

1 **Meal Replacement by Formula Diet Reduces Weight more than a Lifestyle Intervention**  
2 **Alone in Patients with Overweight or Obesity and Accompanied Cardiovascular Risk**  
3 **Factors – the ACOORH Trial**

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5 **Running title: Formula diet and lifestyle intervention in obesity**

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7 Martin Halle<sup>1,2†</sup>, Martin Röhling<sup>3†</sup>, Winfried Banzer<sup>4</sup>, Klaus Michael Braumann<sup>5</sup>, Kerstin  
8 Kempf<sup>3</sup>, David McCarthy<sup>6</sup>, Nina Schaller<sup>1</sup>, Hans Georg Predel<sup>7</sup>, Jürgen Scholze<sup>8</sup>, Dagmar  
9 Führer-Sakel<sup>9</sup>, Hermann Toplak<sup>10</sup>, Aloys Berg<sup>11</sup>, ACOORH study group\*

10

11 <sup>1</sup>Department of Prevention, Rehabilitation and Sports Medicine, Klinikum rechts der Isar,  
12 Technical University of Munich (TUM), Munich, Germany

13 <sup>2</sup>DZHK (German Centre for Cardiovascular Research), Partner Site Munich Heart Alliance,  
14 Munich, Germany

15 <sup>3</sup>West-German Center of Diabetes and Health, Düsseldorf Catholic Hospital Group, Dusseldorf,  
16 Germany

17 <sup>4</sup>Department of Sports Medicine, Institute for Sports and Sport Science, University of Frankfurt,  
18 Frankfurt, Germany

19 <sup>5</sup>Faculty of Psychology and Human Movement Sciences, Department of Sports and Movement  
20 Medicine, University of Hamburg, Hamburg, Germany

21 <sup>6</sup>Public Health Nutrition Research Group, London Metropolitan University, London, UK

22 <sup>7</sup> Institute of Cardiovascular Research and Sports Medicine, German Sport University Cologne,  
23 Cologne, Germany;

24 <sup>8</sup> KARDIOS, Cardiologists in Berlin, Berlin, Germany;

25 <sup>9</sup> Department of Endocrinology, Diabetes and Metabolism and Division of Laboratory Research,  
26 University Hospital Essen, University Duisburg-Essen, Essen, Germany;

27 <sup>10</sup> Department of Medicine, Division of Endocrinology and Diabetology, Medical University of  
28 Graz, Austria;

29 <sup>11</sup> Faculty of Medicine, University of Freiburg, Freiburg, Germany

30 \* A list of authors and their affiliations appears at the end of the paper.

31

32 †These authors contributed equally to this work

33

34 **Corresponding author**

35 Dr. Martin Röhling

36 West-German Center of Diabetes and Health, Düsseldorf Catholic Hospital Group, Dusseldorf,  
37 Germany, Hohensandweg 37, 40591 Dusseldorf, phone: +49 (0)211-56 60 360 76, fax: +49  
38 (0)211-56 60 360 72, E-mail: [martin.roehling@vkkd-kliniken.de](mailto:martin.roehling@vkkd-kliniken.de)

39

40 **Consortium representative**

41 Prof. Dr. Aloys Berg (principal investigator)

42 Faculty of Medicine, University of Freiburg, Freiburg, Germany, Breisacher Str. 153, 79110  
43 Freiburg, phone: +49 (0)172-74 14 771, E-mail: [alloys.berg@klinikum.uni-freiburg.de](mailto:alloys.berg@klinikum.uni-freiburg.de)

44

45 **Abstract**

46 **Background:** As formula diets have demonstrated to be effective in reducing weight, we  
47 hypothesized that in patients with overweight or obesity and accompanied cardiovascular risk  
48 factors, combining a liquid formula diet with a lifestyle intervention is superior in reducing  
49 weight and improving cardiovascular risk factors than lifestyle intervention alone.

50 **Methods:** In this multicenter RCT 463 participants with overweight or obesity (BMI: 27-35  
51 kg/m<sup>2</sup>; at least one additional co-morbidity of the metabolic syndrome) were randomized (1:2)  
52 into either a control group with lifestyle intervention only (CON, n=155) or a lifestyle  
53 intervention group including a liquid meal replacement (INT, n=308). Both groups used  
54 telemonitoring devices (scales and pedometers), received information on healthy diet and were  
55 instructed to increase physical activity. Telemonitoring devices automatically transferred data  
56 into a personalised online portal and acquired data were discussed. INT obtained a liquid meal  
57 replacement substituting three meals/day (~1,200 kcal) within the first week. During weeks 2-4,  
58 participants replaced two meals/day and during weeks 5-26 only one meal/day was substituted  
59 (1,300-1,500 kcal/day). Follow-up was conducted after 52 weeks. Intention-to-treat analyses  
60 were performed. Primary outcome was weight change. Secondary outcomes comprised changes  
61 in cardiometabolic risk factors including body composition and laboratory parameters.

62 **Results:** From the starting cohort 360 (78%, INT: n=244; CON: n=116) and 317 (68%, INT:  
63 n=216; CON: n=101) participants completed the 26-weeks intervention phase and the 52-weeks  
64 follow-up. The estimated treatment difference (ETD) between both groups was -3.2 kg [-4.0; -  
65 2.5] (P<0.001) after 12 weeks and -1.8 kg [-2.8; -0.8] (P<0.001) after 52 weeks.

66 **Conclusions:** A low-intensity lifestyle intervention combined with a liquid meal replacement is  
67 superior regarding weight reduction and improvement of cardiovascular risk factors than lifestyle  
68 intervention alone.

69

70 **Introduction**

71 A high energy intake combined with low physical activity are major determinants for  
72 overweight and obesity and contribute to the overall increase of non-communicable diseases [1].

73 Although lifestyle interventions have been shown to induce clinically relevant effects,  
74 adherence to these approaches remains low overall. Therefore, alternative treatment strategies  
75 need to be considered [2, 3]. In this context, liquid meal replacements have been shown to be an  
76 useful treatment option to manage obesity and diseases such as type 2 diabetes [4-6], leading to  
77 improvements in fat mass, blood pressure, HbA<sub>1c</sub>, or insulin [7, 8]. Furthermore, there is a  
78 positive association between partial and complete meal replacement with weight reduction which  
79 was shown in favor of complete meal replacement in patients with type 2 diabetes [9]. Based on  
80 their positive effects in the management of patients with type 2 diabetes, liquid meal  
81 replacements have been included into current guidelines for baseline treatment of type 2 diabetes  
82 [10-12], but not uniformly for the routine management of overweight and obesity [3]. In this  
83 regard, there is still uncertainty about weight maintenance and long-term effectivity of formula  
84 diets [13, 14] and whether there is a beneficial effect of adding a formula diet to an lifestyle  
85 intervention and/or nutrition counseling alone in patients with overweight and obesity [12].

86 Hence, an international and multicenter RCT, the *Almased Concept against Overweight*  
87 *and Obesity and Related Health Risk* (ACOOHR)-study, was conducted to examine the impact  
88 of a liquid meal replacement together with a low-intensity lifestyle intervention compared to a  
89 low-intensity lifestyle intervention alone on weight loss in patients with overweight or obesity  
90 and accompanied cardiovascular risk factors.

91

92

## 93 **Materials/Subjects and Methods**

94

### 95 *Study design and population*

96           Participating volunteers (n=463) were randomly allocated with a ratio of 1:2 into either a  
97 lifestyle intervention group (CON, n=155) or a meal replacement-based lifestyle intervention  
98 group (INT, n=308). The lifestyle intervention was characterized by a 26-week intervention  
99 phase and a follow-up phase until week 52 and the study design has been described in detail  
100 previously in a predefined subanalysis of the ACOORH study focusing solely on patients with  
101 prediabetes [15]. This multicenter RCT received ethical approval (registered at *drks.de*; ID:  
102 DRKS00006811) for each participating center and the study reporting adheres to CONSORT  
103 guidelines. Informed consent was obtained from all participating volunteers. Study participants  
104 were recruited in all study centers either through direct contacting based on existing patient files,  
105 (2) proactive study enquiry by the participants via the study center homepages, or (3)  
106 advertisements in newspapers. Inclusion and exclusion criteria have been described in detail  
107 previously [15].

108

### 109 *Intervention and diet regime*

110           Both groups were provided with guideline booklets about healthy cooking, received  
111 advices regarding physical activity and a healthy lifestyle including encouragement to lose  
112 weight, and were equipped with telemetric scales (smartLAB scale W; HMM Holding AG,  
113 Dossenheim, Germany) and pedometers (smartLAB walk P+; HMM Holding AG, Dossenheim,  
114 Germany). Probands were recommended to note down a 4-day, unweighted diet record at  
115 baseline and after 12, and 52 weeks of the study and all records (including steps and body

116 weight) were discussed during the study visits (personal contact time  $\approx$  1-2 h per visit). A  
117 detailed description of the study can be found elsewhere [15] and is illustrated in Fig. 1.

118 Additionally, the INT group was provided with the liquid soy-yogurt-honey-based meal  
119 replacement Almased-Vitalkost<sup>®</sup> (protein content: 53.3% (83 % soy-protein-isolate, and 17%  
120 milk protein), glycemic index (GI): 27, energy per 100 g powder: 1507 kJ (360 kcal), Almased-  
121 Wellness-GmbH, Bienenbüttel, Germany [16]) for the first 26 weeks and received an  
122 accompanying booklet containing information about preparing and applying the liquid formula  
123 diet and general advices about low-carbohydrate, low-glycemic and protein-rich meals. The  
124 management of the liquid formula diet regime during the study is described in detail elsewhere  
125 [15]. All booklet records were evaluated at each visit by study nurses and used for nutritional and  
126 lifestyle counselling.

127

## 128 ***Measurements***

129 Measurements were performed at baseline as well as after 4, 12, 26, and after 52 weeks  
130 as described in detail elsewhere [15]. Body composition (Seca medical Body Composition  
131 Analyzer<sup>®</sup> (seca-mBCA 115), Hamburg, Germany [17]) and blood pressure (Mobil-O-Graph  
132 PWA; I.E.M. GmbH, Stolberg, Germany) were determined by using validated devices.  
133 Biochemical blood parameters were determined by venous blood sampling. Adverse and serious  
134 adverse events [18] were documented continuously (participant questionnaire) and were  
135 reviewed by an external monitor.

136

## 137 ***Statistics***

138 Sample size calculation was based on the results of a previous study [19] and its  
139 assumptions, including randomization and number of dropouts, are described in detail elsewhere  
140 [15]. Final sample size per group comprised at least 19 participants for each study center.  
141 However, based on previous experiences in all participating centers with dropout rates greater  
142 than 50% for long-term adherence to weight management programs, at least a number of 40  
143 participants per center was targeted.

144 Primary outcome of the ACOORH study was body weight in kg after 4, 12, 26 and 52  
145 weeks of intervention. Power calculation was performed for the difference of body weight  
146 change after 12 weeks of intervention between INT and CON. Secondary outcomes comprised  
147 changes in anthropometric (fat mass (FM), fat free mass (FFM), and waist circumference (WC))  
148 and clinical parameters (fasting blood glucose (FBG), systolic blood pressure (SBP), diastolic  
149 blood pressure (DBP), total cholesterol, HDL cholesterol (HDL-C), LDL cholesterol (LDL-C),  
150 TG) after 4, 12, 26 and 52 weeks of intervention.

151 An independent institute (ACOMED statistik<sup>®</sup>, Leipzig, Germany) executed the  
152 statistical analysis and a detailed description including statistical tests applied (for parametric and  
153 non-parametric data) and software used can be found elsewhere [15]. Completer (per-protocol  
154 (PP)) and intention-to-treat (ITT) analyses were applied. All statistical tests were two-sided and  
155 significance was assumed at  $\alpha < 0.05$ . Participants who visited all follow-up assessments were  
156 integrated into the PP analysis. Primary analysis focused on the ITT approach as these values are  
157 of more clinical relevance. Last-observation-carried-forward (LOCF) method was applied to  
158 replace missing data for the ITT analysis.

159

160



161 **Results**

162 Four hundred thirty-nine (95%, INT: n=299; CON: n=140) from the starting cohort  
163 finished the first 4 weeks of the intervention phase. Follow-up data after 12, 26 and 52 weeks  
164 were available from 396 (86%, INT: n=270; CON: n=126), 360 (78%, INT: n=244; CON:  
165 n=116) and 317 participants (68%, INT: n=216; CON: n=101). Anthropometric and clinical  
166 parameters of INT and CON at baseline are illustrated in Table 1. Dropouts demonstrated no  
167 statistical difference in comparison to the non-dropout group (Supplementary Table 1).  
168 Participants dropped out because of (1) health issues, (2) work-related issues, (3) personal issues  
169 and (4) other reasons. No acute cardiac event, hospitalization for cardiovascular disease, or other  
170 serious adverse events related to the study participation occurred.

171 Compared to CON, INT significantly lost more weight after 4 weeks (-4.0 kg with 95%  
172 CI [-4.3;-3.8] vs. -1.4 kg [-1.8;-1.1]; P<0.001), 12 weeks (-5.8 kg with 95% CI [-6.3;-5.3] vs. -  
173 2.7 kg [-3.3;-2.1]; P<0.001), 26 weeks (-5.9 kg with 95% CI [-6.5;-5.4] vs. -3.0 kg [-3.8;-2.2];  
174 P<0.001) and 52 weeks (-4.4 kg [-5.0;-3.8] vs. -2.7 kg [-3.0;-2.0]; P<0.001) in the ITT analysis.  
175 The estimated treatment difference (ETD) between both groups was -2.6 kg [-3.5; -1.8]  
176 (P<0.001) after 4 weeks, -3.2 kg [-4.0; -2.5] (P<0.001) after 12 weeks, -2.9 kg [-3.7; -2.1]  
177 (P<0.001) after 26 weeks and -1.8 kg [-2.8; -0.8] (P<0.001) after 52 weeks. These differences  
178 were even stronger in the PP analysis after 4 weeks (-4.5 kg with 95% CI [-4.8;-4.2] vs. -1.6 kg  
179 [-2.0;-1.2] P<0.001), 12 weeks (-6.3 kg with 95% CI [-6.8;-5.8] vs. -3.2 kg [-3.9;-2.6] P<0.001),  
180 26 weeks (-6.8 kg with 95% CI [-7.5;-6.2] vs. -3.6 kg [-4.6;-2.7] P<0.001) and 52 weeks (-5.0 kg  
181 [-5.7;-4.2] vs. -3.5 kg [-4.5;-2.5] P=0.021).

182 Weight reduction was accompanied with changes in WC, FM, FBG, SBP, DBP, total  
183 cholesterol, TG, and LDL-C in both groups following the intervention, with a particularly

184 pronounced effect within the first 12 weeks (Fig. 2) (ITT analysis). These effects were already  
185 evident after 4 weeks of intervention in all parameters in the INT group (all  $P < 0.001$ ) (ITT  
186 analysis), but not in the CON group. Only FM, WC, and SBP (all  $P < 0.001$ ) as well as DBP and  
187 total cholesterol (both  $P < 0.01$ ) significantly changed after 4 weeks in CON (ITT analysis). The  
188 aforementioned 12-week changes remained significantly altered after 26 weeks of intervention in  
189 the INT group in all parameters ( $P < 0.001$ ) (ITT analysis). In contrast, only FM, WC, and SBP  
190 remained significantly changed after 26 weeks in the CON group (all  $P < 0.01$ ) (ITT analysis).

191 Compared to CON, INT significantly reduced more WC, FM, FFM, total cholesterol, and  
192 LDL-C after 12 weeks of intervention (Table 2). These differences remained significant after 52  
193 weeks in FM, FFM, and. INT reduced FM by -3.3 kg with 95% CI [-3.9; -2.7] vs. -2.4 kg [-3.2; -  
194 1.5]  $P = 0.020$ ) and) compared to CON after 52 weeks. INT showed a pronounced loss in FFM  
195 compared to CON after 52 weeks (-0.9 kg [-1.3; -0.6] vs. -0.3 kg [-0.9; 0.2]  $P < 0.001$ ).

196

## 197 **Discussion**

198 The results of the ACOORH trial show that a low-intensity lifestyle intervention  
199 accompanied with a liquid formula diet contributes to larger reductions in body weight in  
200 patients with overweight or obesity and accompanied cardiovascular risk factors compared to a  
201 low-intensity lifestyle intervention alone and these findings remain significantly superior even  
202 after 52 weeks.

203 The weight reduction after 1 year (-5.8 kg [-6.3; -5.3] (ITT analysis)) is comparable to  
204 other lifestyle intervention programs with smaller cohorts ( $n = 19-167$ ), which have also shown a  
205 significant weight loss ranging from -1.43 kg to -12.1 kg [20]. In particular, very intense lifestyle  
206 programs with rigorous meal replacement regimen [21] or intensive support [22] led to mean

207 weight losses greater than 10 kg. Furthermore, study effects and weight loss show a dose-  
208 response pattern in relation to program duration [23] and intensity of support [20]. The longer the  
209 intensive intervention phase and the greater the level of support, the greater the weight loss.

210 A recently published systematic review and meta-analysis demonstrated larger weight  
211 reductions following either very low (<800 kcal/day) or low-calorie (>800 kcal/day) liquid meal  
212 replacements (ranging from 8.9 to 15.0 kg) in patients with obesity (BMI: 36-43 kg/m<sup>2</sup>) [24].  
213 Compared to the present study can be assumed that the weight reduction difference to the studies  
214 in the meta-analysis is resulted by a higher calorie intake per day (1300-1500 kcal/day). In  
215 addition, we chose a more moderate daily energy intake target to increase study compliance and  
216 adherence as well as to minimise dropout rates. In support of this approach, it has been shown  
217 that a moderate and continuous weight loss reduces the risk for adverse outcomes in the long-  
218 term compared to a fast and severe weight loss [25].

219 In the present study, weight reduction was accompanied with further improvements,  
220 (predominantly achieved in the INT-group) during the 12-week intervention phase in  
221 cardiometabolic parameters, including FM, WC, DBP and LDL-C and TC. Furthermore, after 52  
222 weeks of follow-up there was still a significant difference in FM loss between both groups.  
223 These findings are in line with other lifestyle intervention trials with low-calorie diets in patients  
224 with prediabetes [7] or type 2 diabetes [26, 27] or lifestyle interventions with physical activity in  
225 patients with obesity [28].

226 The ACCORH trial and its strengths are characterized by (1) a comparably large sample  
227 size in an (2) international and multicenter design with (3) a randomized controlled trial  
228 approach. Moreover, (4) two intervention groups were followed up over a period of 52 weeks  
229 and this trial was conducted in a (5) real-world setting in which a low-intensity lifestyle

230 intervention was combined with liquid meal replacement. The intention was to design a practical  
231 lifestyle-based intervention program which could be easily implemented into present health care  
232 programs. Moreover, the (6) inclusion of only high-risk participants with at least one additional  
233 co-morbidity of the metabolic syndrome indicates a further strength of the study.

234         There are also limitations in the present trial that have to be considered. We did not  
235 constantly (i) controlled the participants for decreased energy intake or for false food  
236 compositions (e.g., amount of carbohydrates or proteins) by monitoring diet diaries. As it is well-  
237 known that dietary records of patients with obesity are characterized by systematic errors, we,  
238 therefore, had purposely chosen not to constantly monitor these records [29]. However, the  
239 prepared 4-day diet diaries of the probands were used in each study visit as a resource of  
240 information for the lifestyle counseling. Moreover, volunteers of the INT group should record  
241 the number of containers and amount of meal replacement consumed. Thus, we were able, at  
242 least, to evaluate the intake of liquid meal replacement within the first 12 weeks. A second  
243 limitation was the imputation of missing values by the LOCF approach. More sophisticated  
244 imputation methods like multiple imputation could have been performed as this imputation  
245 technique takes the uncertainty of the imputed values more realistic into account. However, the  
246 LOCF procedure was consciously chosen as it is a conservative statistical approach to estimate  
247 treatment effects, which might have even underestimated the results. Concomitantly, the ITT  
248 analysis method performed prevents the overestimation of data and takes the number of dropouts  
249 into account.

250         In sum, a low-intensity lifestyle intervention accompanied with a liquid meal replacement  
251 contributes to a long-term and clinically relevant weight reduction in patients with overweight  
252 and obesity and further cardiovascular risk factors. Furthermore, this weight reduction was

253 characterized with improvements in cardiovascular and cardiometabolic risk factors. The present  
254 findings underline the efficacy of the liquid formula diet tested in individuals with overweight or  
255 obesity and accompanied cardiovascular risk factors when included in a lifestyle intervention  
256 program. This therapy approach should be considered as a valid option for management of  
257 overweight and obesity in clinical, community and health care settings.  
258

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269

270 **Conflict of Interest**

271 W Banzer, A Berg, KM Braumann, M Halle, K Kempf, D McCarthy, HG Predel, J Scholze, D  
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286

287 **Author contributions**

288 A Berg had the initial idea for the study design and initiated the study. The protocol was  
289 designed together with H Toplak and with additional contributions of S Martin. M Halle and M  
290 Röhling drafted the manuscript. All authors critically revised the manuscript and approved the  
291 final version. W Banzer, A Berg, KM Braumann, D McCarthy, M Halle, K Kempf, S Martin,  
292 HG Predel, J Scholze, D Führer-Sakel, and H Toplak collected data at their local sites. A Berg is  
293 the guarantor of this work and all co-authors had full access to all the data in the study and take  
294 responsibility for the integrity of the data and the accuracy of the data analysis.

295

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379

380 **Figure legends**

381 **Fig.1.** Flow diagram.

382

383 **Fig. 2.** Mean changes in secondary outcomes.

384 (A) weight, (B) systolic blood pressure (C) diastolic blood pressure, (D) LDL-C, (E) total

385 cholesterol, (F) fasting blood glucose, (G) waist circumference, (H) triglycerides, and (I) fat

386 mass after 4, 12, 26, and 52 weeks. Within-group changes were analyzed using ANOVA with

387 repeated measures. \*\*\*p<0.001 vs. baseline; \*\*p<0.01 vs. baseline; \*p<0.05 vs. baseline; ITT,

388 intention-to-treat analysis

389

390 **Table legends**

391 **Table 1.** Baseline characteristics.

392 Data are presented as means  $\pm$  standard deviations, or percentages. BMI, body mass index; DBP,

393 diastolic blood pressure; FBG, fasting blood glucose; FM, fat mass; FFM, fat free mass; HC, hip

394 circumference; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; SBP, systolic blood

395 pressure; WC, waist circumference; WHR, waist-to-hip ratio

396

397 **Table 2.** Intra and intergroup changes in the INT and CON-group after 12 and 52 weeks

398 compared to baseline

399 Data are shown as mean [95% CI]. \*\*\*p<0.001 vs. baseline; \*\*p<0.01 vs. baseline; \*p<0.05 vs.

400 baseline. Differences in changes after 12 as well as 52 weeks between both groups were analyzed

401 using ANCOVAs adjusting for baseline values. DBP, diastolic blood pressure; FBG, fasting

402 blood glucose; FM, fat mass; FFM, fat free mass; HDL-C, HDL cholesterol; LDL-C, LDL

403 cholesterol; n.a., not available; SBP, systolic blood pressure; WC, waist circumference

404

405 **Consortium member list (present study\*)**  
406

407 **Germany**

408 **Munich:**

409 Martin Halle<sup>1,2</sup>

410 Nina Schaller<sup>1</sup>

411 <sup>1</sup>Department of Prevention, Rehabilitation and Sports Medicine, Klinikum rechts der Isar,  
412 Technical University of Munich (TUM), Munich, Germany

413 <sup>2</sup>DZHK (German Centre for Cardiovascular Research), Partner Site Munich Heart Alliance,

414 Munich, Germany

415

416 **Dusseldorf:**

417 Martin Röhling<sup>3</sup>

418 Kerstin Kempf<sup>3</sup>

419 <sup>3</sup>West-German Center of Diabetes and Health, Düsseldorf Catholic Hospital Group, Düsseldorf,  
420 Germany

421

422 **Frankfurt:**

423 Winfried Banzer<sup>4</sup>

424 <sup>4</sup>Department of Sports Medicine, Institute for Sports and Sport Science, University of Frankfurt,  
425 Frankfurt, Germany

426

427 **Hamburg:**

428 Klaus Michael Braumann<sup>5</sup>

429 <sup>5</sup>Faculty of Psychology and Human Movement Sciences, Department of Sports and Movement  
430 Medicine, University of Hamburg, Hamburg, Germany

431

432 **Berlin:**

433 Jürgen Scholze<sup>8</sup>

434 <sup>8</sup>KARDIOS, Cardiologists in Berlin, Berlin, Germany

435

436 **Essen:**

437 Dagmar Führer-Sakel<sup>9</sup>

438 <sup>9</sup> Department of Endocrinology, Diabetes and Metabolism and Division of Laboratory Research,  
439 University Hospital Essen, University Duisburg-Essen, Essen, Germany

440

441

442 **Cologne:**  
443 Hans Georg Predel<sup>7</sup>  
444 <sup>7</sup>Institute of Cardiovascular Research and Sports Medicine, German Sport University Cologne,  
445 Cologne, Germany  
446

447 **Freiburg:**  
448 Aloys Berg<sup>11</sup>  
449 <sup>11</sup>Faculty of Medicine, University of Freiburg, Freiburg, Germany  
450

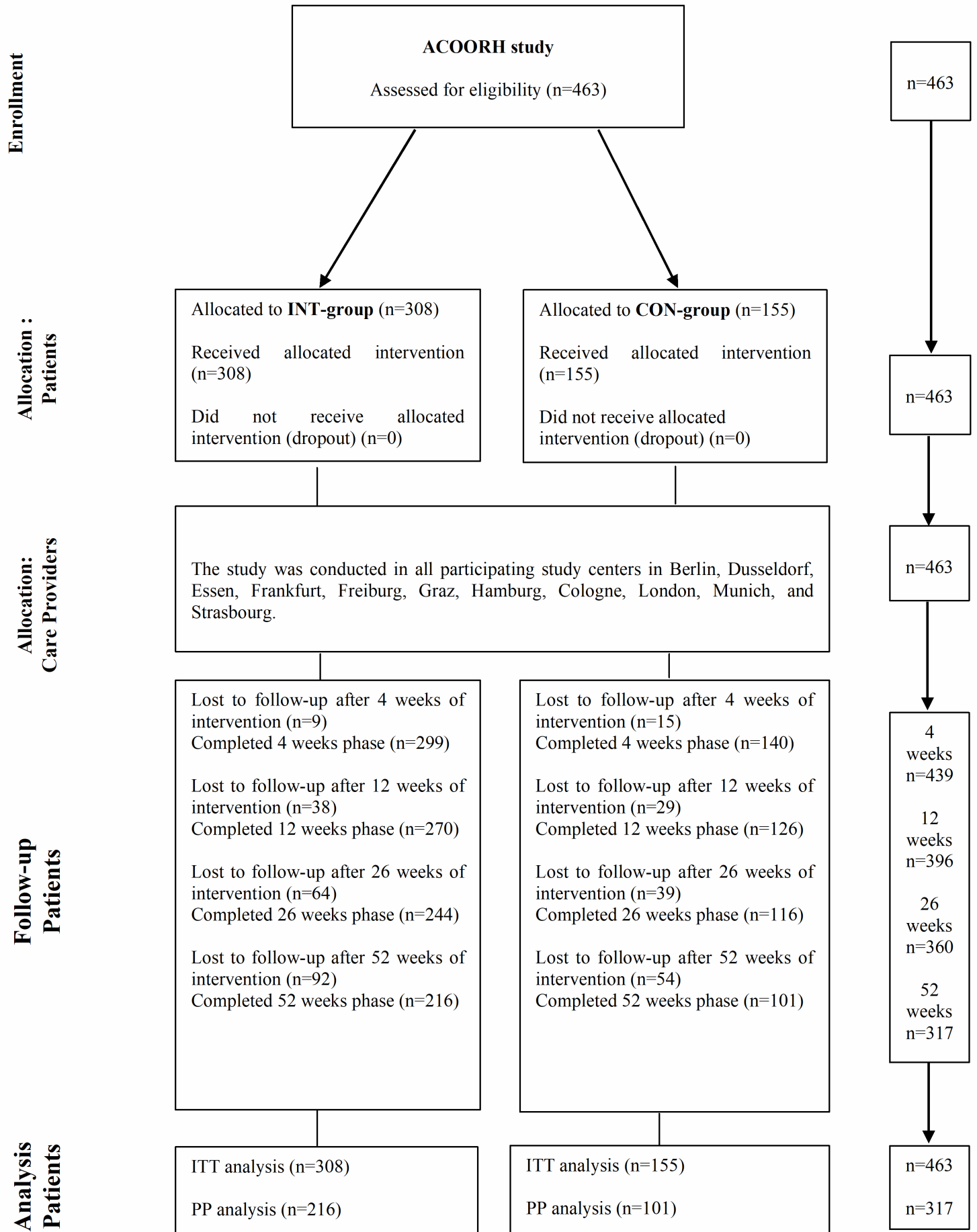
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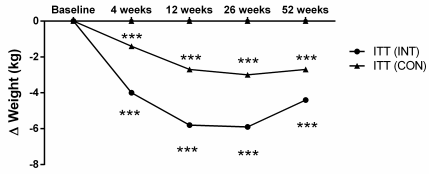
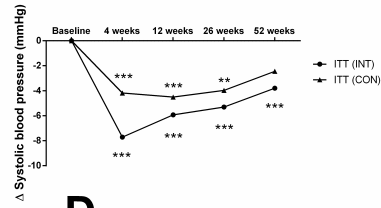
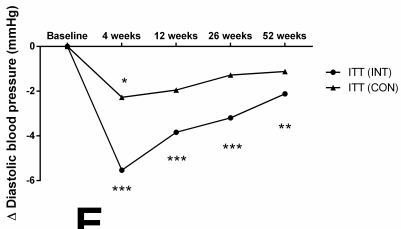
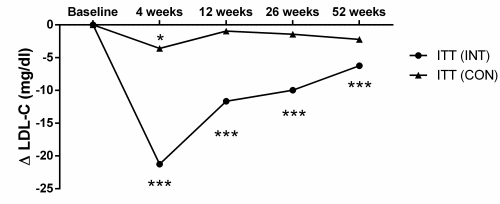
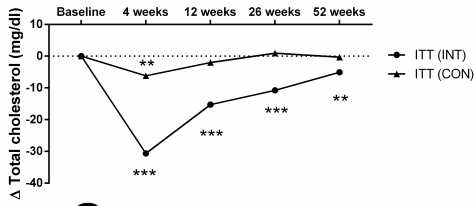
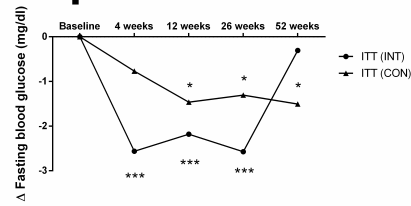
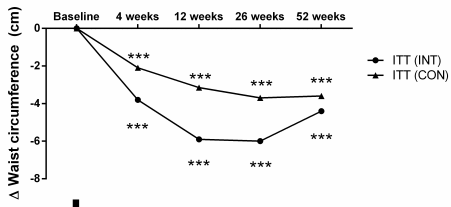
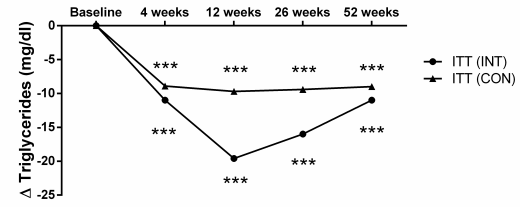
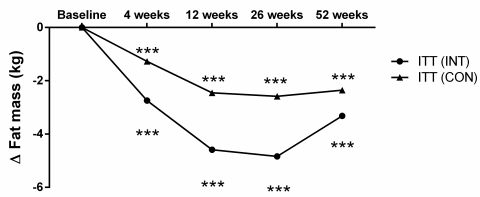
452 **London:**  
453 David McCarthy<sup>6</sup>  
454 <sup>6</sup>Public Health Nutrition Research Group, London Metropolitan University, London, UK  
455

456 **Austria**

457 **Graz:**  
458 Hermann Toplak<sup>10</sup>  
459 <sup>10</sup> Department of Medicine, Division of Endocrinology and Diabetology, Medical University of  
460 Graz, Austria  
461

462 \*A complete list of all consortium members including those who did not met authorship criteria  
463 can be seen in the Supplementary Information.



**A****B****C****D****E****F****G****H****I**

1 **Table 1.** Baseline characteristics

	INT-group (n=308)	CON-group (n=155)
Sex (% male)	32.8	41.3
Age (years)	51 ± 10	50 ± 10
Weight (kg)	92 ± 14	94 ± 12
BMI (kg/m <sup>2</sup> )	31.7 ± 2.4	31.5 ± 2.4
WC (cm)	106 ± 10	107 ± 8
HC (cm)	113 ± 8	112 ± 7
WHR	0.94 ± 0.08	0.95 ± 0.08
FM (kg)	37.0 ± 6.7	37.0 ± 6.6
FFM (kg)	54.9 ± 11.7	56.7 ± 11.5
FBG (mg/dl)	94 ± 12	94 ± 11
SBP (mmHg)	134 ± 15	134 ± 13
DBP (mmHg)	89 ± 12	89 ± 10
Total cholesterol (mg/dl)	221 ± 39	220 ± 45
HDL-C (mg/dl)	56 ± 15	56 ± 15
LDL-C (mg/dl)	141 ± 34	139 ± 39
Triglycerides (mg/dl)	145 ± 83	147 ± 68

2 Data are presented as means ± standard deviations, or percentages. BMI, body mass index;  
3 DBP, diastolic blood pressure; FBG, fasting blood glucose; FM, fat mass; FFM, fat free mass;  
4 HC, hip circumference; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; SBP, systolic  
5 blood pressure; WC, waist circumference; WHR, waist-to-hip ratio



1 **Table 2.** Intra and intergroup changes in the INT and CON-group after 12 and 52 weeks compared to baseline

ITT (INT, n=307; CON, n=154)		12 weeks			52 weeks		
PP (INT, n=266; CON, n=126) 12w		INT	CON	P (INT vs. CON)	INT	CON	P (INT vs. CON)
PP (INT, n=214; CON, n=101) 52w		INT	CON	P (INT vs. CON)	INT	CON	P (INT vs. CON)
Weight (kg)	ITT	-5.8 [-6.3; -5.3]***	-2.7 [-3.3; -2.1]***	<0.001	-4.4 [-5.0; -3.8]***	-2.7 [-3.4; -2.0]***	<0.001
	PP	-6.3 [-6.8; -5.8]***	-3.2 [-3.9; -2.6]***	<0.001	-5.0 [-5.7; -4.2]***	-3.5 [-4.5; -2.5]***	0.021
WC (cm)	ITT	-5.9 [-6.5; -5.2]***	-3.1 [-3.9; -2.4]***	<0.001	-4.4 [-5.2; -3.7]***	-3.6 [-4.7; -2.6]***	0.175
	PP	-6.3 [-7.1; -5.6]***	-3.6 [-4.5; -2.7]***	<0.001	-4.8 [-5.7; -3.8]***	-4.6 [-5.9; -3.3]***	0.725
FM (kg)	ITT	-4.6 [-5.1; -4.1]***	-2.5 [-3.1; -1.8]***	<0.001	-3.3 [-3.9; -2.7]***	-2.4 [-3.2; -1.5]***	0.020
	PP	-5.1 [-5.5; -4.7]***	-2.9 [-3.5; -2.3]***	<0.001	-3.7 [-4.5; -3.0]***	-3.1 [-4.2; -2.0]***	0.248
FFM (kg)	ITT	-1.0 [-1.4; -0.6]***	-0.2 [-0.8; 0.3]	<0.001	-0.9 [-1.3; -0.6]***	-0.3 [-0.9; 0.2]	<0.001
	PP	-1.0 [-1.4; -0.7]***	-0.3 [-0.8; 0.2]	<0.001	-1.0 [-1.6; -0.5]***	-0.4 [-1.2; 0.3]	<0.001
FBG (mg/dl)	ITT	-2.2 [-3.5; -0.9]***	-1.5 [-3.0; 0.0]*	0.577	-0.3 [-1.7; 1.1]	-1.5 [-2.9; -0.1]*	0.169
	PP	-2.5 [-3.8; -1.1]***	-1.7 [-3.5; 0.1]*	0.433	-0.3 [-2.0; 1.4]	-1.4 [-3.4; 0.5]	0.305
SBP (mmHg)	ITT	-5.9 [-8.0; -3.3]***	-4.5 [-7.5; -1.5]**	0.191	-3.8 [-5.9; -1.7]***	-2.4 [-5.4; 0.5]	0.218
	PP	-6.4 [-8.3; -4.5]***	-5.1 [-7.9; -2.3]***	0.207	-4.1 [-6.8; -1.4]**	-1.7 [-5.6; 2.2]	0.093
DBP (mmHg)	ITT	-3.8 [-5.3; -2.3]***	-1.9 [-4.1; 0.2]	0.022	-2.1 [-3.5; -0.7]***	-1.1 [-3.1; 0.9]	0.172
	PP	-4.0 [-5.4; -2.7]***	-2.4 [-4.3; -0.4]*	0.069	-2.0 [-3.8; -0.2]*	-0.9 [-3.5; 1.7]	0.221
Total cholesterol (mg/dl)	ITT	-16 [-19; -13]***	-2 [-6; 2]	<0.001	-6 [-9; -2]**	-0 [-5; 4]	0.076
	PP	-15 [-18; -12]***	-2 [-7; 3]	<0.001	-1 [-5; 3]	2 [-8; 4]	0.639
HDL-C (mg/dl)	ITT	-1 [-2; 0]	0 [-1; 2]	0.002	2 [1; 3]**	2 [0; 3]*	0.858
	PP	-0 [-1; 1]	1 [-1; 2]	0.004	3 [1; 4]***	2 [1; 4]**	0.907

LDL-C (mg/dl)	ITT	-12 [-15; -10]***	-1 [-4; 2]	<b>&lt;0.001</b>	-7 [-10; -4]***	-2 [-6; 1]	0.067
	PP	-12 [-15; -9]***	-0 [-4; 3]	<b>&lt;0.001</b>	-4 [-7; -1]*	-4 [-8; 1]	0.736
Triglycerides (mg/dl)	ITT	-19 [-27; -11]***	-10 [-25; 5]***	0.161	-11 [-20; -3]***	-9 [-20; 3]*	0.618
	PP	-22 [-30; -14]***	-11 [-29; 8]***	0.132	-12 [-21; -4]**	-15 [-30; -1]*	0.840

2 Data are shown as mean [95% CI]. \*\*\*p<0.001 vs. baseline; \*\*p<0.01 vs. baseline; \*p<0.05 vs. baseline. Differences in changes after 12 as well as  
3 52 weeks between both groups were analyzed using ANCOVAs adjusting for baseline values. DBP, diastolic blood pressure; FBG, fasting blood  
4 glucose; FM, fat mass; FFM, fat free mass; HDL-C, HDL cholesterol; LDL-C, LDL cholesterol; n.a., not available; SBP, systolic blood pressure;  
5 WC, waist circumference