucose relative to fasting plasma glucose after lifestyle-induced weight loss stratified by weight loss quartiles Q1-

Q4 in a modeled quadratic dependent on time after LIWL. Data are presented as change in fasting plasma glucose after LIWL. BL= baseline; LIWL= lifestyle-induced weight loss; 1-5= years of follow-up