Long-term Effects of Weight-Reducing Interventions in Hypertensive Patients

Systematic Review and Meta-analysis

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Weight loss is recommended in all major guidelines for antihypertensive therapy. We searched for randomized controlled trials investigating the effects of weight-reducing diets, pharmacologic substances, and invasive interventions for weight reduction on patient-relevant end points and blood pressure (BP) in patients with essential hypertension. No information on the effects on patient-relevant end points was available. Patients assigned to weight loss diets, orlistat, or sibutramine reduced their body weight more effectively than did patients in the usual care/placebo groups. Reduction of BP was higher in patients treated with weight loss diets (systolic BP [SBP]: weighted mean difference [WMD], −6.3 mm Hg; diastolic BP [DBP]: WMD, −3.4 mm Hg) or orlistat (SBP: WMD, −2.5 mm Hg; DBP: WMD, −2.0 mm Hg). Systolic BP increased with sibutramine treatment (WMD, 3.2 mm Hg). In patients with essential hypertension, therapy with a weight loss diet or orlistat resulted in reductions in body weight and BP. Although sibutramine treatment reduced body weight, it did not lower BP.

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Globally, cardiovascular diseases (CVDs) account for 13% of the disease burden in adults and for approximately half of the deaths caused by noncommunicable diseases, that is, 16.7 million. In developed countries, heart disease and stroke are the first and second leading causes of death in adults and together are responsible for 36% of all deaths. Furthermore, the mortality and disease burden resulting from CVD are rapidly increasing in developing regions. Among the major CVD risk factors is high blood pressure (BP). High BP is estimated to lead to more than 7 million deaths each year, approximately 13% of the total deaths worldwide. Lowering BP levels in hypertensive patients has been shown to be a very effective means of reducing patients’ cardiovascular risk, with a significant reduction in cardiovascular morbidity and mortality.

Consistently, epidemiologic investigations have found an association between high BP and different lifestyles, excess body weight among them. Weight reduction is recommended in major guidelines as an initial intervention in the treatment of hypertensive patients. Among the possible means of reducing body weight are lifestyle modifications and pharmacologic and invasive interventions.

METHODS

The review question was to assess the long-term effects of (1) dietary interventions intended to reduce body weight, (2) pharmacologically induced reduction in body weight, and (3) reduction of body weight through invasive interventions on all causes of death, cardiovascular morbidity, adverse events, and BP in people with essential hypertension.

ELIGIBILITY CRITERIA

To be included in this meta-analysis, trials were required to use a randomized controlled design; to compare dietary, pharmacologic, or in-
vative interventions for weight loss with placebo or usual care; and to have follow-up of at least 24 weeks. Combinations of different nonpharmacologic interventions for reducing BP without the possibility of analyzing the different interventions were excluded. In the case of an additional active care (eg, antihypertensive medication), this co-therapy also had to be a component of the comparison group. To be considered, trials had to include patients with essential hypertension aged 18 years or older (excluding pregnant women) and had to report on at least 1 of the following outcomes: mortality, cardiovascular outcomes, adverse events, and BP effects. Publication language had to be English, German, Dutch, French, Italian, Portuguese, or Spanish.

IDENTIFICATION AND SELECTION OF TRIALS

An initial search was performed in June 2006 in MEDLINE, EMBASE, the Cochrane databases, BIOSIS, and CINAHL and in the reference lists of retrieved relevant articles and overviews. Also, study registries and the Internet sites of the European Agency for the Evaluation of Medicinal Products and the Food and Drug Administration were searched. Companies manufacturing sibutramine and orlistat and authors of relevant articles were contacted. In March 2007, we updated the search and extended it to include rimonabant. The updated search was limited to the electronic databases MEDLINE, EMBASE, and CENTRAL.

OUTCOME MEASURES

Outcomes of primary interest were total mortality, cardiovascular morbidity, and adverse events. Other analyzed outcomes were duration and magnitude of BP and body weight reduction.

STUDY SELECTION AND QUALITY ASSESSMENT

Two of us (K.H., K.J., T.W.G., and/or A.S.) independently screened the title, abstract, and key words of each reference identified by the search and applied the inclusion and exclusion criteria. The same procedure was applied to references retrieved for more detailed evaluation. Differences between reviewers were resolved by discussion or a third reviewer (K.H., K.J., T.W.G., or A.S.). Data on quality, patient characteristics, interventions, and relevant outcomes were abstracted by 2 reviewers (K.H., K.J., T.W.G., and/or A.S.) independently.

Quality assessment was based on the adequacy of randomization; allocation of concealment; blinding of participants, study personnel, and outcome assessors; comparability of patients in the different treatment groups for prognostically relevant factors at baseline; follow-up and handling of withdrawals and dropouts in the analyses; statistical methods; and consistency of reporting. Accordingly, the methodological quality of the included studies was graded as no methodological deficiencies detectable (A), slight methodological deficiencies detectable (B), or serious methodological deficiencies detectable (C).

STATISTICAL ANALYSIS

Weighted mean differences (WMDs) were calculated for the changes in BP and body weight. A random-effects model was used for the meta-analyses. Standard deviations were approximated on the basis of P values and, if P values were not available, sample sizes. Heterogeneity between trials was assessed using Higgins I², which describes the percentage of the variability in effect estimates due to heterogeneity. In the case of substantial heterogeneity (Higgins I² > 50%), 6 we planned to perform sensitivity analyses and subgroup analyses for the following items: study quality, per-protocol vs intention-to-treat analyses, sex, age, body mass index, concomitant diseases, ethnicity, BP at baseline, BP goals, concomitant antihypertensive therapy, and socioeconomic status. However, owing to the low number of included trials in the different meta-analyses and the lack of information on most of these items, we could not perform formal sensitivity analyses. A formal statistical test on publication bias was not meaningful because of the low number of included trials. 7

Figure 1 shows the number of trials (1) identified, (2) excluded for vari-
ous reasons, and (3) included in the systematic review. The XENDOS study\textsuperscript{8-10} was included in this review only after additional information was made available through the manufacturer (Hoffmann-LaRoche AG, Basel, Switzerland). This information is publicly available in the Institute for Quality and Efficiency in Health Care report\textsuperscript{6} on this topic.

Seven studies (38 publications) investigated dietary interventions. In 8 studies (10 publications), pharmacologic interventions (orlistat or sibutramine) were compared with placebo. No studies examining surgical interventions or rimonabant satisfying the inclusion criteria were found, mainly because studies were not randomized, had a duration of less than 24 weeks, or did not allow for extraction of results for hypertensive patients.

**DIETARY INTERVENTION STUDIES**

**Trial Characteristics and Quality**

The 7 studies (Croft et al\textsuperscript{11} the Dietary Intervention Study of Hypertension [DISH]\textsuperscript{12-14} Jalkanen\textsuperscript{15} the Oslo Diet and Exercise Study [ODES]\textsuperscript{16-24} Ruvolo et al\textsuperscript{25} the Trial of Antihypertensive Interventions and Management [TAIM]\textsuperscript{26-37} and the Trial of Nonpharmacologic Interventions in the Elderly [TONE]\textsuperscript{38-48}) comparing a dietary intervention for reducing body weight with usual care included a total of 1632 patients. Follow-up lasted 6 to 36 months, and the mean age of patients ranged from 45 to 66 years. For results on study quality, see Table 1.

**Results of Data Synthesis**

Only TONE\textsuperscript{38-48} was designed to evaluate the effects of dietary weight loss vs no such diet on a combined end point, including cardiovascular complications. After 30 months, the hazard ratio for patients in the dietary group to reach the combined end point, consisting of the necessity of reinstating antihypertensive therapy and severe cardiovascular complications, was 0.70 (95% confidence interval [CI], 0.57 to 0.87) compared with patients in the usual care group. No information on possible adverse effects of the different dietary interventions was reported in any publications of the relevant trials.

Based on their design, the reported outcomes, and data, only the studies by Croft et al\textsuperscript{11} and ODES\textsuperscript{16-24} could be included in a meta-analysis on systolic BP (SBP). The meta-analysis found a significant difference in the reduction of SBP in favor of dietary interventions: WMD, −6.26 mm Hg (95% CI, −9.82 to −2.70 mm Hg) (I\textsuperscript{2}=0\%) (Figure 2A). For diastolic BP (DBP), the Croft et al\textsuperscript{11} ODES\textsuperscript{16-24} and TAIM\textsuperscript{26-37} studies were incorporated into the meta-analysis, showing a significant difference in the reduction of DBP in favor of dietary interventions: WMD, −3.41 mm Hg (95% CI, −5.55 to −1.27 mm Hg) (I\textsuperscript{2}=36\%) (Figure 2B).

Of those investigations that could not be included in the meta-analyses, the study by Ruvolo et al\textsuperscript{25} found that a weight loss diet affected BP favorably, whereas in the study by Jalkanen,\textsuperscript{15} dietary interventions were less effective than usual care (Table 2). Two further studies\textsuperscript{12-14,38-48} reported not BP changes but the number of patients needing reinstatement of antihypertensive therapy after stopping all antihypertensive medication use at the beginning of the trials. In both studies, the number of patients eventu-
ally requiring antihypertensive therapy was lower in the diet groups.

Information on body weight change in hypertensive patients was available from 5 studies comparing diet with usual care (Table 2). A meta-analysis including 4 of these studies found a significant reduction in body weight of WMD −4.14 kg (95% CI, −4.98 to −3.30 kg) in patients in the diet groups compared with patients in the usual care groups (Figure 2C). Heterogeneity was I² = 36%. The fifth study, 25 not included in the meta-analysis owing to missing variables of variance, also showed a markedly higher reduction in body weight for patients treated by dietary means (Table 2).

**PHARMACOLOGIC INTERVENTION STUDIES**

**Trial Characteristics and Quality**

We identified 4 studies (Bakris et al, 49 Cocco et al, 50 Guy-Grand et al, 51 and the XENDOS study 8,10) that compared orlistat with placebo in 3132 hypertensive patients with a mean age of 46 to 55 years. Study duration ranged from 6 to 48 months. For sibutramine vs placebo, 4 studies (Fanghanel et al, 52 Faria et al, 53,54 and McMahon et al 55,56) were identified. A total of 610 patients with a mean age of 46 to 53 years were included in these studies. Study duration ranged from 6 to 12 months. For results on study quality, see Table 1.

**Results of Data Synthesis**

None of the studies was designed to investigate the effects of therapy with orlistat or sibutramine on mortality or cardiovascular end points. It remains unclear whether therapy with orlistat or sibutramine will lead to beneficial or even disadvantageous outcomes. Gastrointestinal adverse effects were the adverse events most commonly reported by patients treated with orlistat. Formal statistical testing resulting in a significant difference in favor of placebo was presented in only 1 trial. 49 In this study 49 and in the XENDOS study, 8,10 treatment with orlistat also resulted in a significantly higher proportion of patients experiencing musculoskeletal pain.

Whereas in the investigation by Fanghanel et al, 52 patients in both comparison groups reported comparable rates of adverse events, Faria et al 53,54 and McMahon et al 55,56 found that more patients treated with sibutramine reported dry mouth as an adverse effect than did patients in the placebo group. In one of the studies by McMahon et al, 55 the difference reached statistical significance. Faria et al 53 also reported that arthralgia was more common with sibutramine treatment. Patients in the sibutra-

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**Table 1.**

<table>
<thead>
<tr>
<th>Source</th>
<th>Participants, No.</th>
<th>Mean (SD)</th>
<th>WMD (random) (95% CI)</th>
<th>Weight, %</th>
<th>WMD (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Croft et al, 11</td>
<td>66</td>
<td>−11.00 (15.26)</td>
<td>−6.90 (4.66)</td>
<td>36.1%</td>
<td>−6.50 (4.86)</td>
</tr>
<tr>
<td>ODES 16-24 IG vs CG</td>
<td>16</td>
<td>−8.40 (12.30)</td>
<td>−4.00 (2.80)</td>
<td>36.4%</td>
<td>−3.50 (3.70)</td>
</tr>
<tr>
<td>ODES 16-24 IG + Pa vs CG + Pa</td>
<td>24</td>
<td>−8.30 (10.29)</td>
<td>−4.10 (6.96)</td>
<td>36.1%</td>
<td>−4.20 (6.37)</td>
</tr>
<tr>
<td>Total</td>
<td>106</td>
<td>96</td>
<td>−11.00 (15.26)</td>
<td>50.0%</td>
<td>−4.14 (10.65)</td>
</tr>
<tr>
<td>Heterogeneity: Q = 1.47 (P = .48), I² = 0%</td>
<td>Overall effect: Z score = −3.45 (P = .001), t² = 0.000</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Table 2.**

<table>
<thead>
<tr>
<th>Source</th>
<th>Participants, No.</th>
<th>Mean (SD)</th>
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</tr>
</thead>
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<tr>
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<td>−7.10 (6.37)</td>
<td>−4.10 (6.96)</td>
<td>36.1%</td>
<td>−4.20 (6.37)</td>
</tr>
<tr>
<td>TAIM 26-37 IG vs CG</td>
<td>265</td>
<td>−12.80 (10.00)</td>
<td>−7.10 (4.66)</td>
<td>36.1%</td>
<td>−7.00 (4.86)</td>
</tr>
<tr>
<td>Total</td>
<td>371</td>
<td>360</td>
<td>−7.00 (10.15)</td>
<td>50.0%</td>
<td>−6.00 (10.65)</td>
</tr>
<tr>
<td>Heterogeneity: Q = 4.7 (P = .20), I² = 36.1%</td>
<td>Overall effect: Z score = −3.12 (P = .002), t² = 1.759</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

**Figure 2.** Diet vs usual care: changes in systolic blood pressure (A), diastolic blood pressure (B), and body weight (C). The size of the squares represents the weight of studies in meta-analysis (a numerical representation is given in the “Weight, %” column). The width of the diamond shapes represents the 95%CI (see Cocco et al, 50 Guy-Grand et al, 51 and WMD, weighted mean difference.

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The results of the meta-analysis are presented in Table 2. The overall effect of diet vs usual care was significant for systolic blood pressure (WMD −3.30 kg) in patients in the diet groups (Figure 2A). The heterogeneity was I² = 36%. The fifth study, 25 not included in the meta-analysis owing to missing variables of variance, also showed a markedly higher reduction in blood pressure for patients treated by dietary means (Table 2).

**PHARMACOLOGIC INTERVENTION STUDIES**

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We identified 4 studies (Bakris et al, 49 Cocco et al, 50 Guy-Grand et al, 51 and the XENDOS study 8,10) that compared orlistat with placebo in 3132 hypertensive patients with a mean age of 46 to 55 years. Study duration ranged from 6 to 48 months. For sibutramine vs placebo, 4 studies (Fanghanel et al, 52 Faria et al, 53,54 and McMahon et al, 55,56) were identified. A total of 610 patients with a mean age of 46 to 53 years were included in these studies. Study duration ranged from 6 to 12 months. For results on study quality, see Table 1.

**Results of Data Synthesis**

None of the studies was designed to investigate the effects of therapy with orlistat or sibutramine on mortality or cardiovascular end points. It remains unclear whether therapy with orlistat or sibutramine will lead to beneficial or even disadvantageous outcomes. Gastrointestinal adverse effects were the adverse events most commonly reported by patients treated with orlistat. Formal statistical testing resulting in a significant difference in favor of placebo was presented in only 1 trial. 49 In this study 49 and in the XENDOS study, 8,10 treatment with orlistat also resulted in a significantly higher proportion of patients experiencing musculoskeletal pain.

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mine vs placebo found disadvantageous BP effects for sibutramine (Table 4). A meta-analysis for sibutramine was not possible because, in all the studies, variability measurement data were missing. For the same reason, the results of the studies by Fanghanel et al22 and Faria et al55,56 could not be included in the meta-analysis on DBP. A combined analysis for DBP of the remaining 2 studies by McMahan et al55,56 showed a significant difference between sibutramine and placebo, with a detrimental effect in patients treated with sibutramine: WMD, 3.16 mm Hg (95% CI, 1.40 to 4.92 mm Hg) ($I^2=37\%$) (Figure 3A). Diastolic BP was also significantly reduced in patients treated with orlistat: WMD, −1.92 mm Hg (95% CI, −2.99 to −0.85 mm Hg) ($I^2=47\%$) (Figure 3B).

The 4 studies examining sibutramine vs placebo found disadvantageous BP effects for sibutramine (Table 4). A meta-analysis for sibutramine was not possible because, in all the studies, variability measurement data were missing. For the same reason, the results of the studies by Fanghanel et al22 and Faria et al55,56 could not be included in the meta-analysis on DBP. A combined analysis for DBP of the remaining 2 studies by McMahan et al55,56 showed a significant difference between sibutramine and placebo, with a detrimental effect in patients treated with sibutramine: WMD, 3.16 mm Hg (95% CI, 1.40 to 4.92 mm Hg) ($I^2=37\%$) (Figure 3A). Diastolic BP was also significantly reduced in patients treated with orlistat: WMD, −1.92 mm Hg (95% CI, −2.99 to −0.85 mm Hg) ($I^2=47\%$) (Figure 3B). The 4 studies examining sibutramine vs placebo found disadvantageous BP effects for sibutramine (Table 4). A meta-analysis for sibutramine was not possible because, in all the studies, variability measurement data were missing. For the same reason, the results of the studies by Fanghanel et al22 and Faria et al55,56 could not be included in the meta-analysis on DBP. A combined analysis for DBP of the remaining 2 studies by McMahan et al55,56 showed a significant difference between sibutramine and placebo, with a detrimental effect in patients treated with sibutramine: WMD, 3.16 mm Hg (95% CI, 1.40 to 4.92 mm Hg) ($I^2=37\%$) (Figure 3A). Diastolic BP was also significantly reduced in patients treated with orlistat: WMD, −1.92 mm Hg (95% CI, −2.99 to −0.85 mm Hg) ($I^2=47\%$) (Figure 3B).
**Table 3. Characteristics and Results of Studies Investigating Orlistat**

<table>
<thead>
<tr>
<th>RCT Groups</th>
<th>Participants, No.</th>
<th>Difference, Mean (SD) [SE]^a</th>
<th>Weight, kg</th>
<th>HR, bpm</th>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bakris et al.49 2002</td>
<td>IG: 278</td>
<td>−13.3 (15.2)</td>
<td>−11.4 (8.3)</td>
<td>−5.4 (6.4)</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>CG: 276</td>
<td>−11.0 (15.0)</td>
<td>−9.2 (8.4)</td>
<td>−2.7 (6.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Cocco et al.50 2005</td>
<td>IG: 45</td>
<td>−4.3 (NA)</td>
<td>−3.6 (NA)</td>
<td>−5.4 (NA)</td>
<td>−1.9 (NA)</td>
</tr>
<tr>
<td></td>
<td>CG: 45</td>
<td>−0.9 (NA)</td>
<td>−0.8 (NA)</td>
<td>−2.5 (NA)</td>
<td>1.0 (NA)</td>
</tr>
<tr>
<td>Guy-Grand et al.51 2004</td>
<td>IG: 304</td>
<td>−9.8 [1.0]</td>
<td>−7.5 [0.6]</td>
<td>−5.8 [0.3]</td>
<td>NA</td>
</tr>
<tr>
<td></td>
<td>CG: 310</td>
<td>−9.8 [1.0]</td>
<td>−7.3 [0.6]</td>
<td>−1.8 [0.2]</td>
<td>NA</td>
</tr>
<tr>
<td>XENDOS study,8–10</td>
<td>IG-D vs CG-D</td>
<td>−8.8 (14.8)</td>
<td>−8.1 (9.3)</td>
<td>−6.6 (8.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Bakris et al.49 2001-2006</td>
<td>IG-D: 441</td>
<td>−6.4 (15.1)</td>
<td>−6.2 (9.9)</td>
<td>−3.8 (7.8)</td>
<td>NA</td>
</tr>
<tr>
<td>Sp: industry</td>
<td>CG-D: 407</td>
<td>−11.5 (14.9)</td>
<td>−5.0 (9.9)</td>
<td>−8.8 (8.7)</td>
<td>NA</td>
</tr>
<tr>
<td>Guy-Grand et al.51 (4 y)</td>
<td>IG-S: 516</td>
<td>−8.6 (14.3)</td>
<td>−3.0 (10.4)</td>
<td>−3.2 (7.4)</td>
<td>NA</td>
</tr>
<tr>
<td>Sp: industry</td>
<td>CG-S: 509</td>
<td>−9.1 (12.3)</td>
<td>−17.8 (13.8)</td>
<td>−14.6 (12.8)</td>
<td>NA</td>
</tr>
</tbody>
</table>

Abbreviations: CG, control group; D, DBP of 90 mm Hg or greater at baseline; DBP, diastolic blood pressure; HR, heart rate; IG, intervention group; NA, not available; NS, not significant; RCT, randomized controlled trial; S, SBP 140 mm Hg or greater at baseline; SBP, systolic blood pressure; Sp, sponsoring; XENDOS, XENical in the prevention of Diabetes in Obese Subjects.

^a Difference from the beginning to the end of the study.

**Figure 3. Orlistat vs placebo: changes in systolic blood pressure (A), diastolic blood pressure (B), and body weight (C).** The size of the squares represents the weight of studies in meta-analysis (a numerical representation is given in the “Weight, %” column). The width of the diamond shapes represents the 95% CI (see also WMD [95% CI] column). CG indicates control group; CI, confidence interval; I^2, Higgins I^2; IG, intervention group; D, diastolic blood pressure of 90 mm Hg or greater at baseline; WMD, weighted mean difference; and XENDOS, XENical in the prevention of Diabetes in Obese Subjects. *The SDs are calculated on the basis of P<.03. †The SDs are calculated on the basis of P=.01. ‡The SDs are calculated on the basis of P=.001.
more pronounced decrease in patients with sibutramine therapy.

**COMMENT**

This systematic review attempted to determine the long-term effects of weight loss through dietary, pharmacologic, or invasive interventions on patient-relevant end points, namely, death and cardiovascular complications, in the antihypertensive therapy of patients with essential hypertension but found that currently no randomized controlled trials designed to answer this question are available.

We found that dietary interventions to reduce body weight successfully reduced body weight and lowered BP in 1 year of follow-up in these patients. However, because all the studies except TAIM26-37 and TONE38-49 have major methodological deficiencies, the beneficial effects shown remain afflicted with some degree of uncertainty.

Of the 4 studies on the effects of orlistat included in the present analyses, only 1 was judged as having major deficiencies in study quality. The meta-analyses showed that patients being treated with orlistat could reduce their weight and BP levels significantly more than patients in the placebo groups. Although these results show that orlistat may be a helpful option in the antihypertensive therapy of obese hypertensive patients, some questions still remain. First, patients with orlistat therapy experienced adverse effects to a high degree, foremost of a gastrointestinal nature. This might unfavorably affect the ef-
ffectiveness of the medication in settings outside of scientific studies. Furthermore, it remains unclear whether BP levels will remain low for a longer period or once the medication is discontinued because different investigations found body weight increasing again after 1 year, independent of whether orlistat treatment was continued.37,38

Although sibutramine reduced body weight about the same amount as orlistat, it did not show the same beneficial effects on BP. In 2 studies using a dosage of 20 mg/d, which is higher than the currently (in Germany) approved dosage of 10 to 15 mg/d, BP even rose in patients treated with sibutramine. This finding is further underlined by the results of a head-to-head comparison of orlistat vs sibutramine.39 It found that, whereas in patients in the orlistat group (120 mg 3 times a day) a reduction of −8.4 kg of body weight resulted in a reduction in SBP and DBP of −4.0 and −3.0 mm Hg, respectively, the same loss of body weight of −8.3 kg in the sibutramine group did not cause a change in BP in patients treated with sibutramine, 10 mg/d (0.0 and 0.0 mm Hg). Also, in a meta-analysis by Kim et al40 comparing sibutramine with placebo in patients with or without hypertension at baseline, significant increases in SBP (1.6 mm Hg) and DBP (1.8 mm Hg) were found in the sibutramine treatment group despite a large effect on weight loss in this group.

Four studies (the RIO [Rimonabant in Obesity] studies)61-64 investigated the effects of therapy with rimonabant, 20 and 5 mg/d, compared with placebo in study populations including normotensive and hypertensive (30%-60%) patients. None of these studies was designed to assess the effects on patient-relevant end points. Patients being treated with rimonabant, regardless of the dosage, reduced their body weight significantly more than placebo-treated patients. Contrary to these findings, the studies yielded heterogeneous results concerning BP changes. In particular, therapy with 5 mg of rimonabant showed inconsistent results, with a higher reduction in BP compared with placebo in some studies but less of a reduction in others. Treatment with 20 mg of rimonabant daily showed more uniform findings, with a higher reduction in SBP in all 4 studies (the difference was significant in 2). Also, the reduction in DBP was more pronounced in patients receiving rimonabant, 20 mg, than in placebo-treated patients in 3 studies (the difference was significant in 1), but slightly less in 1 study. Only the publication of the RIO Lipid study61 reported information on a hypertensive subgroup. In hypertensive patients treated with 20 mg of rimonabant, BP was reduced statistically significantly more than in patients in the placebo group (SBP: −5.9 mm Hg and DBP: −3.9 mm Hg). Because no other information on the hypertensive subgroup is given (the article does not even report the percentage of patients with hypertension at baseline), the relevance of these findings remains unclear. Hopefully, more results on hypertensive patients will be published.

A major limitation of this review is that because of the lack of information in the included studies, no conclusions on the effects of the different weight loss interventions on patient-relevant end points can be drawn. Also, because the maximum duration of the included trials was 4 years, and Sjöström et al63 found that BP in patients who successfully reduced their body weight by means of bariatric surgery was still reduced 2 years after surgery but increased again to baseline values after 10 years despite continued weight loss, the long-term effects of weight loss on BP found in this review are uncertain.

In conclusion, in patients with essential hypertension, therapy with dietary interventions to reduce body weight or with orlistat resulted in reductions in BP and body weight. A reduction in body weight of approximately 4 kg was necessary to achieve a reduction of approximately 6 mm Hg in SBP with dietary treatment and of approximately 2.5 mm Hg with orlistat. Although sibutramine treatment reduced body weight it did not lower or might even elevate BP. None of the studies provided data to answer the question whether risk of mortality or other patient-relevant end points can be lowered by weight reduction.