SUPPLEMENTARY MATERIAL

CHARACTERISTICS OF INCLUDED STUDIES AND RISK OF BIAS TABLES

Study Characteristics: Batterham 2001	
Methods	Randomized control trial, not blinded, no placebo
Participants	15 HIV positive patients a) 5 participants, mean age 42, 100% male b) 6 participants (5 completed), mean age 48, 100% male c) 4 participants, mean age 46, 100% male
Interventions	3 arm trial a) Dietary counseling b) Nandrolone decanoate (100mg/ fortnight intramuscular injection) c) Megestrol acetate (400mg/day oral)
Outcomes	Weight Appetite (10 point visual analogue scale) LBM (measurement published: fat free mass by bioelectrical impendence analysis) Plus: dietary intake
Notes	Length of treatment: 12 weeks Quality score: 2 Data request: raw data provided by author Cachexia criteria: unintentional weight loss >5% usual body weight despite adequate nutritional intake for > 1 month Dropout rate: 20% Time of analysis: 12 weeks (14 patients) 5 patients receiving dietary advice then went on to receive either ND (3) or MA (2). Not included in analysis as neither of the 2 patients whom received MA completed the trial.

Risk of Bias: Batterham 2001		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	No information given. Matched baseline characteristics.
Allocation concealment (selection bias)	Unclear risk	No information given
Blinding of participants and personnel (performance bias)	Low risk	Not blinded - however not possible as Nandrolone deconate (ND) is given as IM injection
Blinding of outcome assessment (detection bias)	Low risk	Not blinded - however not possible as Nandrolone deconate (ND) is given as IM injection
Incomplete outcome data (attrition bias)	Low risk	Only 1 dropout - pain at injection site (ND group).
Selective reporting (reporting bias)	High risk	Unclear why results at 24 weeks not published. Raw data provided by author.
Other bias	Low risk	Matched baseline characteristics. No funding from industry.

Study Characteristics: Gołębiewska 2012	
Methods	Clinical trial (open trial), not randomized
Participants	32 end stage renal failure on dialysis (peritoneal or haemodialysis), mean age 70, 56% male
Interventions	Megestrol acetate (160mg/day oral)
Outcomes	Weight HRQOL: modified Hospital Anxiety and Depression Score (HADS), Purpose In Life test (PIL test), Cantril's Ladder, Brief Fatigue Inventory (BFI). HADS used in analysis. Serum albumin Plus: nutritional scores
Notes	Length of treatment: up to 6 months (open trial). Mean length of treatment 3.5 months Data request: raw data provided by author Cachexia criteria: serum albumin </= 3.8g/dL Drop out rate: open trial Time of analysis: 1 month (32 patients), 2 months (26), 3 months (18), 4 months (14), 5 months (12), 6 months (12) Data used: 2 month data (3 month data used for HRQOL)

Risk of Bias: Gołębiewska 2012		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Non-randomized trial
Allocation concealment (selection bias)	High risk	Non-randomized trial
Blinding of participants and personnel (performance bias)	High risk	Non-randomized trial
Blinding of outcome assessment (detection bias)	High risk	Non-randomized trial
Incomplete outcome data (attrition bias)	Low risk	All dropouts accounted for and explained. Reasons for dropouts broadly due to either progression of disease or renal transplant. 11 drop outs due to side effects of drug.
Selective reporting (reporting bias)	Low risk	Data for whole follow up period published. Raw data supplied by author.
Other bias	Low risk	No funding from industry.

Study Characteristics: Graham 1994	
Methods	Clinical trial, not randomized
Participants	14 patients with AIDS, mean age 39, 100% male
Interventions	Megestrol acetate (800mg/day oral)

Outcomes	Weight Plus: plasma drug levels
Notes	Length of treatment: 21 days Data request: not required Cachexia criteria: involuntary weight loss >10% baseline (since diagnosed with HIV infection) Drop out rate: 0% Time of analysis: 21 days Aim of trial was to look at pharmacokinetics of drug.

Risk of Bias: Graham 1994		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Non-randomized trial
Allocation concealment (selection bias)	High risk	Non-randomized trial
Blinding of participants and personnel (performance bias)	High risk	Non-randomized trial
Blinding of outcome assessment (detection bias)	High risk	Non-randomized trial
Incomplete outcome data (attrition bias)	High risk	Unclear why 4 patients not included in analysis (no explanation)
Selective reporting (reporting bias)	Low risk	All data published.
Other bias	Unclear risk	Supported by Bristol Myers Squibb (manufacturer of MA)

Study Characteristics: Lien 1996	
Methods	Pilot study, not randomized
Participants	16 end stage renal failure on dialysis (peritoneal or haemodialysis), mean age 56, 63% male
Interventions	Megestrol acetate (20mg BD oral)
Outcomes	Weight Serum albumin Plus: other nutritional parameters
Notes	Length of treatment: at least 2 months Data request: response - data no longer available Cachexia criteria: serum albumin <3.5mg/dL for > 2 months Drop out rate: 25% Time of analysis: 2 months

Risk of Bias: Lien 1996		
Bias	**Authors' judgement**	**Support for judgement**

Random sequence generation (selection bias)	High risk	Non-randomized trial
Allocation concealment (selection bias)	High risk	Non-randomized trial
Blinding of participants and personnel (performance bias)	High risk	Non-randomized trial
Blinding of outcome assessment (detection bias)	High risk	Non-randomized trial
Incomplete outcome data (attrition bias)	Low risk	All patients included in analysis.
Selective reporting (reporting bias)	High risk	Mean follow up 4.3 months yet no data after 2 months reported.
Other bias	Unclear risk	Funding source not stated.

Study Characteristics: Monfared 2009	
Methods	Randomized control trial, single blinded, placebo controlled*
Participants	22 end stage renal failure on haemodialysis a) 11 participants (9 completed), mean age 54 b) 11 participants (9 completed), mean age 60
Interventions	2 arm trial: a) Megestrol acetate (40mg BD oral) b) Current treatment, no placebo
Outcomes	Weight Serum albumin Plus: other nutritional parameters
Notes	Length of treatment: 2 months Quality score: 3 Data request: no response Cachexia criteria: serum albumin <3.5mg/dL for 2 months Drop out rate: 18% Time of analysis: 2 months This study was designed to look at serum albumin, weight was a secondary outcome and results not published. * No 'placebo' actually given, comparison made to current treatment only

Risk of Bias: Monfared 2009		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of randomization not stated. Unclear if baseline characteristics matched
Allocation concealment (selection bias)	Unclear risk	Method of randomization not stated
Blinding of participants and personnel (performance bias)	High risk	Participants and staff not blinded
Blinding of outcome assessment (detection bias)	Low risk	Analysis of outcome data blinded

Incomplete outcome data (attrition bias)	Unclear risk	4 dropouts. 3 deaths (2 in control group, 1 in intervention group), 1 kidney transplant. Causes of death not stated, but unlikely to be related to intervention.
Selective reporting (reporting bias)	Low risk	Weight data not published (but not primary outcome of study).
Other bias	Unclear risk	Funding source not stated.

Study Characteristics: Mulligan 2007	
Methods	Randomized control trial, double blind, placebo controlled*
Participants	79 HIV positive patients a. 41 participants (37 completed), mean age 37, 100% male b. 38 participants (29 completed) mean ago 39, 100% male
Interventions	2 arm trial: a. Megestrol acetate (800mg/day) with testosterone enanthane (200mg IM injection once every 2 weeks) - MA/TE b. megestrol acetate (800mg/day) with placebo (IM injection once every 2 weeks) - MA/PL
Outcomes	Weight LBM (bioelectrical impedance analysis) Plus: dietary intake, adrenal and gonadal function, sexual function
Notes	Length of treatment: 12 weeks Quality score: 3 Data request: raw data provided by author Cachexia criteria: weight loss >/=5% usual body weight or BMI <20 Drop out rate: 16% Time of analysis: 6 weeks, 12 weeks This study was designed to look at the addition of adding testosterone to MA therapy (thus *placebo was MA with placebo)

Risk of Bias: Mulligan 2007		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Permuted blocks method used. Baseline characteristics not matched.
Allocation concealment (selection bias)	Unclear risk	Unclear if allocation sequence concealed
Blinding of participants and personnel (performance bias)	Unclear risk	Method of blinding not stated
Blinding of outcome assessment (detection bias)	Unclear risk	Method of blinding not stated
Incomplete outcome data (attrition bias)	High risk	7 patients in MA group completed trial but were not included in analysis due 'to missing data' (all in MA/TE group). 4 patients withdrew due to 'adverse events' (1 MA/TE, 3 MA/PL) - no more detail.

Selective reporting (reporting bias)	High risk	Very little raw data published. Weight and LBM data given as medians with interquartile range (? skewed data) - therefore not used in review.
Other bias	Unclear risk	Multiple writers had consulting fees and grant support from Bristol Myers Squibb

Study Characteristics: Mwamburi 2004	
Methods	Randomized control trial, not blinded, no control
Participants	39 HIV positive patients a) 20 participants (18 completed), mean age 41, 65% male b) 19 participants (15 completed), mean age 39, 84% male
Interventions	2 arm trial: a) Megestrol acetate (800mg/day oral) with nutrition counseling b) Oxandrolone 10mg BD with nutrition counseling
Outcomes	Weight LBM (bioelectrical impedance analysis and anthropometric measurements) HRQL: SF12 questionnaire (physical and mental component) Serum albumin Plus: dietary intake, HIV RNA levels
Notes	Length of treatment: 2 months Quality score: 3 Data request: unable to contact author Cachexia criteria: weight loss >5% body weight in last 6/12 Drop out rate: 12.5% Time of analysis: 2 months

Risk of Bias: Mwamburi 2004		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated random numbers. Matched baseline characteristics.
Allocation concealment (selection bias)	Unclear risk	Not clear if allocation sequence concealed
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	5 dropouts - precise reasons for each not implicitly stated, but adverse rates reported.
Selective reporting (reporting bias)	Low risk	No concerns
Other bias	Unclear risk	Bristol Myers Squibb one of the funding sources.

Study Characteristics: Mwamburi 2004a	
Methods	Clinical trial, not randomized

Participants	29 HIV positive patients, mean age 40, 74% male
Interventions	Megestrol acetate (800mg/day oral) plus Oxandrolone (10mg BD) plus nutrition counseling
Outcomes	Weight LBM (bioelectrical impedance analysis and anthropometric measurements) HRQL: SF12 questionnaire (physical and mental component) Serum albumin Plus: dietary intake, HIV RNA levels
Notes	Length of treatment: 2 months either MA plus nutrition counseling or Oxandrolone plus nutrition counseling, then 5 months of all 3 therapies Data request: no response Cachexia criteria: weight loss >5% body weight in last 6/12 Drop out rate: 26% Time of analysis: 7 months Same patients as Mwamburi 2004 - extension of previous study

Risk of Bias: Mwamburi 2004a		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Non-randomized trial
Allocation concealment (selection bias)	High risk	Non-randomized trial
Blinding of participants and personnel (performance bias)	High risk	Non-randomized trial
Blinding of outcome assessment (detection bias)	High risk	Non-randomized trial
Incomplete outcome data (attrition bias)	Unclear risk	5 dropouts - no explanation given.
Selective reporting (reporting bias)	Unclear risk	2 published studies using the same patients.
Other bias	Unclear risk	Bristol Myers Squibb one of the funding sources.

Study Characteristics: Rammohan 2005	
Methods	Clinical trial, not randomized
Participants	16 end stage renal failure on peritoneal dialysis or haemodialysis (data published only for the 10 patients whom completed the trial), mean age 60, 40% male
Interventions	Megestrol acetate (400mg/day oral)
Outcomes	Weight Appetite (part of kidney disease and quality of life questionnaire (version 1.2) - SF36) LBM (measurement published = fat free mass, bioelectrical impedance analysis) HRQOL (kidney disease and quality of life questionnaire (version 1.2) - SF36) Serum albumin Plus: dietary intake, serum leptin and CRP

Notes	Length of treatment: 16 weeks Data request: unable to contact Cachexia criteria: actual body weight < 85% IBW or BMI <20 with at least 1 of following (recent unplanned weight loss >5-10% of their target weight within a 6/12 period not cause by evident intercurrent illness, serum albumin <3.7 for 3 consecutive months) Drop out rate: 38% Time of analysis: 16 weeks

Risk of Bias: Rammohan 2005		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Non-randomized trial
Allocation concealment (selection bias)	High risk	Non-randomized trial
Blinding of participants and personnel (performance bias)	High risk	Non-randomized trial
Blinding of outcome assessment (detection bias)	High risk	Non-randomized trial
Incomplete outcome data (attrition bias)	Low risk	All dropouts accounted for.
Selective reporting (reporting bias)	Low risk	No concerns.
Other bias	Unclear risk	Bristol Myers Squibb one of trial sponsors.

Study Characteristics: Rochon 2003	
Methods	Randomized control trial, double blind, no placebo
Participants	12 patients with HIV a) 6 participants, mean age 36, 100% male b) 6 participants, mean age 44, 100% male
Interventions	2 arm trial: a) Medroxyprogesterone acetate (400mg/day oral) plus nutritional advice, amino acid supplementation and protein supplementation b) Placebo plus nutritional advice, amino acid supplementation and protein supplementation
Outcomes	Weight LBM (anthropometric measurements) Serum albumin Plus: plasma tryptophan, amino acid levels, plasma substrate levels (e.g. insulin, glucose)
Notes	Length of treatment: 5 weeks of nutritional supplementation, medroxyprogesterone/placebo given in the last 3 weeks Data request: no response Cachexia criteria: weight loss (not further specified) Drop out rate: 0% Time of analysis: 5 weeks No defined cachexia criteria

Risk of Bias: Rochon 2003		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of randomization not stated. Matched baseline characteristics.
Allocation concealment (selection bias)	Unclear risk	Method of randomization not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Method of blinding not stated
Blinding of outcome assessment (detection bias)	Unclear risk	Method of blinding not stated
Incomplete outcome data (attrition bias)	Low risk	All patients included in analysis
Selective reporting (reporting bias)	Low risk	No concerns
Other bias	Low risk	No commercial sponsor (charitable)

Study Characteristics: Summerbell 1992	
Methods	Randomized control trial, not blinded, no placebo
Participants	14 patient with HIV a) 7 participants, no baseline characteristics published b) 7 participants, no baseline characteristics published
Interventions	2 arms: a) Megestrol acetate (40mg/day oral, 'increased by 40mg daily on alternate weeks to a maximum dose of 160mg/day if there was no response in weight') b) Cyproheptadine (12mg/day oral)
Outcomes	Weight plus: dietary intake, sexual function questionnaires
Notes	Length of treatment: 3 months Quality score: 1 Data request: unable to contact author Cachexia criteria: weight loss >5kg body weight Drop out rate: 7% Time of analysis: 3 months

Risk of Bias: Summerbell 1992		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	'simple randomization' - no further information. Baseline characteristics not published.
Allocation concealment (selection bias)	High risk	No information given
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded

Incomplete outcome data (attrition bias)	High risk	All patients included in analysis.
Selective reporting (reporting bias)	Low risk	Some data presented in graphical form with no raw data
Other bias	High risk	Funding source not stated.

Study Characteristics: Timpone 1997	
Methods	Randomized control trial, not blinded, no placebo
Participants	50 patients with HIV a) 12 participants (7 completed), mean age 39, 83% male b) 12 participants (10 completed), mean age 46, 83% male c) 13 participants (11 completed), mean age 38, 92% male d) 13 participants (12 completed), mean age 40, 92% male
Interventions	4 arm trial: a) Dronabinol 2.5mg BD oral b) Megestrol acetate 750mg/day oral c) Megestrol acetate 750mg/day oral plus Dronabinol 2.5mg BD oral d) Megestrol acetate 250mg/day oral plus Dronabinol 2.5mg/day oral
Outcomes	Weight Appetite (Visual Analogue Scale for Hunger/ VASH questionnaire) HRQOL (Visual Analogue Scale for Mood/VASM questionnaire) Plus: pharmacokinetic drug levels
Notes	Length of treatment: 12 weeks Quality score: 2 Data request: unable to contact author Cachexia criteria: clinical diagnosis of 'HIV wasting syndrome' with >/= 10% weight loss and/or low BMI (≤20.5kg/m^2 for age 18-34 or ≤22.5kg/m^2 for age ≥35 years) Drop out rate: 20% Time of analysis: 12 weeks Study designed to look at safety and pharmacokinetics

Risk of Bias: Timpone 1997		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of randomization not stated. Matched baseline characteristics.
Allocation concealment (selection bias)	Unclear risk	Method of randomization not stated
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	Dropouts fully explained
Selective reporting (reporting bias)	Low risk	No concerns
Other bias	Low risk	No commercial sponsors

Study Characteristics: Von Roenn 1990	
Methods	Pilot study (open trial), not randomized
Participants	22 patients with HIV, limited baseline characteristics
Interventions	Megestrol acetate 80mg QDS oral
Outcomes	Weight Appetite HRQOL (sense of wellbeing - method not stated) Plus: sexual function questionnaire
Notes	Length of treatment: 2-72 weeks (open trial) Data request: no response Cachexia criteria: weight loss >10% pre-illness body weight and loosing weight at time of enrolment Drop out rate: open trial Time of analysis: unclear 14 patients previously reported in Van Roenn 1988 (same trial)

Risk of Bias: Von Roenn 1990		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	High risk	Non-randomized trial
Allocation concealment (selection bias)	High risk	Non-randomized trial
Blinding of participants and personnel (performance bias)	High risk	Non-randomized trial
Blinding of outcome assessment (detection bias)	High risk	Non-randomized trial
Incomplete outcome data (attrition bias)	High risk	Reasons for withdrawal not stated clearly.
Selective reporting (reporting bias)	Low risk	Raw data clearly presented.
Other bias	Unclear risk	Source of funding not stated. Results for 14 patients in same trial published twice.

Study Characteristics: Von Roenn 1994	
Methods	Randomized control trial, double blind, placebo controlled
Participants	270 patients with AIDS (75 dropouts - not stated how many in each arm of trial) a) 82 participants, mean age 39, 99% male b) 75 participants, mean age 39, 100% male c) 75 participants, mean age 38, 100% male d) 38 participants, mean age 38, 100% male
Interventions	4 arm trial: a) Megestrol acetate 100mg/day oral b) Megestrol acetate 400mg/day oral c) Megestrol acetate 800mg/day oral d) Placebo (no further information)

Outcomes	Weight Appetite LBM (bioelectrical impedance analysis and anthropometric measurements) HRQOL (sense of wellbeing - nine item linear analogue and self assessment questionnaire) Plus: dietary intake, opportunistic infections
Notes	Length of treatment: 12 weeks Quality score: 3 Data request: no response Cachexia criteria: clinically significant weight loss (>20% usual body weight), or 10% below IBW Drop out rate: 28% Time of analysis: 12 weeks

Risk of Bias: Von Roenn 1994		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of randomization not stated. Matched baseline characteristics.
Allocation concealment (selection bias)	Unclear risk	Method of randomization not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Method of blinding not stated. Form of placebo not published (? tablet form)
Blinding of outcome assessment (detection bias)	Unclear risk	Method of blinding not stated
Incomplete outcome data (attrition bias)	High risk	Unclear how many dropouts were from each arm of trial. No CONSORT flow diagram of patients through study.
Selective reporting (reporting bias)	Low risk	Data clearly reported
Other bias	Unclear risk	Supported by Bristol Myers Squibb (manufacturer of MA)

Study Characteristics: Wanke 2007	
Methods	Randomized control trial, not blinded, no placebo
Participants	63 patients with HIV a) 32 participants, mean age 37, 66% male b) 31 participants, mean age 36, 48% male
Interventions	2 arm trial: a) Megestrol acetate concentrated suspension 575mg/day oral b) Megestrol acetate oral suspension 800mg/day oral
Outcomes	Weight Appetite LBM (anthropometric measurements) HRQOL (Bristol Myers Anorexia/Cachexia Recovery Instrument/BACRI, plus Hamilton rating scale for depression/HAMD-17) Serum albumin Plus: serum cortisol

Notes	Length of treatment: 12 weeks Quality score: 3 Data request: no response Cachexia criteria: weight loss >10% body weight or weight <90% ideal body weight Drop out rate: 7% Time of analysis: 12 weeks Study designed to compare efficacy of different strengths of Megestrol acetate suspension

Risk of Bias: Wanke 2007		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	'Randomized 1:1 from a central site with block size 2'. Matched baseline characteristics.
Allocation concealment (selection bias)	Low risk	'Randomized 1:1 from a central site with block size 2'
Blinding of participants and personnel (performance bias)	High risk	Not blinded
Blinding of outcome assessment (detection bias)	High risk	Not blinded
Incomplete outcome data (attrition bias)	Low risk	5 dropouts due to 'adverse events' - no further information. Equally distributed between 2 groups.
Selective reporting (reporting bias)	Low risk	No concerns
Other bias	Unclear risk	Funding source not stated but likely Bristol Myers Squibb (use their assessment tools)

Study Characteristics: Weisberg 2002	
Methods	Randomized control trial, double blind, placebo controlled
Participants	145 patients with COPD a) 72 participants, mean age 68, 64% male b) 73 participants, mean age 66, 62% male
Interventions	2 arm trial: a) Megestrol acetate 800mg/day oral b) Placebo (inert oral suspension)
Outcomes	Weight Appetite LBM (anthropometric measurements) HRQOL (9 item questionnaire) Serum albumin Plus: respiratory muscle strength, ABG levels, subjective perception of disease
Notes	Length of treatment: 8 weeks Quality score: 3 Data request: no response Cachexia criteria: <95% ideal body weight Drop out rate: 12% Time of analysis: 8 weeks

Risk of Bias: Weisberg 2002		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method of randomization not stated. Matched baseline characteristics.
Allocation concealment (selection bias)	Unclear risk	Method of randomization not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Method of blinding not stated
Blinding of outcome assessment (detection bias)	Unclear risk	Method of blinding not stated
Incomplete outcome data (attrition bias)	Low risk	Reasons for dropouts well explained.
Selective reporting (reporting bias)	Low risk	Raw data published
Other bias	Unclear risk	Funding source not stated

Study Characteristics: Yeh 2000	
Methods	Randomized control trial, double blind, placebo controlled
Participants	69 nursing home residents with geriatric cachexia a) 36 participants, mean age 76, 97% male b) 33 participants, mean age 76, 94% male
Interventions	2 arm trial: a) Megestrol acetate 800mg/day oral b) Placebo (20ml in identical containers with non-identifying labels)
Outcomes	Weight Appetite LBM (measurement published = fat free mass by bioelectrical impedance analysis) HRQOL (Depression score, enjoyment score) Serum albumin Plus: nutritional parameters, dietary intake
Notes	Length of treatment: 12 weeks Quality score: 5 Data request: no response Cachexia criteria: weight loss ≥5% usual body weight over preceding 3 months or body weight 20% below ideal body weight Drop out rate: 17% Time of analysis: 12 weeks

Risk of Bias: Yeh 2000		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random numbers table. Matched baseline characteristics.

Allocation concealment (selection bias)	Unclear risk	Unclear if allocation sequence concealed
Blinding of participants and personnel (performance bias)	Low risk	Double blinding method well explained
Blinding of outcome assessment (detection bias)	Low risk	Double blinding method well explained
Incomplete outcome data (attrition bias)	Unclear risk	Dropouts clearly explained, however 18 patients not included in analysis as 'violated entry criteria', and 2 dropouts due to 'lack of weight gain'.
Selective reporting (reporting bias)	Low risk	No concerns. All outcome data clearly published.
Other bias	Unclear risk	Sponsored by Bristol Myer Squibb

Study Characteristics: Yeh 2010	
Methods	Randomized control trial, double blind, no placebo
Participants	9 end stage renal failure on haemodialysis a) 4 participants, mean age 67.5, 100% male b) 5 participants, mean age 75.4, 100% male
Interventions	2 arms: a) Megestrol acetate 800mg/day oral plus physical therapy b) Placebo plus physical therapy
Outcomes	Weight Appetite (5 point Liket scale) LBM (fat mass, bioelectrical impedance analysis) HRQOL (sense of wellbeing questionnaire) Serum albumin Plus: ability to exercise, ability to perform ADLs, nutritional parameters and cytokine levels
Notes	Length of treatment: 20 weeks Quality score: 5 Data request: no response Cachexia criteria: albumin <4, total cholesterol <150, protein catabolic rate (PCR) <0.8, pre-dialysis serum urea nitrogen >60 Drop out rate: 33% Time of analysis: 24 weeks 9 enrolled, 6 included in analysis

Risk of Bias: Yeh 2010		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Random numbers table. Matched baseline characteristics.
Allocation concealment (selection bias)	Unclear risk	Unclear if allocation sequence concealed
Blinding of participants and personnel (performance bias)	Unclear risk	On site statistician and pharmacist aware of allocation
Blinding of outcome assessment (detection bias)	Unclear risk	Not stated

Incomplete outcome data (attrition bias)	Low risk	Dropouts accounted for an evenly distributed
Selective reporting (reporting bias)	Low risk	No concerns
Other bias	Unclear risk	Sponsored by Bristol Myer Squibb