Obesity consultation – stakeholder comments (Health Economics): clinical only
16 March – 11 May 2006

National Institute for Health and Clinical Excellence

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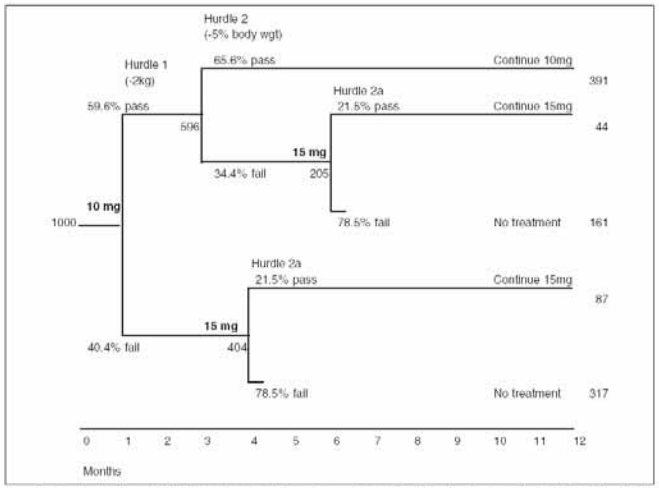
Organisation	Order no.	Document	Page no.	Line no.	Comment	Response
Abbott Laboratories Ltd	6	Full version	710	1–2	For Clarity please insert a diagram to represent the hurdle requirements for progressing treatment e.g. Figure 1 in Reference 9 (Warren et al., 2004)  *Figure 1 Treatment pathway of 1000 obese naive patients. Proportions passing each hurdle are based on an analysis of 161 individuals in the Smith and Goulder[9] trial.*	Thank you. Agreed – diagram inserted. Permission will be sought for this.
Abbott Laboratories Ltd	47	Section 6 Health economic (General)	687–779		Throughout this section, the source of the models referred to is not clear. Clarity in presenting the source of the models used is needed (e.g. previous HTAs, provided by the sponsor, published models, revised version of the sponsors model	Noted with thanks.

					by the collaborating centre, or collaborating centre)	
Abbott Laboratories Ltd	48	Section 6 Health economic (General)	687–779		In stating the cost-effectiveness of interventions from previous HTAs and earlier publications, it should be noted that "based on current NICE guidance, higher cost per QALYs would be expected." Previous recommendations of a 6% discount rate for costs and 1.5% for outcomes, have since been replaced by 3.5% for both costs and outcomes. Consequently, the present value of future cost-savings and future QALY gains in previous models would now be considered lower, giving rise to a higher cost per QALY.	Noted. This point was explained to the group and thus was included in their deliberations on the construction of recommendations. Without recreating the previous modelling, it would have been difficult to estimate the extent to which the change in discounting strategy affected the cost per QALY.
Abbott Laboratories Ltd	49	Section 6 Health economic (General)	687–779		Throughout this section, the design of the model and compared interventions is not clear. Please clearly describe the design and comparator interventions in the models to enable transparency when comparing interventions	Noted with thanks.
Abbott Laboratories Ltd	50	Full version	690	11	Sibutramine is licensed for patients with a BMI of 27kg/m2 or greater. This is based on clinical evidence in patients with a BMI >27 kg/m2. Therefore, the search should not be limited to a	Thank you. Noted and amended as appropriate.

					study population of BMI >28kg/m2, but should be extended to include a study population of >27kg/m2 to ensure all clinically relevant evidence for sibutramine is captured.	
Abbott Laboratories Ltd	51	Full version	690	Table 16.1 (1)	It should be clarified in this table that as a result of "…little evidence specifically on the cost-effectiveness of non-pharmacological interventions…" [insert] the cost-effectiveness of non-pharmacological interventions should be treated as corroborative evidence, rather than definite proof" (as stated on Pg 702, line 27-29).	Thank you. The point is correct. However, this evidence statement is limited to an overview of the published literature.
Abbott Laboratories Ltd	52	Full version	690	Table 16.1 (3)	Please identify each of the non-pharmacological interventions identified, their comparator, and their respective best estimate cost per QALYs, rather than just the range £174-£9,971 for all non-pharmacological interventions. This will enable transparency when comparing with other cost per QALY information for other pharmacological and surgical interventions in the guidance.	Due to the heterogeneity of the types of non-pharmacological interventions (different diets, exercise approaches, behavioural therapies), the group felt that specific cost per QALY for each type of intervention was unhelpful. The reason why comparisons between non-pharmacological and pharmacological interventions were not considered was that they apply to different population groups.
Abbott Laboratories Ltd	53	Full version	690	Table 16.1 (3)	Given that this represents the best-performing practice for non-pharmacological interventions, a range should also be presented	Because of the heterogeneity of intervention under each of the umbrella terms, it was felt that presenting a range in the traditional

					that includes the upper and lower limits of cost-effectiveness from the base case scenario analysis' (e.g. Table 16.13)	way was misleading as the inevitable wide variation is not necessarily representative of uncertainty regarding the potential benefit of the interventions but more the wide range of interventions which could be classified under each term.
Abbott Laboratories Ltd	54	Full version	690	Table 16.1	The cost-effectiveness of these interventions should be presented over the equivalent time horizon, using current discounting rates of 3.5% for both cost and outcomes, to enable a fairer comparison to the other interventions: sibutramine, orlistat, and surgery.	The comparison between different options is not realistic in this case since the interventions are dealing with different populations.
Abbott Laboratories Ltd	55	Full version	699	Table 16.10	Cost per kg lost (£) column for Jones et al. 1999 should be presented to 2 decimal places (i.e. 1215.00) for consistency	Noted and amended with thanks.
Abbott Laboratories Ltd	56	Full version	701	Table 16.13 Table 16.14	What are the non-pharmacological interventions being compared?	The comparator is the trend weight gain over time.
Abbott Laboratories Ltd	57	Full version	703	Table 16.15 (2)	The cost per QALY stated of between £3,200 and £16,700 was based on data available in 2002. Revised modelling by Ara and Brennan (2004) has used the most recently available economic and clinical evidence and calculates the cost per QALY of:	Thank you. Agreed and amended.

					sibutramine + diet +exercise versus diet +exercise alone as £6,349 (range: £4,542-£12,227). In this revised model for sibutramine: -A stronger correlation of weight loss and utility gain to improve regression fit has been derived from the longer-term SAT study. -This study also reflects the experience of using licensed doses of sibutramine in clinical practice, as opposed to trial conditions (e.g. Smith and Goulder The Journal of Family Practice, 2001; 6: 505-512). -The model has also incorporated updated estimates of unit costs and resource utilisation for: monitoring and treating obesity as well as treating the consequences of obesity, diabetes and CHD. -Furthermore, the outcomes (QALYs) in this model have received greater discounting than the previous model in line with current NICE guidance (3.5 and 1.5%, respectively). Use of the previously recommended 6% discount rate for costs and 1.5% for outcomes would result in a lower cost per QALY as the present value of cost savings and future QALY gains with	

					sibutramine would be increased. Therefore, this estimate by Ara and Brennan of £6,349, provides a more appropriate and accurate representation of the cost-effectiveness of sibutramine and should be used instead.	
Abbott Laboratories Ltd	58	Full version	703	Table 16.15 (2)	Please insert that "this cost per QALY (£6,349) represents the benefits and costs of 12 months of treatment with sibutramine over a five year time horizon"	The 12-month treatment is contained within licensing. The 5-year time horizon has been added.
Abbott Laboratories Ltd	59	Full version	703	Table 16.15 (2)	Please insert: "It should be noted that the probability of cost-effectiveness at £10,000 per QALY is 94.5%"	The discussion of the result is contained within the chapter. This table is a distillation of the results.
Abbott Laboratories Ltd	60	Full version	703	Table 16.15 (2)	Please insert that this Cost per QALY of £6,349 is a conservative estimate, as: - "Only two of the commonly associated comorbidities of obesity have been modelled of 10 (Hughes et a J Med Econ. 1999;2:143–53). If all were modelled, the cost per QALY would further decrease due to a greater accumulation of cost offsets. Therefore, the cost per QALY is conservative."	Thank you. The details of the paper are given in adequate depth elsewhere so it was felt that duplication was not helpful. However, this consideration was noted in the construction of recommendations.
Abbott Laboratories Ltd	61	Full version	703	12	Please change "Abbott Technologies" to "Abbott"	Thank you. Noted and amended.

Abbott Laboratories Ltd	62	Full version	703	12	To distinguish between the model provided by Abbott for the HTA published in 2002 and the updated model provided by Abbott (Ara and Brennan) for this guidance, please refer to this as the "….previous model included 1000 patients…" for clarity	Noted and amended with thanks.
Abbott Laboratories Ltd	63	Full version	706	13	It should be noted that the relationship between the weight loss and utility is derived from clinical data on weight loss collected from patients in the sibutramine SAT trial. The Macran publication (reference 31), however, gives the relationship between BMI and utility and does not give the utility gain for a change in weight experienced by patients."	Noted. While the Macran paper looked at weight, rather than weight loss, the stratification of quality of life was considered to be a valuable component of the discussion.
Abbott Laboratories Ltd	64	Full version	707	Table 16.17	The BMI ranges: "21-25, 26-30, 31-39", should be presented as continuous ranges (e.g. 21-25,25-30, 30-39) to correlate with weight, a continuous variable.	Thank you. Amended to show the exhaustiveness of the ranges.
Abbott Laboratories Ltd	65	Full version	708	9–10	It is misleading to suggest, that in men, the cost per QALY for sibutramine is likely to be higher than the range presented by Ara and Brennan, as this is based on weak utility evidence. In the analysis conducted by the collaborating centre, the utility	It was felt that the evidence from Macran on women was relatively consistent with the estimates used by Ara and Brennan. However, the evidence on men suggested that the utility gain assumed by Ara and Brennan was a little optimistic (see below for caveat on this).

					associated with a BMI >39 in men, is based on a small sample size (n=26: Table 16.16), which suggests a trend towards a rise in utility with increasing weight. Based on this data it is suggested that obese patients weighing 143kg (BMI: 35-44) have a greater utility than a patient of 75kg (BMI: 21-25). Inclusion of utility estimates in males >55 years in the 39+BMI group (missing data) would be expected to reduce the average utility for the group. Removal of the outlying 0.88 utility estimate, for the male 39+BMI group would give the expected relationship between weight loss and utility, consistent with that observed in females	We agree that the implication of utility rising with weight is unrealistic. The importance of the highest BMI group is unrealistic due to the point below. However, the overall point that the evidence suggests Ara and Brennan's estimate to be overly optimistic remains valid. We agree that if the 0.88 estimate included the missing data it is highly likely the average utility in this group would fall. However, it is felt to be unlikely that the inclusion of these data would change to the utility gain per kg lost to the figures suggested by Ara and Brennan.
Abbott Laboratories Ltd	66	Full version	708	3–13	It should be stated that " as patients lose weight greater increments of utility are achieved per Kg lost as patients tend towards a BMI of 21-25. Therefore, the benefits of weight loss are not just for the obese, since there are worthwhile benefits for overweight patients also losing weight.	Noted. However, this point was illustrated to the group and is clear from the surrounding discussion.
Abbott Laboratories Ltd	67	Full version	709	13	Reference 32 should be Reference 9 (Warren et al., 2004)	Thank you. Amended.

Abbott Laboratories Ltd	69	Full version	710	12	Change “treatment is continued for the full year instead of discontinued” to: “treatment is continued for the remainder of the year instead of discontinued”	Thank you. Noted and amended.
Abbott Laboratories Ltd	70	Full version	Cost-effectiveness of Orlistat	Section 16.5	The cost-effectiveness estimates for pharmacotherapy (sibutramine and orlistat) can not be fairly compared due to differences in model data and assumptions: It would be instructive for the collaborating centre to conduct an analysis containing these elements: • The comparator should be diet and exercise advice, • Over the same time-horizon (e.g. 5 years) • In the same population (age / BMI / gender). • Inclusion of weight regain • The estimate of utility per Kg lost should be the same. • The discount rate should be 3.5% for both cost and outcomes	You are correct that the direct comparison between the two pharmacotherapy options can not be made from the report. The undertaking of this comparison was considered by the group. However, it was not undertaken since the limited time resources of the group precluded some of the work that might have been beneficial.
Abbott Laboratories Ltd	71	Full version	Cost-effectiveness of Orlistat	Section 16.5	Based on the cost per QALY estimates presented, and that the probability of sibutramine being cost-effectiveness at £10,000 per QALY is 94.5%, it would appear that sibutramine is a more cost-effective pharmacological option when	It was felt that the different process through which weight loss is achieved may lead the two interventions to tend to apply to different patient groups.

					compared to orlistat. It is therefore unclear why sibutramine has not been recommended as a more favourable pharmacological option on cost-effectiveness grounds.	
Abbott Laboratories Ltd	72	Full version	Cost-effectiveness of Orlistat	Section 16.5	It is unclear why one model refers to the "current licensing" and the other refers to the "alternative EMEA licensing" - Please clearly explain this difference between models	The difference between the two approaches taken by the author is given on p. 713. The use of the more exclusory approach reduces the cost per quality adjusted life years (QALY) since it limits the treatment to the most successful responders.
Abbott Laboratories Ltd	73	Full version	712	Table 16.21 (2 and 3)	Please insert ranges associated with these cost-effectiveness estimates of £24,431 (range:10,885-77,196) and £19,005 (range:8,8839-£57,798)	Noted and amended with thanks.
Abbott Laboratories Ltd	74	Full version	712	Table 16.21 (2 and 3)	Please insert time frame at which the benefits and costs are calculated to produce the stated cost per QALY estimates	Thank you. Details of the evidence base are given in depth in the narrative. This level of detail is beyond that usually contained within tables of evidence statements.
Abbott Laboratories Ltd	75	Full version	712	Table 16.21 (2 and 3)	Please note that this cost per QALY presented has not factored in weight regain after treatment, and therefore this value represents the optimum point of cost-effectiveness. Using a longer time horizon would be expected to further increase the cost per QALY for	If weight regain is included, it is reasonable to assume that individuals have a higher quality of life until they reach baseline. Once they reach baseline, it is standard to assume their weight remains at baseline. Thus, extending the time horizon leads to the minimum cost per QALY rather than the

					orlistat.	maximum.
Abbott Laboratories Ltd	76	Full version	712	Table 16.21 (5)	Please clarify where the range of ICERs comparing 48-month regimen to a 12-month regimen (£24,789-£46,524 per QALY) are derived as these do not relate to the sensitivity analysis presented in Table 16.24	Noted and amended with thanks.
Abbott Laboratories Ltd	77	Full version	712	Table 16.21 (5)	It is not clear if the ICERs represent comparing a 0-12 month regimen to a 12-48 month regimen or a 0-48 month regimen? –Please clarify	It refers to the latter.
Abbott Laboratories Ltd	78	Full version	712	Table 16.21 (5)	The cost-effectiveness of 1-year treatment with orlistat should be presented over a longer time-horizon, equivalent to the time-horizon used in the estimates for sibutramine (i.e 5-years).	Point 5 refers to extending the duration of the treatment to 48 months, not to 12 months (thus there is no comparable sibutramine evidence).
Abbott Laboratories Ltd	79	Full version	712	Table 16.21 (5)	Please insert in this table (as per Pg 720, line 7-8): "Based on this model developed by the collaborating centre comparing a 48 month regimen to a 12 month regimen (ICER range £22,099- to £39,308), longer-term use of orlistat cannot be firmly recommended on cost-effectiveness grounds, when compared with other economic analyses in the institute".	Thank you for the suggestion. However, the table refers solely to evidence.

Abbott Laboratories Ltd	80	Full version	715	30	It should be clarified that this section relates to a model independently developed by the collaborating centre	Noted and amended.
Abbott Laboratories Ltd	81	Full version	719	Table 16.24	The incremental cost per QALY should also be presented as orlistat vs placebo over equivalent time-horizons (i.e 5 years) to sibutramine.	The time horizon for this additional modelling is approximately 5 years. The time interval 12 months refers not to the time horizon but to the duration of treatment.
Abbott Laboratories Ltd	82	Full version	721	Table 16.25 (1)	The analysis of cost-effectiveness presented has not compared surgical, non-pharmacological and pharmacological interventions: • against the same comparator, • in the same study design, • over the same time-horizon • in the same population. Additionally, the discount rate should be 3.5% for both cost and outcomes Therefore, it is not possible to suggest that "surgery seems to be a more cost-effective intervention relative to non-surgical options in a typically obese group" – please modify or remove this statement	Noted with thanks. The statements have been amended.
Abbott Laboratories Ltd	83	Full version	721	Table 16.25 (2)	Please state the surgical interventions compared and the comparator used to derive the cost per QALY estimates of	It was decided that using an umbrella term was appropriate as the evidence was similar between interventions.

					£6,289-£8,527	
Abbott Laboratories Ltd	84	Full version	721	Table 16.25 (2)	Please state the time-horizon used to derive the cost per QALY estimates of £6,289-£8,527 (e.g. 20 year time-horizon)	The time horizon is given in the main text.
Abbott Laboratories Ltd	85	Full version	721	Table 16.25 (2)	Please state ranges of the ICERs associated with each of the compared interventions e.g. "Gastric bypass vs usual care: £6,289 (£7,255-£18,278)"	Thank you for the suggestion. It was felt that the HTA approach of not separating the interventions was reasonable.
Abbott Laboratories Ltd	86	Full version	722	23	Change "undated" to "updated"	Noted with thanks.
Abbott Laboratories Ltd	87	Full version	731	11	Please define "usual care" (e.g. diet, exercise, behaviour modification etc)	This has been outlined on a previous page (p. 728).
Abbott Laboratories Ltd	92	NICE version	46	1.2.5.10	Please insert the headline incremental cost per QALY for the comparator intervention vs. orlistat treatment over a 5-year time horizon. Or Define the cost per QALY: (e.g. £24,431(range:10,885-77,196) and £19,005(range:8,8839-£57,798),stating the • Time horizon (e.g. after 1-year of treatment) • Using a longer time horizon would further	Thank you. However, the NICE version focuses on the recommendations, not the evidence underpinning them.

					increase the cost per QALY for orlistat." The Patient population	
Abbott Laboratories Ltd	93		46	1.2.5.15	Please insert the headline incremental cost per QALY for sibutramine + diet + exercise vs diet +exercise as £6,349 (range: £4,542-£12,227) over a 5-ear time-horizon	Thank you. However, the NICE version focuses on the recommendations, not the evidence underpinning them.
Abbott Laboratories Ltd	94	NICE version	48	1.2.7.1	Please insert the headline Incremental cost per QALY for the comparator intervention vs Gastric bypass; vs adjustable silicone gastric band; vs Vertical gastric banding treatment. or define the cost per QALY: stating the • time-horizon (e.g. after 20-years of treatment) • "Using a lifetime horizon would further increase the cost per QALY ." The patient population	The original HTA chose not to report these values since they felt they were not adequately robust to use the point estimates for create incremental cost effectiveness ratios (ICERs). Therefore, the report follows this convention. The figures are found in the body of the text. We do not think that the evidence unequivocally suggests the use of a lifetime horizon would increase the cost per QALY.
Association for the Study of Obesity	5	NICE			The guidance could provide a section on health economics and treatment priorities. Although this is in the full document, this information would be useful in the shortened version.	Thank you for the suggestion. There are a number of items we would have liked to have included in the NICE version. However, it was required that the group prioritise parts of the full guideline and this issue, while of importance, was not prioritised in this process.

Association for the Study of Obesity	101		687		One reference that is missing is the paper by Hughes D et al. The direct cost of obesity in the UK. Journal of Clinical Research, 1999.	Noted. This paper was considered. The £351 million excess cost shows the importance of the issue that the guideline is attempting to tackle. However, the group identified alternatives sources of costing data and causality between obesity and morbidity.
Association for the Study of Obesity	102		689	19/20	Why not consider optimal duration of sibutramine treatment in line with orlistat above?	Noted. That discussion would have been valuable. However, at the time, the group felt the evidence on longer regimen of sibutramine therapy to be inappropriate for economic evaluation.
Association for the Study of Obesity	103		703	18	These hurdles may/are inappropriate for people with diabetes where initial weight loss is slower, but would appear to be less predictive of weight loss at 1 yr. Prediction of response to sibutramine therapy in obese non-diabetic and diabetic patients N. Finer, D. H. Ryan, C. L. Renz and A. C. Hewkin Diabetes, Obesity and Metabolism, 8, 2006, 206–213	Thank you for bringing up this very important point. This was discussed widely in the group, and it was noted that the rate of benefit as weight loss occurs is likely to be higher in a diabetic sub-population. For this reason, we drafted recommendation 1.7.5.8, which states that “Rates of weight loss can be slower in people with diabetes, so less strict goals of weight loss may be appropriate.”
Association for the Study of Obesity	104		708	14	A fundamental issue for these analyses is the assumption that sibutramine will/should be withdrawn at 1 yr. Like any other drug it cannot be expected	Thank you. The extension of Orlistat to 4 years was selected on one specific piece of evidence. It was felt that this 4-year horizon was necessary to judge the

					to 'work' if not being taken, and there are now some longer-term studies with data over >1 yr showing maintained efficacy (STORM, James et al, Lancet; Mathus-Vliegen et al, Eu J CLin Nutr. Long-term maintenance of weight loss with sibutramine in a GP setting following a specialist guided very-low-calorie diet: a double-blind, placebo-controlled, parallel group study (BTW was this included in GP setting comments in 5b?). While the label is for 1 yr use this is an issue that should be commented upon.	continued efficacy of the treatment. The literature search did not identify anything extending sibutramine beyond 2 years. The group was aware that evidence is emerging regarding the suitability of continued prescription and has suggested that prescribers should be aware of the latest evidence.
Association for the Study of Obesity	105		730 and 749	17 3	'ceteris paribus': A classical education as an a priori for starting medicine has not been required for many years!	Noted. In this context, the term is one used widely in cost-effectiveness.
Association for the Study of Obesity	106		755	Table	Throughout this colon cancer is the only cancer considered. Breast cancer must be an equally important if not greater issue not only in terms of frequency but also because there is evidence that in obesity patients present with more advanced disease and have poorer responses to treatment.	Noted. Breast cancer was excluded from the model due to the limited evidence available to accurately predict the increased risk stratified by age, sex and BMI. The report does emphasise that the outcomes of the model should be regarded as conservative as it has not been possible to include all co-morbidities that may arise due to obesity (e.g. musculo-skeletal disease, other cancers, etc.). Where these have been excluded it is on the grounds of insufficient

						data.
Association of British Clinical Diabetologists	60		687		One reference that is missing is the paper by Hughes D et al. The direct cost of obesity in the UK. Journal of Clinical Research, 1999. I can send a copy if needed	Noted. This paper was considered. The £351 million excess cost shows the importance of the issue that the guideline is attempting to tackle. However, the group identified alternatives sources of costing data and causality between obesity and morbidity.
Association of British Clinical Diabetologists	61		689	19/20	Why not consider optimal duration of sibutramine treatment in line with orlistat above?	Noted. That discussion would have been valuable. However, at the time, the group felt the evidence on longer regimen of sibutramine therapy to be inappropriate for economic evaluation.
Association of British Clinical Diabetologists	62		703	18	These hurdles may/are inappropriate for people with diabetes where initial weight loss is slower, but would appear to be less predictive of weight loss at 1 yr. Prediction of response to sibutramine therapy in obese non-diabetic and diabetic patients N. Finer, D. H. Ryan, C. L. Renz and A. C. Hewkin Diabetes, Obesity and Metabolism, 8, 2006, 206–213	Thank you for bringing up this very important point. This was discussed widely in the group, and it was noted that the rate of benefit as weight loss occurs is likely to be higher in a diabetic sub-population. For this reason, we drafted recommendation 1.7.5.8, which states that “Rates of weight loss can be slower in people with diabetes, so less strict goals of weight loss may be appropriate.”
Association of British Clinical Diabetologists	63		708	14	A fundamental issue for these analyses is the assumption that sibutramine will/should be withdrawn at 1 yr. Like any other drug it cannot be expected	Thank you. The extension of Orlistat to 4 years was selected on one specific piece of evidence. It was felt that this 4-year horizon was necessary to judge the

					to 'work' if not being taken, and there are now some longer-term studies with data over >1 yr showing maintained efficacy (STORM, James et al, Lancet; Mathus-Vliegen et al, Eu J CLin Nutr. Long-term maintenance of weight loss with sibutramine in a GP setting following a specialist guided very-low-calorie diet: a double-blind, placebo-controlled, parallel group study (BTW was this included in GP setting comments in 5b?). While the label is for 1 yr use I think this is an issue that should be commented upon.	continued efficacy of the treatment. The literature search did not identify anything extending sibutramine beyond 2 years. The group was aware that evidence is emerging regarding the suitability of continued prescription and has suggested that prescribers should be aware of the latest evidence.
Association of British Clinical Diabetologists	64		730 and 749	17 3	'ceteris paribus': A classical education as an a priori for starting medicine has not been required for many years!	Noted. In this context, the term is one used widely in cost-effectiveness.
Association of British Clinical Diabetologists	65		755	Table	Throughout this colon cancer is the only cancer considered. Breast cancer must be an equally important if not greater issue not only in terms of frequency but also because there is evidence that in obesity patients present with more advanced disease and have poorer responses to treatment.	Noted. Breast cancer was excluded from the model due to the limited evidence available to accurately predict the increased risk stratified by age, sex and body mass index (BMI). The report does emphasise that the outcomes of the model should be regarded as conservative, as it has not been possible to include all co-morbidities that may arise due to obesity (e.g. musculo-skeletal disease, other cancers, etc.). Where these have been excluded it

						is on the grounds of insufficient data.
Department of Health (DH), Scientific Advisory Committee on Nutrition	123			Section 6 Section 6, 687–779	The Health Economic considerations do not appear to have included the costs of training the current healthcare workforce in nutrition and physical activity so that the solutions can be delivered. The cost-effectiveness of interventions is discussed without considering the full costs of implementation. The additional training and personnel required to implement the recommendations will add enormously to the costs and probably reduce the cost-effectiveness accordingly. Starting with a trained dietician to deliver advice, for example, is a lot cheaper than training the dietician from scratch which, given the state of nutritional knowledge among many health professionals, will be necessary.	It is agreed that this plays a significant role in the discussion. However, the issue of service configuration is beyond the remit of the guideline.
Food Standards Agency		General Economics			The paper generally uses methodology that is consistent with the Agency's approach to BMI/obesity measurement and benefit estimation of potential policy interventions. However, as well as considering health effects measured in QALYs the	In line with NICE guidelines on economic evaluation we have chosen to use Cost effectiveness analysis/ Cost utility analysis approaches. Whilst we accept the potential of willingness to pay it is not widely used in valuing health outcomes at present.

					Agency also considers it relevant to analyse mortality and morbidity effects using willingness-to-pay value of life monetisation. In addition the Agency is more concerned with Cost-Benefit than this paper's Cost-Effectiveness analysis. Whilst being logical it is welcome that this paper concludes that the longer the temporal nature of a policy intervention's effect the more cost-effective it is likely to be. As such policies that are more likely to resonate longer term with consumers may be given primacy. The benefits identified require overt discounting for scenarios in excess of a year for two reasons: firstly a person's QALY degrades with age; and secondly the further are future health benefits away from today the less valuable are they compared with policy costs incurred in the present. The relative cost-effectiveness between the three policies could be explored in detail.	Discounting is applied to both costs and outcomes. Incremental cost effectiveness ratios have been presented compared to 'do nothing'. Given the level of data to support the analysis

						incremental ratios between different interventions have not been provided.
					The scenarios envisaged appear too extreme (unrealistic) and could be made more helpful. For example, talking about extending from a year's worth of effect to two, five, ten and then twenty and fifty may give the reader a better feel for the temporal influence.	The scenarios are intended to provide an insight into the effect of extending the duration of effect. Additional analyses can be run if required although it is believed that the current scenarios adequately show the temporal effect.
					The assumption of 75% efficacy appears arbitrary without documented supporting evidence. Similarly the one year intervention success also requires evidential justification.	This is an assumption in the absence of data, and was arrived at in consultation with the GDG. Additional analyses can be run to test the sensitivity of this assumption
					The weight maintenance and 10kg weight loss scenarios/assumptions do not feel natural and would also require justification.	Noted.
					The cumulative effect(s) of diabetes; colon cancer and CHD on QALY penalty seems quite small; are the cumulative effects	A multiplicative approach has been adopted.

					more likely to be multiplicative than additive?	
					The treatment of diabetes as a co-morbidity is not very tractable as it itself leads to further co-morbidities/ causes of death. FSA chose to acknowledge its role but concentrate on measuring CVD/cancer effects. Type 2 diabetes in childhood can lead to irreversible effects.	Noted. Diabetes was included as this was deemed to be a major morbidity arising from obesity.
					Temporal reinforcement of the policy strands could be usefully considered with associated on-going cost increases and the potential resulting efficacy and duration advances.	
					The finding that the benefits of the interventions can decline and even become detrimental as their efficacy is increased probably deserves more analysis that to simply say that it may be a statistical anomaly. This raises questions of the validity of the main findings.	Extensive analyses have lead us to believe that this is truly a statistical (random) anomaly which arises due to small %changes or short term changes to risk factors.
					The potential for obesity's mortality effects to save the NHS/DWP money has not been considered. Whilst not	Mortality is included in the model so anyone who dies will no longer incur any additional costs. However, the potential positive

					presentationally easy this is a genuine potential cost-benefit consideration that is increasingly being considered in dietary analysis.	impact on the public purse of increased mortality arising from obesity has not been considered.
Royal College of Paediatrics and Child Health	67	Full	687		The costing does not take into account the likely inadequacy of current resources to implement recommendations (see previous comment about page 63). Therefore the costs of training sufficient numbers of health professionals to implement both management and prevention strategies need to be considered.	Implementation is beyond the remit of the Guideline Development Group (GDG). It is addressed by the Implementation Unit at NICE.
Royal College of Physicians	97		687		One reference that is missing is the paper by Hughes D et al. The direct cost of obesity in the UK. Journal of Clinical Research, 1999. We can supply a copy if needed.	Noted. This paper was considered. The £351 million excess cost shows the importance of the issue that the guideline is attempting to tackle. However, the group identified alternatives sources of costing data and causality between obesity and morbidity.
Royal College of Physicians	98		689	19/20	Why not consider optimal duration of sibutramine treatment in line with orlistat above?	Noted. That discussion would have been valuable. However, at the time, the group felt the evidence on longer regimen of sibutramine therapy to be inappropriate for economic evaluation.
Royal College of Physicians	99		703	18	These hurdles may/are inappropriate for people with diabetes where initial weight loss is slower, but would appear to be less predictive of weight loss	Thank you for bringing up this very important point. This was discussed widely in the group, and it was noted that the rate of benefit as weight loss occurs is likely to be

					at 1 yr. Prediction of response to sibutramine therapy in obese non-diabetic and diabetic patients N. Finer, D. H. Ryan, C. L. Renz and A. C. Hewkin Diabetes, Obesity and Metabolism, 8, 2006, 206–213	higher in a diabetic sub-population. For this reason, we drafted recommendation 1.7.5.8, which states that "Rates of weight loss can be slower in people with diabetes, so less strict goals of weight loss may be appropriate."
Royal College of Physicians	100		708	14	A fundamental issue for these analyses is the assumption that sibutramine will/should be withdrawn at 1 yr. Like any other drug it cannot be expected to 'work' if not being taken, and there are now some longer-term studies with data over >1 yr showing maintained efficacy (STORM, James et al, Lancet; Mathus-Vliegen et al, Eu J CLin Nutr. Long-term maintenance of weight loss with sibutramine in a GP setting following a specialist guided very-low-calorie diet: a double-blind, placebo-controlled, parallel group study (BTW was this included in GP setting comments in 5b?). While the label is for 1 yr use we think this is an issue that should be commented upon.	Thank you. The extension of Orlistat to 4 years was selected on one specific piece of evidence. It was felt that this 4-year horizon was necessary to judge the continued efficacy of the treatment. The literature search did not identify anything extending sibutramine beyond 2 years. The group was aware that evidence is emerging regarding the suitability of continued prescription and has suggested that prescribers should be aware of the latest evidence.
Royal College of Physicians	101		730 and 749	17 3	'ceteris paribus': A classical education as an a priori for starting medicine has not been required for many years!	Noted. In this context, the term is one used widely in cost-effectiveness.

					[same comment from three SHs?	
Royal College of Physicians	102		755	Table	Throughout this colon cancer is the only cancer considered. Breast cancer must be an equally important if not greater issue not only in terms of frequency but also because there is evidence that obese patients present with more advanced disease and have poorer responses to treatment.	Noted. Breast cancer was excluded from the model due to the limited evidence available to predict accurately the increased risk stratified by age, sex and BMI. The report does emphasise that the outcomes of the model should be regarded as conservative as it has not been possible to include all co-morbidities that may arise due to obesity (e.g. musculo-skeletal disease, other cancers, etc.). Where these have been excluded it is on the grounds of insufficient data.
Slimming World	44	Full	Section 6		It would have been interesting to have seen some inclusion regarding the cost effectiveness of commercial slimming organisations given that information regarding long term weight control is available and also costings for 'slimming on referral' schemes were provided (as a paper under review for publication at the time). It would be beneficial for people have access to as much information as possible in this particular section as has been provided for unpublished work in other areas e.g. Counterweight.	Noted. The cost-effectiveness of a range of non-pharmacological interventions were considered. It was felt that the wide range of approaches that fall under the umbrella term made it difficult to select individual approaches to consider in more depth. Therefore, we looked at the diet, behaviour and exercise approaches that produced the best outcomes for the least resource use to act as 'best practice'.

University College London Hospitals NHS Trust Nutrition and Dietetics		General			There are many facets which are not necessarily measurable with regards to cost-effectiveness- eg – role of personal interaction in motivation/encouragement for weight loss- CBT type approach/? Medication – also, difficult to assess the psychological implications of surgery for obese patients	Agreed. The role of cost-effectiveness is necessarily constrained by the difficulty in modelling the complexity of human behaviour. Thus, its role is limited to the provision of evidence for the consideration of the GDG. The importance of these other areas is that they form the context in which the discussion of the evidence is conducted.
University College London Hospitals NHS Trust Nutrition and Dietetics	31		702	20–22	Cost effectiveness is difficult to assess as the time after intervention is continued - limitations	We are unsure what this comment is suggesting. It is certainly true that the cost-effectiveness of these interventions is difficult to assess given the current literature base. Modelling behaviour change brought about by non-pharmacological interventions introduces significant methodological difficulties.
University College London Hospitals NHS Trust Nutrition and Dietetics	32		711	29–31	Highlight the fact that the benefit of decreased weight loss in obese adolescents with regards to costs is less tangible in adolescents/children – due to effect of psychological benefits? ?measurable	It was felt that this issue was not one which could be analysed quantitatively. However, it played an important role in the discussions on children.
Weight Watchers	9	Full version	687–769		The section on health economics of obesity management will have enormous potential interest to budget holders and decision makers. Weight Watchers proposes to commission a	Noted.

					health economics analysis of its intervention, following the models and formulae presented by others in the draft report. It is anticipated that this will provide additional cost-effectiveness data to add to the 'pool' which will assist those making decisions about weight loss service options at local level. We are now in discussion with the various health economists and plan to undertake this modelling as a matter of urgency.	