Meta- and Cost-Effectiveness Analysis of Commercial Weight Loss Strategies

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Objective: To estimate the incremental cost-effectiveness of clinically proven nonsurgical commercial weight loss strategies for those with BMIs between 25 and 40.

Methods: We performed a systematic literature review to identify randomized controlled trials of commercially available weight loss studies of at least 1 year in duration. Using the results of these trials and publicly available cost data, we quantified the incremental cost per kilogram of weight loss and per quality adjusted life year (QALY) gained. We then use probabilistic sensitivity analyses to quantify uncertainty in our results.

Results: Based on the literature review, two lifestyle programs (Weight Watchers and Vtrim), one meal replacement program (Jenny Craig), and three pharmaceutical products (Qsymia, Lorcaserin, and Orlistat) were included in the analysis. Average cost per kilogram of weight lost ranged from $155 (95% CI: $110-$218) for Weight Watchers to $546 (95% CI: $390-$736) for Orlistat. The incremental cost per QALY gained for Weight Watchers and Qsymia was $34,630 and $54,130, respectively. All other interventions were prohibitively expensive or inferior in that weight loss could be achieved at a lower cost through one or a combination of the other strategies.

Conclusions: Results suggest that, in the absence of other considerations and at current market prices, Weight Watchers and Qsymia represent the two most cost-effective strategies for nonsurgical weight loss.

Introduction

Every year millions of Americans will attempt to lose weight. Many will enroll in commercial weight loss programs and/or take weight loss medication. Currently, the majority of these costs are financed directly by individuals, yet the high prevalence and costs of obesity, greater acknowledgement that obesity is a disease, and growing emphasis on accountable care means that third parties will be increasingly subsidizing some of these costs. As the number of available treatments increases, the decision of which option is right for a given individual, employer, or health plan becomes increasingly complex.

For third party payers, the relative benefits of available treatments are a significant consideration. Yet little information exists that directly compares costs and effectiveness across options. This results because nearly all weight loss trials compare only two arms, and one is typically a low-cost minimal intervention. In the absence of

direct comparisons, several attempts at evaluating the comparative effectiveness have been made. Tsai and Wadden (1) described the cost and efficacy of several major commercial weight loss programs available in the United States but did not include any pharmaceutical interventions. Recently, Yanovski and Yanovski (2) systematically reviewed the effectiveness of medications but excluded commercial programs. To date, there has not been a comprehensive study that compares the incremental costs and benefits of available nonsurgical weight loss interventions including both commercial programs and weight loss medications. This is a significant limitation given that weight loss medications and programs are viable substitutes in many circumstances and because resource allocation decisions should be made on the basis of incremental, as opposed to average, costs and benefits, when one is considering a choice between alternative treatment options (3).

The objective of this study is threefold. First, we identify all commercially available nonsurgical weight loss strategies with published

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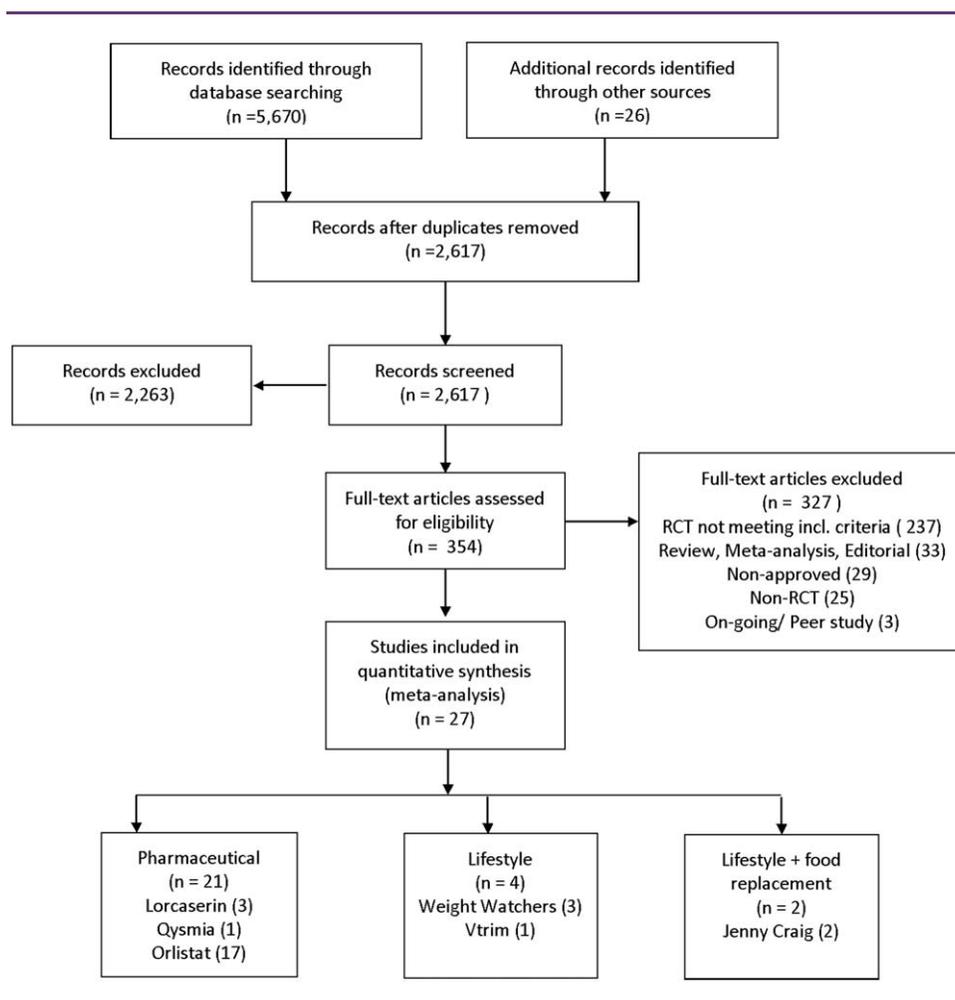
Figure 1 PRISMA flow diagram.

efficacy at 12 months or longer based on randomized controlled trials (RCTs). We then compare the weight loss and costs for each of these interventions and report the average and incremental (relative to the next most expensive strategy) costs per kilogram of weight lost. Third, to put the results into context, we convert the weight loss results into costs per quality adjusted life years (QALYs) saved to allow for comparing results with established benchmarks for cost-effectiveness. These findings will be of relevance to payers and others interested in identifying the relative costs and benefits of commercially available weight loss strategies.

Methods

Search methods

Pubmed, Medline, and Cochrane databases were searched from inception to November 18, 2013. Search strategies used the keywords obesity, overweight, body mass index, treatment, weight loss, and RCT. A keyword search was also conducted by combining the terms weight loss and commercial, weight loss and proprietary, and RCT. This search was further supplemented by a review of relevant bibliographies. The search resulted in the identification of 2,617

studies after removing duplicates (Figure 1). Studies identified underwent a review of the title, abstract, or both to discard nonrelevant articles.

To be included, studies had to be based on an RCT design, focus on adults, have less than 50% attrition, and include as a primary or secondary outcome weight loss results of 12 months or longer based on intention-to-treat (ITT) principles. The strategy must also be currently available in the United States. The goal of this manuscript is to focus on commercially available nonsurgical weight loss interventions that would be appropriate for the vast majority of the overweight/obese population. As a result, we limited the review to trials of nonsurgical interventions that focus on those with average BMI values below 40.

Costs

Costs include any required food costs and program fees for commercial programs, and weight loss medication and physician visit costs for weight loss medications. Annual direct costs for weight loss programs were limited to subscription and/or appointment costs. These costs were based on an online search. For pharmaceutical products, the Medi-Span Price RX database (4) was searched (September

2013) for the lowest listed wholesale acquisition price or average wholesale price for the standard dose. Costs for two physician visits that would be expected to occur in the year that someone starts a weight loss medication was then added to the medication cost (5). We then reduce the total cost estimates based on reported attrition rates from each study, assuming participants quit at 3 months on average (i.e., we give these participants just one quarter of the annual costs).

Jenny Craig is different from the other interventions in that payment for Jenny Craig meals offsets some of the food costs that would occur in the absence of the program. Our analysis focuses solely on the incremental costs that are expected to occur for someone who joins Jenny Craig. To calculate the incremental costs, we use the Hall et al. (6) dynamic energy expenditure model to estimate the number of calories consumed per day for a 46-year-old woman with a BMI of 35, the weighted average of age and BMI from our included studies. We divide this number by average daily food costs from Gallup (7) [inflated to 2013 prices using the consumer price index (CPI) inflator for food (8)] to obtain the average daily cost per calorie while not on the diet. We consider two scenarios. The first quantifies incremental costs for someone with average income (JC_{AI}) and the second quantifies costs for high-income individuals (JC_{HI}) who have greater average food costs, thus lower incremental costs for the Jenny Craig diet. The latter perspective recognizes that individuals who join Jenny Craig typically have higher incomes. To obtain the cost per calorie for Jenny Craig foods, we divide the average cost of Jenny Craig foods consumed in a typical day by the average number of calories in those foods. Next, we estimated the calorie reduction necessary to achieve the weight loss at 12 months reported by the trials for each weight loss intervention. The incremental cost of the diet per day is then calculated as follows:

$$\text{Daily incremental cost of Jenny Craig Diet} = \text{Cal}_{JC} \times \text{Costcal}_{JC} + (\text{Dailycal}_{JC} - \text{Cal}_{JC}) \times \text{Costcal}_{NonJC}$$

where Cal_{JC} is daily calories from Jenny Craig foods, Costcal_{JC} is per calorie cost of Jenny Craig foods, Dailycal_{JC} is calories consumed per day for a 46-year-old woman with a BMI of 35 while on the diet, and Costcal_{NonJC} is cost per calorie for the remaining non-Jenny Craig foods consumed (either average income consumers or high-income consumers). From this cost, the cost of food per day when not on the diet is subtracted and the difference is multiplied by 365 to calculate the average incremental cost per year for those on Jenny Craig, separately for high-income and average income participants.

Effectiveness

Weight loss. Weight loss was measured in terms of absolute change in kilograms lost relative to the control arm. In nearly all studies, the control arm was a low-cost/low-intensity intervention, plus a placebo for the pharmaceutical trials. Two lifestyle interventions did not have a pure control arm (9,10). For comparability, these studies were compared to the weighted average weight loss of those in the control arms for the other lifestyle RCTs. Where multiple studies for the same intervention were included, we use Review Manager Version 5.2 (11) to calculate the pooled estimate of the weight loss effect. Data were combined using a random-effects

model, with DerSimonian and Laird's technique for calculating between-study variance (12). Each study was weighted by the inverse of its reported study variance. In the event that some measure of distribution (e.g., standard error or standard deviation) or absolute or percentage weight loss was not reported, approximate standard errors were generated via the delta method.

QALYs. Conversion from weight loss to annual quality of life (QoL) improvements was estimated using data collected in a randomized double-blind clinical study of Qsymia (13). In brief, 2,487 overweight or obese adults were randomly assigned to receive placebo or one of two doses of Qsymia. Of those enrolled, 1,723 completed a baseline and 1 year weigh-ins and of these, 1,667 also completed an SF-12 version 2 health questionnaire (14). We used the Brazier and Roberts algorithm (15) to convert SF-12 version 2 into a health-related QoL metric for each participant at baseline and 1 year, where $0 = \text{dead}$ and $1 = \text{best imaginable health state}$. This algorithm is widely used in cost-effectiveness analyses (16-18). We then constructed a multivariate linear regression model to assess the impact of weight loss on change in QoL, regardless of study arm. The dependent variable was change in QoL at 1 year and the key independent variables were weight loss (kg) and weight loss squared, controlling for gender, age, baseline BMI, and baseline QALY. To calculate the 1 year change in effectiveness of each intervention in terms of QoL, we simply multiply the betas for weight loss and weight loss squared by our pooled estimate of effectiveness from each of the included studies.

Average and incremental cost-effectiveness ratios. Average and incremental cost-effectiveness ratios (ACERs and ICERs) in terms of cost per kilogram of weight lost and cost per QALYs gained are presented. ACERs compare the ratio of each interventions costs and effectiveness relative to the control intervention. ICERs present the ratio of incremental costs to incremental benefits when compared not to the control intervention but to the next most costly alternative. To calculate the ICERs, first interventions are ordered from lowest to highest cost. Next, dominated strategies are eliminated. These are strategies that are more costly, yet less effective than an alternative (termed simple dominated) or where greater effectiveness could be achieved at a lower cost using a combination of lower and higher cost strategies (termed extended dominated). Once dominated strategies are removed, ICERs for the remaining strategies are calculated simply by dividing the additional costs for each remaining intervention by the additional benefits.

Sensitivity analyses. Confidence intervals for costs, effectiveness, and ACERs were generated using probabilistic sensitivity analyses (PSAs) used on the base case model. We ran the model 1,000 times to assess the effect of uncertainty regarding all input parameters simultaneously. We assumed a normal distribution for costs and effectiveness. For costs, we assumed a standard deviation of 12.5% of mean costs; for effectiveness, we applied the standard errors reported from the trials or obtained through the meta-analysis exercise. We further assume that the relative standard error for QALYs is the same as for weight loss. We also conducted the following additional one-way sensitivity analyses: (1) reducing costs by food cost savings, (2) assuming noncompleters drop out at 6 months instead of 3 months, and (3) assuming effectiveness was compared to zero weight change, as opposed to the weight loss of the control intervention.

TABLE 1 Key components and costs of commercial weight loss programs

	Description	Subscription costs ($)	Other costs ($)	Completer costs ($)	Attrition[a] (%)	Annual cost ITT ($)
Lifestyle						
Weight Watchers[b]	Lifestyle weight loss intervention. Weekly in, person or online group meetings	515	N/A	515	36	377
Vtrim	Lifestyle weight loss intervention. Online group support.	925	N/A	925	35	682
Food substitution						
Jenny Craig Average Income	Lifestyle weight loss intervention with low-calorie meal replacements	340	2,949	3,289	6	3,152
Jenny Craig High Income		340	2,281	2,621	6	2,512
Pharmaceutical						
Lorcaserin	One Lorcaserin hydrochloride 10 mg tablet twice daily	2,394	178	2,572	43	1,743
Orlistat	One 120 mg Orlistat tablet taken three times daily	1,881	178	2,059	35	1,518
Qsymia	Once-daily combination of phentermine 7.5 mg and extended-release topiramate 45 mg	1,693	178	1,871	36	1,366

[a]Based on weighted average of attrition from each included study for each product.
[b]Since 2010 now operating on PointsPlus system, based on new food/exercise calculation method, but adhering to same basic principles. The PointsPlus system has yet to be tested in a randomized controlled trial.

Results

Search results

Six interventions met the inclusion/exclusion criteria: Two lifestyle interventions (Weight Watchers and Vtrim), one lifestyle and food replacement intervention (Jenny Craig), and three pharmaceutical interventions (Orlistat, Qsymia, and Lorcaserin). In total, 27 studies were identified, 3 for Weight Watchers ($n = 1,355$) (10,19,20), 1 for Vtrim ($n = 124$) (9), 2 for Jenny Craig ($n = 512$) (21,22), 3 for Lorcaserin ($n = 7,789$) (23), 17 for Orlistat ($n = 10,875$) (24-40), and 1 for Qsymia ($n = 2,487$) (13). We focus on the most frequently prescribed dose for each pharmaceutical product (Table 1). With the exception of the Orlistat studies, the majority of studies were conducted in the United States. Eleven Orlistat studies were conducted outside the United States (25,27-30,34,36-40). One Weight Watchers study was conducted jointly with participants in Australia and Germany (20). Most studies were 12 months and all reported 12 month results. The average age of participants was 46 and the majority were women (87% of participants in lifestyle programs and 71% in the medication trials). An overview of the included studies is available in the Supporting Information Table 1 and briefly summarized in Table 1.

Costs

Weight Watchers is the least expensive intervention, consisting only of an average subscription fee of $515 (41). Costs are reduced to $377 (95% CI: $291-$471) from the ITT perspective after factoring in dropouts and assuming four equally spaced payments. Annual costs for the 6 month Vtrim program plus 6 month weight mainte-

nance program is $925 (42). This cost is reduced to $682 (95% CI: $521-$854) once attrition is factored in. After factoring in attrition ranging between 35% and 43%, Lorcaserin, Orlistat, and Qsymia were predicted to cost $1,743 (95% CI: $1,311-$2,165), $1,518 (95% CI: $1,149-$1,895), and $1,366 (95% CI: $1,036-$1,674) per year, respectively (4).

Because of the relatively high cost of Jenny Craig food, it is the most expensive intervention. On average, there are 840 calories in Jenny Craig meals for a cost $18.14 (43), therefore, the cost per calorie is 2.2 cents. A 46-year-old woman with a BMI of 35 consumes 2,438 calories per day on average. To generate 7.4 kg of weight loss in 1 year, the same woman would consume 2,163 calories per day, a deficit of 275 calories. Based on Gallup data (7) [inflated to 2013 prices (8)], an average income individual spends $22 per day on food ($8,030 per year), generating a cost per calorie of 0.9 cents. Therefore;

$$\text{Incremental cost of JC}_{AI} \text{ diet}$$
$$= \left(840 \times \frac{\$18.14}{840} + (2,163 - 840) \times \frac{\$22}{2,438}\right)$$
$$\times 365 - \$8,030 = \$2,949$$

After accounting for attrition and adding in the $340 subscription cost, the cost of the Jenny Craig diet for average income individuals is $3,152 (95% CI: $2,378-$3,943). For high-income individuals, the average expenditure per day on food is $26 ($9,490 per year) or 1.1 cents per calorie. The corresponding incremental cost is;

TABLE 2 Average cost effectiveness ratios (weight loss in kg), base-case[a]

	Costs ($) Mean (95% CI)	Effectiveness Mean (95% CI)	ACER ($) Mean (95% CI)
Weight Watchers	377 (291-471)	2.4 (1.8-3.0)	155 (110-218)
Vtrim	682 (521-854)	3.2 (1.4-4.9)	213 (127-493)
Qsymia 7.5/46	1,366 (1,036-1,674)	6.7 (4.7-8.6)	204 (134-317)
Orlistat 3 × 120 mg	1,518 (1,149-1,895)	2.8 (2.4-3.2)	546 (390-736)
Lorcaserin 2 × 10 mg	1,743 (1,311-2,165)	3.2 (2.6-3.8)	545 (399-725)
Jenny Craig average income	3,152 (2,378-3,943)	7.4 (5.7-8.9)	424 (302-594)
Jenny Craig high income	2,512 (1,931-3,124)	7.4 (5.7-8.9)	338 (248-476)

[a]Base-case—Mean costs and effectiveness, no food cost savings, drop out at 3 months, effectiveness based on intention-to-treat sample less weight loss from control arm.

Incremental cost of JC_{HI} diet

$$\left(840 \times \frac{\$18.14}{840} + (2,163-840) \times \frac{\$26}{2,438}\right) \times 365 - \$9,490 = \$2,281$$

Taking attrition and the subscription cost into account, the Jenny Craig diet costs high-income individuals $2,512 (95% CI: $1,931-$3,124).

Weight loss

Average weight loss ranged from 2.4 kg (95% CI: 1.8-3.0) for Weight Watchers to 7.4 kg (95% CI: 5.7-8.9) for Jenny Craig. Those on Orlistat lost 2.8 kg (95% CI: 2.4-3.2), whereas those on Vtrim (95% CI: 1.4-4.9) and Lorcaserin (95% CI: 2.6-3.8) both lost an average of 3.2 kg. Weight loss for those on Qsymia averaged 6.7 kg (95% CI: 4.7-8.6). Meta analyses results are reported in the Supporting Information Table 2.

Cost-effectiveness

ACERs. Cost, effectiveness, and ACERs are presented in Table 2. ACERs ranged from $155 (95% CI: $110-$218) per kg lost (Weight Watchers) to $546 (95% CI: $390-$736) per kg lost (Orlistat).

One-way sensitivity analyses are presented in Table 3. More optimistic assumptions generated significantly lower ACERs. However, the general trend of Weight Watchers being the least expensive and Orlistat and Lorcaserin among the most expensive, in terms of cost per kilogram of weight lost, was maintained across scenarios.

Incremental cost per kilogram lost. Incremental cost per kilogram of weight loss is displayed in Figure 2 and Supporting Information Table 3. Weight Watchers has an ICER (relative to a low-cost control intervention) of $155 per kg of weight lost. Lorcaserin and Orlistat are dominated strategies: they are more expensive and less effective than Qsymia. Vtrim is extended dominated; the same level of weight loss could be achieved at lower cost by giving some individuals Weight Watchers and others Qsymia. Relative to Weight Watchers, Qsymia generates additional weight loss at a cost of $232 per kg. Jenny Craig generates additional weight loss compared to its next most expensive nondominated option, Qsymia, at a cost of $2,448 ($JC_{AI}$) or $1,571 ($JC_{HI}$) per kg. PSAs revealed that Lorcaserin and Orlistat were dominated by Qsymia in 74% and 91% of simulations, respectively. Vtrim was extended dominated in 58% of simulations. In all simulations, Jenny Craig was more expensive than Qsymia; it was also less effective in 31%.

QALYs. Regression results for QoL improvements per kilogram of weight loss based on the Qsymia data are available in the

TABLE 3 Average cost effectiveness ratios (weight loss in kg), sensitivity analyses

|	Weight watchers mean (95% CI)	Vtrim mean (95% CI)	Qsymia 7.5/46 mean (95% CI)	Orlistat 3 × 120 mg mean (95% CI)	Lorcaserin 2 × 10 mg mean (95% CI)	Jenny Craig average income mean (95% CI)	Jenny Craig high income mean (95% CI)
Base-case ($)	155 (110-218)	213 (127-493)	204 (134-317)	546 (390-736)	545 (399-725)	424 (302-594)	338 (248-476)
Less food cost savings ($)	85 (59-119)	166 (85-345)	141 (95-207)	480 (350-637)	478 (350-618)	648 (454-919)	279 (194-385)
Drop out at 6 months ($)	175 (121-245)	267 (141-543)	232 (152-341)	637 (452-864)	609 (428-807)	442 (311-607)	351 (242-469)
Compared to zero baseline ($)	88 (61-120)	138 (88-216)	172 (122-235)	311 (234-396)	259 (198-326)	375 (236-618)	299 (185-483)
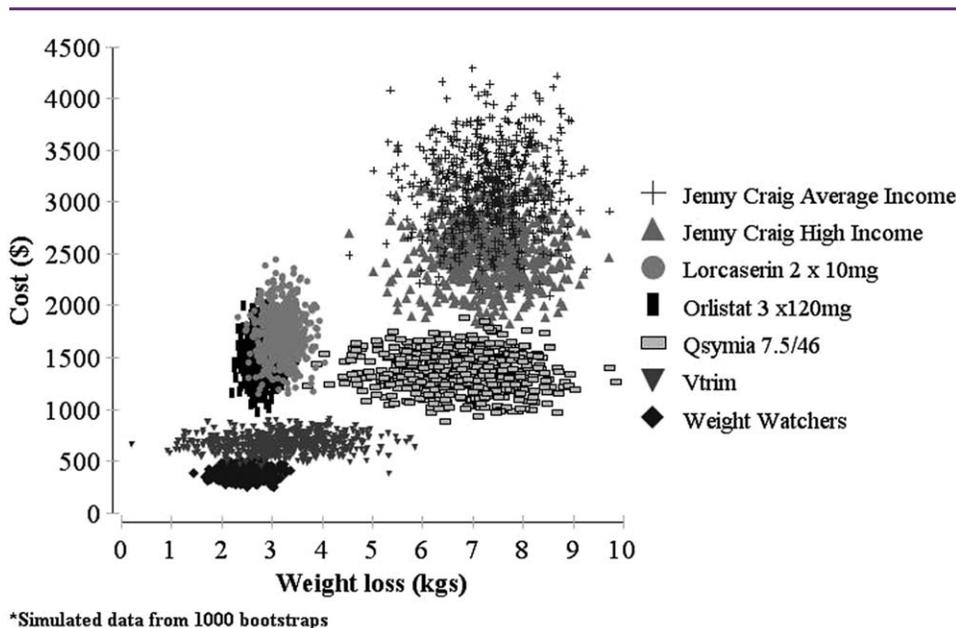
Figure 2 Probability sensitivity analysis (PSA) base case.

Supporting Information Table 4. Based on these results, 1 year of Weight Watchers results in a 0.011 (95% CI: 0.008-0.013) QALY improvement over 4 years, followed by Orlistat at 0.012 (95% CI: 0.01-0.014), Lorcaserin (95% CI: 0.012-0.017), and Vtrim (95% CI: 0.007-0.022) improve QALYs by 0.014, Qsymia by 0.029 (95% CI: 0.021-0.037) and Jenny Craig by 0.032 (95% CI: 0.026-0.039). Using our base case assumption of one year on treatment with benefits linearly decaying to zero in years 2 through to 4, the ICERs for

nondominated strategies are $34,630 and $54,130 for Weight Watchers (relative to control) and Qsymia (relative to Weight Watchers) (Table 4, ICERs rounded to nearest $10). Jenny Craig generates additional QALYs at an incremental cost of more than $350,000 per QALY in the most optimistic scenario (JC_{HI}).

The cost-effectiveness acceptability curves (CEACs) are displayed in Figure 3. The CEACs reveal that at a willingness-to-pay of
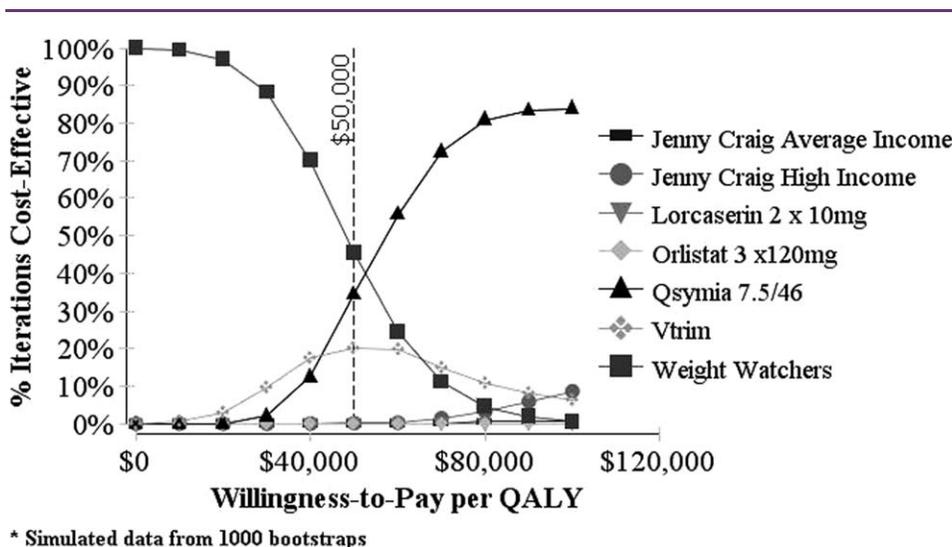

Figure 3 Cost-effectiveness acceptability curves.

TABLE 4 Incremental cost effectiveness ratios per QALY gained

	Incremental costs ($)	Effectiveness	Incremental effectiveness	ACER ($)	ICER ($)	
					Compared to next most expensive, nondominated	Excluding dominated and extended dominated strategies
	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)	Mean (95% CI)		
Weight watchers	377 (115-471)	0.011 (0.008-0.013)	0.011 (0.008-0.013)	34,630 (24,300-49,380)	34,630	34,630
Vtrim	305 (115-497)	0.014 (0.007-0.022)	0.003 (−0.004-0.011)	47,990 (28,730-103,260)	91,700	Extended dominated
Qsymia 7.5/46	684 (330-1,059)	0.029 (0.021-0.037)	0.015 (0.003-0.026)	46,850 (32,010-69,350)	45,760	54,130
Orlistat 3 × 120 mg[a]	152 (−186 to 913)	0.012 (0.01-0.014)	−0.017 (−0.023 to 0.007)	122,640 (88,530-164,440)	Dominated	Dominated
Lorcaserin 2 × 10 mg[a]	378 (−367 to 615)	0.014 (0.012-0.017)	−0.015 (−0.025 to 0.008)	122,640 (89,540-159,810)	Dominated	Dominated
Jenny Craig average income[a]	1,787 (958-2,665)	0.032 (0.026-0.039)	0.003 (−0.007 to 0.013)	97,940 (68,800-134,860)	588,620	588,620
Jenny Craig high income[a]	1,147 (440-1,869)	0.032 (0.026-0.039)	0.003 (−0.007 to 0.013)	78,060 (56,480-108,180)	377,760	377,760

[a]Incremental costs and incremental effectiveness compared to Qsymia.

$50,000 per QALY, which is a commonly cited threshold for cost effectiveness (44,45), Weight Watchers would be optimal in 46% of simulations, Qsymia in 34% and Vtrim, although extended dominated on average, would generated the most QALYs in 20% of simulations. At a willingness-to-pay of $100,000 per QALY Qsymia would be chosen in 84% of simulations.

Discussion

The goal of this study was to provide data on ACERs and ICERs of commercially available nonsurgical weight loss strategies. We identified only six interventions with proven clinical efficacy that met our inclusion criteria. These included three commercial programs and three weight loss medications. Several additional interventions were considered but ultimately excluded. eDiets was excluded as it was found to be no more effective than a control intervention (46). Several meal replacement products were excluded, including Medifast, Optifast, and Slimfast, due to violating one or more inclusion criteria, including failure to report ITT results (47-53), greater than 50% attrition (54), testing a more intensive intervention than what is offered commercially (55), insignificant evidence of weight loss (56,57) or less than 12 months in duration (58). Metformin, an oral diabetic medication, has evidence of weight loss but is not approved for weight loss alone (59). Sibutramine was withdrawn from the market due to serious side effects (60). An additional Qsymia study was excluded for having an average baseline BMI over 40 kg/m^2 (61). Surgical weight loss interventions were excluded because they are typically not considered until more traditional weight loss programs fail.

Results show that average costs per kilogram lost for those studies that met our inclusion criteria ranged from $155 per kg lost (Weight Watchers) to $546 for Orlistat. Extending to QALYs, only three interventions, Weight Watchers, Vtrim, and Qsymia had ACERs below the commonly accepted threshold of $50,000 per QALY gained (44,45). When one considers incremental costs per QALY gained, which is the appropriate perspective for resource allocation decisions, only Weight Watchers and Qsymia are viable options. Weight Watchers is the least expensive intervention and generates improvements at a cost of $34,630 per QALY gained. Qsymia shows greater effectiveness, however, relative to Weight Watchers, additional QALYs are more expensive, costing an average of $54,130 which is slightly above the commonly accepted threshold. Taking into account, uncertainty in cost and effectiveness estimates, at the commonly accepted threshold of $50,000 per QALY, Weight Watchers, Qsymia, and Vtrim would be chosen in 46%, 34%, and 20% of simulations.

It is worth noting that if third party payers financed only a portion of the costs of the interventions, then the results would differ. For example, Jenny Craig would be the most cost-effective intervention from a third party payer's perspective if food costs were excluded. This results because Jenny Craig generates the greatest weight loss, yet the subscription cost is less than that of Weight Watchers ($340 for Jenny Craig vs. $515 for Weight Watchers). In reality, third party payers are unlikely to cover the full costs of Jenny Craig food, so from their perspective, subsidizing Jenny Craig program costs may be highly cost-effective. However, this is the same issue that would occur if third parties do not cover 100% of the weight loss medication costs or costs for the other programs. Future studies should quantify the net costs and benefits of these

strategies based on cost-sharing arrangements likely to occur in the real world.

Aside from prior cost-effectiveness studies of Orlistat, there are few studies available to gauge the veracity of these results. The Orlistat studies report ACERs ranging between US $23,290 and US $102,000 per QALY [converted to USD (62)] (63-76). Although a broad range, all are lower than our estimate of $122,000 per QALY. However, this results because Orlistat costs up to 60% less in Europe (77), where these studies were conducted. If we use a comparable cost estimate, our ACER is reduced to $71,000, which is within the range of the published studies. One Weight Watchers study from Australia found the program (excluding participant costs) to have an average cost effective ratio of $27,000; this is only slightly lower than our estimate of $34,630 (78). These results suggest that our estimates are in line with the published literature.

This analysis has several limitations. First, comparisons are not based on a single randomized trial that includes all studies. As a result, it is possible that uncontrolled differences across interventions may have biased the results. In particular, the intensity of the control intervention may differ between designs. In recognition of this shortfall, we implemented several sensitivity analyses to test the robustness of the results and also provided results comparing weight loss to zero (i.e., no control group). Whereas this improved the cost-effectiveness ratios of some interventions (e.g., Orlistat) more than others (Qsymia, Jenny Craig), the general conclusions were unchanged. Second, because the cost-effectiveness analysis is based on a relatively short time period, we did not use a Markov or other disease progression model nor did we include potential cost offsets from reduced comorbidities. Whereas it would be possible to incorporate these outcomes and extend the duration of analysis, it would require additional assumptions concerning both long term weight maintenance and its relationship to health and cost improvements. The goal of this analysis was to provide a straightforward head-to-head comparison of commercially available weight loss interventions with as few assumptions as possible. We believe that this approach is appropriate until longer term data on weight maintenance is available. Third, we convert weight loss in kilograms to QoL improvements using data from a single randomized trial of Qysmia. Yet our estimate of the effect of weight loss on QoL is similar to published estimates (79,80). For example, averaging results across from two studies using a total of five RCTs of sibutramine (79,80), the relationship between QoL change and weight change was 0.00275, only slightly larger than our estimate of 0.00235. Using our estimate makes the results slightly more conservative. Fourth, the cost-effectiveness analysis did not consider other cost savings and the opportunity costs of participants. Weight Watchers requires regular group meetings, and therefore, high time and transit costs and perhaps additional food purchasing and preparation costs that were not incorporated into our analysis. In fact, when considering time and other opportunity costs, all lifestyle products may be more expensive than the pharmaceutical interventions, which may require fewer changes in behavior to generate the weight loss. Other cost offsets that were not included may include reduced medications for obesity-related conditions, such as for hypertension, diabetes, and dyslipidemia. We note that including these additional cost offsets would improve the cost-effectiveness ratios, although it is unlikely that the rankings would change. An additional limitation is that the benefits of the interventions were expressed exclusively in kilograms or QoL accruing from weight loss. Yet the enjoyment of consuming Jenny Craig food, for example, or the potential disutility of being on a weight loss medication versus losing weight via diet and exercise

alone, may also play into individual's decisions of which intervention is right for them. A full accounting of these additional costs and benefits is beyond the scope of this analysis but should be an area of future research.

The primary results reported here show costs and effectiveness, on average, based on ITT results from clinical trials. In the real world, although results will differ for any given individual, overall weight loss and costs are likely to be lower, partly because individuals are required to pay for the costs of the interventions. We attempted to account for this by showing costs for both ITT and completers, but as both are based on data collected during the trials, neither result may generalize to what a third party payer may experience for their covered population. Future studies should look at the weight loss and cost consequences of offering these programs as part of larger health promotion efforts within employer/insurer groups.

Acknowledgments

References

1. Tsai AG, Wadden TA. Systematic review: an evaluation of major commercial weight loss programs in the United States. *Ann Intern Med* 2005;142:56-66.

2. Yanovski SZ, Yanovski JA. Long-term drug treatment for obesity: a systematic and clinical review. *JAMA* 2013;311:74–86.

3. Siegel JE, Weinstein MC, Russell LB, Gold MR. Recommendations for reporting cost-effectiveness analyses. *JAMA* 1996;276:1339-1341.

4. Medi-Span. Price RX Database. Wolters Kluwer Health. 2013.

5. Medicare. Fee Schedule, Payment and Reimbursement Benefit Guideline, CPT Code Billing. Office visit CPT, E&M code fee schedule - Florida Medicare. 2013. Available at: http://www.medicarepaymentandreimbursement.com/2013/01/office-visit-cpt-e-code-fee-schedule.html. Accessed on January 17, 2014.

6. Hall KD, Sacks G, Chandramohan D, et al. Quantification of the effect of energy imbalance on bodyweight. *Lancet* 2011;378:826-837.

7. Gallup. Americans Spend $151 a Week on Food; the High-Income, $180. August 2, 2012. Available at: http://www.gallup.com/poll/156416/americans-spend-151-week-food-high-income-180.aspx. Accessed on March 3, 2014.

8. Bureau of Labor Studies. CPI Inflation Calculator. 2013. Available at: http://www.bls.gov/data/inflation_calculator.htm. Accessed on March 5, 2014.

9. Gold BC, Burke S, Pintauro S, Buzzell P, Harvey-Berino J. Weight loss on the web: a pilot study comparing a structured behavioral intervention to a commercial program. *Obesity (Silver Spring, Md)* 2007;15:155-164.

10. Dansinger M, Gleason J, Griffith JL, Selker HP, Schaefer EJ. Comparison of the atkins, ornish, weight watchers, and zone diets for weight loss and heart disease risk reduction: a randomized trial. *JAMA* 2005;293:43-53.

11. Collaboration RTC. Review Manager (RevMan). 5.2. The Nordic Cochrane Centre, Copenhagen: The Cochrane Collaboration; 2008.

12. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-188.

13. Gadde KM, Allison DB, Ryan DH, et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. *Lancet* 2011;377:1341-1352.

14. Ware JE Jr, Kosinski M, Keller SD. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;34:220-233.

15. Brazier JE, Roberts J. The estimation of a preference-based measure of health from the SF-12. *Med Care* 2004;42:851-859.

16. Reynolds MR, Zimetbaum P, Josephson ME, Ellis E, Danilov T, Cohen DJ. Cost-effectiveness of radiofrequency catheter ablation compared with antiarrhythmic drug therapy for paroxysmal atrial fibrillation. *Circ Arrhythm Electrophysiol* 2009;2:362-369.

17. Katon W, Russo J, Sherbourne C, et al. Incremental cost-effectiveness of a collaborative care intervention for panic disorder. *Psychol Med* 2006;36:353-363.

18. Bensink M, Wootton R, Irving H, et al. Investigating the cost-effectiveness of videotelephone based support for newly diagnosed paediatric oncology patients and their families: design of a randomised controlled trial. *BMC Health Serv Res* 2007;7:38.

19. Heshka S, Anderson JW, Atkinson RL, et al. Weight loss with self-help compared with a structured commercial program. *JAMA* 2003;289:1792-1798.

20. Jebb SA, Ahern AL, Olson AD, et al. Primary care referral to a commercial provider for weight loss treatment versus standard care: a randomised controlled trial. *Lancet* 2011;378:1485-1492.

21. Rock CL, Flatt SW, Sherwood NE, Karanja N, Pakiz B, Thomson CA. Effect of a free prepared meal and incentivized weight loss program on weight loss and weight loss maintenance in obese and overweight women: a randomized controlled trial. *JAMA* 2010;304:1803-1810.

22. Rock CL, Pakiz B, Flatt SW, Quintana EL. Randomized trial of a multifaceted commercial weight loss program. *Obesity* 2007;15:939-949.

23. O'Neil PM, Smith SR, Weissman NJ, et al. Randomized placebo-controlled clinical trial of lorcaserin for weight loss in type 2 diabetes mellitus: the BLOOM-DM study. *Obesity* 2012;20:1426-1436.

24. Bakris G, Calhoun D, Egan B, Hellmann C, Dolker M, Kingma I. Orlistat improves blood pressure control in obese subjects with treated but inadequately controlled hypertension. *J Hypertens* 2002;20:2257-2267.

25. Broom I, Wilding J, Stott P, Myers N. Randomised trial of the effect of orlistat on body weight and cardiovascular disease risk profile in obese patients: UK multimorbidity study. *Int J Clin Pract* 2002;56:494.

26. Davidson MH, Hauptman J, DiGirolamo M, et al. Weight control and risk factor reduction in obese subjects treated for 2 years with orlistat. *JAMA* 1999;281: 235-242.

27. Derosa G, Cicero AF, D'Angelo A, Fogari E, Maffioli P. Effects of 1-year orlistat treatment compared to placebo on insulin resistance parameters in patients with type 2 diabetes. *J Clin Pharm Ther* 2012;37:187-195.

28. Derosa G, Mugellini A, Ciccarelli L, Fogari R. Randomized, double-blind, placebo-controlled comparison of the action of orlistat, fluvastatin, or both an anthropometric measurements, blood pressure, and lipid profile in obese patients with hypercholesterolemia prescribed a standardized diet. *Clin Ther* 2003;25:1107-1122.

29. Finer N, James W, Kopelman P, Lean M, Williams G. One-year treatment of obesity: a randomized, double-blind, placebo-controlled, multicentre study of orlistat, a gastrointestinal lipase inhibitor. *Int J Obes Relat Metab Disord* 2000;24: 306-313.

30. Hanefeld M, Sachse G. The effects of orlistat on body weight and glycaemic control in overweight patients with type 2 diabetes: a randomized, placebo-controlled trial. *Diabetes Obes Metab* 2002;4:415-423.

31. Hauptman J, Lucas C, Boldrin MN, Collins H, Segal KR. Orlistat in the long-term treatment of obesity in primary care settings. *Arch Fam Med* 2000;9:160.

32. Hollander PA, Elbein SC, Hirsch IB, et al. Role of orlistat in the treatment of obese patients with type 2 diabetes: a 1-year randomized double-blind study. *Diabetes Care* 1998;21:1288-1294.

33. Kelley DE, Bray GA, Pi-Sunyer FX, et al. Clinical efficacy of orlistat therapy in overweight and obese patients with insulin-treated type 2 diabetes: a 1-year randomized controlled trial. *Diabetes Care* 2002;25:1033-1041.

34. Krempf M, Louvet JP, Allanic H, Miloradovich T, Joubert JM, Attali JR. Weight reduction and long-term maintenance after 18 months treatment with orlistat for obesity. *Int J Obes Relat Metab Disord* 2003;27:591-597.

35. Miles JM, Leiter L, Hollander P, et al. Effect of orlistat in overweight and obese patients with type 2 diabetes treated with metformin. *Diabetes Care* 2002;25:1123-1128.

36. Rössner S, Sjöström L, Noack R, Meinders A, Noseda G. Weight loss, weight maintenance, and improved cardiovascular risk factors after 2 years treatment with orlistat for obesity. *Obes Res* 2012; 8:49-61.

37. Sjostrom L, Rissanen A, Andersen T, et al. Randomised placebo-controlled trial of orlistat for weight loss and prevention of weight regain in obese patients. European Multicentre Orlistat Study Group. *Lancet* 1998;352:167-172.

38. Swinburn BA, Carey D, Hills AP, et al. Effect of orlistat on cardiovascular disease risk in obese adults. *Diabetes Obes Metab* 2005;7:254-262.

39. Torgerson JS, Hauptman J, Boldrin MN, Sjöström L. XENical in the Prevention of Diabetes in Obese Subjects (XENDOS) Study A randomized study of orlistat as an adjunct to lifestyle changes for the prevention of type 2 diabetes in obese patients. *Diabetes Care* 2004;27:155-161.

40. Lindgärde F. The effect of orlistat on body weight and coronary heart disease risk profile in obese patients: the Swedish Multimorbidity Study. *J Intern Med* 2000; 248;245-254.

41. Weight Watchers. Weightwatchers.com: Monthly Pass Learn More. 2013. Available at: http://www.weightwatchers.com/templates/marketing/Landing_1col_nonav.aspx?PageId=1080551. Accessed on October 24, 2013.

42. Blake P. Vtrim review. 2013. Available at: http://www.dietspotlight.com/vtrim-review/. Accessed on October 26, 2013.

43. J. Craig. Jenny Craig Cuisine Menu. 2013. Available at: http://www.jennycraig.com/site/cuisine/cuisine.jsp?. Accessed on November 1, 2013.

44. Braithwaite RS, Meltzer DO, King JT Jr, Leslie D, Roberts MS. What does the value of modern medicine say about the $50,000 per quality-adjusted life-year decision rule? *Med Care* 2008;46:349-356.

45. Grosse SD. Assessing cost-effectiveness in healthcare: history of the $50,000 per QALY threshold. *Expert Rev Pharmacoecon Outcomes Res* 2008;8:165-178.

46. Womble LG, Wadden TA, McGuckin BG, Sargent SL, Rothman RA, Krauthamer-Ewing ES. A randomized controlled trial of a commercial internet weight loss program. *Obes Res* 2004;12:1011-1018.

47. Cheskin LJ, Mitchell AM, Jhaveri AD, et al. Efficacy of meal replacements versus a standard food-based diet for weight loss in type 2 diabetes: a controlled clinical trial. *Diabetes Educ* 2008; 34:118-127.

48. Rothacker DQ, Staniszewski BA, Ellis PK. Liquid meal replacement vs traditional food: a potential model for women who cannot maintain eating habit change. *J Am Diet Assoc* 2001;101:345-347.

49. Li Z, Treyzon L, Chen S, Yan E, Thames G, Carpenter CL. Protein-enriched meal replacements do not adversely affect liver, kidney or bone density: an outpatient randomized controlled trial. *Nutr J* 2010;9:72.

50. Ashley JM, St Jeor ST, Schrage JP, et al. Weight control in the physician's office. *Arch Intern Med* 2001;161:1599-1604.

51. Ashley JM, Jeor ST, Perumean-Chaney S, Schrage J, Bovee V. Meal replacements in weight intervention. *Obes Res* 2001;9(Suppl 4):312s-320s.

52. Ditschuneit HH, Flechtner-Mors M, Johnson TD, Adler G. Metabolic and weight-loss effects of a long-term dietary intervention in obese patients. *Am J Clin Nutr* 1999;69:198-204.

53. Ditschuneit HH, Flechtner-Mors M. Value of structured meals for weight management: risk factors and long-term weight maintenance. *Obes Res* 2001: 9(Suppl 4):284S-289S.

54. Leader NJ, Ryan L, Molyneaux L, Yue DK. How best to use partial meal replacement in managing overweight or obese patients with poorly controlled type 2 diabetes. *Obesity (Silver Spring, Md)* 2013;21:251-253.

55. LeCheminant JD, Jacobsen DJ, Hall MA, Donnelly JE. A comparison of meal replacements and medication in weight maintenance after weight loss. *J Am Coll Nutr* 2005;24:347-353.

56. Keogh JB, Clifton P. The effect of meal replacements high in glycomacropeptide on weight loss and markers of cardiovascular disease risk. *Am J Clin Nutr* 2008;87: 1602-1605.

57. Ashley JM, Herzog H, Clodfelter S, Bovee V, Schrage J, Pritsos C. Nutrient adequacy during weight loss interventions: a randomized study in women comparing the dietary intake in a meal replacement group with a traditional food group. *Nutr J* 2007; 6:12.

58. Fontaine KR, Yang D, Gadbury GL, et al. Results of soy-based meal replacement formula on weight, anthropometry, serum lipids & blood pressure during a 40-week clinical weight loss trial. *Nutr J* 2003;2:14.

59. Knowler WC, Barrett-Connor E, Fowler SE, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. *N Engl J Med* 2002;346: 393-403.

60. U.S. Food and Drug Administration. Meridia (sibutramine): market withdrawal due to risk of serious cardiovascular events. 2010. Available at: http://www.fda.gov/safety/medwatch/safetyinformation/safetyalertsforhumanmedicalproducts/ucm228830.htm. Accessed on September 9, 2013.

61. Allison DB, Gadde KM, Garvey WT, et al. Controlled-release phentermine/topiramate in severely obese adults: a randomized controlled trial (EQUIP). *Obesity (Silver Spring, Md)* 2012;20:330-342.

62. XE. XE Live Exchange Rates. 2014. Available at: www.xe.com. Accessed on February 24, 2014.

63. Archer E, Groessl EJ, Sui X, et al. An economic analysis of traditional and technology-based approaches to weight loss. *Am J Prev Med* 2012;43:176-182.

64. Cobiac LJ, Vos T, Barendregt JJ. Cost-effectiveness of interventions to promote physical activity: a modelling study. *PLoS Med* 2009;6:e1000110.

65. Foxcroft D. Orlistat for the treatment of obesity: cost utility model. *Obes Rev* 2005; 6:323-328.

66. Foxcroft D, Milne R. Orlistat for the treatment of obesity: rapid review and cost-effectiveness model. *Obes Rev* 2000;1:121-126.

67. Hertzman P. The cost effectiveness of orlistat in a 1-year weight-management programme for treating overweight and obese patients in Sweden: a treatment responder approach. *Pharmacoeconomics* 2005;23:1007-1020.

68. Iannazzo S, Zaniolo O, Pradelli L. Economic evaluation of treatment with orlistat in Italian obese patients. *Curr Med Res Opin* 2007;24:63-74.

69. Lacey LA, Wolf A, O'Shea D, Erny S, Ruof J. Cost-effectiveness of orlistat for the treatment of overweight and obese patients in Ireland. *Int J Obes* 2005;29:975-982.

70. Lamotte M, Annemans L, Lefever A, Nechelput M, Masure J. A health economic model to assess the long-term effects and cost-effectiveness of orlistat in obese type 2 diabetic patients. *Diabetes Care* 2002;25:303-308.

71. Maahs D, de Serna DG, Kolotkin RL, et al. Randomized, double-blind, placebo-controlled trial of orlistat for weight loss in adolescents. *Endocr Pract* 2006;12:18-28.

72. Maetzel A, Ruof J, Covington M, Wolf A. Economic evaluation of orlistat in overweight and obese patients with type 2 diabetes mellitus. *Pharmacoeconomics* 2003;21:501-512.

73. O'Meara S, Riemsma R, Shirran L, Mather L, Ter Riet G. A rapid and systematic review of the clinical effectiveness and cost-effectiveness of orlistat in the management of obesity. *Health Technol Assess* 2001;5:1-81.

74. Roux L, Kuntz KM, Donaldson C, Goldie SJ. Economic evaluation of weight loss interventions in overweight and obese women. *Obesity* 2006;14:1093-1106.

75. Ruof J, Golay A, Berne C, Collin C, Lentz J, Maetzel A. Orlistat in responding obese type 2 diabetic patients: meta-analysis findings and cost-effectiveness as rationales for reimbursement in Sweden and Switzerland. *Int J Obes* 2005;29:517-523.

76. Van Baal PH, Van Den Berg M, Hoogenveen RT, Vijgen S, Engelfriet PM. Cost-effectiveness of a low-calorie diet and orlistat for obese persons: modeling long-term health gains through prevention of obesity-related chronic diseases. *Value Health* 2008;11:1033-1040.

77. Light DW, Lexchin J. Foreign free riders and the high price of US medicines. *BMJ* 2005;331:958-960.

78. Cobiac L, Vos T, Veerman L. Cost effectiveness of Weight Watchers and the Lighten Up to a Healthy Lifestyle program. *Aust N Z J Public Health* 2010;34:240-247.

79. O'Meara S, Riemsma R, Shirran L, Mather L, ter Riet G. A Systematic Review of the Clinical Effectiveness and Cost-Effectiveness of Sibutramine in the Management of Obesity. Health Technology Assessment; 2002;6.

80. Warren E, Brennan A, Akehurst R. Cost-effectiveness of sibutramine in the treatment of obesity. *Med Decis Making* 2004;24:9-19.