review article

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REVIEW ARTICLE

Pharmacotherapy for overweight/obesity in ethnic minorities and White Caucasians: a systematic review and meta-analysis

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Ethnic minorities in the West exhibit a higher prevalence of obesity and also under-achieve in weight management compared to White Caucasians. A systematic review of randomized controlled trials (RCTs) in adults (mean age ≥18 years, duration ≥6 months and published in the English language) was undertaken to evaluate the effectiveness of antiobesity drugs in ethnic minorities and White Caucasians. Data sources between 1990 and 2010 were searched including MEDLINE, EMBASE, Cochrane Controlled Trials Register, CINAHL and references cited in the included studies of other reviews. Eighteen RCTs that met the inclusion criteria were included in this review (6 sibutramine and 12 orlistat). A random effects model was used for meta-analysis. An indirect comparison of weight loss in sibutramine-treated patients in ethnic minorities was significantly lower than in White Caucasians: −2.7 kg (95% CI: −3.1 to −2.3) versus −4.4 kg (95% CI: −5.0 to −3.8), respectively. For orlistat, weight loss was similar in the two groups: −2.3 kg (95% CI: −2.6 to −2.0) in ethnic minorities and −2.8 kg (95% CI: −5.1 to −0.5) in White Caucasian participants. Overall, there were few studies of weight loss pharmacotherapy for comparison of this review and it was not possible to analyse data based on ethnic groupings. More ethnically tailored studies are needed to assess the most effective weight loss strategies in these most metabolically vulnerable groups.

Keywords: antiobesity drug, antiobesity medications, ethnic minorities, weight loss therapy, White Caucasians

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Introduction

Minority non-White ethnic groups in Western countries (including Blacks, non-White Hispanics, Asians and Native Americans) [1] exhibit a higher prevalence of obesity and obesity-related complications compared to people of White European ancestry [2]. In the USA, the prevalence of overweight or obesity among adults between 2003 and 2004 was 66.3% in the general population, 64.2% in White Caucasians, 76.1% in Blacks and 75.8% in Mexican Americans [3]. In England, data from the 2004 Health Survey for England showed that Black Caribbeans had the highest prevalence of obesity (25%), whereas for women, Black African (38%), Black Caribbean (32%) and Pakistani ethnic groups (28%) had higher obesity prevalence rates compared to the general adult population (23–25%) [2].

Additionally, ethnic minorities under-achieve in weight management programmes compared to their White Caucasian counterparts [4–9]. Ethnic disparities in obesity rates and weight management interventions are explained in part by increased genetic predisposition [10–14], social pressures and cultural influences which contribute to 'obesity-tolerant' attitudes (e.g. African American and Hispanic women are less likely to be dissatisfied with their body weight even when overweight), thus, promoting weight gain and limiting the efficacy of weight loss interventions in certain ethnic groups [15–18].

Antiobesity medications such as sibutramine (withdrawn in Europe) and orlistat have been recommended for patients with a body mass index (BMI) ≥27 kg/m^2 (with one or more obesity-related disorders) or ≥30 kg/m^2 (without obesity-related disorders) and are used in conjunction with lifestyle modification [19,20]. Sibutramine acts to suppress appetite and increase satiety primarily by modifying central nervous system neurotransmission of serotonin. Orlistat inhibits intestinal fat absorption and works by inhibiting pancreatic and other lipases [21]. Of previous published reviews on pharmacotherapy for obesity [19–27], none included subgroup analysis of ethnic minorities. This review therefore compared the effectiveness of antiobesity medications in ethnic minorities and White Caucasians.

Methods

Inclusion/Exclusion Criteria and Outcomes

The search included (i) randomized placebo-controlled trials of antiobesity medications approved/licensed for medium to long-term use in the UK or USA. These include sibutramine

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and orlistat, (ii) studies with ≥6 months duration, (iii) studies involving White and ethnic minority adult participants (aged ≥18 years) or only ethnic minority participants and (iv) trials that evaluated changes in weight/BMI (primary outcome) with at least one secondary outcome (waist circumference, blood pressure, fasting lipid and glucose levels and HbA1c). If a study reported both weight loss and weight maintenance phases, only data from the weight loss phase was used in this review, (v) only studies published in the English language and (vi) studies of short-term duration (<6 months) or reported weight/BMI change as the only outcome or full text not published in the English language were excluded.

Search Strategy

Bibliographic database were searched for published articles from January 1990 to June 2010. The following sources were searched: MEDLINE, EMBASE, COCHRANE, CCTR, CINAHL, DARE, Current Science meta-register of controlled trials and examined reference lists of identified trials and reviews. The key words used were 'Minority or Black or African American or American Indian or Mexican American or Hispanic or Latino or Asian' and 'obesity or overweight or weight loss or weight control' in combination with 'pharmacotherapy or antiobesity medication or sibutramine or orlistat' using various suffices. Electronic searches, scanning the identified references and data extraction of included studies were performed by one reviewer (G. O.-A.) and checked by another (I. K.). Any disagreements were resolved by consensus.

For studies made up of White Caucasians and ethnic minority participants, authors were contacted for subgroup results/analysis of ethnic minorities and White Caucasians wherever possible (n = 4).

Data Extraction and Meta-analysis

Results of included studies were extracted and analysed by the two reviewers. A preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement [28] was used to describe how studies/references identified through the searches were processed. Methodological quality was assessed descriptively using the Verhagen Delphi list [29], because numerical scores can be inaccurate and poorly reproducible when used to differentiate between high- and low-quality studies [30].

Results of trials that were comparable were pooled using STATSDIRECT statistical software version 2.6.6 (Altrincham, Cheshire, UK) [31] in a meta-analysis using random effect models.

Publication bias was assessed using Egger et al.'s test for asymmetry of the funnel plot [32].

Heterogeneity in Meta-analysis/Publication Bias

The classical measure of heterogeneity is Cochran's Q, which is calculated as the weighted sum of squared differences between individual study effects and the pooled effect across studies, with the weights being those used in the pooling method. Despite a lack of significant statistical heterogeneity found between the included studies 'random effects' was used in the analysis to allow the study outcomes to vary in a normal distribution between studies. Many investigators consider the random effects approach to be a more natural choice than fixed effects [33].

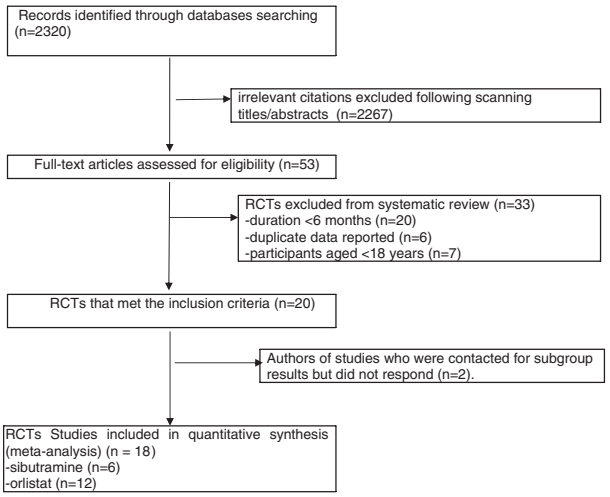

Figure 1. PRISMA flow chart (articles published from January 1990 to June 2010).

Results

Search results are summarized in the PRISMA flow chart (figure 1). Twenty studies met the inclusion criteria. However, when authors were contacted for subgroup results on ethnic minorities and White Caucasians (n = 4), two did not respond. Thus, a total of 18 studies representing 6 sibutramine [9,34–38] and 12 orlistat [39–50] trials were included in the review. Table 1 shows the key characteristics of included studies. All studies took place in the USA except one in the UK [43]. Mean attrition rate was 16.4 and 25.2% in the sibutramine and orlistat trials, respectively. Reasons for attrition included lack of cooperation, protocol violations, adverse events (clinical adverse events or adverse laboratory findings), loss to follow-up and refusal of treatment.

The methodological quality of included trials is summarized in Table 2. For majority of the studies, the method of randomization was adequate (14/18), allocation to treatment groups concealed (14/18), baseline data similar in treatment groups (12/18), eligibility criteria specified (18/18) and use of intention to treat analysis (13/18).

Sibutramine

Six trials were identified which included 341 subjects from ethnic minorities and 964 White Caucasians. Average age and BMI of participants was 49.2 years and 35.8 kg/m^2 [9,34–38], respectively. Only one study was made up of one ethnic minority group [9].

Outcomes. Pooled results in ethnic minorities indicated a weight loss of −2.7 kg (95% CI: −3.1 to −2.3) (figure 2A) and in White Caucasians, there was a significantly (p = 0.0326)

Table 1. Key characteristics of included studies.

Study	Population	Mean age (years)	Mean BMI (kg/m^2)	Intervention versus control	Attrition percentage (treatment/control)
McMahon [34]	White Caucasians (n = 180) and ethnic minority (Black and Mexican American) (n = 50) hypertensive patients	51.1	34.0	Sibutramine 20 mg once daily (n = 146) + dietary advice versus placebo + dietary advice (n = 74)	1.4/5.4
Dujovne [35]	White Caucasians (n = 179) and ethnic minority (Black, Mexican American and Indian/Pakistani) (n = 51) patients with cardiovascular risk factors	45.2	35.3	Sibutramine 20 mg once daily + dietary advice (n = 124) versus placebo + dietary advice (n = 114)	38.7/47.4
Fujioka [36]	White Caucasians (n = 91) and ethnic minority (Blacks and others) (n = 47) patients with type 2 diabetes	54.5	34.0	Sibutramine 20 mg + dietary advice (n = 70) versus placebo + dietary advice (n = 68)	14.3/10.3
Porter [37]	White Caucasians (n = 382) and ethnic minorities (Blacks, Mexican Americans and Indian/Pakistani) (n = 76)	48.4	38.8	Sibutramine 15 mg + dietary advice (n = 257) versus placebo (n = 201) + dietary advice	13.2/31.2
McMahon [9]	White Caucasians (n = 130) and African American (n = 94) patients with hypertension	53.0	34.4	Sibutramine 20 mg + dietary advice (n = 150) versus placebo + dietary advice (n = 74)	5.3/6.8
Wadden [38]	White Caucasians (n = 75) and ethnic minorities (Blacks and non-White Hispanics) (n = 38)	42.7	38.1	Sibutramine 15 mg (n = 58) + dietary advice versus placebo + lifestyle change (n = 55)	10.0/7.0
Poston [39]	White Caucasians (n = 26), ethnic minorities (Blacks and Asians) (n = 111)	43.0	36.9	Orlistat 120 mg 3× daily + brief counselling (n = 82) versus brief counselling (n = 85)	34.1/67.1
Poston [40]	Mexican American women (n = 108)	41.0	36.0	Orlistat 120 mg 3× daily + tailored lifestyle change (n = 56) versus tailored lifestyle change (n = 52)	42.9/34.6
Garcia [41]	Mexican American women (n = 48)	44	36.8	Orlistat 120 mg 3× daily + dietary advice (n = 25) versus no intervention (n = 23)	0/0
Davidson [42]	White Caucasians (n = 711) and ethnic minorities (Blacks and Mexican Americans) (n = 160)	43.7	36.4	Orlistat 120 mg 3× daily + dietary advice (n = 650) versus placebo + dietary advice (n = 221)	31.3/38.3
Dixon [43]	South Asians with type 2 diabetes (n = 40)	Not reported	28.2	Orlistat 120 mg 3× daily + dietary advice (n = 18) versus placebo + dietary advice (n = 22)	11.1/31.8
Hauptman [44]	White Caucasians (n = 377) and ethnic minorities (Blacks, American Indians and non-White Hispanics) (n = 45)	42.7	36.3	Orlistat 120 mg 3× daily + dietary advice (n = 210) versus placebo + dietary advice (n = 212)	28.0/43.0
Heymsfield [45]	White Caucasians (n = 494) and ethnic minorities (Blacks, Asians and non-White Hispanics) (n = 81)	44.2	36.2	Orlistat 120 mg 3× daily + calorie restriction (n = 359) versus placebo + calorie restriction (n = 316)	31.3/31.5
Hill [46]	White Caucasians (n = 317) and ethnic minorities (Blacks, non-White Hispanics and Asians) (n = 46)	46.3	32.8	Orlistat 120 mg 3× daily + calorie restriction (n = 179) versus placebo + calorie restriction (n = 184)	30.4/26.6
Hollander [47]	White Caucasians (n = 281) and ethnic minority (Blacks, non-White Hispanics and others) (n = 40) patients with type 2 diabetes	54.8	34.6	Orlistat 120 mg 3× daily + calorie restriction (n = 167) versus placebo + calorie restriction (n = 159)	15.0/27.0

Table 1. Continued.

Study	Population	Mean age (years)	Mean BMI (kg/m^2)	Intervention versus control	Attrition percentage (treatment/control)
Kelley [48]	White Caucasians (n = 385) and ethnic minority (Blacks, Asians and others) (n = 150) patients with type 2 diabetes	57.9	35.4	Orlistat 120 mg 3× daily + calorie restriction (n = 266) versus placebo + calorie restriction (n = 269)	3.0/2.5
Miles [49]	White Caucasians (n = 412) and ethnic minority (Blacks and others) (n = 92) patients with type 2 diabetes	52.5	35.8	Orlistat 120 mg 3× daily + calorie restriction (n = 250) versus placebo + calorie restriction (n = 254)	2.0/2.7
Harrison [50]	White Caucasians (n = 28) and ethnic minority (Blacks, non-White Hispanics and Asians) (n = 13) patients with non-alcoholic steatohepatitis	47.0	36.4	Orlistat 120 mg 3× daily + dietary advice (n = 23) versus placebo + dietary advice (n = 18)	13.0/33.3

Table 2. Summary of methodological quality.

Study	Randomization adequate	Allocation concealment	Baseline similarity	Eligibility criteria specified	Patient blinded	Care provider blinded	Outcome assessor blinded	Point and measures of variability for the primary outcome	ITT analysis
McMahon [34]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Dujovne [35]	Y	Y	Y	Y	Y	Y	Y	Y	N
Fujioka [36]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Porter [37]	Y	Y	N	Y	Y	Y	Y	Y	Y
McMahon [9]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Wadden [38]	Y	N	U	Y	N	N	N	Y	Y
Poston [39]	U	Y	Y	Y	Y	Y	Y	Y	Y
Poston [40]	N	N	N	Y	N	N	U	Y	Y
Garcia [41]	N	N	N	Y	N	N	N	Y	U
Davidson [42]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Dixon [43]	N	N	U	Y	N	N	N	Y	U
Hauptman [44]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Heymsfield [45]	Y	Y	N	Y	Y	Y	Y	N	Y
Hill [46]	Y	Y	Y	Y	Y	Y	Y	Y	N
Hollander [47]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Kelley [48]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Miles [49]	Y	Y	Y	Y	Y	Y	Y	Y	Y
Harrison [50]	Y	Y	Y	Y	Y	Y	Y	Y	U

ITT, intention to treat; N, no; Y, yes; U, unreported.

greater weight loss than in ethnic minorities of −4.4 kg (95% CI: −5.0 to −3.8) (figure 2B).

Treatment with sibutramine resulted in significant improvements in waist circumference (both minorities and White Caucasians) and HDL and triglyceride in White Caucasians only. However, sibutramine was associated with significant increases in systolic (minorities) and diastolic (both minorities and White Caucasians) blood pressures as well as pulse rate (both minorities and White Caucasians) (Table 3).

Orlistat

Twelve trials using orlistat in ethnic minorities were identified, which included 934 participants. Three studies were made up of a mono-ethnic group: Mexican Americans [40,41] and South Asians [43]. Nine of the trials also involved White Caucasians: a total of 2166 participants. Average age and BMI of participants was 46.4 years and 35.2 k/m^2, respectively.

Outcomes. Pooled results showed a weight loss of −2.3 kg (95% CI: −2.6 to −2.0) in ethnic minorities and −2.8 kg (95% CI: −5.1 to −0.5) in White Caucasians (figure 3A, B, respectively). There was no significant difference between the two groups in weight loss for orlistat (p = 0.373).

Weight loss with orlistat resulted in significant improvements in systolic (both minorities and White Caucasians) and diastolic (only in White Caucasians) blood pressure. There were also significant improvements in fasting blood glucose, HbA1c, total and LDL cholesterol in both minorities and White Caucasians (Table 3).

Publication Bias

When publication bias of the primary outcome (weight loss) was assessed using funnel plot and statistical analysis, no evidence of significant asymmetry of the funnel plots or bias was

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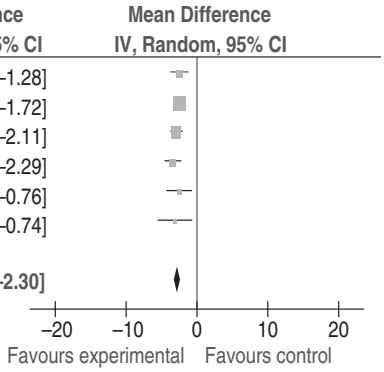
Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean Difference IV, Random, 95% CI
Dujovne 2001	−4	2	30	−1.5	2.3	21	11.8	−2.50 [−3.72, −1.28]
Fujioka 2000	−3	1.3	16	−0.6	0.5	16	37.4	−2.40 [−3.08, −1.72]
McMahon 2000	−4.2	1.7	67	−1.3	1.8	27	27.8	−2.90 [−3.69, −2.11]
McMahon 2002	−4.5	3.2	40	−1.1	0.8	10	14.2	−3.40 [−4.51, −2.29]
Porter 2004	−5.4	2.7	45	−2.9	4.4	31	5.8	−2.50 [−4.24, −0.76]
Wadden 2005	−8.9	2.5	18	−5.8	4.7	20	3.1	−3.10 [−5.46, −0.74]
Total (95% CI)			**216**			**125**	**100.0%**	**−2.72 [−3.14, −2.30]**

Heterogeneity: Tau² = 0.00; Chi² = 2.77, df = 5 (P = 0.73); I² = 0%
Test for overall effect: Z = 12.77 (P < 0.00001)



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Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean Difference IV, Random, 95% CI
Dujovne 2001	−5.9	4.7	89	−1.4	3.8	90	15.1	−4.50 [−5.75, −3.25]
Fujioka 2000	−4.8	1.4	46	−1.2	1.5	45	26.6	−3.60 [−4.20, −3.00]
McMahon 2000	−5.9	2.3	40	−1.6	1.9	19	17.1	−4.30 [−5.41, −3.19]
McMahon 2002	−5.5	4.3	116	−0.8	1.2	64	21.9	−4.70 [−5.54, −3.86]
Porter 2004	−6.8	5.5	212	−1.4	5.4	170	17.3	−5.40 [−6.50, −4.30]
Wadden 2005	−12.8	9.8	40	−6.5	9.5	33	2.0	−6.30 [−10.74, −1.86]
Total (95% CI)			**543**			**421**	**100.0%**	**−4.46 [−5.11, −3.81]**

Heterogeneity: Tau² = 0.32; Chi² = 10.86, df = 5 (P = 0.05); I² = 54%
Test for overall effect: Z = 13.48 (P < 0.00001)

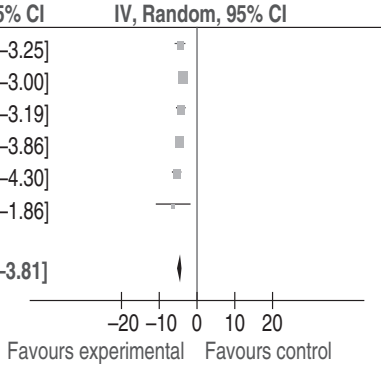

Figure 2. (A) Meta-analysis plot for weight loss with sibutramine in minorities and (B) meta-analysis plot for weight loss with sibutramine in White Caucasians.

Table 3. Secondary outcomes.

	Sibutramine		Orlistat	
Outcomes	Minorities	White Caucasians	Minorities	White Caucasians
Waist circumference (cm)	−2.7 (−3.46 to −1.91)	−3.12 (−4.04 to −2.19)	−0.6 (−3.02 to 1.82)	—
Systolic blood pressure (mmHg)	4.2 (2.42 to 6.03)	0.8 (−1.64 to 3.28)	−1.0 (−1.8 to −0.3)	−1.3 (−2.34 to −0.28)
Diastolic blood pressure (mmHg)	3.0 (1.71 to 4.35)	2.6 (1.64 to 3.47)	−0.8 (−2.2 to −0.7)	−1.7 (−2.24 to −1.09)
Pulse rate (beats/min)	4.9 (3.56 to 6.15)	4.56 (2.26 to 6.87)	—	—
Total cholesterol (mmol/l)	0.014 (−0.18 to 0.21)	0.5 (−0.27 to 1.22)	−0.2 (−0.42 to −0.04)	−0.3 (−0.47 to −0.06)
HDL cholesterol (mmol/l)	0.09 (0.08 to 0.10)	0.12 (0.03 to 0.20)	0.01 (−0.02 to 0.02)	−0.01 (−0.07 to 0.05)
LDL cholesterol (mmol/l)	0.11 (0.05 to 0.17)	0.04 (−0.08 to 0.17)	−0.3 (−0.4 to −0.2)	−0.2 (−0.35 to −0.13)
Triglyceride (mmol/l)	−0.4 (−0.89 to −0.07)	−0.38 (−0.72 to −0.03)	0.02 (−0.12 to 0.15)	−0.2 (−0.34 to −0.004)
Fasting glucose (mmol/l)	−0.14 (−0.49 to 0.19)	0.05 (−0.28 to 0.39)	−0.28 (−0.46 to −0.10)	−0.5 (−0.8 to −0.19)
HbA1c (%)	—	—	−0.3 (−0.53 to −0.15)	−0.3 (−0.44 to −0.24)

Pooled weighted mean difference (95% CI).

detected for orlistat [figure 4, Egger: bias = −0.629724 (95% CI: −1.515902 to 0.256453), p = 0.1444].

Discussion

The review evaluated 18 randomized controlled trials (RCTs) of approved/licensed antiobesity medications with ≥6 months duration in ethnic minorities and White Caucasians. One trial involved only South Asians [43] and two trials consisted of Mexican Americans [40,41]. The rest of the included trials were made up of multiethnic participants (White Caucasians, Blacks, Mexican Americans, Asians and Native Americans).

In RCTs ≥ 6 months, weight loss in sibutramine-treated ethnic minority patients was significantly lower than in White

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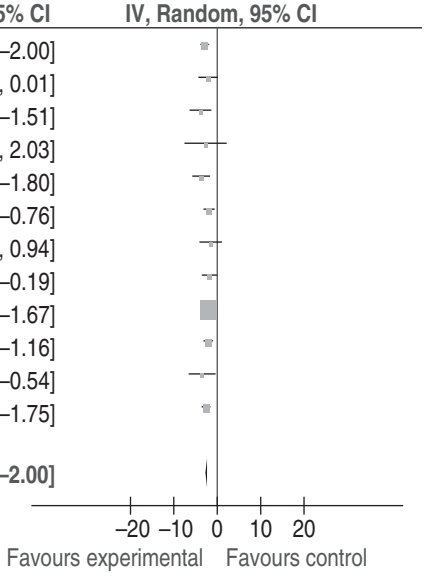
Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean Difference IV, Random, 95% CI
Davidson 1999	–8	3.6	116	–5.1	2.1	44	10.9	–2.90 [–3.80, –2.00]
Dixon 2008	–3.1	4.5	18	–1	0.9	22	2.0	–2.10 [–4.21, 0.01]
Garcia 2006	–7.26	2.3	25	–3.4	5.3	23	1.6	–3.86 [–6.21, –1.51]
Harrison 2009	–4.5	2.6	9	–1.8	4.5	4	0.4	–2.70 [–7.43, 2.03]
Hauptman 2000	–7.2	4.7	26	–3.5	1.3	19	2.5	–3.70 [–5.60, –1.80]
Heymsfield 2001	–5.7	3.3	43	–3.8	1.8	38	6.8	–1.90 [–3.04, –0.76]
Hill 1999	–7.4	5.1	26	–5.9	3.3	20	1.5	–1.50 [–3.94, 0.94]
Hollander 1998	–5.9	2.8	21	–4.1	2.4	19	3.4	–1.80 [–3.41, –0.19]
Kelley 2002	–3.8	1.3	77	–1.7	1.4	73	47.4	–2.10 [–2.53, –1.67]
Miles 2002	–4.6	2.6	39	–2.5	1.7	53	10.2	–2.10 [–3.04, –1.16]
Poston 2003	–5.9	8.2	56	–2.4	7.5	52	1.0	–3.50 [–6.46, –0.54]
Poston 2006	–4	2.9	57	–1.4	1.5	54	12.2	–2.60 [–3.45, –1.75]
Total (95% CI)			**513**			**421**	**100.0%**	**–2.30 [–2.60, –2.00]**

Heterogeneity: Tau² = 0.00; Chi² = 8.91, df = 11 (P = 0.63); I² = 0%
Test for overall effect: Z = 15.12 (P < 0.00001)



B

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight (%)	Mean Difference IV, Random, 95% CI
Davidson 1999	–9.8	35.6	372	–5.9	20.2	105	18.9	–3.90 [–9.19, 1.39]
Harrison 2009	208	42	14	210	45	14	0.5	–2.00 [–34.24, 30.24]
Hauptman 2000	–8	33.5	102	–4.8	29.1	83	6.5	–3.20 [–12.23, 5.83]
Heymsfield 2001	–6.8	32.4	216	–4.8	28.5	191	15.1	–2.00 [–7.92, 3.92]
Hill 1999	–9.6	35.2	107	–6.7	30.8	123	7.1	–2.90 [–11.51, 5.71]
Hollander 1998	–6.9	35.8	120	–4.6	37.1	102	5.7	–2.30 [–11.94, 7.34]
Kelley 2002	–4.9	33.7	91	–2.3	24.4	88	7.2	–2.60 [–11.20, 6.00]
Miles 2002	–5.5	27.9	211	–3	26.3	201	19.3	–2.50 [–7.73, 2.73]
Poston 2006	–4.6	8.2	16	–1.8	5.3	10	19.7	–2.80 [–7.99, 2.39]
Total (95% CI)			**1249**			**917**	**100.0%**	**–2.82 [–5.12, –0.51]**

Heterogeneity: Tau² = 0.00; Chi² = 0.27, df = 8 (P = 1.00); I² = 0%
Test for overall effect: Z = 2.40 (P = 0.02)

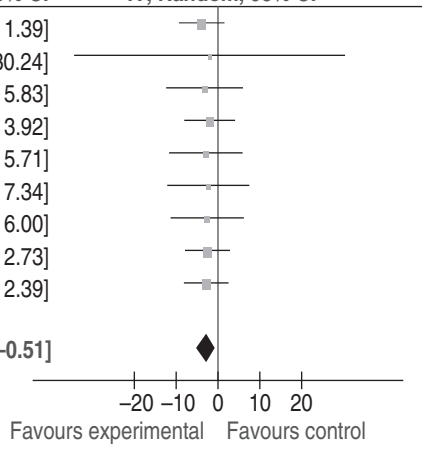


Figure 3. (A) Meta-analysis plot for weight loss with orlistat in minorities and (B) meta-analysis plot for weight loss with orlistat in White Caucasians.

Caucasian patients. For orlistat, weight loss was insignificantly higher in White Caucasians than in minorities. These results are consistent with previous studies of pharmacologically induced weight loss in the general population which suggest that the maximum average weight loss is <5 kg [22–27]. Our results together with other reviews [19,20,22–24] have also shown that weight loss achieved by using sibutramine is greater than that achieved by using orlistat in both ethnic minorities and White Caucasians. This may be because of the difference in mechanism of action of the two drugs. Sibutramine acts as a serotonin and noradrenaline reuptake inhibitor which promotes weight loss by generating feelings of satiety [21]. Orlistat, on the other hand, is a gastro-intestinal lipase inhibitor which acts by blocking the absorption of approximately 30% of dietary fat [21]. Orlistat-treated patients are encouraged to eat a nutritionally balanced low-fat diet and therefore treatment with Orlistat needs greater engagement from the patient over long periods of time compared to sibutramine treatment.

Our results suggest that weight loss with sibutramine was more successful in White Caucasians. It is difficult to explain this, as none of the studies were designed to examine the effect of ethnicity on response to treatment and it is likely that the studies were underpowered for this outcome. In most of the trials, White Caucasian participants outnumbered ethnic minorities by two to three times. This highlights the underrepresentation of ethnic minorities in clinical trials despite the increased metabolic morbidity in these groups of patients [51]. To increase the participation rate of ethnic minorities in trials,

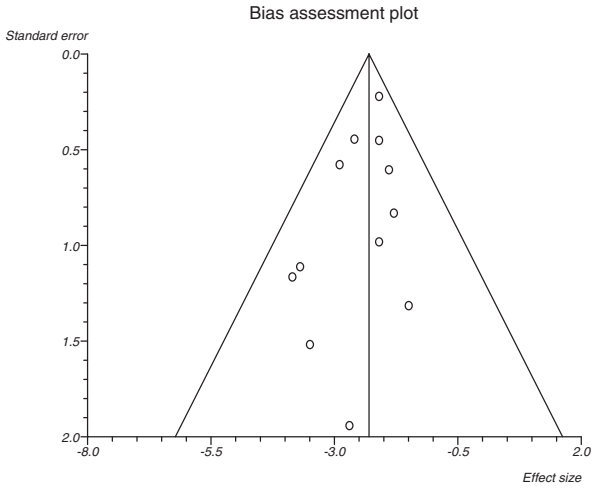


Figure 4. Funnel plot for orlistat.

it has been suggested that trials must be culturally sensitive by providing, for example, a setting that incorporates features probably to be familiar to minority participants [52] and the use of researchers/investigators who are members of the particular minority group [52].

There were also differing effects of weight loss on secondary outcomes in ethnic minorities and White Caucasians by sibutramine and orlistat. While sibutramine resulted in significant improvements in waist circumference (both groups) and HDL and triglyceride in only White Caucasians, orlistat was associated with significant improvements in systolic blood pressure, fasting blood glucose, HbA1c, total and LDL cholesterol (both groups) and diastolic blood pressure (only White Caucasians). These results are difficult to explain but it should be noted that, while some trials were powered to detect significant changes in the primary outcome, no trial was powered to detect secondary outcomes; therefore these results should be interpreted with some caution.

The decision to prescribe an antiobesity drug involves careful assessment of the risks and benefits to the patient. On the basis of recent evidence from the Sibutramine Cardiovascular Outcome (SCOUT) trial, the European Medicines Agency (EMA) has suspended the prescribing license for sibutramine in Europe [53]. The SCOUT study was an RCT involving approximately 10 000 obese and overweight patients with cardiovascular disease and/or type 2 diabetes treated over a 6-year period. Patients treated with sibutramine experienced a 16% increased risk of cardiovascular events compared with placebo-treated patients [hazard ratio 1.161 (95% CI: 1.029 to 1.311); $p = 0.016$]. Although most of the patients enrolled within SCOUT would not qualify for treatment with sibutramine on current clinical criteria, the EMA felt that the cardiovascular risk would be relevant to routine clinical care because it is not always possible to identify underlying cardiovascular disease in patients who are obese or overweight and withdrew the license in Europe. The US Food and Drug Administration's (FDA) review of SCOUT is ongoing. In the meantime, the FDA has initiated a label change and the product remains on the market in the USA. Australia's Therapeutic Goods Administration (TGA) has also taken a similar action. Data from the SCOUT study are as yet not widely available and it is not clear if a subgroup analysis of data from ethnic groups has been performed.

It is well known that there are significant differences in metabolic disease risk between ethnic groupings [2]. It is not clear if this is because of different disease processes at work or if this just reflects an alteration in risk threshold. It cannot therefore be assumed that people from different ethnic backgrounds would respond differently to pharmacological interventions. We acknowledge that combining different ethnic minorities into one group is problematic. Authors were contacted for detailed subgroup analysis but because of underrepresentation of these groups in clinical trials and lack of separate data for each ethnic group, it was not possible to obtain results for every minority ethnic group. Although this does impose limitations in the interpretation of these review data, this does not diminish the message that there may be differences between ethnic minorities and Whites with respect to response to pharmacological treatments of obesity: a message that has implications both for clinical care and future research.

Other antiobesity medications like phentermine and fluoxetine were not included in the review as they did not meet the inclusion criteria: the inclusion of only approved/licensed antiobesity medications, duration (≥6 months) and randomized placebo-controlled trial. These inclusion criteria were used because it was thought the 6-month duration is the period within which the effectiveness of a weight management intervention should be evaluated [24]. Additionally, RCTs are a better estimate of effect size [54].

This review does provide evidence to support the effectiveness of antiobesity medications, in addition to lifestyle approaches, in overweight and obese patients from minority ethnic groups and, despite the limitations of the available data, most of these RCTs showed positive weight management results. However, more studies need to be performed in minority ethnic groups to develop a greater understanding as to how weight loss interventions may be tailored to provide maximum benefit to individual patients.

Conflict of Interest

G. O.-A., Y. A., I. K., S. K. and K. M. designed this study. G. O.-A., Y. A., I. K. and K. M conducted and collected data. G. O.-A., Y. A. and K. M. analysed the data. G. O.-A., Y. A., S. K. and K. M. wrote the manuscript. KM has received support to attend conferences from Roche. All other authors have no competing interests.

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