

Supplementary Material

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Supplementary Material 1 Characteristics of psychiatric inpatients versus controls.

	Psychiatric inpatients (n=21)	Controls (n=38)	<i>P</i> value ^a
Age in years, mean (<i>SD</i>)	40.0 (13.1)	46.7 (16.3)	0.11
Male gender, no (%)	14 (66.7%)	18 (47.4%)	0.12
Higher education, no (%)	5 (23.8%)	30 (78.9%)	< 0.001
BMI (kg/m ²), mean (<i>SD</i>)	26.9 (7.8)	24.4 (3.6)	0.11
Dutch Nationality, no (%)	14 (66.7%)	38 (100%)	< 0.001
Alcohol ≥ 14 U/wk, no (%)	1 (4.8%)	12 (31.6%)	0.02
Current smoker, no (%)	21 (100%)	15 (39.5%)	< 0.001
Recreational drugs, no (%)	8 (38.1%)	0 (0%)	< 0.001
Unmarried, no (%)	21 (100.0%)	10 (26.3%)	< 0.001
Physically active, no (%)	5 (23.8%)	18 (47.4%)	0.07
Psychotropic use, no (%)	21 (100.0%)	0 (0.0%)	< 0.001

Note. Data are number of participants (with percentages in parentheses) or means (with standard errors in parentheses). BMI=Body Mass Index.

^a Chi-square values have been computed for categorical variables, t-test for independent samples for interval variables.

Supplementary Material 2 Comparison of dietary intake of food groups and micro(nutrients) in psychiatric inpatients versus controls.

	Psychiatric inpatients (n=21)	Controls (n=38)	Adjusted Mean difference	P value ^a
Total caloric intake ^b	1700 (120.8)	2016 (90.7)	-316 (-620; -13)	< 0.001
Total protein, g	69.0 (2.9)	72.6 (2.1)	-3.71 (-11.4; 3.96)	0.34
Vegetable protein, g	31.9 (1.7)	30.9 (1.2)	1.00 (-3.34; 5.34)	0.65
Animal protein, g	37.1 (3.0)	41.7 (2.2)	-4.65 (-12.6; 3.27)	0.24
Total fat, g	62.3 (2.6)	63.7 (1.9)	-1.32 (-8.09; 5.45)	0.70
Saturated fatty acids, g	23.6 (1.2)	23.8 (0.8)	-0.19 (-3.23; 2.84)	0.90
Mono unsaturated fatty acids, g	20.7 (1.1)	22.4 (0.8)	-1.71 (-4.57; 1.15)	0.24
Poly unsaturated fatty acids, g	12.1 (0.9)	11.2 (0.7)	0.90 (-1.55; 3.36)	0.47
Trans fatty acids, g	1.22 (0.1)	1.48 (0.1)	-0.26 (-0.49; -0.03)	0.03
α-Linolenic acid (ALA, mg)	0.98 (0.1)	0.94 (0.01)	0.04 (-0.13; 0.20)	0.68
Eicosapentaenoic acid (EPA, mg)	0.02 (0.02)	0.06 (0.01)	-0.04 (-0.08; 0.001)	0.056
Docosahexaenoic acid (DHA, mg)	0.04 (0.02)	0.10 (0.02)	-0.06 (-0.12; -0.004)	0.035
Cholesterol, mg	140 (12)	200 (8.6)	-60.8 (-92.2; -29.5)	< 0.001
Total carbohydrates, g	262 (7.9)	224 (5.6)	38.1 (17.6; 58.7)	< 0.001
Total mono and disaccharides, g	149 (6.8)	105 (4.8)	44.1 (26.4; 61.7)	< 0.001
Total polysaccharides, g	112 (6.0)	119 (4.3)	-6.32 (-21.9; 9.31)	0.42
Total dietary fibre, g	20.7 (1.3)	23.2 (0.9)	-2.53 (-6.00; 0.92)	0.15
Calcium (mg)	919 (78.5)	857 (56.1)	62.2 (-143; 267)	0.55
Iron (mg)	11.2 (0.5)	11.7 (0.3)	-0.50 (-1.71; 0.72)	0.41
Zinc (mg)	7.8 (0.4)	9.0 (0.3)	-1.17 (-2.21; -0.12)	0.03
Copper (mg)	2.6 (0.3)	1.3 (0.2)	1.25 (0.58; 1.92)	< 0.001
Magnesium (mg)	327 (13.6)	336 (9.7)	-9.18 (-44.7; 26.3)	0.61
Selenium (µg)	34.1 (1.9)	43.2 (1.4)	-9.15 (-14.2; -4.06)	0.001
Iodine (µg)	27.0 (3.2)	46.1 (2.3)	-19.1 (-27.5; -10.7)	< 0.001
Vitamin A (retinol, mg)	305 (136.3)	624 (97.4)	-319 (-675; 37.5)	0.08
Beta carotene (g)	2.50 (0.2)	2.03 (0.2)	0.47 (-0.14; 1.08)	0.13
Thiamin (vitamin B1,mg)	1.03 (0.1)	1.14 (0.0)	-0.11 (-0.25; 0.03)	0.12
Riboflavin (vitamin B2,mg)	1.41 (0.1)	1.30 (0.1)	0.11 (-0.15; 0.36)	0.40
Niacin (Vitamin B3, mg)	15.4 (0.9)	18.4 (0.7)	-2.97 (-5.35; -0.59)	0.02
Pyridoxine (vitamin B6, mg)	1.35 (0.1)	1.70 (0.0)	-0.36 (-0.54; -0.18)	< 0.001
Folates naturally occurring,(µg)	198 (11.6)	201 (8.3)	-2.89 (-33.2; 27.4)	0.85
Cobalamin (vitamin B12, µg)	3.18 (0.5)	4.23 (0.4)	-1.05 (-2.42; 0.33)	0.13
Vitamin C (mg)	106 (9.1)	97.8 (6.5)	8.36 (-15.4; 32.1)	0.48
Vitamin D (µg)	1.74 (0.3)	2.57 (0.2)	-0.83 (-1.49; -0.16)	0.02
Vitamin E (mg)	9.45 (0.7)	9.35 (0.5)	0.10 (-1.75; 1.95)	0.91

Data are (adjusted) means (with standard errors in parentheses) and adjusted mean differences (with 95% confidence intervals in parentheses). Adjusted values were calculated with analysis of variance adjusted for gender, age, BMI, and total caloric intake.

Supplementary Material 4 Doses of previous studies including the current study.

	Previous studies									PSYVA
	Schoenthaler 1997	Schoenthaler 2000	Gesch 2002	Zaalberg 2010	Adams ^a 2011	Long 2013	Tammam 2016	Raine 2016	Rucklidge ^b 2018	
Minerals										
Potassium (mg)			4	4	50	40		40	192	
Calcium (mg)	122	200	100	100	100	162		162	1056	
Manganese (mg)	3	1	3	3	3	2	2	2	7.7	5
Iron (mg)	18	9	12	12		5	12	7.2	10.8	8
Zinc (mg)	15	8	15	15	12	5	15	8.3	38.4	7.5
Copper (mg)	2	1	2	2		0.5	1	0.9	5.8	0.5
Magnesium (mg)	59	80	30	100	100	100	94	20	480	
Molybdenum (µg)	250	120	250	250	150	50			120	13
Selenium (µg)	100	50	50	50	22	30	55		168	75
Chromium (µg)	100	50	200	200	70	40	50		504	13
Iodine (µg)	150	75	140	140	100	100	130	160	163	150
Lithium (µg)					500					
Sulfur (mg)					500					
Phosphorus (mg)						125			672	
Chloride (mg)						36.3				
Vitamins										
A (Retinol, mg)	1.5	0.75	0.75	0.75	0.6	0.8	0.4	0.8	1.4	
A (Beta carotene, mg)		–	–	0.13						6
B1 (Thiamin, mg)	4.5	0.75	1.2	1.2	20	1.4	6	1.4	48	15
B2 (Riboflavin, mg)	5.1	0.9	1.6	1.6	20	1.75	3	1.75	14.4	15
B3 (Niacinamide, mg)	60	10	18	18	25	20	18	20	72	20
B5 (Pantothenic acid, mg)	30	5	4	4	15	7.5	6	7.5	24	15
B6 (Pyridoxine, mg)	30	1	2	2	40	2	8	2	56	5
Folic acid / B11 (µg)	400	200	400	400	100	200	400	200	640	400
B12 (Canocobalamin, µg)	18	3	3	3	500	2.5	15	2.5	720	25
Biotin (µg)		150	100	100	150	62.5	75		864	25
C (Ascorbic acid, mg)	120	40	60	60	600	100	80	100	480	100
D3 (Cholecalciferol, µg)	5	5	10	5	7.5	5	20	5	60	25
E (D-alpha-tocopherol, mg)	80	10	10	10	270	15	8	15	200	53
K (µg)	50	50				30		30	96	
Other										
Inositol (mg)	40				100				144	
Benzoic acid (mg)	50									
Choline (mg)	40				250				432	
Fatty acids										
Linoleic acid (mg)			1260			10		400		
γ-Linolenic acid (mg)			160	100						
EPA (mg)			80	400			165	200		329
DHA (mg)			44	400		673	116	300		219

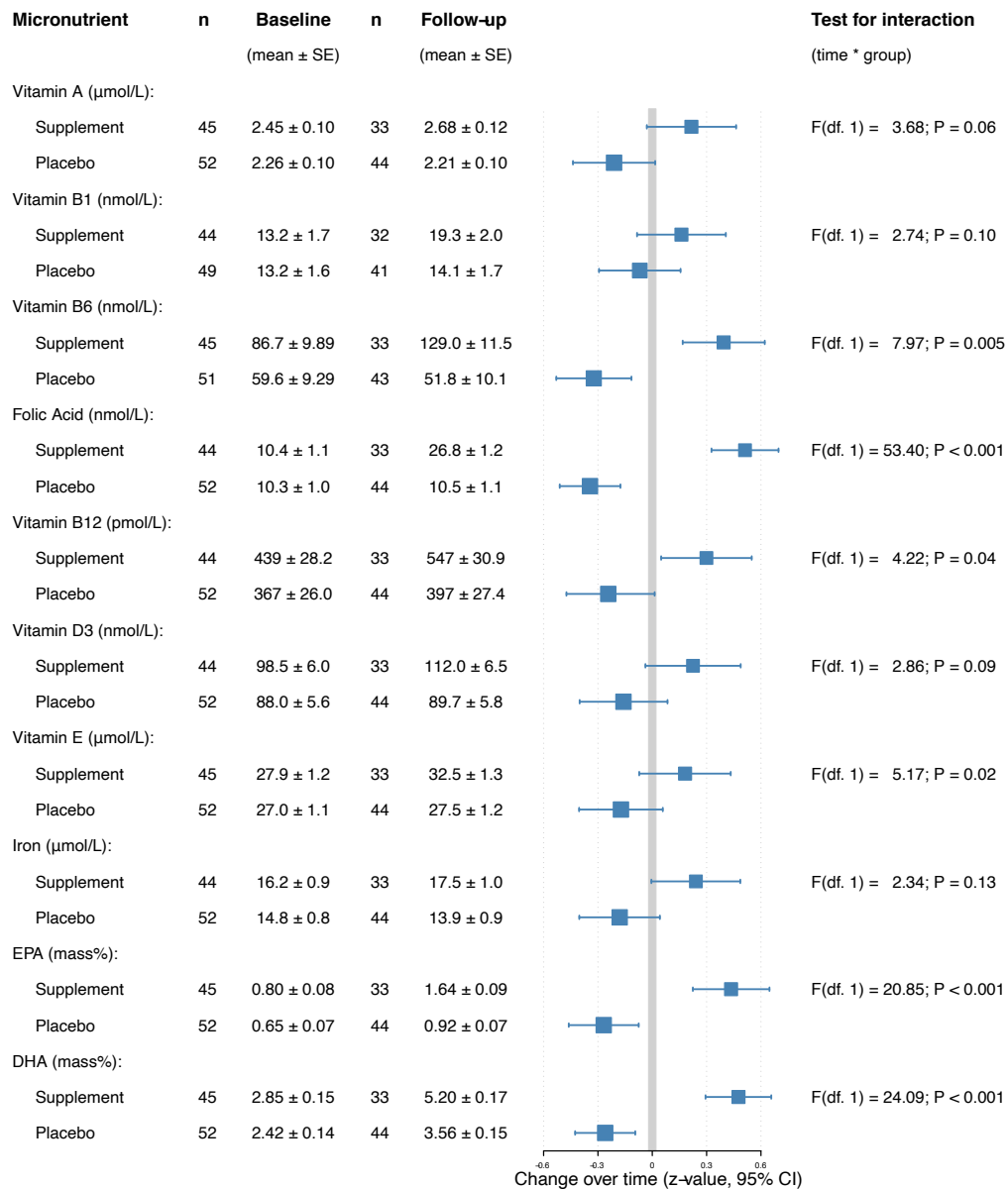
^a Dosage was adjusted based on baseline measured body weight up to a maximum of 100 lbs. The dosage shown is for a 60 lbs child.

^b Target dose was based on the response rates.

Supplementary Material 5 Average costs (in €) per patient year, by randomization group.

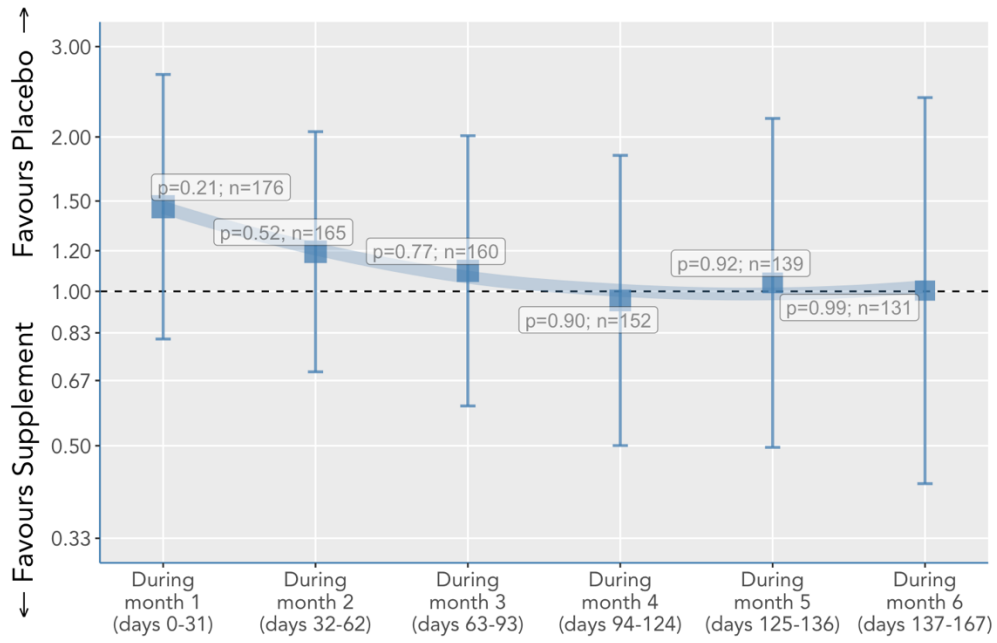
	Supplementation		Placebo		Difference	
	Frequency	Costs	Frequency	Costs	Costs	<i>p</i> value
Supplements ^a		314		0	314	-
Distribution		79		0	79	-
Total intervention costs		393		0	393	-
Verbal incidents	3.9	197	2.3	114	83	0.16
Physical against objects	1.4	122	0.9	76	46	0.20
Physical self-harm	1.9	223	1.9	224	-1	0.99
Physical against others	15.2	2,985	16.5	3,241	-256	0.79
Total aggression costs	22.4	3,526	21.5	3,655	-128	0.90
Total healthcare costs		3,919		3,655	264	0.81

^a Reported costs are for the supplements used in the study. Less expensive supplements are available for €69 per patient year

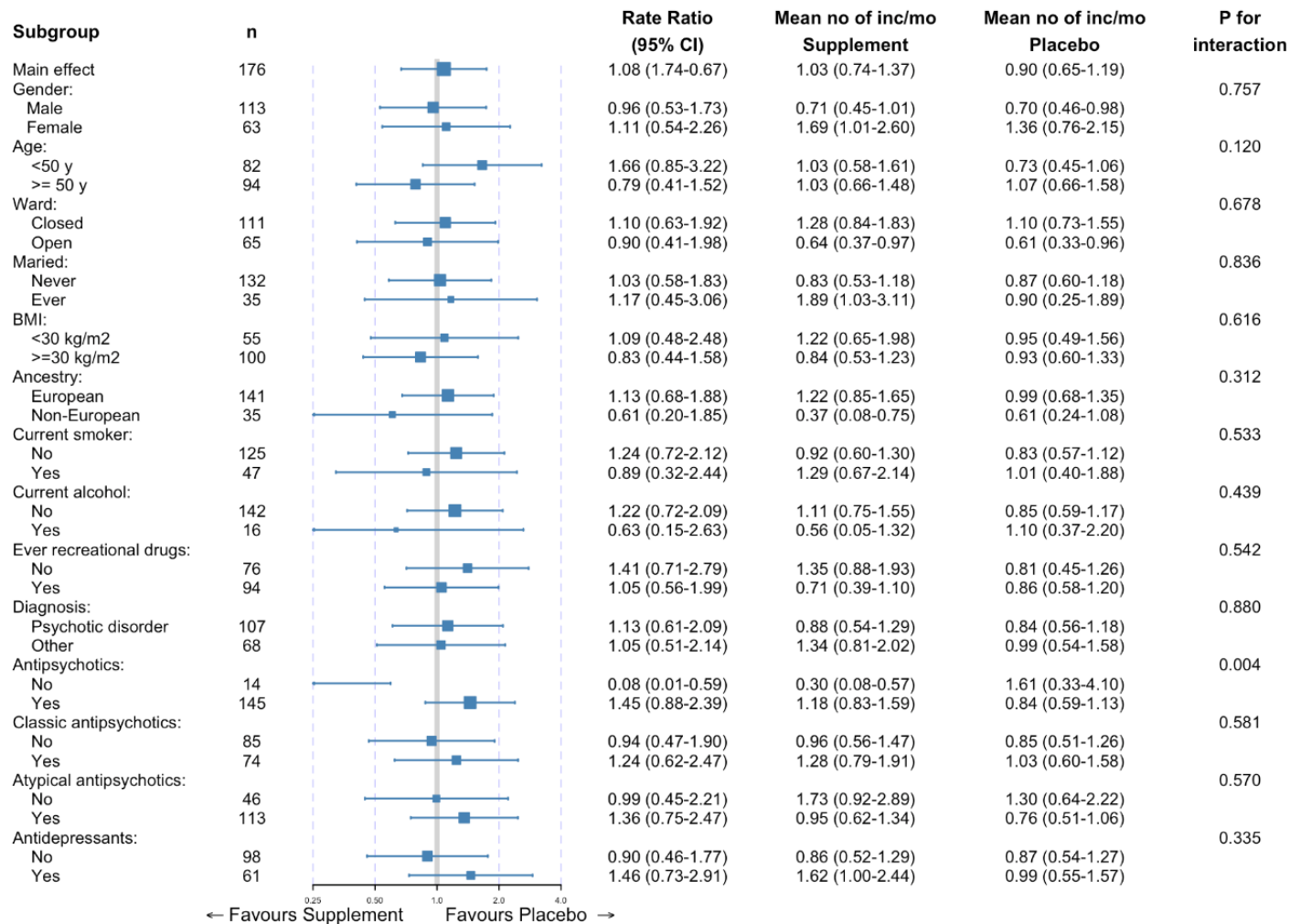


Supplementary Material 6 Changes in micronutrient levels between supplementation and placebo.

Note. Reference values as used by the LUMC: Vitamin A=0.7 – 2.6; Vitamin B1=78 – 143; Vitamin B6=51 – 183; Folic acid=8.8 – 60.8; Vitamin B12=150 – 700; Vitamin D=50 – 250; Vitamin E=16.0 – 41.0; Iron=♂ 14 – 35; Iron=♀ 10 – 25.



Supplementary Material 7 Effect on aggressive incidents over time during 6 months of supplementation.



Supplementary Material 8 Subgroup analyses of the effect of supplementation on aggressive incidents according to demographic and clinical data.

Supplementary Material 9 Adverse effects in both groups.

Side effect	Placebo	Supplements	<i>p</i> value
Any side effect, no (%)	15 (20.5%)	17 (23.0%)	0.72
Nauseous, no (%)	4 (5.6%)	2 (2.7%)	0.39
Diarrhea, no (%)	3 (4.2%)	6 (8.2%)	0.31
Burping, no (%)	2 (2.8%)	8 (11.1%)	0.049
Tiredness, no (%)	3 (4.2%)	4 (5.5%)	0.71
Rash, no (%)	0 (0.0%)	4 (5.5%)	0.04
Headache, no (%)	3 (4.2%)	3 (4.1%)	0.99
Sleep problems, no (%)	2 (2.8%)	3 (4.1%)	0.66
Weight gain, no (%)	2 (2.8%)	2 (2.7%)	0.99
Weight loss, no (%)	3 (4.2%)	1 (1.4%)	0.30
Other, no (%)	5 (6.9%)	3 (4.1%)	0.44