**Fasting, ketogenic and anti-inflammatory diets stabilized active relapsing-remitting multiple sclerosis over 18 months – a randomized, controlled study**

**Supplement**

**Suppl. table 1*.*** Adverse events in the Intention-to-Treat population of the NAMS study

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**Supplemental table 1*.*** Adverse events in the Intention-to-Treat population of the NAMS study

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Adverse events (%)** | **All** | **SD** | **FD** | **KD** |
| Sample size (n) | 105 | 34 | 35 | 36 |
| General diseases and complaints at the administration site | 27 | 15 | 26 | 39 |
| Eye diseases | 4 | 0 | 9 | 3 |
| Endocrine diseases | 6 | 0 | 9 | 8 |
| Diseases of the respiratory, thoracic and mediastinum | 16 | 21 | 11 | 17 |
| Diseases of the skin and subcutaneous tissue | 10 | 3 | 11 | 14 |
| Diseases of the kidney and urinary tract | 9 | 9 | 9 | 8 |
| Diseases of the blood and lymphatic system | 16 | 15 | 17 | 17 |
| Gastrointestinal diseases | 25 | 21 | 34 | 19 |
| Diseases of the immune system (including allergies) | 7 | 9 | 3 | 8 |
| Diseases of the nervous system | 21 | 12 | 31 | 19 |
| Diseases of the ear and labyrinth | 6 | 3 | 9 | 6 |
| Vascular diseases | 2 | 0 | 3 | 3 |
| Benign, malignant, unspecified neoplasm (including cysts and polyps) | 3 | 3 | 3 | 3 |
| Heart diseases | 4 | 0 | 6 | 6 |
| Infection and parasitic diseases | 57 | 47 | 69 | 56 |
| Liver and gallbladder diseases | 3 | 0 | 0 | 8 |
| Psychiatric disorders | 7 | 12 | 0 | 8 |
| Musculoskeletal, connective tissue and bone disorders | 34 | 29 | 43 | 31 |
| Metabolic and nutritional disorders | 16 | 9 | 17 | 22 |
| Examinations | 2 | 3 | 3 | 0 |
| Injury, poisoning, and procedure-related complications | 7 | 3 | 6 | 11 |
| Pregnancy, childbirth, and perinatal diseases | 7 | 6 | 3 | 11 |
| Surgical and medical procedures | 10 | 9 | 6 | 14 |
| Social circumstances | 1 | 0 | 3 | 0 |

FD, fasting diet; KD, ketogenic diet; SD, standard diet

**Supplemental table 2.** Serious adverse events in the Intention-to-Treat population of the NAMS study

|  |  |  |  |
| --- | --- | --- | --- |
| **Serious adverse events (n)** | **SD** | **FD** | **KD** |
| Imminently life-threatening | 1 | 0 | 1 |
| Hospital stay or extension | 1 | 1 | 5 |
| Coronavirus disease (COVID-19) | 0 | 1 | 1 |

FD, fasting diet; KD, ketogenic diet; SD, standard diet

**Supplemental table 3.** Outcome data of the NAMS study at baseline in the Full Analysis Set (FAS)

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FAS Baseline | All (n) | mean (StD) | median (Q3-Q1) | KD (n) | mean (StD) | median (Q3-Q1) | FD (n) | mean (StD) | median (Q3-Q1) | SD (n) | mean (StD) | median (Q3-Q1) |
| Age (years) | 81 | 43 (10) | 44 (50-33) | 26 | 42 (10) | 43 (51-32) | 30 | 42  (9) | 43 (50-35) | 25 | 44 (10) | 46 (51-35) |
| EDSS score | 71 | 2.1 (1.0) | 2.0 (2.5-1.5) | 24 | 2.2 (1.2) | 2.0 (3.1-1.5) | 24 | 1.9 (0.9) | 2.0 (2.5-1.5) | 23 | 2.1 (0.8) | 2.0 (2.5-1.5) |
| T2 lesions, number (n) | 81 | 55.3 (58.1) | 34.0 (76.0-18.0) | 26 | 48.2 (58.3) | 29.0 (50.3-15.8) | 30 | 48.8 (38.1) | 39.0 (59.8-20.3) | 25 | 70.8 (74.7) | 36.0 (88.0-19.0) |
| T2 lesions, volume (mm3) | 81 | 6.7 (8.9) | 3.5 (8.4-1.2) | 26 | 7.0 (10.8) | 2.2 (7.7-1.0) | 30 | 6.4 (6.6) | 4.4 (9.6-1.5) | 25 | 6.9 (9.5) | 3.5 (7.3-1.5) |
| FSS score | 80 | 3.7 (1.8) | 3.7 (5.3-2.1) | 26 | 3.5 (1.6) | 3.5 (4.8-2.2) | 29 | 3.9 (1.8) | 3.9 (5.2-2.6) | 25 | 3.7 (1.9) | 3.8 (5.3-1.8) |
| BDI-II score | 81 | 9.0 (8.0) | 8.0 (12.0-3.0) | 26 | 8.7 (8.7) | 6.0 (10.8-3.0) | 30 | 9.5 (7.4) | 9.0 (13.0-5.3) | 25 | 8.5 (8.1) | 7.0 (12.0-2.0) |
| SDMT score | 77 | 56.0 (11.3) | 56.0 (62.0-49.0) | 25 | 55.1 (13.3) | 57.0 (65.0-47.0) | 27 | 56.0 (10.0) | 56.0 (61.5-49.0) | 25 | 56.8 (11.0) | 54.0 (62.0-51.0) |
| 6-MWT (min) | 79 | 558.3 (102.1) | 566.5 (616.2-502.5) | 25 | 556.0(94.4) | 564.1 (608.1-487.6) | 29 | 559.2 (124.7) | 561.5 (638.1-502.7) | 25 | 559.6 (82.5) | 570 (609.8-510.8) |
| Hand grip strength (kg) | 78 | 33.6 (9.1) | 32.5 (37.1-27.6) | 26 | 35.2 (10.3) | 33.6 (38.6-27.6) | 28 | 32.0 (8.9) | 31.8 (36.4-25.9) | 24 | 33.9 (8.0) | 32.1 (36.6-27.8) |
| MSQOL54 Physical Health score | 80 | 69.6 (14.5) | 71.3 (78.5-63.4) | 25 | 68.3 (12.8) | 70.1 (77.6-65.9) | 30 | 70.7 (12.6) | 71.8 (76.6-65.8) | 25 | 69.5 (18.2) | 70.3 (85.2-54.2) |
| MSQOL54 Mental Health score | 80 | 68.1 (15.7) | 74.2 (79.9-57.7) | 25 | 65.7 (16.2) | 73.6 (79.8-57.5) | 30 | 68.5 (14.8) | 74.2 (78.8-59.2) | 25 | 67.0 (16.7) | 76.8 (83.1-57.8) |
| Average MSFC hpt dominant hand (sec) | 79 | 20.5 (3.4) | 19.8 (21.9-18.5) | 25 | 20.3 (3.9) | 19.3 (20.8-18.3) | 29 | 20.4 (2.6) | 19.9 (21.6-18.6) | 25 | 21.0 (3.7) | 20.8 (22.0-19.2) |
| Average MSFC t25fw (sec) | 78 | 4.3 (0.7) | 4.2 (4.7-3.8) | 25 | 4.3 (0.7) | 4.1 (4.8-3.9) | 28 | 4.3 (0.8) | 4.4 (4.7-3.9) | 25 | 4.1 (0.6) | 4.1 (4.5-3.7) |
| Z Score t25fw | 78 | 0.0 (1.1) | 0.1 (0.6-(-0.5)) | 25 | -0.1 (1.1) | 0.2 (0.4-(-0.9)) | 28 | -0.1 (1.2) | -0.1 (0.6-(-0.7)) | 25 | 0.2 (0.9) | 0.2 (0.8-(-0.3)) |
| Z Score PASAT | 78 | 0.1 (0.8) | 0.3 (0.8-(-0.4)) | 24 | 0.2 (0.7) | 0.2 (0.825-(-0.3)) | 29 | -0.2 (0.8) | -0.3 (0.6-(-0.6)) | 25 | 0.4 (0.7) | 0.6 (0.9-0.2) |
| Z Score hpt | 79 | -0.1 (1.0) | 0.0 (0.5-(-0.6)) | 25 | 0.1 (1.1) | 0.2 (0.56-(-0.2)) | 29 | -0.1 (0.8) | 0.0 (0.5-(-0.4)) | 25 | -0.2 (1.1) | -0.3 (0.3-(-0.7)) |
| Overall Z Score | 77 | 0.0 (0.7) | 0.2 (0.5-(-0.3)) | 24 | 0.1 (0.7) | 0.3 (0.6-(-0.2)) | 28 | -0.1 (0.7) | -0.1 (0.3-(-0.4)) | 25 | 0.1 (0.7) | 0.2 (0.6-(-0.1)) |
| Disease duration from first manifestation (years) | 81 | 9.2 (7.7) | 6.7 (14.8-2.3) | 26 | 10.4 (8.1) | 8.6 (16.5-2.9) | 30 | 9.0 (6.7) | 8.5 (14.6-4.2) | 25 | 8.2 (8.4) | 3.2 (12.7-1.9) |
| Disease duration from first diagnosis (years) | 80 | 6.1 (5.9) | 3.6 (10.1-1.4) | 26 | 6.4 (6.5) | 4.6 (9.6-1.3) | 30 | 7.0 (5.4) | 5.5 (12.0-2.1) | 24 | 4.5 (5.8) | 1.8 (5.1-1.1) |
| BMI (kg/m2) | 81 | 24.9 (4.1) | 24.3 (26.3-22.3) | 26 | 25.0 (5.2) | 23.7 (25.8-22.2) | 30 | 24.3 (3.7) | 23.7 (25.9-21.5) | 25 | 25.5 (3.4) | 25.0 (27.1-23.7) |
| Body fat (%) | 78 | 29.6 (8.1) | 29.7 (34.4-24.7) | 25 | 29.5 (9.9) | 29.1 (32.5-24.1) | 29 | 29.0 (6.8) | 29.3 (33.5-24.9) | 24 | 30.2 (7.7) | 32.3 (34.6-25.9) |
| Total cholesterol (mg/dL) | 67 | 192 (35) | 188 (212-173) | 22 | 187.6 (36.3) | 182 (205-156) | 22 | 195 (36) | 196 (214-176) | 23 | 193 (33) | 188 (206-179) |
| LDL cholesterol (mg/dL) | 67 | 119 (30) | 113 (142-97) | 22 | 119 (32) | 119 (145-93) | 22 | 117 (32) | 109 (132-97) | 23 | 122 (28) | 113 (137-106) |
| HDL cholesterol (mg/dL) | 67 | 70 (17) | 71 (80-57) | 22 | 69 (16) | 71 (79-54) | 22 | 74 (19) | 79 (83-57) | 23 | 69 (14) | 68 (79-62) |
| Triglycerides (mg/dL) | 62 | 88 (40) | 77 (100-66) | 22 | 85 (37) | 77 (84-66) | 19 | 96 (39) | 91 (118-67) | 21 | 85 (44) | 70 (98-66) |
| Insulin (mU/L) | 81 | 8.5 (5.1) | 7.0 (9.5-5.8) | 26 | 8.9 (6.1) | 6.5 (8.6-6.1) | 30 | 8.0 (4.5) | 7.0 (9.3-5.1) | 25 | 8.8 (4.7) | 7.4 (9.6-5.9) |
| Leptin (μg/L) | 75 | 11.3 (8.8) | 9.6 (15.0-5.1) | 22 | 11.8 (10.9) | 9.5 (14.3-5.2) | 28 | 10.3 (8.7) | 8.6 (14.2-4.2) | 25 | 11.9 (6.9) | 9.7 (17.3-6.9) |
| Adiponectin (μg/mL) | 79 | 9.5 (5.1) | 8.4 (12.1-5.6) | 24 | 10.1 (4.8) | 8.9 (13.2-6.3) | 30 | 9.1 (5.5) | 8.7 (11.4-4.5) | 25 | 9.4 (5.1) | 8.0 (11.7-6.3) |
| Vitamin D (nmol/L) | 79 | 101.6 (35.9) | 97.9 (119.6-79.5) | 25 | 103.2 (33.4) | 97.9 (117.3-86.6) | 29 | 93.8 (35.7) | 92.2 (119.5-70.1) | 25 | 108.9 (38.2) | 103.9 (125.7-82.1) |
| Beta-hydroxybutyrate (mmol/L) | 79 | 0.14 (0.18) | 0.09 (0.17-0.04) | 24 | 0.19 (0.17) | 0.11 (0.23-0.08) | 30 | 0.13 (0.23) | 0.07 (0.12-0.04) | 25 | 0.11 (0.12) | 0.07 (0.15-0.04) |
| NfL (pg/mL) | 55 | 11.5 (7.1) | 9.8 (12.8-7.3) | 12 | 12.3 (6.7) | 10.2 (14.3-8.1) | 25 | 12.5 (8.7) | 10.1 (13.7-7.2) | 17 | 10.0 (4.5) | 9.1 (11.6-7.3) |

FD, fasting diet; KD, ketogenic diet; SD, standard diet

**Supplemental table 4.** Outcome data of the NAMS at 9 months in the Full Analysis Set (FAS)

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FAS 9 months | All (n) | mean (StD) | median (Q3-Q1) | KD (n) | mean (StD) | median (Q3-Q1) | FD (n) | mean (StD) | median (Q3-Q1) | SD (n) | mean (StD) | median (Q3-Q1) |
| T2 lesions, number (n) | 79 | 57 (58) | 35 (78-20) | 24 | 51 (61) | 30 (56-17) | 30 | 50 (39) | 41 (59-21) | 25 | 70.1 (72) | 36 (87-20) |
| T2 lesions, volume (mm3) | 79 | 7.3  (9.7) | 3.9 (9.5-1.3) | 24 | 8.1  (12.1) | 2.7 (9.5-1.1) | 30 | 6.7  (6.8) | 4.72 (9.9-1.56) | 25 | 7.4  (10.4) | 3.6 (8.2-1.5) |
| Brain atrophy measured by percentage of brain volume change | 79 | -0.3 (0.5) | -0.3 (0.1-(-0.6)) | 24 | -0.4 (0.5) | -0.4 (-0.2-(-0.7)) | 30 | -0.2 (0.5) | -0.2 (0.1-(-0.4)) | 25 | -0.2 (0.4) | -0.2 (0.2-(-0.5)) |
| FSS score | 79 | 3.8 (1.7) | 3.8 (5.1-2.4) | 25 | 3.6 (1.6) | 3.3 (4.6-2.4) | 29 | 4.0 (1.7) | 4.4 (5.0-2.7) | 25 | 3.9 (1.8) | 3.7 (5.6-2.2) |
| BDI-II score | 81 | 9.8 (9.4) | 8.0 (14.0-3.0) | 26 | 10.3 (12.4) | 5.5 (14.8-2.0) | 30 | 8.2 (7.2) | 7.5 (12.8-3.0) | 25 | 11.2 (8.1) | 10.0 (15.0-8.0) |
| SDMT score | 79 | 56.7 (12.2) | 57.0 (66.0-47.5) | 24 | 58.0 (14.9) | 60.0 (71.0-47.8) | 30 | 56.4 (11.6) | 56.5 (63.8-50.3) | 25 | 55.9 (10.5) | 57.0 (65.0-47.0) |
| 6-MWT (min) | 78 | 567.9 (85.4) | 580.0 (629.4-518.5) | 23 | 576.4 (70.9) | 582.0 (619.7-541.0) | 30 | 562.7 (100.6) | 569.2 (644.8-488.2) | 25 | 566.3 (80.5) | 572.4 (630.4-522.2) |
| Hand grip strength (kg) | 79 | 33.6 (9.5) | 32.8 (36.8-27.8) | 24 | 35.0 (9.3) | 34.1 (37.1-28.9) | 30 | 31.2 (10.3) | 31.3 (34.2-25.1) | 25 | 35.0 (8.6) | 33.8 (40.6-28.5) |
| MSQOL54 Physical Health score | 76 | 69.8 (14.8) | 72.5 (82.3-60.9) | 24 | 69.4 (14.9) | 74.1 (82.4-55.8) | 28 | 70.2 (13.9) | 68.8 (78.4-62.1) | 24 | 69.8 (16.3) | 73.6 (84.2-57.9) |
| MSQOL54 Mental Health score | 77 | 66.0 (16.8) | 69.7 (80.1-57.2) | 25 | 64.5 (19.6) | 68.2 (81.2-53.0) | 27 | 66.6 (16.6) | 70.0 (77.8-58.8) | 25 | 67.0 (14.4) | 69.7 (77.8-59.5) |
| Average MSFC hpt dominant hand (sec) | 79 | 20.3 (3.2) | 19.7 (21.5-17.9) | 24 | 19.8 (3.1) | 19.5 (21.1-17.0) | 30 | 20.72 (3.4) | 19.76 (23.1-18.1) | 25 | 20.3 (3.1) | 19.7 (20.8-18.5) |
| Average MSFC t25fw (sec) | 78 | 4.5 (2.1) | 4.2 (4.7-3.8) | 23 | 4.2 (0.6) | 4.2 (4.6-3.8) | 30 | 4.3 (0.7) | 4.2 (4.8-3.8) | 25 | 4.9 (3.5) | 4.2 (4.6-3.9) |
| Z Score t25fw | 78 | -0.4 (3.2) | 0.2 (0.7-(-0.8)) | 23 | 0.1 (1.0) | 0.2 (0.7-(-0.6)) | 30 | -0.1 (1.1) | 0.0 (0-7-(-0.9)) | 25 | -1.0 (5.4) | 0.2 (0.5-(-0.6)) |
| Z Score PASAT | 78 | 0.1 (0.9) | 0.3 (0.7-(-0.4)) | 23 | 0.2 (0.7) | 0.4 (0.7-(-0.2)) | 30 | -0.3 (1.0) | -0.3 (0.5-(-0.9)) | 25 | 0.3 (0.8) | 0.6 (0.9-(-0.1)) |
| Z Score hpt | 79 | 0.0 (1.0) | 0.1 (0.7-(-0.5)) | 24 | 0.2 (1.0) | 0.2 (1.1-(-0.4)) | 30 | -0.1 (1.0) | 0.0 (0.7-(-0.8)) | 25 | -0.0 (0.9) | 0.0 (0.5-(-0.3)) |
| Overall Z Score | 77 | -0.1 (1.2) | 0.1 (0.5-(-0.3)) | 22 | 0.2 (0.6) | 0.3 (0.7-(-0.2)) | 30 | -0.2 (0.7) | -0.1 (0.3-(-0.6)) | 25 | -0.2 (1.9) | 0.2 (0.5-(-0.2)) |
| Disease duration from first manifestation (years) | 81 | 9.2 (7.7) | 6.7 (14.8-2.3) | 26 | 10.4 (8.1) | 8.6 (16.5-2.9) | 30 | 9.0 (6.7) | 8.5 (4.2-14.6) | 25 | 8.2 (8.4) | 3.2 (12.7-1.9) |
| Disease duration from first diagnosis (years) | 80 | 6.1 (5.9) | 3.6 (10.1-1.4) | 26 | 6.4 (6.5) | 4.6 (9.6-1.3) | 30 | 7.0 (5.4) | 5.5 (12.0-2.1) | 24 | 4.5 (5.8) | 1.8 (5.1-1.1) |
| BMI (kg/m2) | 78 | 24.0 (2.9) | 23.6 (25.5-22.3) | 23 | 23.4 (2.5) | 22.9 (24.6-22.5) | 30 | 23.5 (2.8) | 23.1 (25.1-21.6) | 25 | 25.1 (3.3) | 24.9 (26.6-23.1) |
| Body fat (%) | 79 | 27.7 (7.0) | 27.9 (32.3-24.3) | 24 | 26.4 (8.3) | 27.1 (30.8-23.4) | 30 | 27.6 (5.9) | 27.2 (31.7-24.3) | 25 | 29.0 (6.8) | 30.9 (33.7-25.9) |
| Total cholesterol (mg/dL) | 70 | 185 (37) | 182 (208-160) | 20 | 189 (40) | 178 (203-164) | 29 | 186 (40) | 187 (211-147) | 21 | 179 (30) | 175 (194-156) |
| LDL cholesterol (mg/dL) | 71 | 111 (33) | 109 (129-90) | 20 | 118 (34) | 112 (132-98) | 29 | 108 (36) | 100 (126-85) | 22 | 109 (28) | 109 (123-91) |
| HDL cholesterol (mg/dL) | 71 | 71 (20) | 72 (81-59) | 20 | 75 (24) | 77 (83-64) | 29 | 75 (20) | 79 (83-59) | 22 | 63 (13) | 66 (71-54) |
| Triglycerides (mg/dL) | 69 | 78 (32) | 70 (89-54) | 20 | 61 (18) | 53 (72-48) | 29 | 85 (33) | 75 (109-62) | 20 | 85 (36) | 79 (92-69) |
| Insulin (mU/L) | 69 | 7.7 (3.7) | 6.9 (9.8-5.1) | 19 | 7.6 (2.9) | 7.1 (9.0-5.8) | 30 | 7.0 (3.3) | 6.7 (8.7-4.4) | 20 | 9.0 (4.5) | 7.5 (12.4-5.3) |
| Leptin (μg/L) | 68 | 8.8 (5.2) | 7.8 (12.4-4.5) | 17 | 7.2 (3.2) | 7.5 (8.5-4.5) | 29 | 8.7 (5.9) | 5.9 (12.6-4.5) | 22 | 10.3 (5.3) | 10.8 (14.3-5.7) |
| Adiponectin (μg/mL) | 71 | 10.8 (5.9) | 9.7 (13.0-6.7) | 19 | 13.1 (6.9) | 12.4 (17.1-8.2) | 30 | 10.3 (5.9) | 9.9 (11.8-6.0) | 22 | 9.3 (4.2) | 9.0 (10.9-6.8) |
| Vitamin D (nmol/L) | 68 | 110.0 (38.8) | 108.5 (130.6-83.4) | 19 | 124.8 (44.5) | 113.6 (133.7-96.1) | 29 | 96.3 (36.4) | 94.8 (116.9-75.8) | 20 | 115.9 (30.5) | 114.3 (139.9-93.3) |
| Beta-hydroxybutyrate (mmol/L) | 72 | 0.31 (0.41) | 0.11 (0.46-0.04) | 20 | 0.69 (0.57) | 0.62 (0.78-0.37) | 30 | 0.16 (0.18) | 0.07 (0.25-0.04) | 22 | 0.18 (0.22) | 0.08 (0.29-0.04) |
| NfL (pg/mL) | 55 | 10.3 (4.4) | 8.9 (12.1-7.5) | 12 | 10.4 (4.5) | 10.1 (13.0-6.2) | 25 | 10.4 (5.0) | 8.2 (14.5-7.2) | 18 | 10.0 (3.6) | 8.9 (10.8-7.8) |

**Supplemental table 5.** Outcome data of the NAMS at 18 months in the Full Analysis Set (FAS)

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FAS 18 months | All (n) | mean (StD) | median (Q3-Q1) | KD (n) | mean (StD) | median (Q3-Q1) | FD (n) | mean (StD) | median (Q3-Q1) | SD (n) | mean (StD) | median (Q3-Q1) |
| T2 lesions, number (n) | 79 | 55 (57) | 35 (68-20) | 25 | 48 (59) | 28 (45-16) | 30 | 50 (39) | 41 (63-22) | 24 | 70 (71) | 37 (101-20) |
| T2 lesions, volume (mm3) | 79 | 7.5 (10.4) | 3.6 (9.5-1.3) | 25 | 8.0 (12.4) | 2.7 (9.4-1.2) | 30 | 7.0 (7.1) | 5.0 (11.1-1.6) | 24 | 7.8 (11.8) | 3.3 (8.8-1.4) |
| Brain atrophy measured by percentage of brain volume change | 79 | -0.6 (0.8) | -0.5 (-0.1-(-0.8)) | 25 | -0.7 (0.8) | -0.7 (-0.2-(-1.0)) | 30 | -0.4 (0.8) | -0.2 (0.2-(-0.7)) | 24 | -0.6 (0.6) | -0.5 (-0.2-(-0.7)) |
| FSS score | 81 | 3.9 (1.8) | 4.1 (5.3-2.2) | 26 | 3.8 (1.7) | 3.6 (5.1-2.7) | 30 | 4.1 (1.8) | 4.8 (5.6-2.7) | 25 | 3.6 (1.9) | 3.6 (4.9-1.8) |
| BDI-II score | 81 | 9.3 (9.7) | 7.0 (13.0-2.0) | 26 | 9.7 (9.8) | 6.0 (11.8-3.3) | 30 | 7.5 (7.7) | 7.0 (10.5-2.0) | 25 | 11.0 (11.4) | 9.0 (14.0-3.0) |
| SDMT score | 81 | 58.0 (11.8) | 57.0 (68.0-48.0) | 26 | 59.4 (13.3) | 57.5 (73.0-48.0) | 30 | 57.7 (10.7) | 57.5 (67.3-49.0) | 25 | 56.8 (11.6) | 57.0 (64.0-49.0) |
| 6-MWT (min) | 81 | 559.2 (90.4) | 578.0 (625.3-485.0) | 26 | 552.0 (96.5) | 576.3 (600.6-509.4) | 30 | 558.7 (87.2) | 561.3 (620.9-502.3) | 25 | 567.4 (91.2) | 593.5 (636.0-517.3) |
| Hand grip strength (kg) | 78 | 33.8 (9.4) | 32.6 (37.1-27.8) | 24 | 35.7 (38.5-28.2) | 36.1 (38.5-28.2) | 29 | 31.5 (10.1) | 31.2 (34.6-25.9) | 25 | 34.7 (7.8) | 33.6 (37.6-28.5) |
| MSQOL54 Physical Health score | 79 | 70.4 (16.8) | 76.3 (81.9-59.7) | 25 | 69.4 (15.5) | 75.3 (80.5-56.6) | 29 | 72.2 (14.6) | 76.0 (81.9-66.5) | 25 | 69.3 (20.6) | 79.3 (84.2-50.2) |
| MSQOL54 Mental Health score | 81 | 67.3 (16.6) | 71.3 (80.5-58.9) | 26 | 65.9 (17.1) | 70.2 (80.7-52.5) | 30 | 67.8 (15.2) | 70.0 (80.1-58.9) | 25 | 68.1 (18.2) | 73.7 (80.5-62.2) |
| Average MSFC hpt dominant hand (sec) | 80 | 20.1 (3.3) | 19.5 (21.1-17.7) | 25 | 19.4 (3.1) | 18.9 (20.2-17.7) | 30 | 20.9 (3.5) | 20.7 (21.8-18.5) | 25 | 19.8 (3.2) | 19.3 (21.0-17.7) |
| Average MSFC t25fw (sec) | 81 | 4.4 (0.7) | 4.2 (4.7-3.9) | 26 | 4.4 (0.9) | 4.2 (4.8-3.9) | 30 | 4.4 (0.6) | 4.3 (4.8-3.9) | 25 | 4.2 (0.5) | 4.1 (4.5-3.9) |
| Z Score t25fw | 81 | -0.2 (1.1) | 0.1 (0.6-(-0.7)) | 26 | -0.2 (1.4) | 0.2 (0.6-(-0.8)) | 30 | -0.2 (1.0) | -0.1 (0.4-(-0.8)) | 25 | -0.0 (0.8) | 0.1 (0.6-(-0.4)) |
| Z Score PASAT | 80 | 0.2 (1.0) | 0.4 (0.9-(-0.1)) | 25 | 0.2 (0.9) | 0.4 (0.8-0.1) | 30 | -0.1 (1.1) | 0.2 (0.7-(-0.6)) | 25 | 0.4 (0.8) | 0.7 (1.0-0.2) |
| New Z Score hpt | 80 | 0.1 (1.0) | 0.1 (0.8-(-0.4)) | 25 | 0.3 (1.0) | 0.3 (0.9-(-0.1)) | 30 | -0.2 (1.0) | -0.3 (0.6-(-0.6)) | 25 | 0.2 (1.0) | 0.2 (0.8-(-0.4)) |
| Overall Z Score | 79 | 0.1 (0.7) | 0.3 (0.5-(-0.3)) | 24 | 0.2 (0.8) | 0.4 (0.6-0.1) | 30 | -0.2 (0.7) | 0.0 (0.3-(-0.5)) | 25 | 0.2 (0.6) | 0.3 (0.6-(-0.2)) |
| Disease duration from first manifestation (years) | 81 | 9.2 (7.7) | 6.7 (14.8-2.3) | 26 | 10.4 (8.1) | 8.6 (16.5-2.9) | 30 | 9.0 (6.7) | 8.5 (14.6-4.2) | 25 | 8.2 (8.4) | 3.2 (12.7-1.9) |
| Disease duration from first diagnosis (years) | 80 | 6.1 (5.9) | 3.6 (10.1-1.4) | 26 | 6.4 (6.5) | 4.6 (9.6-1.3) | 30 | 7.0 (5.4) | 5.5 (12.0-2.1) | 24 | 4.5 (5.8) | 1.8 (5.1-1.1) |
| BMI (kg/m2) | 81 | 24.4 (3.5) | 24.3 (26.0-22.2) | 26 | 24.5 (4.4) | 24.5 (25.7-22.3) | 30 | 23.5 (2.6) | 23.4 (25.5-21.7) | 25 | 25.2 (3.3) | 24.8 (26.9-23.1) |
| Body fat (%) | 77 | 28.4 (7.4) | 30.6 (32.8-23.6) | 23 | 27.8 (9.8) | 30.8 (33.4-21.1) | 29 | 27.9 (5.7) | 28.5 (31.5-23.6) | 25 | 29.6 (6.6) | 31.2 (34.5-26.5) |
| Total cholesterol (mg/dL) | 55 | 190 (40) | 187 (211-162) | 12 | 186 (39) | 180 (211-156) | 25 | 197 (42) | 190 (228-170) | 18 | 182 (39) | 182.5 (200-152) |
| LDL cholesterol (mg/dL) | 55 | 115 (34) | 110 (135-91) | 12 | 109 (27) | 111 (122-86) | 25 | 120 (38) | 114 (140-94) | 18 | 111 (33) | 105 (130-84) |
| HDL cholesterol (mg/dL) | 55 | 71 (19) | 69 (83-57) | 12 | 74 (25) | 66 (92-54) | 25 | 75 (17) | 71 (88-64) | 18 | 62 (16) | 63 (69-53) |
| Triglycerides (mg/dL) | 54 | 80 (28) | 75 (90-63) | 12 | 71 (11) | 72 (78-65) | 25 | 82 (32) | 72 (98-58) | 17 | 85 (30) | 83 (90-67) |
| Insulin (mU/L) | 53 | 7.7 (3.8) | 6.8 (9.3-5.3) | 11 | 7.4 (2.4) | 7.1 (7.4-6.2) | 24 | 6.3 (2.7) | 5.7 (7.0-4.6) | 18 | 9.8 (4.7) | 9.3 (12.7-5.7) |
| Leptin (μg/L) | 52 | 9.7 (6.5) | 9.0 (12.4-5.0) | 10 | 9.0 (5.4) | 9.3 (12.3-4.1) | 25 | 10.0 (6.5) | 9.6 (13.7-5.0) | 17 | 9.6 (7.5) | 8.7 (11.1-4.9) |
| Adiponectin (μg/mL) | 53 | 9.8 (4.3) | 8.9 (12.2-7.0) | 11 | 11.0 (4.7) | 9.5 (14.9-7.6) | 25 | 9.7 (4.1) | 9.5 (11.2-7.0) | 17 | 9.4 (4.5) | 7.6 (12.5-6.4) |
| Vitamin D (nmol/L) | 53 | 114.7 (42.7) | 107.6 (143.5-85.0) | 11 | 126.4 (40.0) | 129.1 (152.8-88.3) | 24 | 107.5 (47.4) | 93.8 (123.5-77.7) | 18 | 117.2 (37.9) | 119.4 (139.1-92.6) |
| Beta-hydroxybutyrate (mmol/L) | 54 | 0.31 (0.51) | 0.12 (0.31-0.04) | 12 | 0.90 (0.81) | 0.74 (1.14-0.30) | 24 | 0.09 (0.06) | 0.07 (0.12-0.03) | 18 | 0.2 (0.25) | 0.07 (0.31-0.04) |
| NfL (pg/mL) | 55 | 11.3 (7.2) | 9.4 (13.8-7.0) | 12 | 13.5 (12.5) | 9.8 (16.0-6.8) | 25 | 10.6 (4.0) | 9.2 (14.1-6.9) | 18 | 10.9 (6.2) | 9.4 (11.7-7.3) |

**Supplemental table 6: Dietary intake data for all participants**

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **all data as mean (SD)** | **all (n = 77)** | |  |  | **n = 69** | |  | |  | **n = 72** | |  | |  | |
|  | **Baseline** | | **DACH Reference** | **Delta Reference** | **9 months** | | **DACH Reference** | | **Delta Reference** | **18 months** | | **DACH Reference** | | **Delta Reference** | |
| **Energy (kcal)** | 1821 (426) | | 2050 | -229 | 1812 (847) | | 2050 | | -238 | 1774 (502) | | 2050 | | -276 | |
| **Fat (%)** | 40 (9) | | 30 | 10 | 45 (16) | | 30 | | 15 | 45 (13) | | 30 | | 15 | |
| **Fat (g)** | 83 (33) | | 0 | 83 | 92 (48) | | 0 | | 92 | 92 (45) | | 0 | | 92 | |
| **Carbohydrate (%)** | 39 (10) | | 50 | -11 | 33 (16) | | 50 | | -17 | 34 (13) | | 50 | | -16 | |
| **Carbohydrate (g)** | 151 (78) | | 0 | 151 | 137 (177) | | 0 | | 137 | 137 (83) | | 0 | | 137 | |
| **Protein (%)** | 16 (4) | | 15 | 1 | 16 (4) | | 15 | | 1 | 16 (4) | | 15 | | 1 | |
| **Protein (g)** | 70 (21) | | 52 | 18 | 70 (25) | | 52 | | 18 | 66 (18) | | 52 | | 14 | |
| **" / bodyweight (mg/kg)** | 21.9 (130.2) | | 0.8 | 21.1 | 29.3 (167.2) | | 0.8 | | 28.5 | 13.9 (109.6) | | 0.8 | | 13.1 | |
| **Water (l)** | 2.34 (0.88) | | 2.52 | -0.18 | 2.49 (1.28) | | 2.52 | | -0.03 | 2.41 (0.92) | | 2.52 | | -0.11 | |
| **Retinolequivalent (mg)** | 1.42 (1.423) | | 0.775 | 0.645 | 2.195 (8.773) | | 0.775 | | 1.42 | 1.246 (0.648) | | 0.775 | | 0.471 | |
| **Vitamine A (Retinol) (mg)** | 0.56 (1.151) | | 0.775 | -0.215 | 0.458 (0.914) | | 0.775 | | -0.32 | 0.358 (0.205) | | 0.775 | | -0.417 | |
| **Vitamine D (Calciferol) (µg)** | 3 (4) | | 2 | 1 | 3 (3) | | 2 | | 1 | 3 (3) | | 2 | | 1 | |
| **Vitamine E (Tocopherol) (mg)** | 15 (9) | | 13 | 2 | 16 (8) | | 13 | | 3 | 16 (8) | | 13 | | 3 | |
| **Vitamine K (µg)** | 172 (126) | | 65 | 107 | 187 (152) | | 65 | | 122 | 162 (120) | | 65 | | 97 | |
| **Vitamine B1 (Thiamin) (mg)** | 1.17 (0.53) | | 1.12 | 0.05 | 1.12 (0.78) | | 1.12 | | 0.00 | 1.03 (0.32) | | 1.12 | | -0.08 | |
| **Vitamine B2 (Riboflavin) (mg)** | 1.36 (0.53) | | 1.22 | 0.14 | 1.33 (0.53) | | 1.22 | | 0.11 | 1.16 (0.34) | | 1.22 | | -0.05 | |
| **Niacinequivalent (mg)** | 28.5 (8.77) | | 13.67 | 14.83 | 28.69 (11.53) | | 13.67 | | 15.02 | 26.72 (7.58) | | 13.67 | | 13.06 | |
| **Pantothenic acid (mg)** | 4 (2) | | 5 | -1 | 4 (2) | | 5 | | 1 | 4 (1) | | 5 | | -1 | |
| **Vitamine B6 (Pyridoxin) (mg)** | 1.5 (0.6) | | 1.5 | 0 | 1.5 (1.1) | | 1.5 | | 0 | 1.3 (0.4) | | 1.5 | | -0.2 | |
| **Biotin (µg)** | 50 (24) | | 40 | 10 | 53 (48) | | 40 | | 13 | 49 (19) | | 40 | | 9 | |
| **Total Folate (mg)** | 0.3 (0.1) | | 0.3 | 0 | 0.3 (0.4) | | 0.3 | | 0 | 0.3 (0.1) | | 0.3 | | 0 | |
| **Vitamine B12 (Cobalamin) (µg)** | 4 (3) | | 4 | 0 | 4 (2) | | 4 | | 0 | 3 (2) | | 4 | | -1 | |
| **Vitamine C (Ascorbin acid) (mg)** | 123.1 (173.1) | | 102.5 | 20.6 | 141.2 (369.7) | | 102.5 | | 38.8 | 96.8 (66.4) | | 102.5 | | -5.7 | |
| **Sodium (g)** | 1.9 (0.7) | 1.5 | | 0 | | 1.7 (0.7) | 1.5 | 0.2 | | | 1.6 (0.7) | | 1.5 | | 0.1 |
| **Potassium (g)** | 2.8 (0.8) | 4 | | -1 | | 3 (4) | 4 | -1 | | | 3 (1) | | 4 | | -1 |
| **Calcium (g)** | 1 (0) | 1 | | 0 | | 1 (1) | 1 | 0 | | | 1 (0) | | 1 | | 0 |
| **Magnesium (mg)** | 0.367 (0.119) | 0.325 | | 0.042 | | 0.419 (0.265) | 0.325 | 0.09 | | | 0.401 (0.154) | | 0.325 | | 0.076 |
| **Phosphoride (mg)** | 1.2 (0.3) | 0.7 | | 0.5 | 1.3 (0.5) | | 0.7 | | 0.6 | 1.2 (0.3) | | 0.7 | | 0.5 | |
| **Iron (mg)** | 11.84 (3.7) | 11.67 | | 0.17 | | 11.92 (5) | 11.67 | 0.25 | | | 12.52 (4.45) | | 11.67 | | 0.85 |
| **Cink (mg)** | 10 (3) | 11 | | -1 | | 10 (4) | 11 | -1 | | | 9 (3) | | 11 | | -2 |
| **Copper (mg)** | 1.96 (0.71) | 1.25 | | 0.71 | | 2.09 (0.92) | 1.25 | 0.84 | | | 2.09 (0.69) | | 1.25 | | 0.84 |
| **Manganese (mg)** | 5.8 (2.9) | 3.5 | | 2.3 | | 5.76 (3.6) | 3.5 | 2.3 | | | 6.2 (3.1) | | 3.5 | | 2.7 |
| **Fluoride (mg)** | 0.93 (0.57) | 3.45 | | -2.53 | | 0.88 (0.56) | 3.45 | -2.57 | | | 0.96 (0.52) | | 3.45 | | -2.49 |
| **Iodide (mg)** | 0.104 (0.058) | 0.175 | | -0.071 | | 0.103 (0.07) | 0.175 | -0.07 | | | 0.088 (0.046) | | 0.175 | | -0.087 |
| **Fibre (g)** | 23 (10) | 30 | | -7 | | 26 (14) | 30 | -4 | | | 26 (10) | | 30 | | -4 |
| **Sucrose (%)** | 8 (4) | 10 | | -2 | | 7 (6) | 10 | -3 | | | 7 (4) | | 10 | | -3 |
| **Sucrose (beet sugar) (g)** | 38 (24) | 50 | | -12 | | 40 (112) | 50 | -10 | | | 31 (20) | | 50 | | -19 |
| **Cholesterin (g)** | 0.3 (0.2) | 0.3 | | 0 | | 0.2 (0.3) | 0.3 | -0.1 | | | 0.3 (0.9) | | 0.3 | | 0 |
| **Alcohol (g)** | 5 (8) | 0 | | 5 | | 5 (7) | 0 | 5 | | | 4 (7) | | 0 | | 4 |
| **Saturated fatty acids (%)** | 32 (14) | 33 | | -1 | | 31 (17) | 33 | -2 | | | 32 (15) | | 33 | | -1 |
| **Saturated fatty acids (g)** | 16 (5) | 0 | | 16 | | 15 (6) | 0 | 15 | | | 16 (5) | | 0 | | 16 |
| **n-3 fatty acids (%)** | 2.1 (2.7) | 0.5 | | 1.6 | | 3 (3.2) | 0.5 | 2.5 | | | 2.9 (2.8) | | 0.5 | | 2.4 |
| **n-3 fatty acids (g)** | 257 (1011) | 0 | | 257 | | 462 (2806) | 0 | 462 | | | 249 (1176) | | 0 | | 249 |
| **n-6 fatty acids (%)** | 5.9 (3.5) | 2.5 | | 3.4 | | 7.6 (3.9) | 2.5 | 5.1 | | | 7.3 (3.3) | | 2.5 | | 4.8 |
| **n-6 fatty acids (g)** | 12 (9) | 0 | | 12 | | 15(9) | 0 | 15 | | | 15 (10) | | 0 | | 15 |

DACH = Germany, Austria, Switzerland

**Supplemental table 7: Dietary intake data for standard diet group**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **all data as mean (SD)** | **Standard diet**  **(n = 25)** |  |  | **n = 20** |  |  | **n = 21** |  |  |
|  | **Baseline** | **DACH Reference** | **Delta Reference** | **9 months** | **DACH Reference** | **Delta Reference** | **18 months** | **DACH Reference** | **Delta Reference** |
| **Energy (kcal)** | 1923 (400) | 2050 | -127 | 2042 (1301) | 2050 | -8 | 1845 (484) | 2050 | -205 |
| **Fat (%)** | 36 (6) | 30 | 6 | 35 (10) | 30 | 5 | 40 (7) | 30 | 10 |
| **Fat (g)** | 78 (22) | 0 | 78 | 72 (18) | 0 | 72 | 85 (27) | 0 | 85 |
| **Carbohydrate (%)** | 43 (7) | 50 | -7 | 44 (12) | 50 | -6 | 39 (8) | 50 | -11 |
| **Carbohydrate (g)** | 172 (89) | 0 | 172 | 211 (298) | 0 | 211 | 155 (86) | 0 | 155 |
| **Protein (%)** | 15 (3) | 15 | 0 | 15 (3) | 15 | 0 | 15(3) | 15 | 0 |
| **Protein (g)** | 73 (19) | 52 | 21 | 72 (24) | 52 | 20 | 67 (17) | 52 | 15 |
| **" / bodyweight (mg/kg)** | 1 (0.3) | 0.8 | 0.2 | 1.1 (0.5) | 0.8 | 0.3 | 1 (0.3) | 0.8 | 0.2 |
| **Water (l)** | 2.29 (0.98) | 2.52 | -0.22 | 2.94 (1.64) | 2.52 | 0.42 | 2.65 (0.78) | 2.52 | 0.14 |
| **Retinolequivalent (mg)** | 1.349 (0.664) | 0.775 | 0.574 | 5.101 (16.204) | 0.775 | 4.326 | 1.592 (0.759) | 0.775 | 0.817 |
| **Vitamine A (Retinol) (mg)** | 0.486 (0.307) | 0.775 | -0.289 | 0.253 (0.153) | 0.775 | -0.522 | 0.278 (0.17) | 0.775 | -0.497 |
| **Vitamine D (Calciferol) (µg)** | 3 (2) | 2 | 1 | 3 (2) | 2 | 1 | 3 (2) | 2 | 1 |
| **Vitamine E (Tocopherol) (mg)** | 12 (7) | 13 | -1 | 14 (9) | 13 | 1 | 19 (7) | 13 | 6 |
| **Vitamine K (µg)** | 169 (121) | 65 | 104 | 240 (205) | 65 | 175 | 201 (127) | 65 | 136 |
| **Vitamine B1 (Thiamin) (mg)** | 1.27 (0.67) | 1.12 | 0.15 | 1.49 (1.26) | 1.12 | 0.37 | 1.15 (0.28) | 1.12 | 0.03 |
| **Vitamine B2 (Riboflavin) (mg)** | 1.47 (0.6) | 1.22 | 0.26 | 1.59 (0.49) | 1.22 | 0.37 | 1.28 (0.35) | 1.22 | 0.06 |
| **Niacinequivalent (mg)** | 28.98 (9.2) | 13.67 | 15.31 | 31.32 (14.19) | 13.67 | 17.65 | 27.38 (6.74) | 13.67 | 13.71 |
| **Pantothenic acid (mg)** | 5 (2) | 5 | 0 | 6 (4) | 5 | 1 | 4 (1) | 5 | -1 |
| **Vitamine B6 (Pyridoxin) (mg)** | 1.5 (0.6) | 1.5 | 0 | 1.9 (1.8) | 1.5 | 0.4 | 1.5 (0.4) | 1.5 | 0 |
| **Biotin (µg)** | 49 (24) | 40 | 9 | 69 (82) | 40 | 29 | 48 (16) | 40 | 8 |
| **Total Folate (mg)** | 0.3 (0.1) | 0.3 | 0 | 0.5 (0.6) | 0.3 | 0.2 | 0.3 (0.1) | 0.3 | 0 |
| **Vitamine B12 (Cobalamin) (µg)** | 4 (2) | 4 | 0 | 3 (2) | 4 | -1 | 3 (1) | 4 | -1 |
| **Vitamine C (Ascorbin acid) (mg)** | 94.7 (79.1) | 102.5 | -7.8 | 264.3 (677.8) | 102.5 | 161.8 | 111 (84) | 102.5 | 8.2 |
| **Sodium (g)** | 2 (0.8) | 1.5 | 0.5 | 1.9 (0.8) | 1.5 | 0.4 | 1.7 (0.8) | 1.5 | 0.2 |
| **Potassium (g)** | 3 (1) | 4 | -1 | 5 (6) | 4 | 1 | 3 (1) | 4 | -1 |
| **Calcium (g)** | 1 (0) | 1 | 0 | 1 (1) | 1 | 0 | 1 (0) | 1 | 0 |
| **Magnesium (mg)** | 0.392 (0.117) | 0.325 | 0.067 | 0.569 (0.405) | 0.325 | 0.244 | 0.467 (0.189) | 0.325 | 0.142 |
| **Phosphoride (mg)** | 1.4 (0.4) | 0.7 | 0.7 | 1.5 (0.6) | 0.7 | 0.8 | 1.3 (0.3) | 0.7 | 0.6 |
| **Iron (mg)** | 12.35 (4.04) | 11.67 | 0.68 | 14.4 (5.92) | 11.67 | 2.79 | 14.46 (4.77) | 11.67 | 2.79 |
| **Cink (mg)** | 11 (3) | 11 | 0 | 11 (5) | 11 | 0 | 10 (2) | 11 | -1 |
| **Copper (mg)** | 1.88 (0.54) | 1.25 | 0.63 | 2.3 (1.09) | 1.25 | 1.01 | 2.25 (0.6) | 1.25 | 1 |
| **Manganese (mg)** | 5.7 (2.9) | 3.5 | 2.2 | 6.6 (3.2) | 3.5 | 3.1 | 7.2 (2.8) | 3.5 | 3.7 |
| **Fluoride (mg)** | 0.92 (0.57) | 3.45 | -2.53 | 0.95 (0.58) | 3.45 | -2.5 | 1.1 (0.58) | 3.45 | -2.35 |
| **Iodide (mg)** | 0.127 (0.074) | 0.175 | -0.048 | 0.119 (0.097) | 0.175 | -0.056 | 0.09 (0.054) | 0.175 | -0.085 |
| **Fibre (g)** | 23 (8) | 30 | -7 | 33 (19) | 30 | 3 | 30 (10) | 30 | 0 |
| **Sucrose (%)** | 9 (4) | 10 | -1 | 9 (10) | 10 | 1 | 7 (2) | 10 | -3 |
| **Sucrose (beet sugar) (g)** | 44 (31) | 50 | -6 | 76 (205) | 50 | 26 | 34 (15) | 50 | -16 |
| **Cholesterin (g)** | 0.2 (0.1) | 0.3 | -0.1 | 0.2 (0.1) | 0.3 | -0.1 | 0.5 (1.6) | 0.3 | 0.2 |
| **Alcohol (g)** | 7 (12) | 0 | 7 | 5 (6) | 0 | 5 | 6 (9) | 0 | 6 |
| **Saturated fatty acids (%)** | 33 (14) | 33 | 0 | 24 (9) | 33 | -9 | 26 (11) | 33 | -7 |
| **Saturated fatty acids (g)** | 15 (4) | 0 | 15 | 12 (5) | 0 | 12 | 12 (3) | 0 | 12 |
| **n-3 fatty acids (%)** | 2 (2.7) | 0.5 | 1.5 | 2 (2.3) | 0.5 | 1.5 | 3.4 (1.8) | 0.5 | 2.9 |
| **n-3 fatty acids (g)** | 102 (498) | 0 | 102 | 1144 (5097) | 0 | 1144 | 362 (1626) | 0 | 362 |
| **n-6 fatty acids (%)** | 4.5 (3) | 2.5 | 2 | 5.9 (2.4) | 2.5 | 3.4 | 7.4 (3.2) | 2.5 | 4.9 |
| **n-6 fatty acids (g)** | 9 (5) | 0 | 9 | 11 (4) | 0 | 11 | 16 (8) | 0 | 16 |

DACH = Germany, Austria, Switzerland

**Supplemental table 8: Dietary intake data for fasting diet group**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **all data as mean (SD)** | **Fasting diet**  **(n = 28)** |  |  | **n = 26** |  |  | **n = 28** |  |  |
|  | **Baseline** | **DACH Reference** | **Delta Reference** | **9 months** | **DACH Reference** | **Delta Reference** | **18 months** | **DACH Reference** | **Delta Reference** |
| **Energy (kcal)** | 1738 (419) | 2050 | -313 | 1560 (537) | 2050 | -490 | 1667 (463) | 2050 | -383 |
| **Fat (%)** | 40 (11) | 30 | 10 | 38 (8) | 30 | 8 | 39 (7) | 30 | 9 |
| **Fat (g)** | 81 (35) | 0 | 81 | 67 (27) | 0 | 67 | 74 (24) | 0 | 74 |
| **Carbohydrate (%)** | 39 (11) | 50 | -11 | 41 (8) | 50 | 9 | 40 (9) | 50 | -10 |
| **Carbohydrate (g)** | 144 (71) | 0 | 144 | 150 (70) | 0 | 150 | 161 (73) | 0 | 161 |
| **Protein (%)** | 15 (3) | 15 | 0 | 15 (3) | 15 | 0 | 15 (5) | 15 | 0 |
| **Protein (g)** | 65 (20) | 52 | 13 | 56 (20) | 52 | 4 | 60 (16) | 52 | 8 |
| **" / bodyweight (mg/kg)** | 58 (213) | 0.8 | 57.6 | 75.7 (269.1) | 0.8 | 75 | 34.1 (175.8) | 0.8 | 33.3 |
| **Water (l)** | 2.48 (0.73) | 2.52 | -0.03 | 2.45 (1.03) | 2.52 | -0.07 | 2.3 (0.93) | 2.52 | -0.21 |
| **Retinolequivalent (mg)** | 1.275 (0.966) | 0.775 | 0.5 | 0.919 (0.37) | 0.775 | 0.144 | 1.076 (0.563) | 0.775 | 0.301 |
| **Vitamine A (Retinol) (mg)** | 0.413 (0.359) | 0.775 | -0.362 | 0.58 (1.46) | 0.775 | -0.195 | 0.338 (0.165) | 0.775 | -0.437 |
| **Vitamine D (Calciferol) (µg)** | 3 (4) | 2 | 1 | 2 (1) | 2 | 0 | 2 (1) | 2 | 0 |
| **Vitamine E (Tocopherol) (mg)** | 16 (9) | 13 | 3 | 13 (7) | 13 | 0 | 13 (7) | 13 | 0 |
| **Vitamine K (µg)** | 160 (100) | 65 | 95 | 138 (88) | 65 | 73 | 159 (135) | 65 | 94 |
| **Vitamine B1 (Thiamin) (mg)** | 1.11 (0.43) | 1.12 | -0.01 | 0.9 (0.37) | 1.12 | -0.22 | 1 (0.32) | 1.12 | -0.11 |
| **Vitamine B2 (Riboflavin) (mg)** | 1.17 (0.43) | 1.22 | -0.04 | 0.97 (0.36) | 1.22 | -0.25 | 1.08 (0.32) | 1.22 | -0.14 |
| **Niacinequivalent (mg)** | 27.85 (9.28) | 13.67 | 14.18 | 23.45 (8.6) | 13.67 | 9.78 | 24.38 (6.14) | 13.67 | 10.71 |
| **Pantothenic acid (mg)** | 4 (2) | 5 | -1 | 3 (1) | 5 | -2 | 4 (2) | 5 | -2 |
| **Vitamine B6 (Pyridoxin) (mg)** | 1.4 (0.4) | 1.5 | -0.1 | 1.2 (0.5) | 1.5 | -0.3 | 1.1 (0.3) | 1.5 | -0.4 |
| **Biotin (µg)** | 46 (19) | 40 | 7 | 38 (14) | 40 | -2 | 43 (17) | 40 | 3 |
| **Total Folate (mg)** | 0.3 (0.1) | 0.3 | 0 | 0.2 (0.1) | 0.3 | -0.1 | 0.3 (0.1) | 0.3 | 0 |
| **Vitamine B12 (Cobalamin) (µg)** | 4 (2) | 4 | 0 | 3 (2) | 4 | -1 | 3 (1) | 4 | -1 |
| **Vitamine C (Ascorbin acid) (mg)** | 81.3 (59.1) | 102.5 | -21.2 | 74.5 (48.8) | 102.5 | -28 | 76.8 (64.5) | 102.5 | -25.7 |
| **Sodium (g)** | 1.8 (0.8) | 1.5 | 0.3 | 1.4 (0.6) | 1.5 | -0.1 | 1.6 (0.7) | 1.5 | 0.1 |
| **Potassium (g)** | 3 (1) | 4 | -1 | 2 (1) | 4 | -2 | 2 (1) | 4 | -2 |
| **Calcium (g)** | 1 (0) | 1 | 0 | 1 (0) | 1 | 0 | 1 (0) | 1 | 0 |
| **Magnesium (mg)** | 0.341 (0.1) | 0.325 | 0.016 | 0.323 (0.142) | 0.325 | -0.002 | 0.347 (0.129) | 0.325 | 0.022 |
| **Phosphoride (mg)** | 1.1 (0.3) | 0.7 | 0.4 | 1 (0.4) | 0.7 | 0.3 | 1.1 (0.3) | 0.7 | 0.4 |
| **Iron (mg)** | 11.68 (3.25) | 11.67 | 0.01 | 10.62 (4.32) | 11.67 | -1.05 | 11.36 (3.91) | 11.67 | -0.31 |
| **Cink (mg)** | 9 (3) | 11 | -2 | 8 (3) | 11 | -3 | 8 (3) | 11 | -3 |
| **Copper (mg)** | 1.97 (0.58) | 1.25 | 0.72 | 1.84 (0.72) | 1.25 | 0.59 | 1.93 (0.7) | 1.25 | 0.68 |
| **Manganese (mg)** | 6.4 (3.4) | 3.5 | 2.9 | 5.7 (4.6) | 3.5 | 2.2 | 5.8 (3.7) | 3.5 | 2.3 |
| **Fluoride (mg)** | 1.02 (0.71) | 3.45 | -2.43 | 0.98 (0.68) | 3.45 | -2.47 | 0.95 (0.53) | 3.45 | -2.5 |
| **Iodide (mg)** | 0.088 (0.049) | 0.175 | -0.087 | 0.086 (0.048) | 0.175 | -0.089 | 0.094 (0.044) | 0.175 | -0.081 |
| **Fibre (g)** | 22 (8) | 30 | -8 | 21 (11) | 30 | -9 | 22 (7) | 30 | -8 |
| **Sucrose (%)** | 8 (4) | 10 | -2 | 8 (3) | 10 | -2 | 8 (4) | 10 | -2 |
| **Sucrose (beet sugar) (g)** | 35 (19) | 50 | -15 | 31 (19) | 50 | -19 | 36 (26) | 50 | -14 |
| **Cholesterin (g)** | 0.2 (0.3) | 0.3 | -0.1 | 0.3 (0.4) | 0.3 | 0 | 0.2 (0.1) | 0.3 | -0.1 |
| **Alcohol (g)** | 5 (6) | 0 | 5 | 7 (8) | 0 | 7 | 5 (7) | 0 | 5 |
| **Saturated fatty acids (%)** | 30 (15) | 33 | -3 | 23 (11) | 33 | -10 | 27 (10) | 33 | -6 |
| **Saturated fatty acids (g)** | 15 (5) | 0 | 15 | 13 (3) | 0 | 13 | 14 (4) | 0 | 14 |
| **n-3 fatty acids (%)** | 2.1 (2.6) | 0.5 | 1.6 | 2.7 (2.2) | 0.5 | 2.2 | 2.5 (2) | 0.5 | 2 |
| **n-3 fatty acids (g)** | 314 (1201) | 0 | 314 | 110 (534) | 0 | 110 | 5 (4) | 0 | 5 |
| **n-6 fatty acids (%)** | 6.8 (3.8) | 2.5 | 4.3 | 7.2 (4.7) | 2.5 | -2.7 | 6.5 (2.8) | 2.5 | 4 |
| **n-6 fatty acids (g)** | 14 (9) | 0 | 14 | 12 (7) | 0 | 12 | 12 (6) | 0 | 12 |

DACH = Germany, Austria, Switzerland

**Supplemental table 9: Dietary intake data for ketogenic diet group**

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **all data as mean (SD)** | **ketogenic diet**  **(n = 24)** |  |  | **n = 23** |  |  | **n = 23** |  |  |
|  | **Baseline** | **DACH Reference** | **Delta Reference** | **9 months** | **DACH Reference** | **Delta Reference** | **18 months** | **DACH Reference** | **Delta Reference** |
| **Energy (kcal)** | 1811 (455) | 2050 | -239 | 1895 (548) | 2050 | -155 | 1840 (559) | 2050 | -210 |
| **Fat (%)** | 43 (9) | 30 | 13 | 63 (10) | 30 | 33 | 56 (15) | 30 | 26 |
| **Fat (g)** | 89 (39) | 0 | 89 | 136 (52) | 0 | 136 | 121 (61) | 0 | 121 |
| **Carbohydrate (%)** | 36 (9) | 50 | -14 | 15 (10) | 50 | -35 | 23 (15) | 50 | -27 |
| **Carbohydrate (g)** | 136 (71) | 0 | 136 | 57 (50) | 0 | 57 | 93 (75) | 0 | 93 |
| **Protein (%)** | 16 (4) | 15 | 1 | 18 (4) | 15 | 3 | 17 (4) | 15 | 2 |
| **Protein (g)** | 72 (22) | 52 | 20 | 83 (25) | 52 | 31 | 73 (21) | 52 | 21 |
| **" / bodyweight (mg/kg)** | 1 (0.3) | 0.8 | 0.2 | 1.2 (0.4) | 0.8 | 0.4 | 1 (0.3) | 0.8 | 0.2 |
| **Water (l)** | 2.22 (0.96) | 2.52 | -0.3 | 2.13 (1.09) | 2.52 | -0.39 | 2.3 (1.01) | 2.52 | -0.21 |
| **Retinolequivalent (mg)** | 1.662 (2.246) | 0.775 | 0.887 | 1.113 (0.407) | 0.775 | 0.338 | 1.138 (0.529) | 0.775 | 0.363 |
| **Vitamine A (Retinol) (mg)** | 0.809 (2.007) | 0.775 | 0.034 | 0.499 (0.288) | 0.775 | -0.276 | 0.454 (0.242) | 0.775 | -0.321 |
| **Vitamine D (Calciferol) (µg)** | 4 (5) | 2 | 2 | 4 (4) | 2 | 2 | 4 (4) | 2 | 2 |
| **Vitamine E (Tocopherol) (mg)** | 15 (9) | 13 | 3 | 21 (8) | 13 | 8 | 16 (8) | 13 | 3 |
| **Vitamine K (µg)** | 190 (158) | 65 | 125 | 197 (144) | 65 | 132 | 130 (83) | 65 | 65 |
| **Vitamine B1 (Thiamin) (mg)** | 1.13 (0.49) | 1.12 | 0.02 | 1.06 (0.4) | 1.12 | -0.06 | 0.96 (0.35) | 1.12 | -0.15 |
| **Vitamine B2 (Riboflavin) (mg)** | 1.46 (0.52) | 1.22 | 0.24 | 1.51 (0.51) | 1.22 | 0.29 | 1.16 (0.33) | 1.22 | -0.06 |
| **Niacinequivalent (mg)** | 28.76 (7.99) | 13.67 | 15.09 | 32.34 (10) | 13.67 | 18.67 | 28.97 (9.22) | 13.67 | 15.31 |
| **Pantothenic acid (mg)** | 5 (2) | 5 | 0 | 4 (2) | 5 | 1 | 4 (1) | 5 | -1 |
| **Vitamine B6 (Pyridoxin) (mg)** | 1.5 (0.7) | 1.5 | 0 | 1.5 (0.4) | 1.5 | 0 | 1.3 (0.3) | 1.5 | -0.2 |
| **Biotin (µg)** | 55 (28) | 40 | 15 | 56 (20) | 40 | 16 | 57 (22) | 40 | 17 |
| **Total Folate (mg)** | 0.3 (0.2) | 0.3 | 0 | 0.3 (0.1) | 0.3 | 0 | 0.3 (0.1) | 0.3 | 0 |
| **Vitamine B12 (Cobalamin) (µg)** | 5 (4) | 4 | 1 | 5 (2) | 4 | 1 | 4 (2) | 4 | 0 |
| **Vitamine C (Ascorbin acid) (mg)** | 201.3 (281) | 102.5 | 98.8 | 109.7 (53.3) | 102.5 | 7.2 | 108.6 (43.5) | 102.5 | 6.1 |
| **Sodium (g)** | 1.9 (0.6) | 1.5 | 0.4 | 1.8 (0.7) | 1.5 | 0.3 | 1.4 (0.8) | 1.5 | -0.1 |
| **Potassium (g)** | 3 (1) | 4 | -1 | 3 (1) | 4 | -1 | 3 (1) | 4 | -1 |
| **Calcium (g)** | 1 (0) | 1 | 0 | 1 (0) | 1 | 0 | 1 (0) | 1 | 0 |
| **Magnesium (mg)** | 0.369 (0.139) | 0.325 | 0.044 | 0.396 (0.142) | 0.325 | 0.071 | 0.405 (0.128) | 0.325 | 0.08 |
| **Phosphoride (mg)** | 1.2 (0.3) | 0.7 | 0.5 | 1.4 (0.5) | 0.7 | 0.7 | 1.2 (0.3) | 0.7 | 0.5 |
| **Iron (mg)** | 11.5 (3.91) | 11.67 | -0.17 | 11.23 (4.19) | 11.67 | -0.49 | 12.16 (4.35) | 11.67 | 0.49 |
| **Cink (mg)** | 10 (3) | 11 | -1 | 11 (4) | 11 | 0 | 10 (3) | 11 | -1 |
| **Copper (mg)** | 2.03 (0.97) | 1.25 | 0.78 | 2.23 (0.93) | 1.25 | 0.98 | 2.14 (0.74) | 1.25 | 0.89 |
| **Manganese (mg)** | 5 (2.2) | 3.5 | 1.5 | 5.1 (2.3) | 3.5 | 1.6 | 5.7 (2.5) | 3.5 | 2.2 |
| **Fluoride (mg)** | 0.82 (0.34) | 3.45 | -2.63 | 0.71 (0.37) | 3.45 | -2.74 | 0.85 (0.45) | 3.45 | -2.6 |
| **Iodide (mg)** | 0.097 (0.042) | 0.175 | -0.078 | 0.109 (0.061) | 0.175 | -0.066 | 0.078 (0.04) | 0.175 | -0.097 |
| **Fibre (g)** | 25 (13) | 30 | -5 | 24 (8) | 30 | -6 | 27 (10) | 30 | -3 |
| **Sucrose (%)** | 8 (3) | 10 | -2 | 4 (2) | 10 | -6 | 5 (3) | 10 | -5 |
| **Sucrose (beet sugar) (g)** | 35 (18) | 50 | -15 | 19 (13) | 50 | -31 | 22 (13) | 50 | -28 |
| **Cholesterin (g)** | 0.3 (0.1) | 0.3 | 0 | 0.3 (0.2) | 0.3 | 0 | 0.3 (0.1) | 0.3 | 0 |
| **Alcohol (g)** | 5 (6) | 0 | 5 | 2 (4) | 0 | 2 | 1 (3) | 0 | 1 |
| **Saturated fatty acids (%)** | 34 (12) | 33 | 1 | 46 (19) | 33 | 13 | 42 (19) | 33 | 9 |
| **Saturated fatty acids (g)** | 17 (5) | 0 | 17 | 21 (5) | 0 | 21 | 20 (5) | 0 | 20 |
| **n-3 fatty acids (%)** | 2.1 (2.7) | 0.5 | 1.6 | 4.3 (4.3) | 0.5 | 3.9 | 3 (4.1) | 0.5 | 2.5 |
| **n-3 fatty acids (g)** | 351 (1177) | 0 | 351 | 268 (985) | 0 | 268 | 444 (1388) | 0 | 444 |
| **n-6 fatty acids (%)** | 6.4 (3.1) | 2.5 | 3.9 | 9.6 (3.3) | 2.5 | 7.1 | 8.1 (3.8) | 2.5 | 5.6 |
| **n-6 fatty acids (g)** | 14 (11) | 0 | 14 | 21 (12) | 0 | 21 | 18 (14) | 0 | 18 |

DACH = Germany, Austria, Switzerland