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SUPPLEMENTARY MATERIAL

A network meta-analysis of anorexia treatments in disease and old age: pharmacogenomics, the gut-brain axis and artificial neural nets. Where are we?

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Key words: old-age, cancer, anorexia, pharmacogenomics, machine-learning.

Study registration: PROSPERO: CRD42024622025

Search Arguments

PubMed via NLM First search 15 December 2023 – Last search 30/12/2024 Title: Anorexia Treatment		
	Search terms	
Population		
1	(((((((anorexia) AND (treatment)) OR (appetite loss)) AND (treatment)) OR (appetite stimulant) AND (treatment) OR (anorexia)) AND (therap*)) OR (appetite loss)) AND (therap*)	
Study design: randomized controlled trials and other trials (filter: PubMed clinical queries, therapy, broad) [1]		
7	((clinical[Title/Abstract] AND trial[Title/Abstract]) OR clinical trials[Mesh] OR clinical trial[Publication Type] OR random*[Title/Abstract] OR random allocation[Mesh] OR therapeutic use[Mesh Subheading])	
Reviews PubMeds "Clinical Queries" filter		
8	systematic[sb]	
Combined sets		
9	3 AND 6	
10	3 AND 6 AND 7	
Combined sets with limits		
11	8 AND 9 AND Filters activated: Last 65 years	
12	9 AND Filters activated: Publication date from 1960/01/01 to 2024/12/30 Reviews	

The search result, usually found at the end of the documentation, forms the list of abstracts

[MeSH] = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
[MeSH:NoExp] = Does not include terms found below this term in the MeSH hierarchy
[MAJR] = MeSH Major Topic
[Title/Abstract] = Title or abstract
[Title] = Title
[AU] = Author
[TW] = Text Word
Systematic[SB] = Filter for retrieving systematic reviews
* = Truncation
“ “ = Citation Marks; searches for an exact phrase

Cochrane Library

Title: Anorexia Treatment		
	Search terms	**Items found**
Population		
1	[mh "anorexia"] OR [mh "appetite"]	24
2	treatment OR therapy*:ti,ab,kw	24
3	1 AND 2	24
Intervention		
4	[mh "pharmaco*"]	59
Combined sets		
7	1 AND 4	
Limits		
8	7 AND Publication Year from 1960 to 2024	CDSR/2 DARE/19 Central/221 CRM/1 HTA/9 EED/2

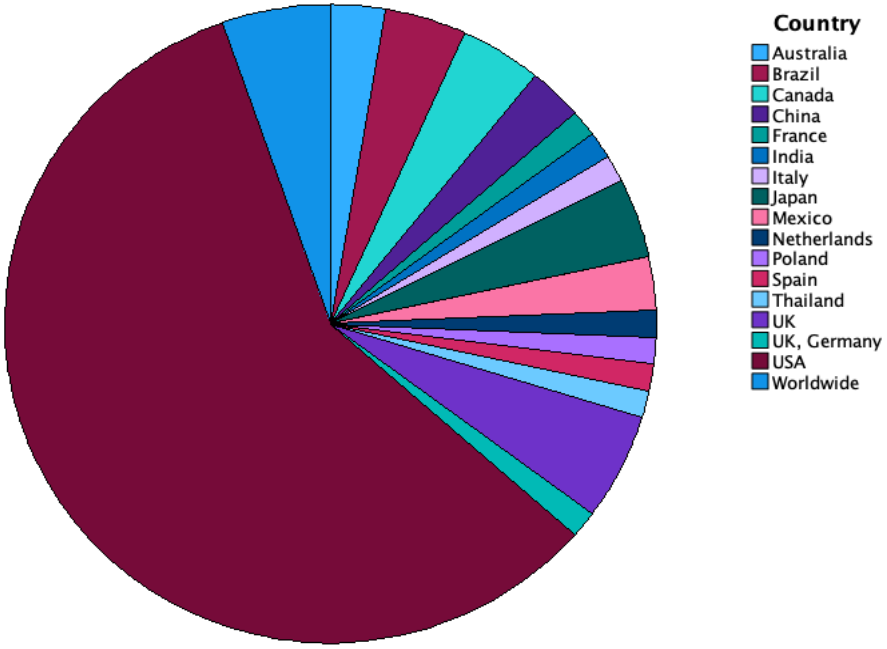
The search result, usually found at the end of the documentation, forms the list of abstracts
[mh] = Term from the Medline controlled vocabulary, including terms found below this term in the MeSH hierarchy
[ti,ab,kw] = Title, abstract, keywords
* = Truncation
" " = Citation Marks; searches for an exact phrase
CDSR = Cochrane Database of Systematic Review
CENTRAL = Cochrane Central Register of Controlled Trials, "trials"
CRM = Method Studies
DARE = Database Abstracts of Reviews of Effects, "other reviews"
EED = Economic Evaluations
HTA = Health Technology Assessments

Embase via Elsevier Title: Anorexia Treatment		
	Search terms	
Population		
1	anorexia:ti,ab,kw AND treatment:ti,ab,kw AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [systematic review]/lim OR [randomized controlled trial]/lim OR [meta analysis]/lim) AND [1960-2024]/py	
2	'appetite loss':ti,ab,kw AND treatment:ti,ab,kw AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [systematic review]/lim OR [randomized controlled trial]/lim OR [meta analysis]/lim) AND [1960-2024]/py	
3	anorexia:ti,ab,kw AND therapy:ti,ab,kw AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [systematic review]/lim OR [randomized controlled trial]/lim OR [meta analysis]/lim) AND [1960-2024]/py	
3	1 OR 2	

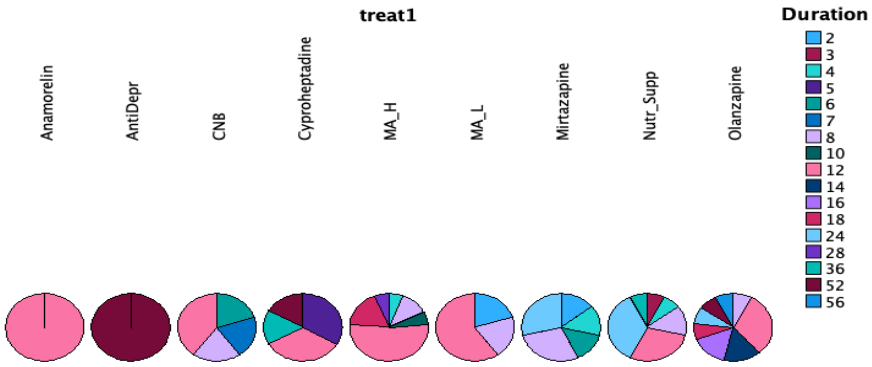
4	1 OR 2 OR 3	
5	'appetite stimulant':ti,ab,kw AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [systematic review]/lim OR [randomized controlled trial]/lim OR [meta analysis]/lim) AND [1960-2024]/py	
Intervention		
6	**pharmacotherapy**	
	(anorexia:ti,ab AND ('drug therapy'/exp OR 'drug therapy':ti,ab,kw OR 'drug treatment':ti,ab,kw OR 'medicament therapy':ti,ab,kw OR 'medicament treatment':ti,ab,kw OR 'medication':ti,ab,kw OR 'medicinal therapy':ti,ab,kw OR 'medicinal treatment':ti,ab,kw OR 'pharmaceutical therapy':ti,ab,kw OR 'pharmaceutical treatment':ti,ab,kw OR 'pharmaco-therapy':ti,ab,kw OR 'pharmaco-treatment':ti,ab,kw OR 'pharmacological therapy':ti,ab,kw OR 'pharmacological treatment':ti,ab,kw OR 'pharmacotherapy':ti,ab,kw OR 'pharmacotreatment':ti,ab,kw OR 'therapeutic uses':ti,ab,kw OR 'therapy, drug':ti,ab,kw OR 'therapy, pharmacological':ti,ab,kw OR 'treatment, drug':ti,ab,kw OR 'treatment, pharmacological':ti,ab,kw) AND (('randomized controlled trial'/exp OR 'controlled trial, randomized' OR 'randomised controlled study' OR 'randomised controlled trial' OR 'randomized controlled study' OR 'randomized controlled trial' OR 'trial, randomized controlled') OR ('systematic review (topic)'/exp OR 'systematic review (topic)' OR 'systematic reviews' OR 'systematic reviews as topic') OR ('meta analysis (topic)'/exp OR 'meta analysis (topic)' OR 'meta-analysis as topic' OR 'metaanalyses'))) AND [1960-2024]/py	
Intervention		
8	6 OR 7	
Limits:		
8	7 AND ([article]/lim OR [article in press]/lim OR [review]/lim) AND [1960-2024]/py	

/de= Term from the EMTREE controlled vocabulary
/exp= Includes terms found below this term in the EMTREE hierarchy
/mj = Major Topic
:ab = Abstract
:au = Author
:ti = Article Title
:ti:ab = Title or abstract
* = Truncation
“ “ = Citation Marks; searches for an exact phrase

Study Demographics



Selected Studies, publication year and country of origin.



Treatment duration in weeks for each treatment type. AntiDepr=antidepressants, CNB=Cannabinoids, MA_H=Megestrol Acetate High dose, MA_L=Megestrol Acetate Low dose, Nutr_Supp=all dietetic approaches

Reviewed Studies

Dietetic Interventions **Ages, Weights and BMI values are mean values, unless otherwise specified, Weight is in kg, BMI is in kg/m2, Age is in years, Height is in meters**					
Study Name & IV type	**Patients & Setting**	**Baseline BMI/Weight**	**EOT & F/U Results – BMI/Weight**	**Type of Study**	**Risk of Bias**
Fearon 2006[1] EPA2 vs EPA4 vs Placebo	Ntot=518 (355M/163F) Ages 18-80 Median age 66 GI & Lung Cancer Patients with anorexia and cachexia 231 Lung Ca 198 Upper GI Ca 83 Lower GI Ca 6 Unclassified Ca	Placebo 123M/48F EPA2 117M/58F EPA4 115M/57F EPA2 N= 94/175 BMI 20.9 W 59.8 Range 29.5 to 114.3 EPA4 N= 92/172 BMI 21.4 W 59.5 Range 37.5 to 100.0 Placebo N= 84/171 BMI 20.9 W 58.8 Range 29.9 to 120.6	Analysis of covariance for weight between the three groups at 8 weeks was borderline nonsignificant (P .066). When compared with the placebo group, the mean weight change for the group receiving 2 g EPA daily had an increase of 1.2 kg (95% CI, 0.0 kg to 2.3 kg). For the group receiving 4 g EPA daily the mean weight change was an increase of 0.3 kg (0.9 kg to 1.5 kg). Compared with weight at baseline, patients receiving placebo lost a mean of 0.7 kg over 8 weeks. Those receiving 2g EPA daily gained a median of 0.4 kg and those receiving 4 g EPA lost a median of 0.4 kg.	RCT 8 weeks Rx	Low
Jatoi 2004[2] MA600mg liquid + placebo cans vs EPA + placebo cans vs EPA + MA600	Ntotal = 421, F+M Mean age 66 yrs Cancer	MA N=140 MA+EPA N=140 EPA N=141	Weight Appetite QoL Conclusion: EPA supplementation has no benefit	RCT	Unclear High Reporting of results unclear, no starting/ending weights or BMIs. MA included in two arms of the RCT, placebo is included in two arms of the RCT

Pharmacological					
Cyproheptadine					
Study Name	**Patients & Setting**	**Baseline**	**Results**	**Type of Study**	**Risk of Bias**
Summerbell 1992[3] CY vs MA	Ntotal = 14,M+F HIV CY = 12mg MA = 40-160mg Outpatients	N MA = 7 N CY = 7	5/7 MA Group + m 3.6 kg, 2 stable. 3/7 CY + m 3.1 kg, 2 lost weight (2.6 kg, 4.6 kg), 1 stable 1 died No difference between MA and CY	RCT Low 35 days No followup	Low
Homnick 2004[4] CY v Placebo	Ntotal =12/16 CH1 :15.8 years (5 F, 2 M) CH2: 14.5 years (3 F, 2 M) CF Outpatients	CY 4mg QDS Baseline CH1 N=5 W 38.20 SD 10 H 147.00 SD 15.44 BMI 17.18 SD 1.46 CH2 N=7 W 49.78 SD 8.48 H 162.14 9.79 BMI 18.80 SD 1.82	At 12 months followup CH1 N=5 W 39.07 SD 9.79 H 149.29 SD 14.29 BMI 17.19 SD 1.41 CH2 N=7 W 53.56 SD 7.66 H164.72 7.63 BMI 19.62 SD 2.51	RCT 9 months 12 months followup Unclear Small sample sizes	Unclear
Chansane 2021[5] Cyproheptadine vs no treatment	N=125,M+F Outpatients Elderly with anorexia and weight loss Age 78.38±11.68 Older CY 4mg	H 157.2±9.54 W 52.46 11.11 BMI 21.16±3.64	Over 12 months W 52.61 SD 10.98 BMI 21.24 SD 3.64	Retrospective study 12 mo Very Low	Unclear
Kim 2021[6] Cyproheptadine vs placebo Cyproheptadine approved for anorexia in Korea	Ntotal =375 Ages 19-64,M+F ARFID – Underweight Adults Outpatients	N CY = 141/189 N PL = 141/186 CY H 162.92 (7.16) CY W 55.67 (8.44) CY BMI 20.91 (2.28) PL H 163.98 (8.01) PL W 56.26 (8.37) PL BMI 20.87 (2.19)	After 8 weeks Percent weight change, % CY +0.53 (0.16) PL –0.15 (0.16) CY BMI 0.37 ± 0.13 [0.12, 0.62] p 0.0037 W + 0.27 (0.09) kg PL BMI -0.10 ± 0.09 W –0.10 (0.09) kg Cyproheptadine statistically significant better than placebo	RCT High 8 weeks	Low
Epifanio 2012[7]	Ntotal = 25	N CY = 9/11	After 12 weeks	RCT	Moderate

Cyproheptadine v Placebo	Ages 5-18, M+F CY Mean Age 11 Control Mean Age 9 CF Inpatients	W 36.94±11.82, H 142.81±19.19 BMI 17.67±1.80 N Control = 12/14 W 31.16±12.14, H 133.82±19.35 BMI 16.78±1.69	Changes from baseline CY W +1.61±1.28 (v Control p = 0.036) BMI + 0.46±0.65 (v Control p = 0,027) Control W 0.67±0.83 BMI -0.07±0.47	12 weeks High	
Mainguet 1972 [8] Cyproheptadine v placebo	Ntotal=97, M+F Ages 15 – 79 Mean age 43 IBS Outpatients	CY = 12 mg/day CY N=50 PL N=47	After 12 weeks CY more effective than PL p <0.001 CY Group + 5.5kg vs PL Group +1.1kg	RCT 12 weeks	Moderate
Kardinal 1990[9] Cyproheptadine v placebo	N = 293, M+F Ages 18-86 Median age 65 Cancer Outpatients	N CY = 72/143 N PL = 81/150	After 36 days average maximum CY 0.9 pounds v Pl 0.5 pounds (P = 0.78); 18% on cyproheptadine versus 17% on placebo gained at least 5 pounds (P = 0.79).	RCT 36 days	Moderate

Cannabinoids					
Study Name	**Patients & Setting**	**Baseline**	**Results**	**Type of Study**	**Risk of Bias**
Volicer 1997[10] Dronabilon v Placebo	Ntotal=12/15 Age 72.7SD 4.9 Range 65–82 11M+1F Elderly in nursing homes w/out dementia, with anorexia and food refusal	N Exp=6 N Placebo=6 BMI 22.6 SD 2.5 Range 16.9– 26.2	Body weight increased during the 12-week study period, regardless of the order in which the treatment was given F(time)=3.64, df 5,143, p=0.006 Patients on dronabilon gained 7.0 SD 1.5 lb and 2.3 SD 1.7 lb v Placebo 4.6 SD 1.3 lb and 1.7 SD 2:3 lb Improvement in neuropsychiatric dementia symptoms and agitation	RCT crossover 12 wks	Moderate
Kasvis 2019[11] Dronabilon v Placebo	Ntotal=51/54 Age 62.1±13.5, M+F Non-cachexia (n=156) Pre-cachexia (n=105) Cachexia (n=136) Refractory (n=61) Cannabis (n=54) Age 47.3±16.1 Cancer anorexia & cachexia	W 70.7±14.6 kg	3-month follow-up: W 71.0±14.8 kg).	Retrospective Chart Review F/U 3 mo	Moderate
Beal 1995 [12] Dronabilon 2.5mg BD v placebo	Ntotal = 139,M+F Ages 38.3 +8.54 HIV Outpatients	N Dronab = 45/72 N Placebo = 36/67	After 6 weeks Dronabinol mean + 0.1 kg vs - 0.4 kg placebo (P =0.14).	RCT Multi Center RCT 6 weeks Low	Moderate
Strasser 2006[13] THC vs CE vs placebo	NTotal = 164/243, M+F Mean Age 61 Cancer	N THC (Dronab) = 65/100 N CE = 66/95 N Pl = 33/48	After 6 weeks Degree of weight loss lower (11.9%) than in other trials (17% and 13%) No differences between groups in body weight at baseline or week 6 (average, 61 kg) or in weight loss (average, 600 g in 6 weeks) were reported.	RCT 6 wks	Moderate
Turcott 2018[14] Nabilone vs placebo	Ntotal= 47/65, M+F Ages Nabilon 61.1 ± 10.6 Placebo 52.6 ± 11.8 Cancer	Nabilone N=14/22 W 51.6 SD 11.37 BMI 21.2 SD 4.3 Placebo N = 19/25 W 51.1 SD 9.4 BMI 21.3 SD 2.8	After 8 weeks – less than baseline Nabilone (N=9) W 50.2 ± 11.6 (− 1.4 ± 1.6), p 0.032 BMI 20.6 ± 4.3 (− 0.6 ± 0.7), p 0.0.29 Placebo (N=13) W 50.06 ± 9.1 (− 1.09 ± 2.6), p 0.119 BMI 20.8 ± 2.8 (− 0.5 ± 1.2), p 0.111	RCT 8 weeks	Moderate Unclear Discrepancy between Table 1 and Table 2 in both Nabilon and Placebo baseline BMI and Weights

Cote 2015[15] Nabilone v Placebo	Ntotal = 56, M+F Mean age 64 Cancer Nabilone dose=0.5mg	N=19/28 Nabilone N= 13/28 Placebo	EOT Fluctuation of weight similar in both groups (p = .1454).	RCT 7 weeks Low	Moderate

Ghrelin Analogues					
Study Name	**Patients & Setting**	**Baseline**	**Results**	**Type of Study**	**Risk of Bias**
Katakami 2018[16] - ONO-7643 Anamorelin v Placebo	Ntotal=174, M+F Age, mean Anam 67.6SD 9.9 PL 67.2 SD 7.9 Cancer	N Anamorelin = 55/84 N Placebo = 63/90 Anamorelin BMI 19.81 SD 2.60 W 52.23 SD 9.43 Placebo BMI 19.27 SD 2.31 W 49.73 SD 8.32	After 12 wks weight mean change Anamorelin +1.06 ± 0.20 Placebo -0.50 ± 0.19 p <0·0001	RCT Moderate 12 weeks	Low
Temel 2016[17] ROMANA I Anamorelin v Placebo	Ntotal = 352/484, M+F Mean Age 62 Cancer	N Anamorelin 284/323 N Placebo 141/161 Anamorelin W 67.6 ± 13.0 Kg BMI 23·2 (3·6) Placebo W 68.0 ± 13.3 BMI 23·3 (3·7)	Mean weight changes Anamorelin +2.20kg SD 0.33 vs Placebo + 0.14kg SD 0.36 p <0·0001	RCT 12 wks Followup yes	Low
Temel 2016[17] ROMANA II Anamorelin v Placebo	Ntotal = 351/495, M+F Mean Age 62 Cancer	N anamorelin 268/330 N Placebo 136/165 Anamorelin W 63.9 ± 13.3 BMI 22·5 (3·7) Placebo W 62.7 ± 12.9 BMI 22·1 (3·7)	Mean weight changes Anamorelin +0.95kg SD 0.39 vs Placebo -0.57kg SD 0.44 p <0·0001	RCT 12 wks Followup yes	Low
Currow 2017[18] **ROMANA III** Anamorelin v Placebo	Ntotal = 513, M+F Mean Age 62 SD 8.5 Cancer Pts from ROMANA1 228 Pts from ROMANA2 285	Anamorelin, N= 273/345 Placebo, N= 131/168 Anamorelin W 67.6 ± 13.0 Kg BMI 23.3 SD 3.6 Placebo W 68.5 ± 13.5	Mean weight changes – 24wks Anamorelin +3.160.6 kg; (CI: 1.8, 4.3) vs Placebo 0.960.7 kg; (CI: 0.5, 2.3) p <0·0001 group treatment difference: 2.160.5 kg; (CI: 1.3, 3.0).	RCT 24 wks Followup yes	Low

		BMI 22.8 SD 3.6			
Takayama 2016[19] Anamorelin v Placebo	Ntotal= 181, M+F Age 55-75 Cancer	N Anamorelin 50mg=42/65 W 51.10 ± 8.53 BMI 19.33 ± 2.57 N Anamorelin 100mg=31/55 W 52.30 ± 11.57 BMI 20.23 ± 3.21 N Placebo = 42/60 W 52.31 ± 10.29 BMI 19.80 ± 2.86	Mean weight changes – 12 wks Anamorelin 50 mg +0.54 kg Anamorelin 100 mg +1.77kg Placebo −0.93 kg p=0.0002	RCT 12 weeks	Low
Garcia 2015[20] Anamorelin 50mg v Placebo	Ntotal = 82, M+F Ages 19-94 Cancer	N Anamorelin = 23/44 N Placebo = 23/38 Anamorelin W 62·4 (36·2–85·0) BMI 21·5 (13·8–30·6) Placebo W 62·6 (35·2–100·4) BMI 21·1 (13·8–29·2)	Over 12 weeks, lean body mass increased in 38 patients in the anamorelin group by a least-squares mean of 1·89 kg (95% CI 0·84 to 2·95) compared with a decrease of a least-squares mean of –0·20 kg (–1·23 to 0·83) for 36 patients in the placebo group (difference 2·09 kg [0·94–3·25]; p=0·0006).	RCT 12 wks	Low

Antipsychotics					
Study Name	**Patients & Setting**	**Baseline**	**Results**	**Type of Study**	**Risk of Bias**
Yeung 2017[21] Olanzapine V Risperidone V Aripiprazole	N=115 N=169 Ages 60+, M+F Older anorexia	N Aripiprazole = 18 N Risperidone = 57 N Olanzapine = 49 N No Antipsy = 17	Weight Changes Aripiprazole group (−2.0 kg; −2.30% from baseline) Olanzapine group (+0.7 kg; 1.87% from baseline; $p < 0.05$), Risperidone group −0.4 kg; −0.45% from baseline Clinically significant weight gain >7% increase in body weight) 14.3% of the olanzapine patients 3.5% in the risperidone group.	Retrospective	High
Sandhya 2023[22] Olanzapine 2.5mg/day v Placebo	N Total =124,M+F (66% M) Ages 18-78 Older Age, Cancer chemotherapy-related nausea, anorexia	N Olanz = 58/63 W 53 (34-69) BMI 20.7 (13-30) N Placebo = 54/61 BMI 20.6 (13.7-33.8) W 53 (33-77)	Weight Change after 12 weeks Olanzapine W 56 (31-73) BMI 21.6 (13.8-32.4) Placebo W 51.5 (32-73) BMI 20.1 (13.8-30.3) Patients in the olanzapine group had an increase in mean weight from 53.1 kg (SD 8.9) to 55.7 kg (SD 9.0) Patients in the placebo group had a decrease in mean weight from 53.6 kg (SD 9.9) to 51.7 kg (SD 9.7)	RCT 12 weeks	Low
Okamoto 2015[23] Olanzapine 1.5-5mg/day	Ntotal=80 Age 60.4±15.7, M+F Mean Olanzapine dose=1.5mg/day Cancer patients with anorexia and cachexia	NR	Significant improvement in appetite and food intake but not weight at a low dose of 1.5mg Food intake increase 149% on average ($p<0.0001$)	Retrospective The observation period was 3 days before and after the start of OLZ treatment, because most inpatients whose food intake increased were discharged in 3 days.	High
Naing 2015[24] Olanzapine 2.5-20mg/day	Ntotal=31/39 Ages 28-84,M+F Cancer patients with anorexia and cachexia	NR	The slopes in weight prior to study(from approximately 6 months prior to study initiation today 1 of the study) had a mean value of−0.35 (95 % confidence interval,−0.44,−0.27;$p< 0.0001$) Slopes in weight during study had a mean value of−0.11	RCT	

			(95 % CI,−0.41, 0.19;p= 0.46). The mean change in slope from before to after the study was 0.24 (95 % CI,−0.08, 0.56;p= 0.13) indicating that treatment had a modest effect in changing the trajectory of weight loss		
Street 2001l[25] Olanzapine 5-10-15mg	Ntotal=206 Ages 65+, M+F Older patients with dementia and mixed chronic illness			RCT 6wks – 18wks	
Street 2000[26] Olanzapine 1-8mg	Ntotal=222 Ages 65+, M+F Older patients with dementia and mixed other chronic illness			RCT 8wks – 14wks	
Deberdt 2005[27] Olanzapine 2.5-10mg	Ntotal=78 Ages 65+, M+F Older patients with dementia and mixed chronic illness			RCT 10-16weeks	
De Deyn 2004[28] Olanzapine 1-7.5mg	Ntotal=561 Ages 65+, M+F Older patients with dementia and mixed chronic illness			RCT 16wks in total	
Kinon 2003 [29] Olanzapine 2.5-20mg	Ntotal=231 Ages 65+, M+F Older patients with dementia and mixed chronic illness			Open Label 8 weeks	
Kinon 2004 [30] Olanzapine 2.5-20mg Risperidone	Ntotal=202 Ages 65+, M+F Older patients with dementia and mixed chronic illness			Open Label 13 months	
Kennedy 2005[31] Olanzapine	Ntotal=249 Ages 65+, M+F Older patients with dementia and mixed chronic illness			RCT 12-14 weeks	
Navari 2010[32] MA800 vs MA800+Olanz	Ntotal=80 Ages 39-81,M+F Cancer patients with anorexia and cachexia	N MA800+Olanz5=39/40 BMI 23.6 W 151 lbs H 67 inch N MA800=37/40 BMI 23 W 143 lbs H 66 inch	Weight improvement - greater than or equal to 5% weight gain	Prospective RCT 8 weeks	

Antidepressants - Mirtazapine					
Study Name	**Patients & Setting**	**Baseline**	**Results**	**Type of Study**	**Risk of Bias**
Mihara 2005[33] The Impact of Mirtazapine Compared with Non-TCA Antidepressants on Weight Change in Nursing Facility Residents	N=185, M+F Age 65+, Mean age 80 Older, Nursing home residents	(Median values) N=11 Citalopram 153lb N Fluox = 23 W 143lb N Parox = 69 W 132lb N Sertraline = 26 123lb N Trazodone = 17 W 135lb N Venlafaxine = 9 W 122lb N Others = 7 W 126lb N Mirtaz = 27 W 120lb	Mirtaz v Others at 3mo F-test = 0.0507 R2 = 0.0883 Adjusted R2 = 0.0425 P 0.71 Mirtaz v Others at 6mo P = 0.88 F-test = 0.0015 R2 = 0.1369 Adjusted R2 = 0.0935 Fluoxetine + 3.84 lb at three months relative to mirtazapine (p = 0.05) Hypertension and diabetes more weight gain female sex less weight gain Mirtazapine not associated with weight gain or loss when compared with other non-TCA antidepressants	Retrospective cohort study 3m and 6m	High
Rigler 2001 [34] Anti-depressants in nursing homes	N Total = 6,009 Weight loss, Anorexia of the Elderly	N None = 4852 N TCA = 243 N SSRI = 814 N Other = 100 Baseline weights without antidepressant use Amitriptyline & trazodone not included	Antidepressant group change in lb None - 0.17 - 0.2 lb loss (SD 10.5) TCA +0.37 - 0.4 lb gain (SD 11.9) SSRI -1.56 - 2.6 lb loss (SD 12.2) Other -2.9 - 2.9 lb loss (SD 13.5) Pairwise differences in weight changes P-value None vs TCA 0.8651 None vs SSRI 0.0151 None vs Other 0.2481 TCA vs SSRI 0.0464 TCA vs Other 0.1658 SSRI vs Other 0.9591	Retrospective cohort design using the Minimum Data Set—Plus (MDS 1).	High
Versiani 2005[35] Mirtaz v Fluox mirtazapine 15–60 mg/day or fluoxetine 20–40 mg/day	Ntotal=297, M+F Ages 18-65 MDD+weight loss	N Mirtaz = 145/147 N Fluox = 147/152 Median (range) Mirtazapine H 165 (145–184) W 64 (41–117) Fluoxetine H 165 (140–194) W 67 (34–134)	Weight Changes after 8 wks Mirtazapine +0.8 ± 2.7kg vs Fluoxetine - 0.4 ± 2.1kg (p < 0.001)	RCT 8 weeks	Moderate

Howard 2019[36] Mirtazapine Dronabilon MA	N=38,M+F Mean Age 66 ARFID Inpatients	N Dronab =5 W 77 ± 25 BMI 22 ± 6 N Mirtaz = 15 W 80 ± 25 BMI 29 ± 8 N MA = 10 W 68 ± 11 BMI 26 ± 5 N Others = 7 W 76 ± 22 BMI 24 ± 6	DC W Dronabilon 77 ± 25 DC W MA 70 ± 14 DC W Mirtaz 86 ± 28 DC W Others 70 ± 23	Retrospective cohort study Median Hospital stay 15 days	Low
Hunter 2021[37] Mirtazapine 15mg nocte v Placebo	Ntotal=120, M+F Age 55.4 (11.5) Cancer anorexia and cachexia	N Mirtaz =48/60 W 62.6 (12.9) BMI 23.5 (4.3) N Placebo = 52/60 W 58.3 (11.1) BMI 23 (4.7	Mirtazapine 15mg at night for 28 days is no better than placebo Body weight change at 56 days Mirtazapine (n=28) -0.4 SD 4.2 Placebo (n=44) – 1.53 SD 2.85	RCT 28 days Followup at 56 days	High Placebo weight loss significantly less than mirtazapine
Jiang 2016[38] Mirtaz vs Others (vs Parox, vs TAU)	Ntotal = 60, M+F Ages 20-55 ARFID + Functional Dyspepsia and weight loss	N Mirtaz = 20 H 163.81 ± 12.36 W 49.77 ± 6.79 BMI 18.73 ± 5.62 N Parox = 20 H 162.36 ± 10.06, W 48.93 ± 5.89 BMI 18.65 ± 4.73 N TAU = 20 H 160.72 ± 10.63, W 48.22 ± 5.57 BMI 18.84 ± 6.38	Weight Changes at 8 wks Mirtazapine + 3.58 ± 1.57 kg, BMI 20.07 ± 5.23. p 0.05 Paroxetine + 0.53 ± 0.44 kg TAU +0.56 ± 0.45 kg p < 0.05	RCT 8 weeks	Low
Mullin 1996[39] Mirtazapine 20-60mg/day v Amitriptyline 75-225mg/day	N=156,M+F Ages 20-65 MDD with weight and appetite loss	N Mirtaz = 64/79 W 64.9 SD 13 H 163.4 (8.3) N Amitript = 59/77 W 64.5 SD 14.1 H 164.8 (8.8)	Mirtazapine +0.5 kg Amitriptyline 3.4 kg.	RCT 6 wks	Low
Megestrol Acetate					
Study Name	**Patients & Setting**	**Baseline**	**Results**	**Type of Study**	**Risk of Bias**
Almeida 2023[40] Mirtaz30 vs MA320	Ntotal=52, M+F 65.8 SD 8.4 years Cancer	N MA = 22/26, 10F, 16M N Mirtaz = 10/26, 15F, 11M Megestrol Median BMI	Improvement after 8 weeks (megestrol vs. mirtazapine) p 0.65 Megestrol Median BMI	RCT 8 weeks	Very low Mirtazapine group size

		22.9 (19.2–24.7) Mirtazapine Median BMI 23.6 (18.8–28.5)	22.6 (19.1–25.2) Mirtazapine Median BMI 24.8 (18.5–29.8)		MA dose 320mg is known to be ineffective
De Conno 1998 [41] Megestrol Acetate v Placebo	Ntotal=42,M+F Ages MA 63 SD 8 Placebo 58 SD 12 Cancer Outpatients MA360 (160mg BD)	N=12/15 MA360 Weight 57Kg SD8 Height 1.68 SD 10 N=11/16 Placebo Weight 63Kg SD10 Height 1.68 SD 5	MA Body Weight Change Day 14 Mean difference MA360 v Placebo MA360 +1.06 SD 1.95 Placebo -0.34 SD 1.01 p 0.015	RCT a 14-day double-blind placebo controlled phase (phase A) and a 76-day open phase (phase B). Low	Low
Von Roenn 1994 [42, 43] MA variable doses	Ntotal=195/271,M+F Ages 30-40 HIV	MA 100mg N= 61/82 MA 400mg N=53/75 MA 800mg N= 53/75 Placebo = 28/38	MA vs Placebo 400 or 800 P< 0.0001 Weight Increase 2.27kg P=0.001, t-test MA 800mg vs PL P=0.006 t-test MA 800mg vs MA 100mg P=0.005 t-test MA800mg vs MA400mg Mean weight change in lb Placebo -1.6 SD 1.2 MA100 19.9 SD 1.3 MA400 4.2 SD 1.3 MA800 7.8 SD 1.3	RCT 12 weeks Moderate	Unclear
Eubanks 2002[44] MA v Placebo	N=17, M+F Ages 6-25 CF Outpatients	N MA = 10 W 26.9 ± 11.8 H 131.9 ± 24.2 N Pl = 7 W 29.1 ± 12.0 H 136.9 ± 23.3	Change in kg MA +4.3kg SD 2.9 PL +1.3 SD 1.4 At 3mo MA 4.3 ± 2.9 vs Pl 1.3 ± 1.4 kg p < .025 At 6mo MA 5.3 ± 3.6 kg versus PL 1.5 ± 1.6 kg p < .03	RCT 3 months Follow up 6months	Moderate
Wanke 2007[45] MA Liquid vs MA tablet Dose 800mg/day	Ntotal = 63, M+F Ages 25-50 HIV	MA Liquid N=32 BMI 19.8 ± 4.1 W 55.6 ± 13.4 MA 800mg = 31 BMI 20.1 ± 3.11 W 54.4 ± 10.5	MA Liquid better than tablet MA Liquid weight (5.4 kg) MA tablet weight (3.5 kg, P = 0.024). MA Liq BMI diff 1.9 ± 1.93 MA800 BMI Diff 1.3 ± 1.51	RCT 12 weeks Moderate	Moderate
Timpone 1996 [46] Megestrol Acetate v Dronabilon BD, alone and combined	Ntotal=39/52,M+F Ages 19-50 HIV	N Dronabinol BD = 12 BMI 20.5 (2.7) W 61.2 (9.0)	EOT M750 and M750+D BMI +2 (from baseline)	RCT 12 weeks	Moderate

		N MA750 =12 BMI 19.1 (2.1) W 60.7 (10.7) N MA750+Dronab =13 BMI 20.3 (2.9) W 63.3 (12.8) N MA250+Dronab =13 BMI 20.2 (2.9) W 63.2 (11)	Mean Weight Change +/- SE D, -2.0 +/- 1.3 kg M750, +6.5 +/- 1.1 kg M759+D, +6.0 +/- 1.0 kg M250+D, -0.3 +/- 1.0 kg Difference among treatment arms p = 0.0001		
Mwamburi 2004[47] MA800 or OXA10 for 2 months Vs MA800+OXA10 for 5 months	Ntotal=39,M+F Mean age 40.2 (7.9) HIV	Whole sample BMI 21 SD 2.1 W 62.5 (9.9) MA800 N=20, W 60.7 ± 9.2 OXA10 N=19, W 64.4 ± 10.4	At 2 months N=33 Weight Incr 2.6kg SD 4.2 BMI incr 1.1 $p < 0.01$ BMI increased from 21.0 to 22.1 At 7 months N=29 BMI increase 2.1 Weight Incr 5.3kg SD 8.5 $p < 0.01$ BMI increased from 21.0 to 23.1	RCT 2 months and 5 months Unclear	Low
Batterham 2001 [48] MA400mg vs Nandrolone decanoate (ND) 100mg IM dietary counselling,	N=15, M+F randomized to receive ND (100 mg/fortnight), or MA (400 mg/day) or dietary counselling for 12 weeks. Mean Age 43 SD 10 HIV Outpatients	Mean BMI 20.5 SD 2.76 (whole sample) N Diet=5 W 66.69 SD 8.62 N ND=5/6 W 64.75 SD 9.84 N MA=4 W 52.91 SD 10.20 Diet group randomised N ND =3 N MA =0/2	Weight Changes after 12 wks Dietary counselling Mean increase 1.13 kg SD 0.36 W 67.82 SD8.87 Nandrolone mean increase 4.01 kg SD1.68 W 68.77 SD 9.99 MA mean increase 10.20 kg SD 4.51 W 63.11 SD 12.71 $p < 0.05$ paired t-test	RCT 12 weeks trial Followup 24 weeks	Unclear, Moderate
Currow 2021[49] MA480 vs DEX4mg vs Pl 4 weeks	Ntotal = 190, M+F Ages MA 71.4 (10.9) DEX 71.2 (12.7) PL 74.7 (10.0) Anorexia secondary to advanced Cancer	MA N = 52/61 - W 63.1 (14.0) H 167.6 (9.9), BMI 22.36 (3.95) DEX N = 44/67 – W 62.5 (14.6), H 167.1 (10.2) , BMI 21.97 (4.00) Pl N = 42/62 –	EOT Weight stable MA 87% DEX 74% PL 85% **p 0.2417**	RCT 4weeks	

		W 62.9 (13.9) H 168.2 (10.2), BMI 22.22 (3.55)			
Fietkau 1997[50] MA160 vs PL	Ntotal =61/64, M+F Ages MA 48 Control 52 H&N CA	MA160 N=31 CONTROL N=30 MA160 W 64.3kg SD 9.9 Placebo W 63.6kg SD 10.6	At 12 wks Weight loss MA 0.8kg vs Pl. 4.1kg P = 0.0004 At F/U (Week 18) MA160 - W 63.5kg SD 10.3 Placebo - W 60kg SD 8.2	RCT 12 weeks Followup week 18	Moderate
Loprinzi 1990 [51] MA v Placebo Megestrol Acetate 800mg/day	Ntotal=133/136, M+F Median Ages MA 69 (30-84) Pl 67 (42-86) Cancer	N=66 MA N=67 Placebo NR	A weight gain of 15 lb or more over baseline was seen in 11/67 (16%) patients MA v 66 (2%) placebo (p =0.003). Mean Absolute %weight gain MA 3% v Placebo -0.5%	RCT 10 wks	Moderate
Loprinzi 1994[52-54] Megestrol Acetate variable doses	Ntotal = 321/342, M+F Ages 45-75 Median 67 Cancer	N MA160=88, W139 ± 3 lb N MA480=86, W 144 + 3 lb N MA800=85, W 141 ± 3 lb N MA1280=83, W 145 ± 3lb	After 18 wks MA160 84 pts Mean % WIncr 0.31 MA480 84 pts Mean % WIncr 0.91 MA800 76 pts Mean % WIncr 3.6 MA1280 77 pts Mean % WIncr 2.6	RCT 18 wks	Moderate
Loprinzi 1999 [55] MA 800mg/day v Fluoxymesterone (20 mg/day) v Dexamethasone 3 mg/day	Cancer Ntotal = 475,M+F Mean ages 64-66 yrs old	N DEX=120/159 N MA800=114/158 N Fluox=114/158 MA W 65.7 kg Fluo W 64.7 kg Dex W 65.7kg	Mean Weight gain in kgs MA 2.50 Fluo 2.01 Dex 1.77 MA800 vs Dex Weighted p 0.537 MA800 vs F Weighted p 0.62 Pts max weight gain >= 10% from baseline MA800 (N=114) vs Dex (N=120) p .42 MA800 (N=114) vs F (N=114) p .08 Rest pts weight gain MA800 vs Dex p 0.55 MA800 vs F p 0.68	RCT Monthly monitoring, unclear ift duration	Moderate
Yeh 2009[56] MA800 Liquid vs Placebo	Ntotal=51,M+F Ages 75-80 Anorexia-cachexia syndrome in the elderly	N MA=26, W 136 lb.+4.0 N Placebo=25 W133.9 lb +5.3	At F/U (c. 25 wks) MA 6.5lb+3.1 (n = 21) Placebo -1lb+1.9 (n = 23)	RCT 12 weeks Followup 3 months Moderate	Low

	CAD Dementia Depression GERD/PUD Urology Problems CVA Constipation Hip Fractures COPD DM		0.043 (t-test)		
Golebiewska 2012[57] MA160	Ntotal = 12/32 Ages 38-85 Mean 69.97±10.8 Dialysis patients with anorexia	Weight (kg) 63.58±12.38 BMI (kg/m2) 23.06±3.26	After 2 mo (N=26) W 64.78±11.97 BMI 23.68±3.63 After 6 mo (N=12) W 65.58±12.53 BMI 24.66±4.23 p < 0.001	Multicentre prospective study 6 mo	Moderate
Herrejon 2011 [57] MA380 v Placebo MA dose = 380mg/day	Ntotal=38,M+F Ages 50-70 COPD Outpatients	N COPD = 19 MA W 55,7 (8,7) MA BMI 20,0 (2,1) N Placebo = 19 PL W 54,3(9,5) PL BMI19,4 (2,5)	MA W +2.3kg vs Control W +0,1 kg (p < 0,04)	RCT 8 weeks Moderate	Moderate
Weisberg 2002[58] MA800 v Placebo MA dose = 800mg/day	Ntotal=128/145,M+F Ages 45-70 COPD	N MA=66/72, W 53.1 (9.1) N Placebo=62/73 W 51.7 (8.6)	EOT Body weight +3.2 kg MA group + 0.7 kg Placebo group (p < 0.001) Week 8 MA W 56.3 (9.5) Placebo W 52.4 (9.4) Diff 3.2 SD 0.7, p 0.001	RCT 8 weeks Moderate	Moderate
Zheng 2019[59] MA_L 160mg vs TAU	Ntotal=46,M+F Ages 65+ Elderly patients with CKD	N MA160=18/23 BMI 19.81 ± 2.01 W 53.14 ± 5.71 N Placebo=23/23	EOT BMI 20.60 ± 2.11 EOT Body weight 55.28 ± 5.97	RCT 12 weeks	Moderate

CAD; coronary artery disease, COPD: chronic obstructive pulmonary disease, CVA: cerebral vascular accident, DM: Diabetes mellitus, GERD: gastric oesophageal reflux disease, PUD: peptic ulcer disease.

Older Adults
Ages, Weights and BMI values are mean values, unless otherwise specified. Weight is in kg, BMI is in kg/m2, Age is in years

Study Name	Patients & Setting	Baseline	Results	Type of Study	Risk of Bias

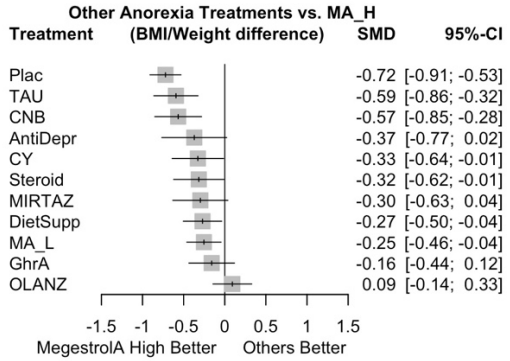
Beck 1996[60] Feeding NG Voluntary & Compulsory	N=11 Ages 55-75 AN	BMI 11.6 SD 3.9	BMI 15.50 SD 2.3	Case Series	High
Price 1985[61]	N=1 Age=68, F AN	BMI 17.9 H 64 inches W 104 pounds	Weight gain of 9.5 lb over the following 10-12 months	Case Report	High
Launer 1978[62]	N=1 Age=70, F AN-BP	W 30.6 kg H 172.6 cm	Rx Chlorpromazine +clomipramine 6 month hospital stay Weight gain of 14 kg	Case report 6 mo admission	High
Ramell 1987[63]	N=1 Age67,F AN	W41kg H 1.50	Rx Chlorpromazine + Insulin After 3.5 weeks W 48 kg	Case Report	High
Malik 2014[64]	N=1 Age=81, M Lost weight, medical complications	BMI 17	BMI 17.5 Rx Dietician	Case Report	High
Parke 2008[65]	N=1 Age=72, M EDNOS, Cognitive disorder NOS, Asperger's syndrome and Schizotypal traits, Dementia	BMI 16.7 H 5 ft, 9 in W 113 lb	After 5 weeks Rx Fluoxetine BMI 19.9 Discharged to a nursing home	Case Report	High
Ronch 1985[66]	N=1 Age=75, M AN	H 5' 4" W 80lbs	Weight 92lbs after 10-12 mo Rx Clorazepate (Benzodiazepine) 3.75 mg every 2nd night for anxiety long care facility 15-min sessions with psychiatrist Weight goals Dietician	Case Report	High
Segers 2014[67] Mirtazapine 15-60mg	N=20/22, M+F Ages 68 to 94 Alzheimer's and Mixed Dementia with appetite or weight loss MMSE 18±6.	BMI 20.5±2.9 Weight 52.4±9.3 kg	Absolute weight change from baseline after 6 months (mean in kg, SD) 3mo +1.93kg (2.90) 6mo +2.11 (4.41)	Retrospective Open-label Study	High
ECT Bernstein 1972[68]	N=1 Age 94,F	5 Treatments W 36kg	W 38.7 + 2.7 kg	Case Report	High
ECT Hill 2001[69]	N=1, F Age 77 AN-R MDD Citalopram, Doxepin, Temazepam	9 Treatments BMI 16.5	BMI 17.00 Gained 2kg	Case Report	High
Wouters-Wesseling 2002[70] Liquid nutrition supplement	N=35/42, M+F Age=60+	N Nutr=19 N Placebo=16	A statistically significant improvement was observed for body weight (difference between groups 2.2 kg, P=0.03), and homocysteine, vitamin	RCT 12 weeks	Moderate

v Placebo	2 x psychogeriatric nursing homes, elderly with appetite and weight loss Dementia Depression	micronutrient-enriched liquid nutrition supplement of 125 ml and 0.6 MJ (135 kcal) or placebo twice daily during daytime between main meals.	B1, TDF, vitamin B6, vitamin B12, folate and vitamin D in the supplement group compared to the placebo group.		
Faxen-Irving 2002[71] Liquid nutrition supplement V Control	Ntotal=36 Age=82+ Geriatric nursing home residents with dementia and weight loss	N Nutr=22 BMI 22.2 SD 4.1 W 55.4 SD 10.4 N Control=14 BMI 24.6 SD 2.9 W 62.2 SD 8.2	After 6 mo The weight of the residents in the intervention group increased by 3.4 (3) kg (P< 0.001) at follow-up, whereas the weight remained unchanged in the control N Nutr BMI 23.5 SD 4.4, W 58.8 SD 11.2 N Control BMI 24.5 SD 3.8 W 61.9 SD 10.4	NRCT 6 months	Moderate
Kamphuis 2011[72] Nutritional Supplement V Control	Ntotal= 212,M+F Age=73+ Geriatric patients with AD dementia and weight loss	N NutSupp=105 BMI 26.2 ± 4.8 N Control =106 BMI 26.2 ± 3.5	BMI of the NutSupp Group increased after 12 weeks p < 0.03	RCT 12 weeks	High
Parrott 2006[73] **&** **Young 2004** Nutritional Supplementation V Control	Ntotal=29/34 Age=82+ Geriatric nursing home residents with/without dementia and weight loss	BMI = 23.7 SD 3.8 N Group1=13 BMI 23.4 SD 3.9 N Group2 = 18 BMI 24.1 SD 3.7	BMI increased significantly from before to after the intervention (p<001); this increase was sustained post supplementation p<.001 vs baseline. BMI 24.3 SD 4.0 Nutrition supplements were least likely to enhance habitual energy intake in subjects who would normally be targeted for nutrition intervention those with low body weight status. Those likely to benefit include those with higher body mass indices, less aberrant motor problems, less mental disorganization, and increased attention	RCT, Crossover 3 weeks	Moderate
Young 2005[74] High Carbohydrate Diet (HCD) at dinner V Control	Ntotal=20/32 Age=87+ Geriatric nursing home residents with/without dementia and weight loss	N Group1=18 BMI 24.1SD 3.7 N Group2=14 BMI 23.6 SD 3.8	In 3 weeks Increase of mean body weight 0.3661.12 kg, p< .076)	RCT 3 weeks	Moderate
Pivi 2011[75] Nutritional Suppl V Nutritional Education V Placebo	Ntotal=78/90,M+F Age=75+ Geriatric patients with dementia and weight loss	N Control Group (CG)= 27 BMI 24.81 - 24.32 N Educat. Group (EG) = 25 BMI 22.71 - 22.84 N Nut.Supl Group (SG)=26 BMI 21.66 – 22.98	Oral nutritional supplementation is more effective compared to nutrition education in improving nutritional status. BMI significantly higher in the nutritional suppl. Group v control - Weight (H calc = 22.12, p<0.001), BMI (H calc = 21.94, p<0.001)	Randomized, prospective 6-month study	Moderate

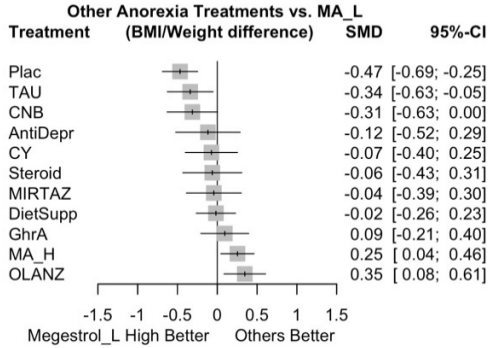
Suominen 2015[76] Nutritional Support& Education Home Visits V None	Ntotal=78 Age=87+ Geriatric patients living at home with/without dementia and weight loss	N IVgroup=40 W 75.4 ± 14.4 BMI 26.3 ± 3 N Control=38 W 74.0 ± 9.3 BMI 25.9 ± 2.9	The mean BMI remained fairly stable at +0.32 kg/m2 (95%CI -0.06 to 0.70) in the intervention group, and +0.42 kg/m2(95% CI 0.06 to 0.79) in the control group. Changes in body weight between the control and intervention groups showed no statistical differences (p = 0.68).	RCT 12 mo	Unclear
Salas 2005[77] Nutritional Supplement V Control	Ntotal=53,M+F Mean age 83+ Dementia, lack of appetite and weight loss 4 nursing homes	N NutSupp=29 W 51.5 SD 10.4 22.3SD 10.4 N Control=24 W 48.6 SD 10.7 BMI 21.7 SD 3.6	After 3mo BMI NutSupp +2.06 SD 1.90 v BMI Control +0.32 SD 3.04 p< 0.007	RCT 3mo	Moderate
Simmons 2008[78] Assisted nutrition V Control	Ntotal=124,M+F Mean age 83+ Depression, Dementia, lack of appetite and weight loss 4 nursing homes	N Nutr=61 N Control=63	0.75 unit change in final BMI value (R-squared = 0.073, p < .05) and a 4.2 pound gain in body weight (R-squared = 0.079, p < .05). Overall, 56% of participants maintained or gained weight during intervention compared to 28% during control.	RCT 24 wks	Moderate
Planas 2004[79] Nutritional Supplement V Control	Ntotal=44, M+F Mean age 72+ Dementia, lack of appetite and weight loss	N NutSupp=23 BMI 25.4 SD 4.4 N Control=21 24.4SD 2.6	After 6 months BMI NutSupp: 26.5 SD 4.5 BMI Control 26.0 SD 3.5 p<0.055	RCT 6mo	Moderate
Reinders 2019[80] Nutritional Supplement V Control	Ntotal=389 Mean age 75+ Dementia, lack of appetite and weight loss	N NutSupp=221 BMI 25.4 SD 4.4 N Control=168 24.4SD 2.6	Dietary counselling in combination with ONS had a larger intervention effect on meaningful weight gain compared to dietary counselling alone (P-value<0.001), but no statistically significant greater effect compared to ONS alone (P-value<0.54). In addition, no statistically significant difference in intervention effect was observed for dietary counseling compared to ONS alone (P-value<0.55).	Pooled estimates	Low

Additional Results for individual treatments

Treatment results for Megestrol Acetate High dose (MA_H) and Megestrol Acetate Low (MA_L) dose are shown in the figures respectively. Megestrol Acetate high dose was second best to Olanzapine and better than all other treatments. Olanzapine, MA_H, Anamorelin (GhrA), Diet supplementation, Cyproheptadine (CY) and Mirtazapine (MIRTAZ) performed better than MA_L.



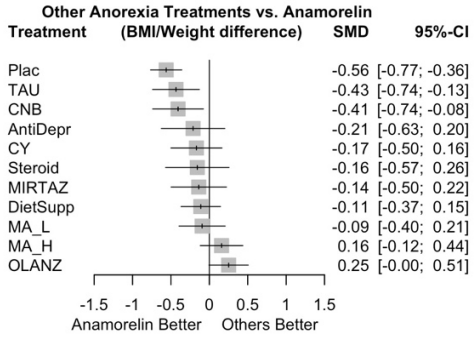
A.



B.

Subgroup analysis for cancer patients - Megestrol Acetate High dose results compared to other treatments (A). Megestrol Acetate Low dose results (B) compared to other treatments. AntiDepr=antidepressants – all classes except mirtazapine, CNB=cannabinoids (dronabilon and nabilon), CY=cyproheptadine, DietSupp= diet supplementation, GhrA=ghrelin analogues (anamorelin), MA_H=megestrol acetate high dose, MA_L= megestrol acetate low dose, MIRTAZ= mirtazapine, OLANZ=olanzapine, Plac=Placebo, TAU= Treatment as Usual, Steroid=corticosteroids.

In the figure below, we can see the performance of anamorelin, a ghrelin analogue compared to other treatments for cancer patients. Anamorelin has been used for cancer patients almost exclusively with satisfactory results. Olanzapine and MA_H performed better than anamorelin. All other treatments were less effective compared to anamorelin. Figure 7B shows the performance of cyproheptadine for all patients compared to other tratments. Results are inconclusive as antidepressants, placebo, treatment as usual and steroids are less effective than cyproheptadine.



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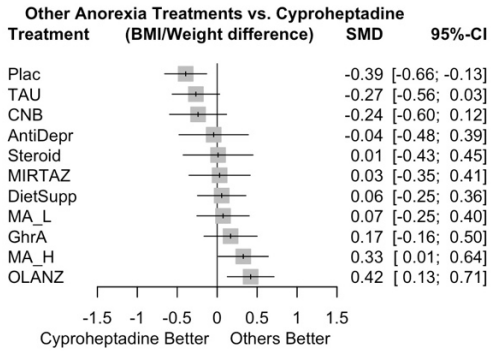
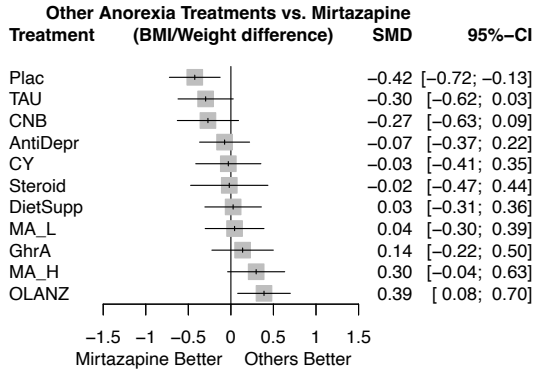


B.

Subgroup analysis for cancer patients - Anamorelin results compared to other treatments (A). Cyproheptadine results for all patients, in (B) indicate inadequate performance for for all patient groups, and as a result, they are inconclusive. It was not possible to establish treatment efficacy. AntiDepr=antidepressants – all classes except mirtazapine, CNB=cannabinoids (dronabilon and nabilon), CY=cyproheptadine, DietSupp= diet supplementation, GhrA=ghrelin analogues (anamorelin), MA_H=megestrol acetate high dose, MA_L= megestrol acetate low dose, MIRTAZ= mirtazapine, OLANZ=olanzapine, Plac=Placebo, TAU= Treatment as Usual, Steroid=corticosteroids.

Treatment results for all patient groups for mirtazapine and cannabinoids (nabilon and dronabilon mainly) are shown in figures below respectively. Dietiary interventions, anamorelin, MA_H and olanzapine performed better than mirtazapine (8A). All treatments performed better than cannabinoids (8B).



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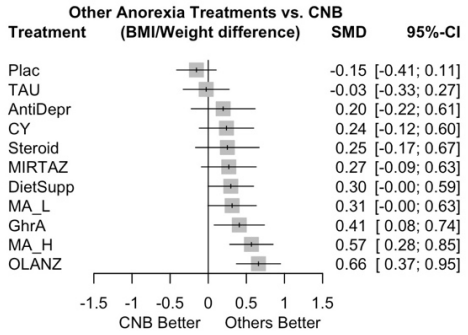
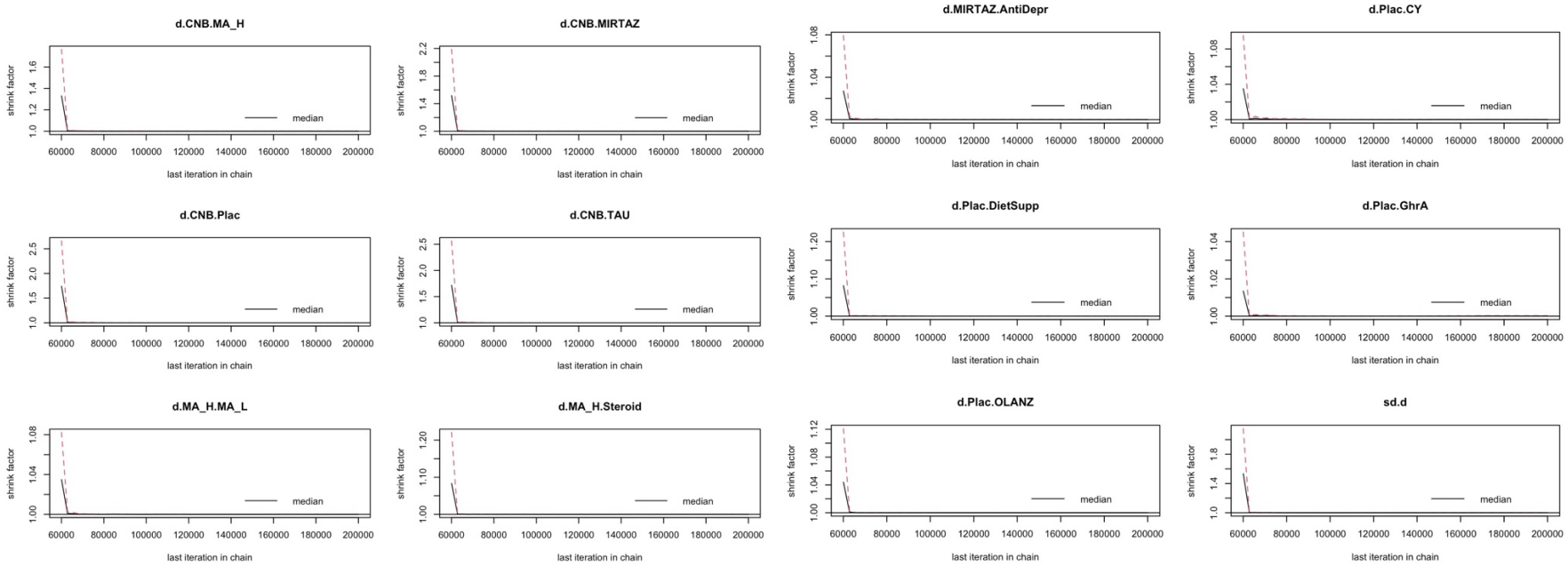


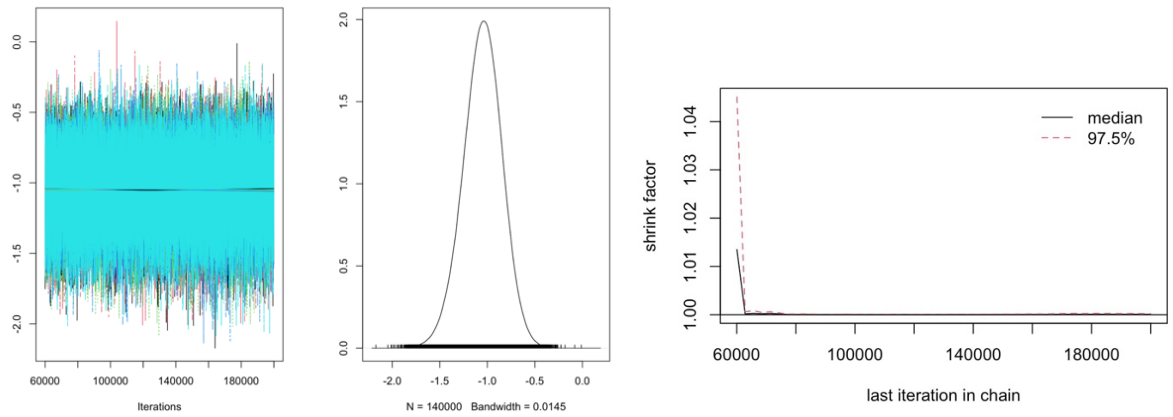
B.

All patient analysis - Mirtazapine results compared to other treatments (A). Cannabinoids (CNB) results (B) compared to other treatments. AntiDepr=antidepressants – all classes except mirtazapine, CNB=cannabinoids (dronabilon and nabilon), CY=cyproheptadine, DietSupp= diet supplementation, GhrA=ghrelin analogues (anamorelin), MA_H=megestrol acetate high dose, MA_L= megestrol acetate low dose, MIRTAZ= mirtazapine, OLANZ=olanzapine, Plac=Placebo, TAU= Treatment as Usual, Steroid=corticosteroids.

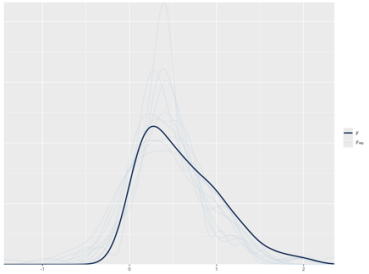
Gelman Plots NMA

Gelman plots for pairwise treatment comparison.

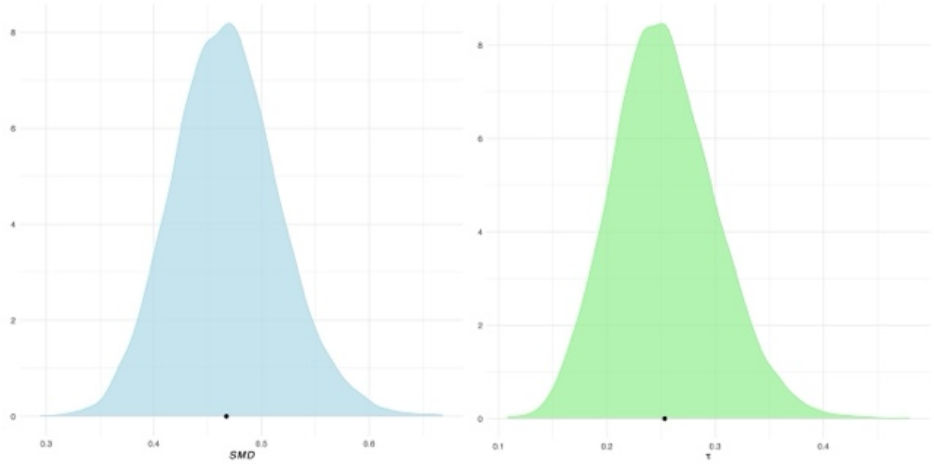




Trace for Olanzapine treatment , bayesian analysis, network training, last iteration in chain



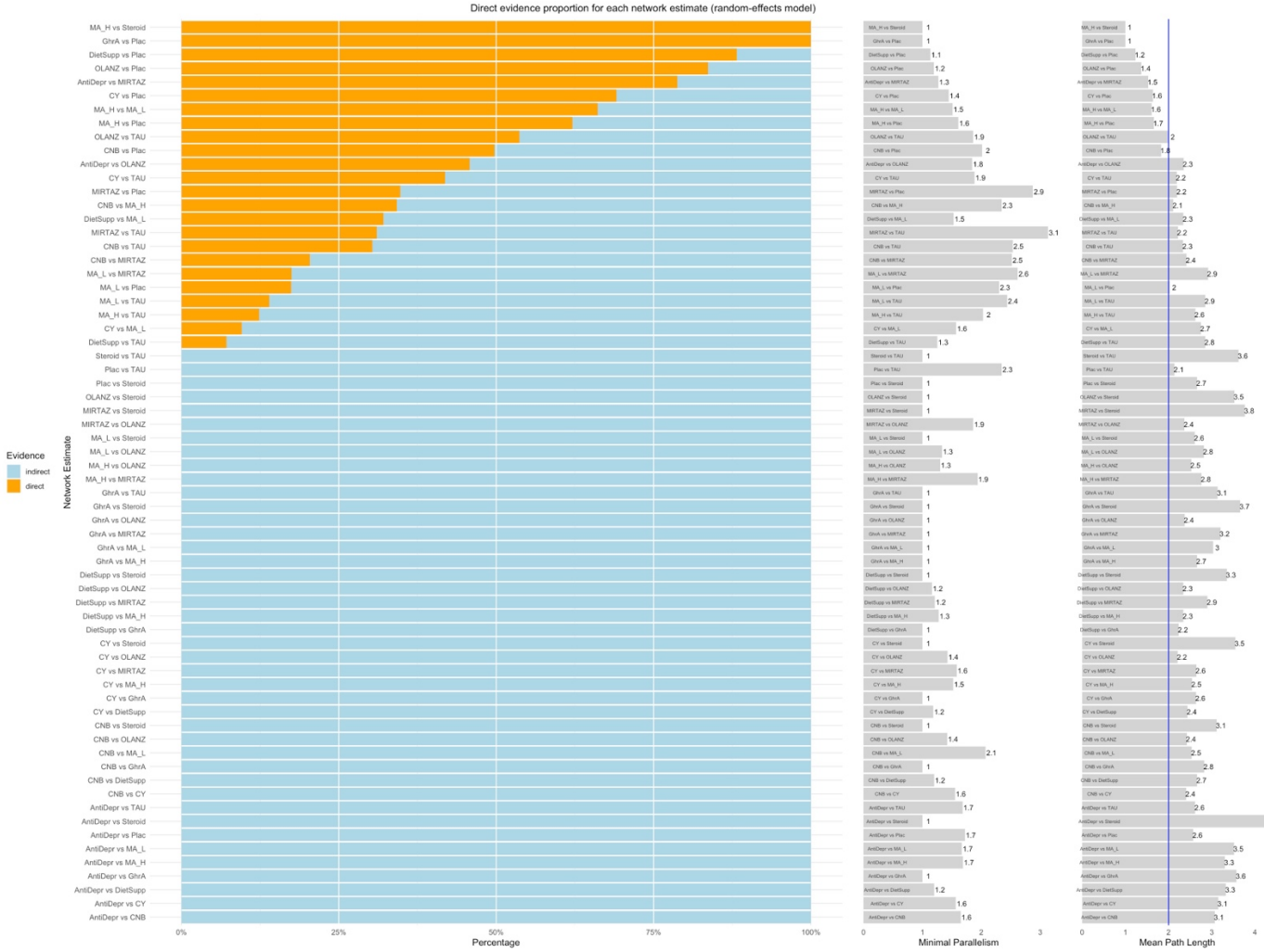
Prior distribution, bayesian analysis



A. **B.**

Bayesian Analysis, Anorexia network, SMD distribution (17A), Tau distribution (17B).

Network estimates and pairwise comparisons



Network, estimated effect sizes

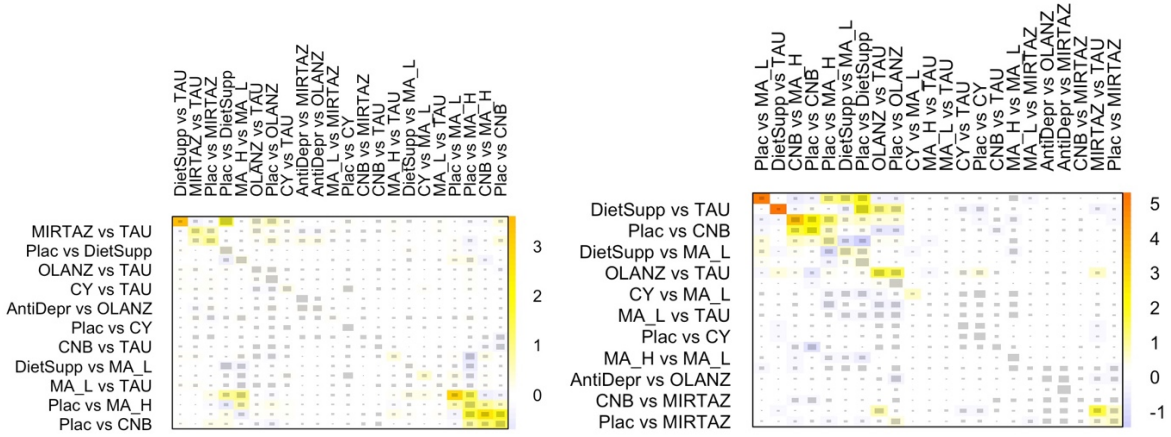
	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12
1	AntiDepr	.	.	.	.	.	.	-0.11 (-0.44; 0.22)	-0.36 (-0.89; 0.17)	.	.	.
2	0.20 (-0.22; 0.61)	CNB	.	.	.	-0.97 (-1.45; -0.48)	.	-0.23 (-1.02; 0.57)	.	0.38 (0.01; 0.75)	.	0.02 (-0.53; 0.57)
3	-0.04 (-0.48; 0.39)	-0.24 (-0.60; 0.12)	CY	.	.	.	0.27 (-0.79; 1.33)	.	.	0.42 (0.10; 0.73)	.	0.16 (-0.30; 0.62)
4	-0.10 (-0.49; 0.29)	-0.30 (-0.59; 0.00)	-0.06 (-0.36; 0.25)	DietSupp	.	.	0.04 (-0.40; 0.48)	.	.	0.42 (0.25; 0.58)	.	1.29 (0.29; 2.29)
5	-0.21 (-0.63; 0.20)	-0.41 (-0.74; -0.08)	-0.17 (-0.50; 0.16)	-0.11 (-0.37; 0.15)	GhrA	.	.	.	.	0.56 (0.36; 0.77)	.	.
6	-0.37 (-0.77; 0.02)	-0.57 (-0.85; -0.28)	-0.33 (-0.64; -0.01)	-0.27 (-0.50; -0.04)	-0.16 (-0.44; 0.12)	MA_H	0.32 (0.06; 0.57)	.	.	0.59 (0.35; 0.83)	0.32 (0.01; 0.62)	0.37 (-0.39; 1.14)
7	-0.12 (-0.52; 0.29)	-0.31 (-0.63; 0.00)	-0.07 (-0.40; 0.25)	-0.02 (-0.26; 0.23)	0.09 (-0.21; 0.40)	0.25 (0.04; 0.46)	MA_L	0.17 (-0.66; 1.00)	.	0.94 (0.41; 1.47)	.	0.18 (-0.59; 0.95)
8	-0.07 (-0.37; 0.22)	-0.27 (-0.63; 0.09)	-0.03 (-0.41; 0.35)	0.03 (-0.31; 0.36)	0.14 (-0.22; 0.50)	0.30 (-0.04; 0.63)	0.04 (-0.30; 0.39)	MIRTAZ	.	0.19 (-0.32; 0.69)	.	0.58 (-0.01; 1.16)
9	-0.46 (-0.82; -0.11)	-0.66 (-0.95; -0.37)	-0.42 (-0.71; -0.13)	-0.36 (-0.58; -0.15)	-0.25 (-0.51; 0.00)	-0.09 (-0.33; 0.14)	-0.35 (-0.61; -0.08)	-0.39 (-0.70; -0.08)	OLANZ	0.84 (0.67; 1.01)	.	0.63 (0.32; 0.94)
10	0.35 (-0.01; 0.71)	0.15 (-0.11; 0.41)	0.39 (0.13; 0.66)	0.45 (0.29; 0.61)	0.56 (0.36; 0.77)	0.72 (0.53; 0.91)	0.47 (0.25; 0.69)	0.42 (0.13; 0.72)	0.81 (0.66; 0.97)	Plac	.	.
11	-0.05 (-0.55; 0.44)	-0.25 (-0.67; 0.17)	-0.01 (-0.45; 0.43)	0.05 (-0.34; 0.43)	0.16 (-0.26; 0.57)	0.32 (0.01; 0.62)	0.06 (-0.31; 0.43)	0.02 (-0.44; 0.47)	0.41 (0.02; 0.79)	-0.41 (-0.76; -0.05)	Steroid	.
12	0.22 (-0.16; 0.61)	0.03 (-0.27; 0.33)	0.27 (-0.03; 0.56)	0.32 (0.06; 0.59)	0.43 (0.13; 0.74)	0.59 (0.32; 0.86)	0.34 (0.05; 0.63)	0.30 (-0.03; 0.62)	0.69 (0.46; 0.91)	-0.13 (-0.35; 0.10)	0.28 (-0.13; 0.68)	TAU

	AntiDepr	CNB	CY	DietSupp	GhrA	MA_H	MA_L	MIRTAZ	OLANZ	Plac	Steroid	TAU
AntiDepr	0	0.2	-0.04	-0.1	-0.21	-0.37	-0.12	-0.07	-0.46	0.35	-0.05	0.22
CNB	-0.2	0	-0.24	-0.3	-0.41	-0.57	-0.31	-0.27	-0.66	0.15	-0.25	0.03
CY	0.04	0.24	0	-0.06	-0.17	-0.33	-0.07	-0.03	-0.42	0.39	-0.01	0.27
DietSupp	0.1	0.3	0.06	0	-0.11	-0.27	-0.02	0.03	-0.36	0.45	0.05	0.32
GhrA	0.21	0.41	0.17	0.11	0	-0.16	0.09	0.14	-0.25	0.56	0.16	0.43
MA_H	0.37	0.57	0.33	0.27	0.16	0	0.25	0.3	-0.09	0.72	0.32	0.59
MA_L	0.12	0.31	0.07	0.02	-0.09	-0.25	0	0.04	-0.35	0.47	0.06	0.34
MIRTAZ	0.07	0.27	0.03	-0.03	-0.14	-0.3	-0.04	0	-0.39	0.42	0.02	0.3
OLANZ	0.46	0.66	0.42	0.36	0.25	0.09	0.35	0.39	0	0.81	0.41	0.69
Plac	-0.35	-0.15	-0.39	-0.45	-0.56	-0.72	-0.47	-0.42	-0.81	0	-0.41	-0.13

Steroid	0.05	0.25	0.01	-0.05	-0.16	-0.32	-0.06	-0.02	-0.41	0.41	0	0.28
TAU	-0.22	-0.03	-0.27	-0.32	-0.43	-0.59	-0.34	-0.3	-0.69	0.13	-0.28	0

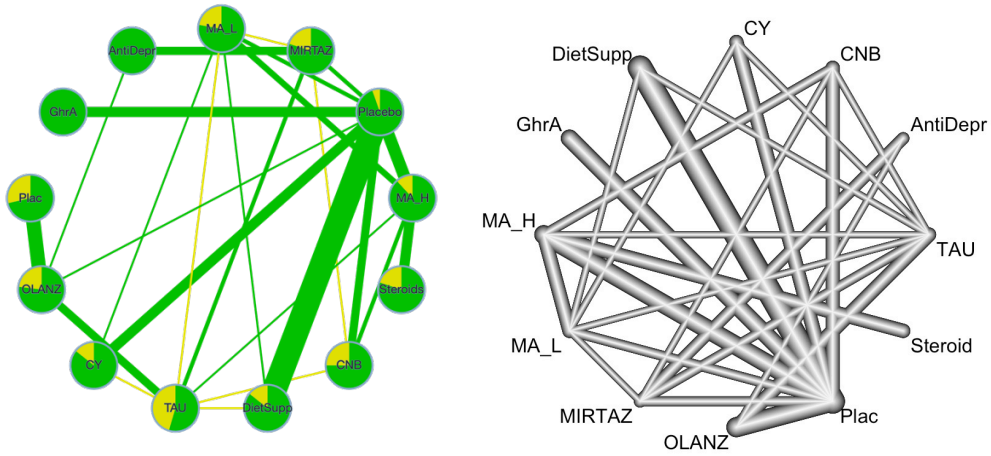
Netheat Plots

NMA result validity as well as network inconsistency for both analyses were examined with netheat plots and netsplit plots as per Veroniki et al[81], Balduzzi et al[82] and Schwarzer et al[82]. The netheat plot for the anorexia network shows some inconsistency as can be seen in figure below.



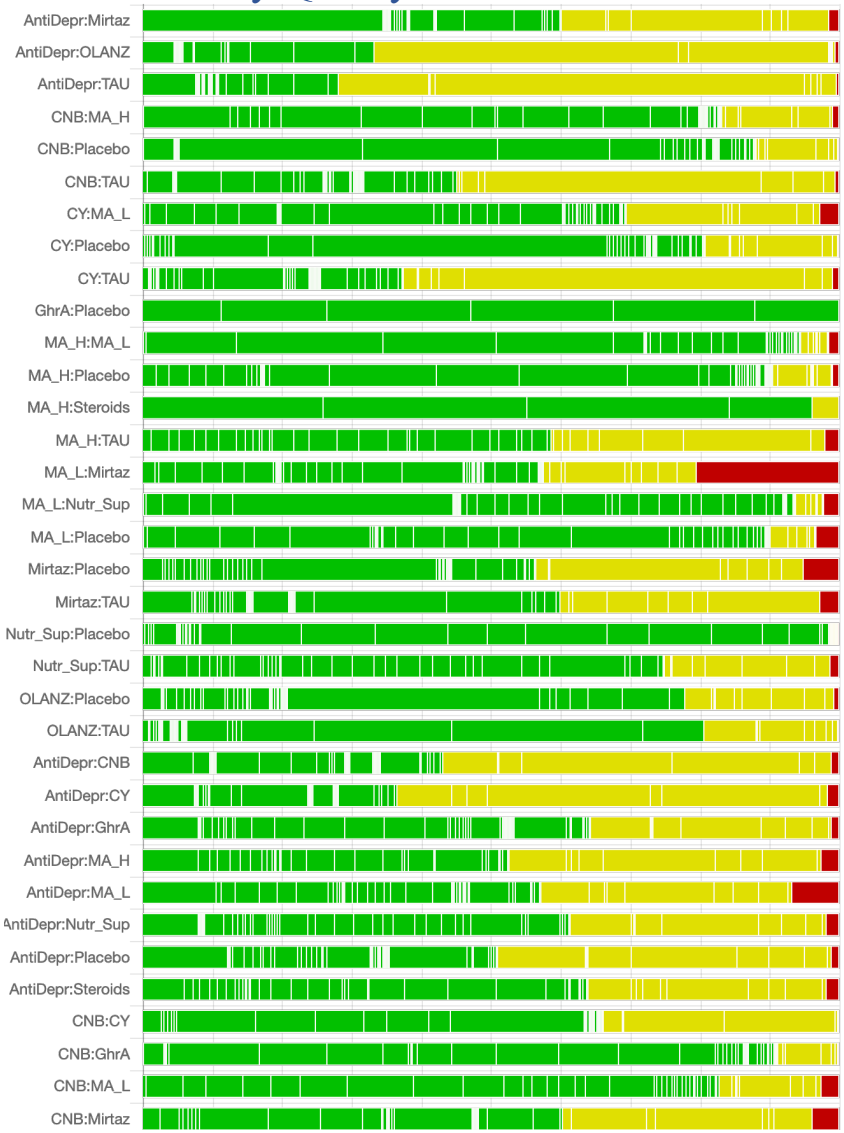
Netheat plots. Network consistency analysis for each intervention. The anorexia network shows some inconsistency as can be seen at the top left boxes that are marked red and orange. The grey squares show the contribution of direct estimate of one design, in the column vs. the network estimate in the row. Colours show the change in inconsistency when the assumption of consistency is relaxed for the effects of single designs. The diagonal colours show the inconsistency of the corresponding design. The off-diagonal colours show the inconsistency change between direct and indirect evidence. Warm colours indicate a decrease, whilst cool colours an increase. AntiDepr=antidepressants – all classes except mirtazapine, CNB=cannabinoids (dronabilon and nabilon), CY=cyproheptadine, DietSupp= diet supplementation, GhrA=ghrelin analogues (anamorelin), MA_H=megestrol acetate high dose, MA_L= megestrol acetate low dose, MIRTAZ= mirtazapine, OLANZ=olanzapine, Plac=Placebo, TAU= Treatment as Usual, Steroid=corticosteroids.

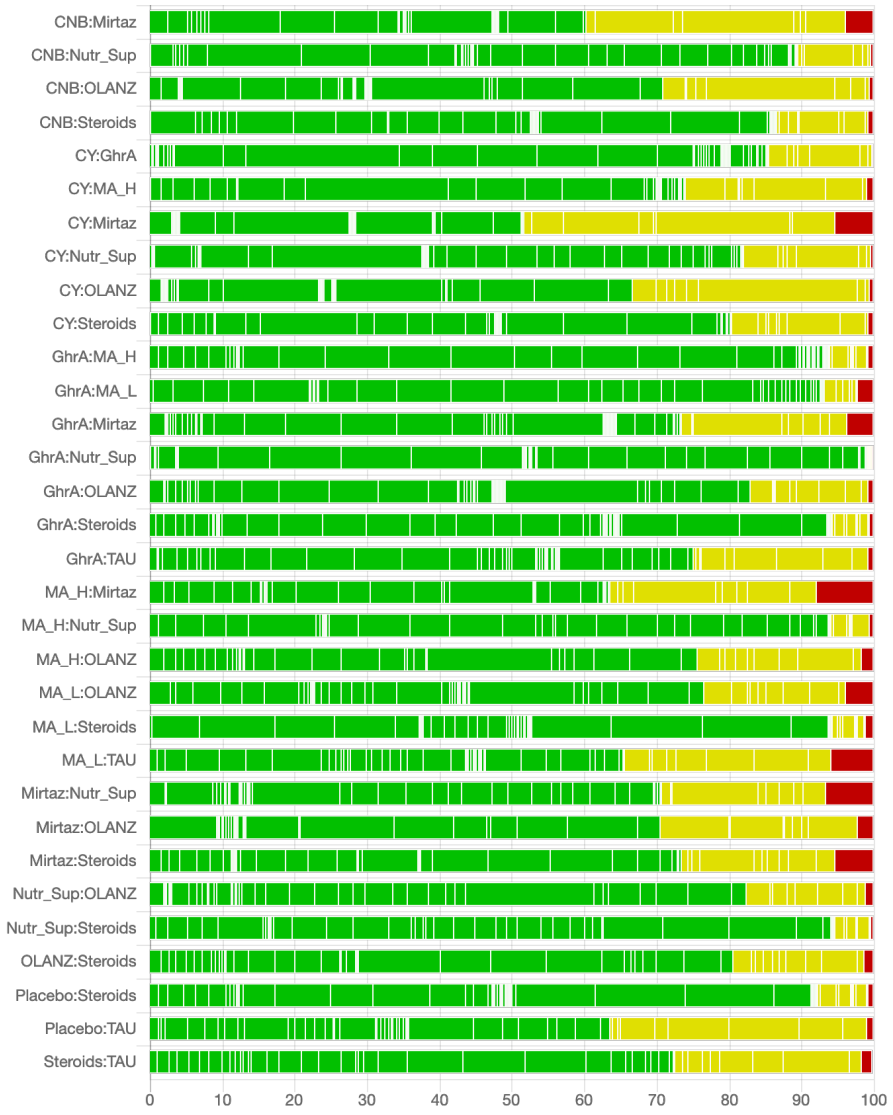
Cinema Confidence ratings



Cinema confidence ratings (quality of studies) for the anorexia network left. Node size by: Equal size, Node color by: Risk of Bias, Edge width by: Number of studies, Edge color by: Average risk of bias-ROB, Colour key: Red=major concerns, yellow= some concerns, green=no concerns. The network architecture can be seen more clearly on the right. AntiDepr=antidepressants – all classes except mirtazapine, CNB=cannabinoids (dronabilon and nabilon), CY=cyproheptadine, DietSupp= diet supplementation, GhrA=ghrelin analogues (anamorelin), MA_H=megestrol acetate high dose, MA_L= megestrol acetate low dose, MIRTAZ= mirtazapine, OLANZ=olanzapine, Plac=Placebo, TAU= Treatment as Usual, Steroid=corticosteroids.

Cinema - Study Quality





Cinema – Quality of Studies, cont.

Comparison	Number of studies	Within-study bias	Reporting bias	Imprecision	Heterogeneity	Incoherence	Confidence rating
AntiDepr:MIRTAZ	4	No concerns	Low risk	No concerns	Some concerns	No concerns	High
AntiDepr:OLANZ	1	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:MA_H	2	No concerns	Low risk	No concerns	No concerns	No concerns	High
CNB:MIRTAZ	1	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:Placebo	4	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:TAU	1	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CY:MA_L	1	No concerns	Low risk	No concerns	No concerns	No concerns	High
CY:Placebo	5	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CY:TAU	1	Some concerns	Low risk	No concerns	Some concerns	No concerns	High
DietSupp:MA_L	1	No concerns	Low risk	No concerns	No concerns	No concerns	High
DietSupp:Placebo	12	No concerns	Low risk	No concerns	Some concerns	No concerns	High
DietSupp:TAU	1	No concerns	Low risk	No concerns	Some concerns	Some concerns	High
GhrA:Placebo	5	No concerns	Low risk	No concerns	No concerns	No concerns	High
MA_H:MA_L	3	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MA_H:Placebo	6	No concerns	Low risk	No concerns	No concerns	No concerns	High
MA_H:Steroids	5	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MA_H:TAU	1	No concerns	Low risk	No concerns	No concerns	No concerns	High
MA_L:MIRTAZ	1	No concerns	Low risk	No concerns	No concerns	No concerns	High
MA_L:Placebo	2	No concerns	Low risk	No concerns	Some concerns	Some concerns	High
MA_L:TAU	1	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MIRTAZ:Placebo	2	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MIRTAZ:TAU	2	No concerns	Low risk	No concerns	Some concerns	No concerns	High
OLANZ:Plac	7	No concerns	Low risk	No concerns	No concerns	No concerns	High
OLANZ:Placebo	1	No concerns	Low risk	No concerns	No concerns	No concerns	High
OLANZ:TAU	4	No concerns	Low risk	No concerns	No concerns	No concerns	High
AntiDepr:CNB	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High

AntiDepr:CY	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
AntiDepr:DietSupp	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
AntiDepr:GhrA	0	No concerns	Low risk	Some concerns	No concerns	No concerns	High
AntiDepr:MA_H	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
AntiDepr:MA_L	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
AntiDepr:Plac	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
AntiDepr:Placebo	0	No concerns	Low risk	Some concerns	No concerns	No concerns	High
AntiDepr:Steroids	0	No concerns	Low risk	Some concerns	No concerns	No concerns	High
AntiDepr:TAU	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:CY	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:DietSupp	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:GhrA	0	No concerns	Low risk	Some concerns	No concerns	No concerns	High
CNB:MA_L	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:OLANZ	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:Plac	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CNB:Steroids	0	No concerns	Low risk	Some concerns	No concerns	No concerns	High
CY:DietSupp	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
CY:GhrA	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CY:MA_H	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
CY:MIRTAZ	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
CY:OLANZ	0	No concerns	Low risk	Some concerns	No concerns	No concerns	High
CY:Plac	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
CY:Steroids	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
DietSupp:GhrA	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
DietSupp:MA_H	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
DietSupp:MIRTAZ	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
DietSupp:OLANZ	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
DietSupp:Plac	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
DietSupp:Steroids	0	No concerns	Low risk	No concerns	No concerns	No concerns	High

GhrA:MA_H	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
GhrA:MA_L	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
GhrA:MIRTAZ	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
GhrA:OLANZ	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
GhrA:Plac	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
GhrA:Steroids	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
GhrA:TAU	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MA_H:MIRTAZ	0	No concerns	Low risk	Some concerns	No concerns	No concerns	High
MA_H:OLANZ	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
MA_H:Plac	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
MA_L:OLANZ	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MA_L:Plac	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
MA_L:Steroids	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MIRTAZ:OLANZ	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
MIRTAZ:Plac	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
MIRTAZ:Steroids	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
OLANZ:Steroids	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
Plac:Placebo	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
Plac:Steroids	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
Plac:TAU	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High
Placebo:Steroids	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
Placebo:TAU	0	No concerns	Low risk	No concerns	No concerns	No concerns	High
Steroids:TAU	0	No concerns	Low risk	No concerns	Some concerns	No concerns	High

Cinema - League Table

AntiDepr	**-0.496 (-1.505, 0.512)**	**-0.684 (-1.721, 0.353)**	**-0.883 (-1.847, 0.081)**	**-1.082 (-2.048, -0.116)**	**-0.847 (-1.824, 0.131)**	**-0.561 (-1.317, 0.196)**	**-0.775 (-1.720, 0.171)**	**-0.772 (-1.724, 0.180)**	**-0.302 (-1.234, 0.630)**	**-0.866 (-1.882, 0.149)**	**0.041 (-0.878, 0.960)**
0.496 (-0.512, 1.505)	CNB	-0.188 (-0.784, 0.408)	-0.387 (-0.845, 0.071)	-0.586 (-1.032, -0.140)	-0.351 (-0.828, 0.127)	-0.065 (-0.732, 0.602)	-0.278 (-0.705, 0.148)	-0.276 (-0.905, 0.353)	0.194 (-0.191, 0.580)	-0.370 (-0.914, 0.174)	0.537 (-0.102, 1.177)
0.684 (-0.353, 1.721)	0.188 (-0.408, 0.784)	CY	-0.199 (-0.716, 0.319)	-0.398 (-0.920, 0.124)	-0.163 (-0.707, 0.381)	0.123 (-0.586, 0.832)	-0.090 (-0.581, 0.400)	-0.088 (-0.762, 0.586)	0.382 (-0.072, 0.837)	-0.182 (-0.791, 0.426)	0.725 (0.042, 1.409)
0.883 (-0.081, 1.847)	0.387 (-0.071, 0.845)	0.199 (-0.319, 0.716)	GhrA	-0.199 (-0.556, 0.157)	0.036 (-0.352, 0.424)	0.322 (-0.276, 0.920)	0.108 (-0.201, 0.417)	0.111 (-0.444, 0.666)	0.581 (0.334, 0.828)	0.016 (-0.458, 0.491)	0.924 (0.357, 1.491)
1.082 (0.116, 2.048)	0.586 (0.140, 1.032)	0.398 (-0.124, 0.920)	0.199 (-0.157, 0.556)	MA_H	0.235 (-0.034, 0.504)	0.521 (-0.080, 1.122)	0.308 (0.006, 0.610)	0.310 (-0.248, 0.868)	0.780 (0.523, 1.037)	0.216 (-0.097, 0.529)	1.123 (0.554, 1.693)
0.847 (-0.131, 1.824)	0.351 (-0.127, 0.828)	0.163 (-0.381, 0.707)	-0.036 (-0.424, 0.352)	-0.235 (-0.504, 0.034)	MA_L	0.286 (-0.333, 0.905)	0.072 (-0.250, 0.395)	0.075 (-0.502, 0.652)	0.545 (0.246, 0.844)	-0.020 (-0.432, 0.393)	0.888 (0.301, 1.475)
0.561 (-0.196, 1.317)	0.065 (-0.602, 0.732)	-0.123 (-0.832, 0.586)	-0.322 (-0.920, 0.276)	-0.521 (-1.122, 0.080)	-0.286 (-0.905, 0.333)	Mirtaz	-0.214 (-0.781, 0.354)	-0.211 (-0.788, 0.366)	0.259 (-0.285, 0.803)	-0.305 (-0.983, 0.372)	0.602 (0.081, 1.123)
0.775 (-0.171, 1.720)	0.278 (-0.148, 0.705)	0.090 (-0.400, 0.581)	-0.108 (-0.417, 0.201)	-0.308 (-0.610, -0.006)	-0.072 (-0.395, 0.250)	0.214 (-0.354, 0.781)	Nutr_Sup	0.003 (-0.517, 0.522)	0.473 (0.287, 0.658)	-0.092 (-0.526, 0.343)	0.816 (0.288, 1.343)
0.772 (-0.180, 1.724)	0.276 (-0.353, 0.905)	0.088 (-0.586, 0.762)	-0.111 (-0.666, 0.444)	-0.310 (-0.868, 0.248)	-0.075 (-0.652, 0.502)	0.211 (-0.366, 0.788)	-0.003 (-0.522, 0.517)	OLANZ	0.470 (-0.027, 0.967)	-0.094 (-0.734, 0.546)	0.813 (0.462, 1.165)
0.302 (-0.630, 1.234)	-0.194 (-0.580, 0.191)	-0.382 (-0.837, 0.072)	-0.581 (-0.828, -0.334)	-0.780 (-1.037, -0.523)	-0.545 (-0.844, -0.246)	-0.259 (-0.803, 0.285)	-0.473 (-0.658, -0.287)	-0.470 (-0.967, 0.027)	Placebo	-0.564 (-0.969, -0.160)	0.343 (-0.167, 0.853)
0.866 (-0.149, 1.882)	0.370 (-0.174, 0.914)	0.182 (-0.426, 0.791)	-0.016 (-0.491, 0.458)	-0.216 (-0.529, 0.097)	0.020 (-0.393, 0.432)	0.305 (-0.372, 0.983)	0.092 (-0.343, 0.526)	0.094 (-0.546, 0.734)	0.564 (0.160, 0.969)	Steroids	0.908 (0.258, 1.557)
-0.041 (-0.960, 0.878)	-0.537 (-1.177, 0.102)	-0.725 (-1.409, -0.042)	-0.924 (-1.491, -0.357)	-1.123 (-1.693, -0.554)	-0.888 (-1.475, -0.301)	-0.602 (-1.123, -0.081)	-0.816 (-1.343, -0.288)	-0.813 (-1.165, -0.462)	-0.343 (-0.853, 0.167)	-0.908 (-1.557, -0.258)	TAU

Meta-regression using Machine Learning - Multi-layer perceptron

Notes

Output Created		09-JAN-2025 16:20:26
Comments		
Input	Data	/SPSS/Others.ANDataset.08.01.2025.sav
	Active Dataset	DataSet10
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	74
Missing Value Handling	Definition of Missing	User- and system-missing values are treated as missing.
	Cases Used	Statistics are based on cases with valid data for all variables used by the procedure.
Weight Handling		not applicable
Syntax		MLP treat1 (MLEVEL=N) BY PtGroup treat2 WITH Duration TE /RESCALE COVARIATE=NORMALIZED /PARTITION TRAINING=7 TESTING=3 HOLDOUT=0 /ARCHITECTURE AUTOMATIC=NO HIDDENLAYERS=1 (NUMUNITS=AUTO) HIDDENFUNCTION=TANH OUTPUTFUNCTION=TANH /CRITERIA TRAINING=BATCH OPTIMIZATION=SCALEDCONJUGATE LAMBDAINITIAL=0.0000005 SIGMAINITIAL=0.00005 INTERVALCENTER=0 INTERVALOFFSET=0.5 MEMSIZE=1000 /PRINT CPS NETWORKINFO SUMMARY CLASSIFICATION SOLUTION IMPORTANCE /PLOT NETWORK ROC GAIN LIFT PREDICTED /STOPPINGRULES ERRORSTEPS= 1 (DATA=AUTO) TRAININGTIMER=ON (MAXTIME=15) MAXEPOCHS=AUTO ERRORCHANGE=1.0E-4 ERRORRATIO=0.001 /MISSING USERMISSING=EXCLUDE .
Resources	Processor Time	00:00:01.10
	Elapsed Time	00:00:01.00

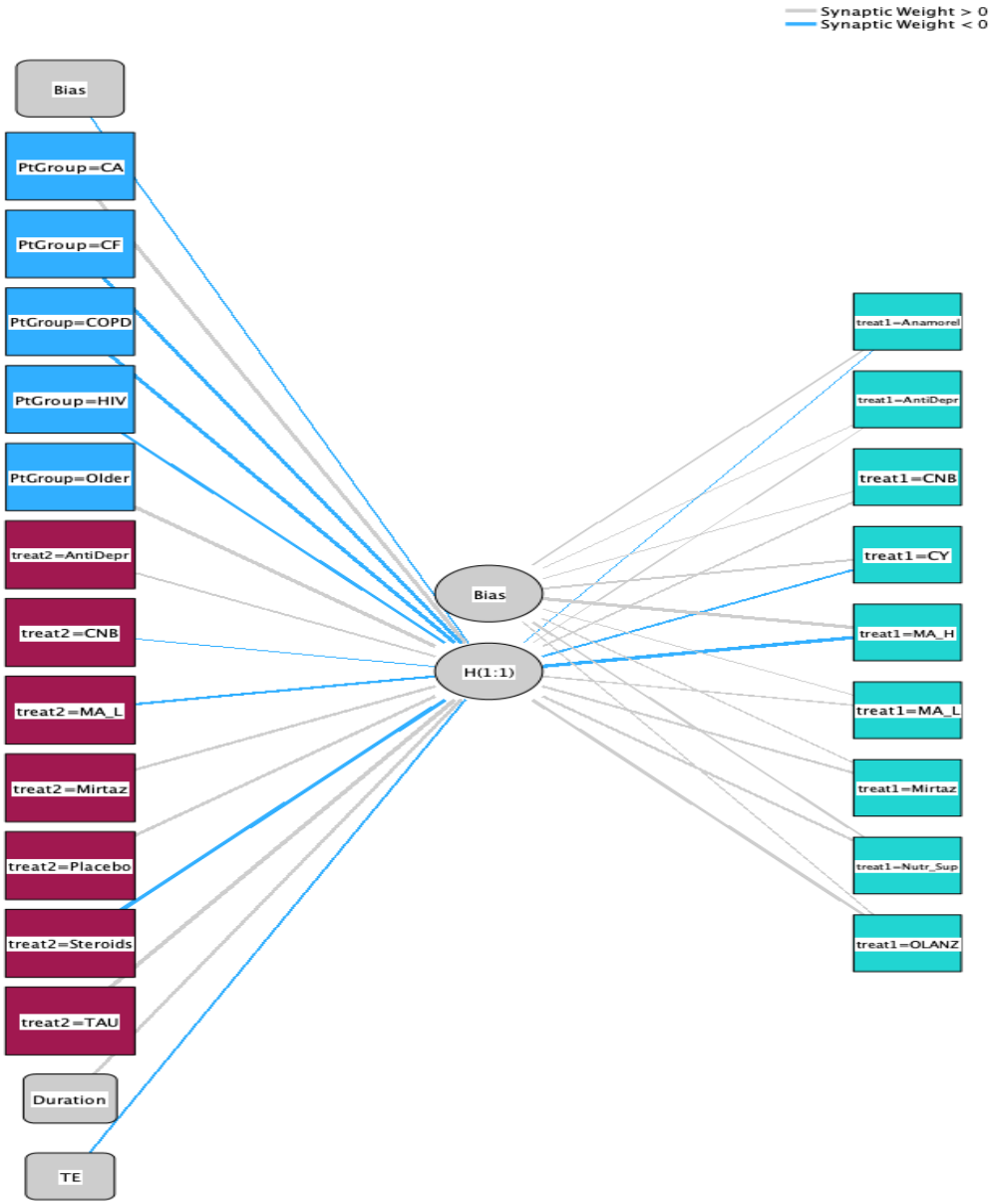
Case Processing Summary

		N	Percent
Sample	Training	55	74.3%
	Testing	19	25.7%
Valid		74	100.0%
Excluded		0	
Total		74	

Network Information

Input Layer	Factors	1	PtGroup
		2	treat2
	Covariates	1	Duration
		2	TE
	Number of Units[a]		14
	Rescaling Method for Covariates		Normalized
Hidden Layer(s)	Number of Hidden Layers		1
	Number of Units in Hidden Layer 1[a]		1
	Activation Function		Hyperbolic tangent
Output Layer	Dependent Variables	1	treat1
	Number of Units		9
	Activation Function		Hyperbolic tangent
	Error Function		Sum of Squares

a. Excluding the bias unit



Hidden layer activation function: Hyperbolic tangent

Output layer activation function: Hyperbolic tangent

Model Summary

Training	Sum of Squares Error	19.686
	Percent Incorrect Predictions	63.6%
	Stopping Rule Used	1 consecutive step(s) with no decrease in error[a]
	Training Time	0:00:00.01
Testing	Sum of Squares Error	7.616
	Percent Incorrect Predictions	68.4%

Dependent Variable: treat1

a. Error computations are based on the testing sample.

Parameter Estimates

			Predicted			
		Hidden Layer 1	Output Layer			
Predictor		H(1:1)	[treat1=Anamorel]	[treat1=AntiDepr]	[treat1=CNB]	[treat1=CY]
Input Layer	(Bias)	-.066				
	[PtGroup=CA]	.401				
	[PtGroup=CF]	-.358				
	[PtGroup=COPD]	-.473				
	[PtGroup=HIV]	-.225				
	[PtGroup=Older]	.674				
	[treat2=AntiDepr]	.108				
	[treat2=CNB]	-.024				
	[treat2=MA_L]	-.220				
	[treat2=Mirtaz]	.241				
	[treat2=Placebo]	.254				
	[treat2=Steroids]	-.541				
	[treat2=TAU]	.716				
	Duration	.244				
	TE	-.087				
Hidden Layer 1	(Bias)		.070	.003	.024	.132
	H(1:1)		-.002	.032	.079	-.109

Parameter Estimates

		Predicted Output Layer				
Predictor		[treat1=MA_H]	[treat1=MA_L]	[treat1=Mirtaz]	[treat1=Nutr_Sup]	[treat1=OLANZ]
Input Layer	(Bias)					
	[PtGroup=CA]					
	[PtGroup=CF]					
	[PtGroup=COPD]					
	[PtGroup=HIV]					
	[PtGroup=Older]					
	[treat2=AntiDepr]					
	[treat2=CNB]					

	[treat2=MA_L]						
	[treat2=Mirtaz]						
	[treat2=Placebo]						
	[treat2=Steroids]						
	[treat2=TAU]						
	Duration						
	TE						
Hidden Layer 1	(Bias)	.668	.026	.054	.079	.043	
	H(1:1)	-.861	.075	.134	.213	.266	

Classification

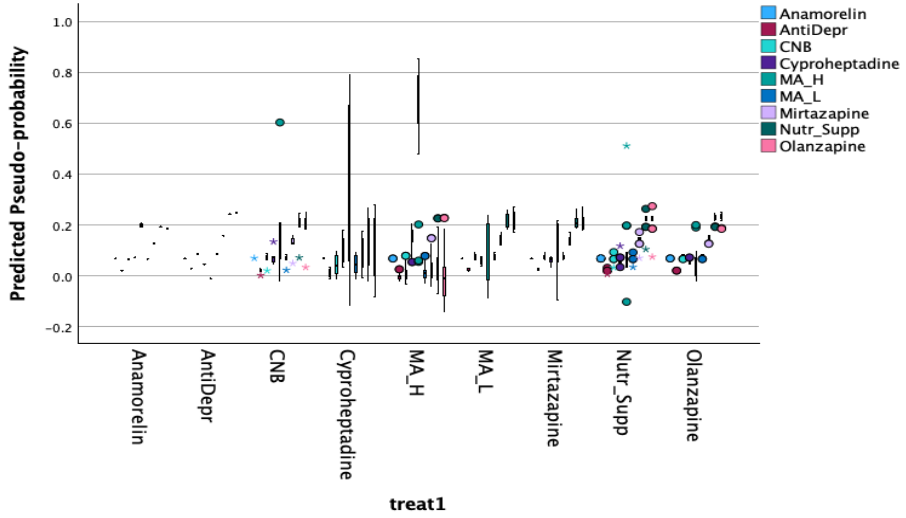
Sample	Observed	Predicted						
		Anamorelin	AntiDepr	CNB	Cyproheptadine	MA_H	MA_L	Mirtazapine
Training	Anamorelin	0	0	0	0	4	0	0
	AntiDepr	0	0	0	0	0	0	0
	CNB	0	0	0	0	1	0	0
	Cyproheptadine	0	0	0	0	3	0	0
	MA_H	0	0	0	0	13	0	0
	MA_L	0	0	0	0	2	0	0
	Mirtazapine	0	0	0	0	3	0	0
	Nutr_Supp	0	0	0	0	2	0	0
	Olanzapine	0	0	0	0	0	0	0
	Overall Percent	0.0%	0.0%	0.0%	0.0%	50.9%	0.0%	0.0%
Testing	Anamorelin	0	0	0	0	2	0	0
	AntiDepr	0	0	0	0	0	0	0
	CNB	0	0	0	0	2	0	0
	Cyproheptadine	0	0	0	0	1	0	0
	MA_H	0	0	0	0	2	0	0
	MA_L	0	0	0	0	1	0	0
	Mirtazapine	0	0	0	0	0	0	0
	Nutr_Supp	0	0	0	0	1	0	0
	Olanzapine	0	0	0	0	1	0	0
	Overall Percent	0.0%	0.0%	0.0%	0.0%	52.6%	0.0%	0.0%

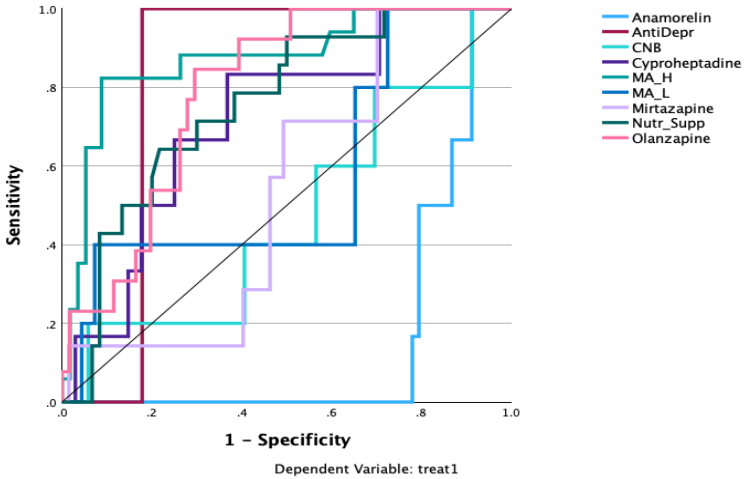
Classification

Sample	Observed	Predicted		
		Nutr_Supp	Olanzapine	Percent Correct
Training	Anamorelin	0	0	0.0%
	AntiDepr	0	1	0.0%
	CNB	0	2	0.0%
	Cyproheptadine	0	2	0.0%
	MA_H	0	2	86.7%
	MA_L	0	1	0.0%
	Mirtazapine	1	2	0.0%
	Nutr_Supp	1	7	10.0%

	Olanzapine	2	6	75.0%
	Overall Percent	7.3%	41.8%	36.4%
Testing	Anamorelin	0	0	0.0%
	AntiDepr	0	0	0.0%
	CNB	0	0	0.0%
	Cyproheptadine	0	0	0.0%
	MA_H	0	0	100.0%
	MA_L	0	1	0.0%
	Mirtazapine	1	0	0.0%
	Nutr_Supp	0	3	0.0%
	Olanzapine	0	4	80.0%
	Overall Percent	5.3%	42.1%	31.6%

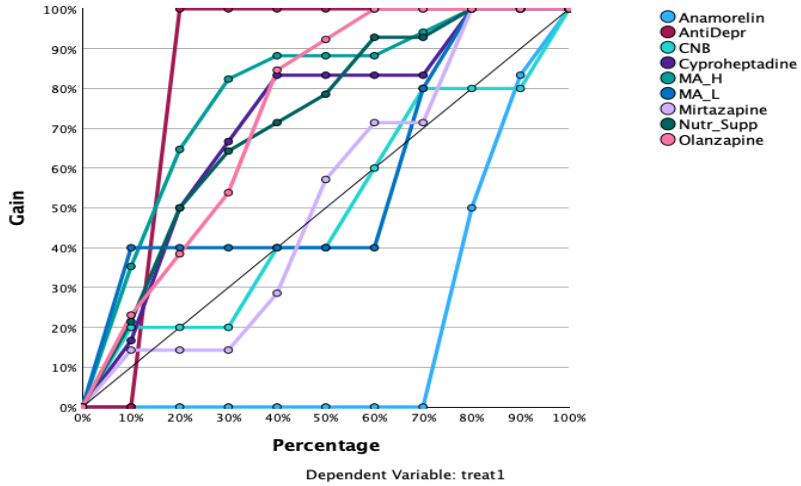
Dependent Variable: treat1

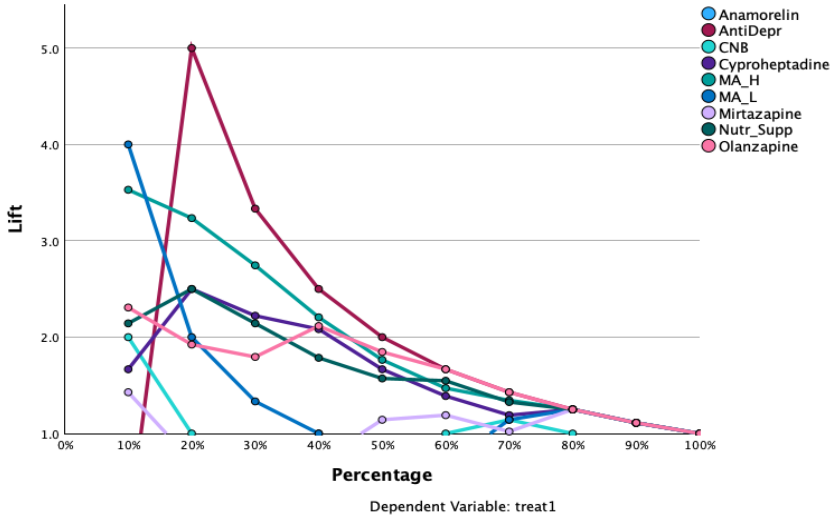




Area Under the Curve

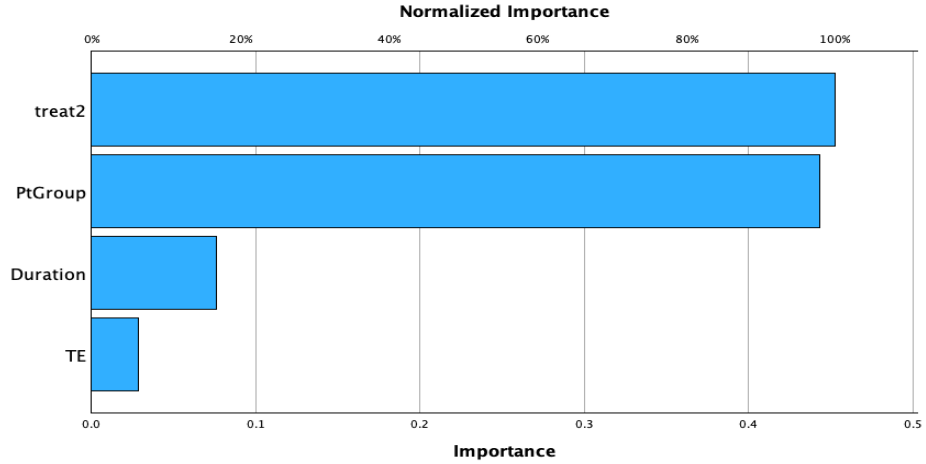
		Area
treat1	Anamorelin	.157
	AntiDepr	.822
	CNB	.472
	Cyproheptadine	.721
	MA_H	.874
	MA_L	.571
	Mirtazapine	.537
	Nutr_Supp	.758
	Olanzapine	.792





Independent Variable Importance

	Importance	Normalized Importance
PtGroup	.443	97.9%
treat2	.453	100.0%
Duration	.076	16.8%
TE	.028	6.3%



Multilayer Perceptron

Notes

Output Created		09-JAN-2025 16:22:21
Comments		
Input	Data	/Others.ANDataset.08.01.2025.sav
	Active Dataset	DataSet10
	Filter	<none>
	Weight	<none>
	Split File	<none>
	N of Rows in Working Data File	74
Missing Value Handling	Definition of Missing	User- and system-missing values are treated as missing.
	Cases Used	Statistics are based on cases with valid data for all variables used by the procedure.
Weight Handling		not applicable
Syntax		MLP TE (MLEVEL=S) BY PtGroup treat1 WITH Duration seTE

		/RESCALE COVARIATE=NORMALIZED /PARTITION TRAINING=7 TESTING=3 HOLDOUT=0 /ARCHITECTURE AUTOMATIC=NO HIDDENLAYERS=1 (NUMUNITS=AUTO) HIDDENFUNCTION=TANH OUTPUTFUNCTION=TANH /CRITERIA TRAINING=BATCH OPTIMIZATION=SCALEDCONJUGATE LAMBDAINITIAL=0.0000005 SIGMAINITIAL=0.00005 INTERVALCENTER=0 INTERVALOFFSET=0.5 MEMSIZE=1000 /PRINT CPS NETWORKINFO SUMMARY CLASSIFICATION SOLUTION IMPORTANCE /PLOT NETWORK ROC GAIN LIFT PREDICTED /STOPPINGRULES ERRORSTEPS= 1 (DATA=AUTO) TRAININGTIMER=ON (MAXTIME=15) MAXEPOCHS=AUTO ERRORCHANGE=1.0E-4 ERRORRATIO=0.001 /MISSING USERMISSING=EXCLUDE .
Resources	Processor Time	00:00:00.54
	Elapsed Time	00:00:00.00

Warnings

One or more cases in the testing or holdout sample have factor or dependent variable values that do not occur in the training sample. These cases are excluded from the analysis.

Case Processing Summary

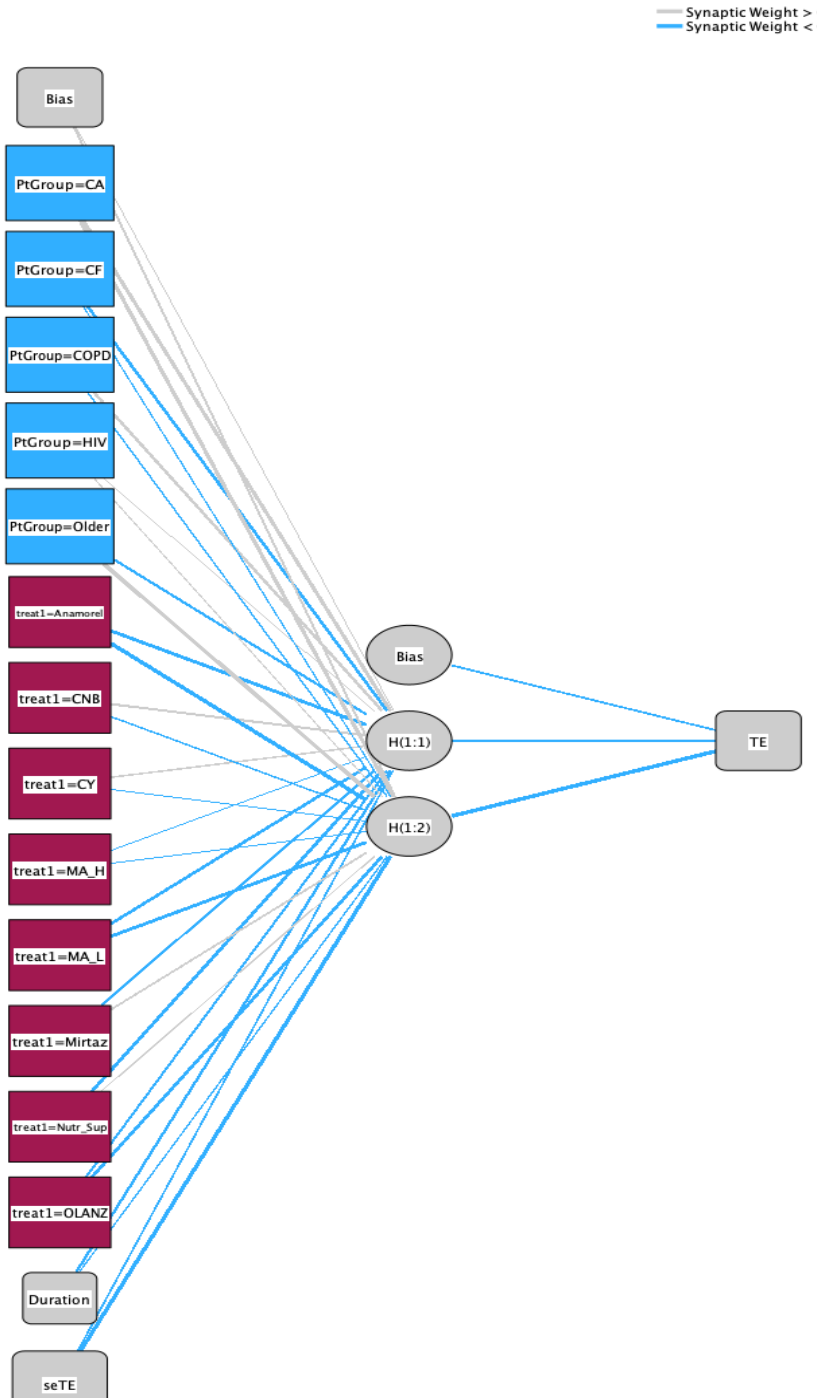
		N	Percent
Sample	Training	45	61.6%
	Testing	28	38.4%
Valid		73	100.0%
Excluded		1	
Total		74	

Network Information

Input Layer	Factors	1	PtGroup
		2	treat1
	Covariates	1	Duration
		2	seTE
	Number of Units[a]		15
	Rescaling Method for Covariates		Normalized
Hidden Layer(s)	Number of Hidden Layers		1

	Number of Units in Hidden Layer 1[a]		2
	Activation Function		Hyperbolic tangent
Output Layer	Dependent Variables	1	TE
	Number of Units		1
	Rescaling Method for Scale Dependents		Adjusted normalized
	Activation Function		Hyperbolic tangent
	Error Function		Sum of Squares

a. Excluding the bias unit


Synaptic Weight > 0
Synaptic Weight < 0
Bias
PtGroup=CA
PtGroup=CF
PtGroup=COPD
PtGroup=HIV
PtGroup=Older
treat1=Anamorel
treat1=CNB
treat1=CY
treat1=MA_H
treat1=MA_L
treat1=Mirtaz
treat1=Nutr_Sup
treat1=OLANZ
Duration
seTE
Bias
H(1:1)
H(1:2)
TE

Model Summary

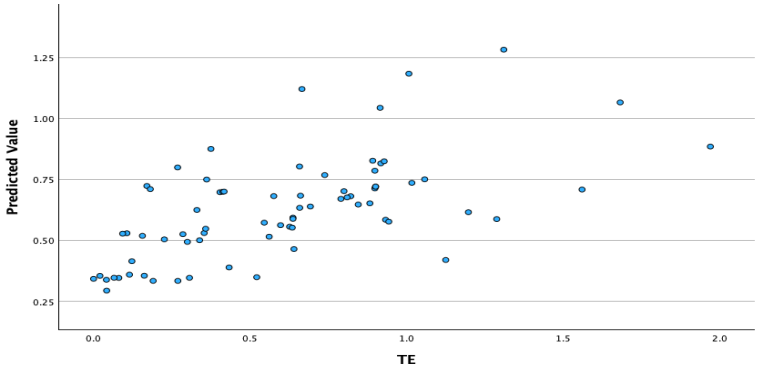
Training	Sum of Squares Error	2.044
	Relative Error	.489
	Stopping Rule Used	1 consecutive step(s) with no decrease in error[a]
	Training Time	0:00:00.01
Testing	Sum of Squares Error	1.982
	Relative Error	.903

Dependent Variable: TE

a. Error computations are based on the testing sample.

Parameter Estimates

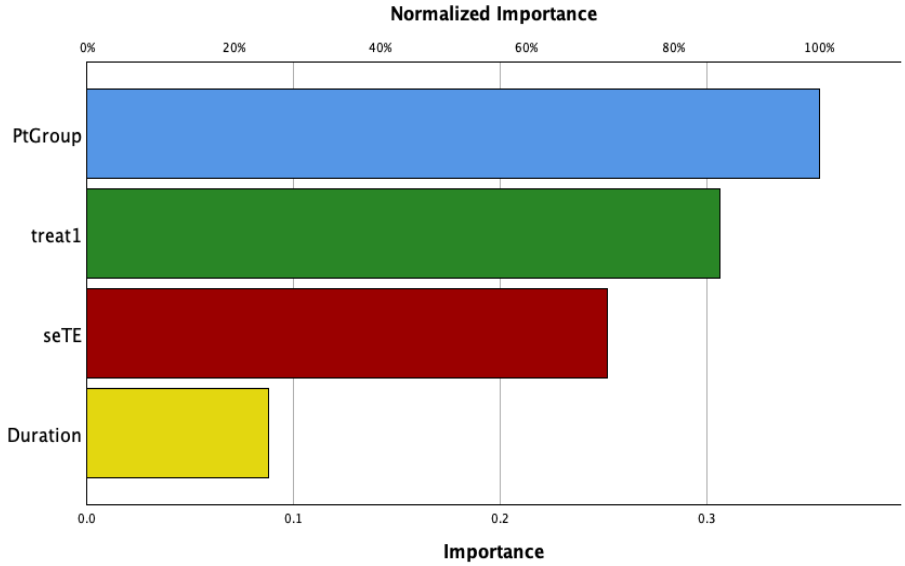
		Predicted		
		Hidden Layer 1		Output Layer
Predictor		H(1:1)	H(1:2)	TE
Input Layer	(Bias)	.059	.243	
	[PtGroup=CA]	.433	.494	
	[PtGroup=CF]	-.361	-.131	
	[PtGroup=COPD]	.353	-.148	
	[PtGroup=HIV]	.047	.104	
	[PtGroup=Older]	-.315	.535	
	[treat1=Anamorel]	-.414	-.639	
	[treat1=CNB]	.287	-.163	
	[treat1=CY]	.184	-.052	
	[treat1=MA_H]	-.020	-.051	
	[treat1=MA_L]	-.365	-.401	
	[treat1=Mirtaz]	-.313	.240	
	[treat1=Nutr_Sup]	-.400	.110	
	[treat1=OLANZ]	-.263	-.369	
	Duration	-.317	-.136	
	seTE	-.237	-.622	
Hidden Layer 1	(Bias)			-.243
	H(1:1)			-.333
	H(1:2)			-.757



Independent Variable Importance

	Importance	Normalized Importance
PtGroup	.354	100.0%
treat1	.306	86.4%
Duration	.088	24.8%
seTE	.252	71.1%

In the figure below, we see how the ANN classified the importance of covariates and factors in predicting treatment efficiency. The ANN correctly identified that the patient group (i.e patient illness type) is the most important factor, followed by intervention type – i.e. which drug was used. It is noted that for patients with chronic illness, or old age, where life expectancy is low, treatment type was significantly more important than the duration of the treatment.



Factor importance analysis multi-layer perceptron classifications. PtGroup is a grouping variable for the type of condition – cancer, CF, HIV/AIDS, COPD, elderly with mixed conditions, with or without dementia, treat1 is another grouping variable AntiDepr=antidepressants – all classes except mirtazapine, CNB=cannabinoids (dronabilon and nabilon), CY=cyproheptadine for Nutr_Supp= diet supplementation, GhrA=ghrelin analogues (anamorelin), MA_H=megestrol acetate high dose, MA_L= megestrol acetate low dose, MIRTAZ= mirtazapine, OLANZ=olanzapine, Plac=Placebo, TAU= treatment as usual, Steroid=corticosteroids, duration of treatment in weeks, seTE= pooled weighted standard error of effect size

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