EUnetHTA JA3 WP4 - Other technologies, OTCA26
External review by external experts on Surgical procedures for treatment of obesity

Comment from *Insert your name, title and affiliation*	**Page number** *Insert 'general' if your comment relates to the whole document*	**Line/ section number**	**Comment and suggestion for rewording** *Please insert each new comment in a new row.*	**Character of comment** • 'major'[a] =1 • 'minor'[b] = 2 • 'linguistic'[c] =3 *Please indicate your choice by writing the according number in this field, e.g. for major choose "1".*	**Author's reply**
Judith Aron-Wisnewsky	20		• *Reversal or improvement in A1C (e.g. <7.0%),* Why use 7%?? The ada definition of complete remission is 6.0% partial remission is defined as <6.5% (buse et al diabetes care 2009)		Agree, complete remission should be 6.0%, and has been corrected. It should be noted that we in the report have focussed on complete remissiion, as this is what is reported in most studies. In addition it is typically a more well-defined outcome than partial remission.
Judith Aron-Wisnewsky	38		There is a problem of visualisation of the different pictures of the technics. This should be reformated		Illustrations have been added to the text where the procedures are described.
Judith Aron-Wisnewsky	39		Why is the RYGB complication section only micronutrient deficiencies and duming syndrom are listed and not surgical complication ? (most complications are listed at the bottom of the page 42 most importantly reactive hypoglycemia (or late dumping syndrom?) i don't think that early and late dumping should be mixed together because their physiopathology differs and the treatments options also.		The section on clinical outcomes has been removed. These data are formally assessed in SAF and EFF. Distinction between early and late dumping syndrome added.
Summary					
Description and technical characteristics of the technology					
Judith Aron-Wisnewsky	40		Why in the banding section the indication encompasses BMI from 30 to 40? It is not really performed anymore so not in the indication of metabolic surgery (from 30 to 35) and also why not above 40?		This text has been deleted. The cited literature suggested that AGB is most suitable for those with lower levels of obesity and no comorbidities, but I will remove that criteria if you feel this does not reflect clinical practice.

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					Only one manufacturer engaged with NIPH so I cannot confirm the indications for which AGBs are currently CE marked, but based on the information provided on the manufacturers websites, in general AGBs are not currently indicated for those with a BMI of 30-35. It is possible that manufacturers are in the process of expanding the indications, but we cannot confirm this.
Judith Aron-Wisnewsky	50		A national document has been produced in france with the nimber of surgery performed each years (60 000 in 2016 p 29) by IGAS inspection général of health) i think this document should be cited and the number of intervention added		I have retrieved the relevant citation: https://www.igas.gouv.fr/IMG/pdf/2017-059R_Tome_I_.pdf The text has been updated to more accurately reflect the level of surgical activity in France
Judith Aron-Wisnewsky	60		The table with obesity complication should be reformated by means of prevalence and some comorbidities should be placed on other columns: - For cardiovascular system start with hypertension and dyslipidemia and then others - For cancer list them in order of prevalence breast and colon are the first ones - For metabolic disorders add NASH Cirrhosis should be put with NASH because this is the reason why		I have not reviewed the epidemiological literature for each of these complications, therefore I cannot reliably re-order the listed complications in order of prevalence, however, I have moved the comorbidities you have suggested.

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			they could develop cirrhosis - Nephropathy and chronic kidney disease is the same leave only nephropathie that can lead to chronic kidney failure - For musculoskeletal put osteoarthritis , add functional limitation in activities of daily living , before varicose veins - PCOS should be put within metabolic disorders (it is linked to insulin resistance) - Idiopathic intracranial hypertension should be added (it is also one of the defined comorbidities that enable bariatric surgery for BMI>35 - Reduced quality of life should be put in psychological complications ?		
Judith Aron-Wisnewsky	63		Add that the WHO table of BMI s true for Caucasian ethnicity and other values are true for Asian populations		Further clarification and footnote added.
Judith Aron-Wisnewsky	64		Similar to BMI a line stating that different waist circumference values that are at risk differs according to ethnicity		Footnote added
Judith Aron-Wisnewsky	69 end of page		Why is the target population and prevalence not addressed ? there is blank with nothing in those chapters ??		These questions have been repeated in errror while pasting into the template. The questions are addressed on page 58.
Judith Aron-Wisnewsky	71 line 18		State whteher the studies that included patients with grade I obesity were also with T2D in an attempt to see whether this addresses		We've added a sentence claifying which studies that included people with class 2 obesity and T2DM..." of which in two of the studies all

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			metabolic surgery? Add how many studies evaluated adverse events linked to bariatric surgery.		participants had T2DM (Courcoulas, and Schauer)." We've added a paragraph 'Outcomes' referring to the summary of reported outcomes in TableA8 Matrix of outcomes in the included studies, which also describes the number of studies reporting on AEs linked to bariatric surgery.. " "The type of outcomes reported in the included studies are summarised in Table A8 Matrix of outcomes reported in the included studies. All studies reported one or more measure of weight change. All but three studies reported on adverse events related to the surgery (Biter, Himpens, Keidar)."
Health problem and current use					
Judith Aron-Wisnewsky	71	35-41	Studies included in this analyses included different technics: RYGB; BPD-DS; AGB; OAGB; B-RYGB; SR-RYGB, and D-RYGB While RYGB , AGB and SG are the most frequent ones worldwide, B-RYGB and SR-RYGB are (i) a modified version of RYGB (ii) probably relatively similar together since they include a band on the		When we talk about combined procedures it is important to distinguish between those for which the procedure of interest cannot be performed without first performing other surgical techniques (e.g. sleeve gastrectomy can be a standalone procedure, but is also the first step in BPD-DS or SADI-S and thus combines

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			RYGB. These technics are not commonly performed (the prevalence worldwide should be indicated. Furthermore, the indication as why they were tested needs to be precised: reactive hypoglycemia ? weight regain ? Likewise for SR-SG (add the worldwide prevalence, to me it remains very low: was it to test whether it was effective for GERD reduction? I think that before comparing the efficacy of different technics the reason why some modification to the original technic have been proposed should be clarified. I am not at ease to propose comparision of these technics for example SR-SG and SG (that are not so often proposed SR SG for instance) just because there is some RCT available for comparison. While the level of proof is less important when longitidunal cohort studies are published as compared to RCT, the number of published results on the three main technics (AGB, SG, RYGB) is very important and represent a lot of patients operated worldwide. This should be clarified in the result section as well as the discussion.		sleeve gastrectomy with intestinal bypass) or atypical combinations. I think the original publications should be referred to in order to identify the rationale for the modification to the procedure. Is it possibly that the silastic ring is added to prevent stretching of the stomach over time and enhance the restrictive component of the procedure? As we did not state that these procedures would be excluded at the protocol stage, then we have no justifiable reason to exclude them entirely from the systematic review. If there is doubt about their relevance they could be removed from the NMA and discussed narratively, highlighting that they are not commonly used in clinical practice.
Judith Aron-Wisnewsky	72		Add how many studies addressed 10 years data and how many patients? This is the novelty of the work.		We've added the following sentence on p.72 "It should be noted that only two studies comparing

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					AGB and RYGB (N=?) provided data at 10 years follow up (Angrisani, Nguyen). "
Judith Aron-Wisnewsky	76-84		Not sure to understand if the conclusion at 3 years for weight loss is in favors of AGB. If so I am not sure that this is exact, or due to a lack of power since studies (not RCT) have clearly shown that RYGB is better than AGB? In general I think this part of the document is very hard to understand (methodology), maybe a small explanation of methods should be added to better understand those finding as well as clear clinical conclusion at the end of each results ?		Thank you. We have now added clear conclusions and changed to wording. Additionally, we provided texts to make the figures easier to understand.
Judith Aron-Wisnewsky	84 line 4	Wording	Why does this part does not address T2D or HTN occurrence after surgery in the long term ?(I e development of comorbidities ? If not comorbidities should be replaced by secondary events of the surgery since this is more what is described in this chapter rather than obesity related diseases (= comorbidities) What does progression of obesity means ? not very clear whether it is weight history following bariatric surgery?		Both question D0006 and D0011 can potentially cover T2DM and HTN (they are at present covered in the latter). We have interpreted progression of obesity to include weight regain, and insufficient weight loss after surgery, but may also include progression/development of co-morbidities, see comment above. We have added a paragraph with results for relapse, worsening, unchanged or de novo T2D, HTN, and dyslipidemia at follow up.

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Judith Aron-Wisnewsky	86		In weight regain part, the final weight of patients after surgery should be stated since weight regain might be similar but the overall effect of the surgery might differ (in links with my remark above (page 76-80) The definition used to say weight regain should be stated in each part as has been done for the comparison between SG and RYGB Likewise insufficient weight loss should be defined in each part What were the proposed surgery for RYGB conversion in those studies ??		We have added the final weight at last follow up to the text when available. We have added the definitions for weight regain used in the studies when available. Different definitions were used. Same as above. We have added definitions for insufficient weight loss used in the included studies when available. "In one study (21) four patients in the AGB group received conversion surgery of which two to BPD and two to RYGB. In one study (49) four AGB patients received conversion to SG and one patient to RYGB. In a third study (30) the reason for conversion was not clear (and the conversion procedure unknown). Insufficient weight loss (treatment failure) was in one study defined as EWL <20% and the need for conversion surgery to another bariatric procedure (49), and in another study (21) insufficient weight loss was described as BMI

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					>35 kg/m² at 5 yrs."
Judith Aron-Wisnewsky	89		Why add gastrointestinal reflux in this part (line 15) it has already been treated in the previous part ?		We have moved all GERD outcomes to the safety section.
Clinical effectiveness					
Judith Aron-Wisnewsky	90		For blood pressure and lipid values do we have the number of patients treated ? does it reduce differently between procedures ? I do not think the simple value of blood pressure or any lipid concentrations can be analyzed without taking into account whether patients are treated or even whether their treatment has been reduced in dosage …		We have the number patients included in the analyses in the forest plots, but I guess what you are asking for is the number of patients with hypertension at baseline? For the dichotomous outcome HTN remission we take into account the number at baseline, and the number with remission and without HTN treatment at follow up. Typically not all patients included in a study suffer from hypertension. The differences in comorbidities across studies is a problem when interpreting the results,
Judith Aron-Wisnewsky	92		While diabetes remission is an important parameter, what about patients without remission? does one type of surgery performs better ? ie less treatment ? better glucose controle HbA1c? Why not add the RCT from shauer in this analysis which compared SG and RYGB in T2D patients ? Similar remark as above for HTN and lipid concentrations ? did you take into account the treatments ?		We did not take into account the treatment In the NMAs (i.e. when analysing the continuous HTN, and lipid outcomes), but did so for the dichotomous outcomes for which reaching a target cut-off and stopping medication were both required. We have added available information on drug treatment to the text. Schauer is included.

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Judith Aron-Wisnewsky	93		Line 13 were patients from each groups receiving vitamin and mineral supplementation? Usually it is mandatory after RYGB but after sleeve some teams do not systematically give them. I think it is major to state this to be able to compare nutritional deficiencies between the two technics.		We have added a sentence indicating that there were no information on supplementation after surgery in either group in this study.
Judith Aron-Wisnewsky	98 line 28		The references are missing (same line 41)		Sorted
Judith Aron-Wisnewsky	106		Line 15: did the study assessing quality of life also assessed whether GERD was increased? Maybe state whether quality of life differed according to GERD? Or at least mention that this was not explored ?		We've added a sentence saying that it was not explored in the studies reporting this outcome.
Safety					
Judith Aron-Wisnewsky	107		In the limitation section, maybe state that this analysis only included RCT and a small number which maybe precludes from definitive conclusions. Other results might have been found if longitudinal cohorts had also been included (yet will less power to conclude)?		We've added a paragraph discussing the potential limitation of including only RCTs.
Judith Aron-Wisnewsky	107	18	The number of lost to follow up should be mentioned since this is a very big problem of bariatric surgery worldwide.		The number of lost to follow up is reported in the study level RoB table. We've also mentioned in the discussion that some studies had large losses to follow up.
Judith Aron-Wisnewsky		29	Also note that treatment for dyslipidemia and hypertension should be mentioned to evaluate the complete benefit of the bariatric surgery in terms of improvement of dyslipidemia and hypertension, not solely		We have addressed this comment by adding the following paragraph to the discussion: "Approximately 31% of all deaths worldwide is

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			blood pressure values or lipid concentrations.		due to cardiovascular disease (CVD), with obesity being one of the major risk factors (WHO). The World Health Organization (WHO) emphasizes the need for management of intermediate risk factors such as hypertension, dyslipidemia, and diabetes mellitus, in order to prevent CVD. Despite this, less than half of the included studies reported on blood pressure, lipids, and related medication use, while this presumably is patient data that are routinely collected at follow up, and therefore should be readily available to be included in studies on the effects of obesity surgery procedures. Effects on all CVD risk factors should be assessed to evaluate the complete benefit of bariatric surgery. "
Judith Aron-Wisnewsky	108	Line 18	The report state the difference with another analyses which only included AGB, SG and RYGB… however these are the three main surgical intervention performed worldwide with a lot of published data on longitudinal follow-up. While not all studies published on bariatric surgery are RCT they still give a lot of important information. This should be mentioned in the discussion section.		We have mentioned in the discussion that the review could have benefited by from the inclusion of non-randomised evidence. We have however also added a paragraph describing the problems with including observational study design.

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Appendix					
Judith Aron-Wisnewsky			Overall, I think that in the objective part, le document should mention that this analysis was meant to evaluate whether one technic was superior or better at least than others for different outcomes.		We have added a sentence clarifying this.
Judith Aron-Wisnewsky			One of the important result of this analysis is the fact that most studies do not use the same classification for adverse events so it makes it difficult to make comparision. I think this point should also be added in the conclusion section.		Agree, we've added this important point to the conclusion.
Laurent Genser	3		My first name is Laurent and not "Laurant"	1	Apologies Laurent, this spelling mistake has been corrected.
Summary					
Laurent Genser			Ok no comments		
Description and technical characteristics of the technology					
Laurent Genser	35	28	Please replace "biliopancreatic limb of 50 cm" with "biliopancreatic limb of 50-100 cm" ref Obes Surg. 2016 Mar;26(3):660-71		Added this information to the report. (plus the ref)
Laurent Genser		41	I woiuld add "Lack of standardisation poses further problems with interpretation and comparison of scientific literature. The review by mahawar et al (Obes Surg. 2016 Mar;26(3):660-71.)concluded concluded that a range of 100-200 cm for combined length of biliopancreatic or alimentary limb gives optimum results with Roux-en-Y gastric bypass in most patients.		Added this information to the report. (plus the same ref as above) The clinical effectiveness and safety are formally assessed in SAF and EFF.

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Laurent Genser	36	6	I would add the concerns on severe malnutrition requiring conversion as stated by the RCT by Robert et al (Lancet)		This paper has been cited as suggested, but long0term clinical complications are not discussed in full as this is the aim of the EFF and SAF domains.
Laurent Genser	45	37	Remove "to ensure"		Removed
Health problem and current use					
Laurent Genser			No comments		
Clinical effectiveness					
Laurent Genser			No comments		
Safety					
Laurent Genser			No specific comparison data in the present work nor mortality data The mortality rate after sleeve gastrectomy is higher than other bariatric procedure which does not fit with the rates reported in retrospective studies (zellmer et al am j surg 2015)	2	We have moved the results for GERD to the safety section. There were no early deaths in the SG studies included in our report.
Appendix					
Laurent Genser	14		TABLE 0-2:Replace "Indirekt" with indirect		Spelling mistake corrected.
Rune Sandbu	General		"Discussion and Conclusion". I am overall impressed by the first Draft of the OTCA review. You have managed to extract and present core information about status of surgical treatment of obesity although the		We have listed the main procedures in the first paragraph of the conclusion.

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			different studies included vary greatly in how outcomes are defined and reported. I will recommend that the five bariatric procedures included in this analysis are listed. It should be stated that no study on effectiveness of SASI or SADI met the inclusion criteria.		In addition, we've added the following 'No evidence was found for the effectiveness of SADI-S or SASI'
Rune Sandbu	106	41-05	Repetition from page 105, line 35-44.		Removed repetitive paragraph
Rune Sandbu	72	23	"For details see the risk of bias section." Couldn't find that section.		Links added to the ROB section
Tom Mala Consultant surgeon			I find the report a bit challenging to read. Substantial space is given to details outside the scope to explain the context. This is perhaps due to a standard template for the report (?).	1 general	An attempt will be made to streamline the final version. However, as noted, there are a series of mandatory questions that are required in the standard assessment template.
Tom Mala Consultant			A main comment is the limited high quality data avilable including long-term observations, the heterogenity in reporting of important outcome measures and the selection of only RCTs. Multiple comparions are made. Combined this make evaluations challenging and limiting relevance of the report – in part commented on in the report.	1	This is an important point. We've added a paragraph to address this issue to the discussion. "A majority of the included RCTs were at high risk of bias. Only a handful of RCTs provided high quality evidence, mainly for the comparison of SG vs, RYGB. There was a lack of studies with long-term follow up (>5 years). The limited availability of long-term follow-up data is a major limitation in the literature at the present time. Nevertheless, this work represents a synthesis of the highest quality evidence. Updates to this systematic review will be necessary as long-

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					term evidence becomes available." "The selection of only RCTs is another potential limitation, and it may be argued that well-performed cohort studies with longer follow up could have provided valuable evidence for our research questions. However, allocation of participants to groups in non-randomised studies is typically based on patient preference, clinical decision-making or shared clinical decison-making, and results from non-randomised studies, therefore, may be biased because the characteristics of populations selected for a particular procedure may differ, limiting the usefulness of this evidence, in particular in the evaluation of head-to-head comparisons" "Heterogeneity in reporting, multiple comparisons, and great variations in comorbidities across included studies makes evaluations and interpretations of findings challenging. Definitions of comorbidity resolution, improvement or relapse/worsening, and adverse event classification (late and early

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					complications; major and minor complications; SAEs only) were heterogenous across studies which presents challenges for comparison of results. This highlights the need for adopting standardised definitions for incorporation into core outcome sets to facilitate consistent reporting. "
Summary					
Tom Mala Consultant			Summary not yet finished	2	Sorted
Description and technical characteristics of the technology					
Tom Mala Consultant			I don't quite understand that "Description of technical characteristics of Technology" page 33 and "Health problems and current use of the technology" page 57 are research questions with separate results part rather than background? But again, perhaps due to the use of a special template.	2 general	These are mandatory questions are in the assessment template.
Health problem and current use					
Tom Mala Consultant			[B0003][A0021][A0011] – What is the phase of development and implementation, current 2 use and reimbursement status of the different bariatric procedures in Europe?		
Tom Mala Consultant			Page 49/Figure 3: In Norway there are also recommendations for	1	In the 2014 HTA it was stated that *"In Norway bariatric surgery is offered to persons with morbid obesity (body mass index (BMI) ≥ 35*

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			considering bariatric surgery in pts with BMI 30-35 with diabetes.		*kg/m 2 with at least one obesity related comorbidity or KMI ≥ 40 kg/m 2)".* It is unclear if a recommendation to expand indications was made, and if this was implemented in clinical practice. https://www.fhi.no/en/publ/2014/long-term-effects-of-bariatric-surgery/"
Clinical effectiveness					
Tom Mala Consultant			How was the comparisons made selected like why BPD-DS vs RYGB and not vs SG/D-RYGB/OAGB etc?		We chose RYGB as the main comparaator as it is by many considered the gold standard.
Tom Mala Consultant			Page 19: it is stated that comparison exclude: "long vs short leg": This comparison is anyway done in the report for RYGB vs. D-RYGB?	2	We had stated in the protocol that we would include both RYGB and D-RYGB, but not other variants with different lengths of short- and/or long leg, robotic surgery, or different types of suturing etc.).
Tom Mala Consultant			Page 19 statement: banded gastric bypass not included. B-SG and B-RYGB does that anyway included banded or does the B signify something else?	2	The B indeed stands for a banded procedure. In an intermediate stage of the production of this report we decided to include combined procedures (i.e. B-RYGB and B-SG). These procedures are reported in recent publications, and guidelines, and appears to be still in use. We have added information regarding this in the

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					paragraph *deviations from the protocol.*
Tom Mala Consultant			Page 19 states that BPD without duodenal switch is not included but in Figure 5-2, 5.6 and 5.8 BPD appears to be included?	2	We did in the end include BPD (and DS) procedures in the report, as these procedures appears to be still in use, even though they are not very common. Also a recent bariatric surgery guideline refer to pooled results of all three procedures (BPD-DS, BPD, and DS). We have added information regarding this in the paragraph *deviations from the protocol*
Tom Mala Consultant			Page 20: diabetes both primary and secondary outcome?	2	This is in accordance with the published protocol. The primary outcome of diabetes control (continous variable) capture any *improvement in diabetes control* (Improved HbA1c and reduced medication), while the secondary diabetes outcome (dichotomous) capture *remission of diabetes* (cardivasular risk reduction) with HbA1c lower than 6.0% and stopped diabetic medication.
Tom Mala Consultant			Page 20: "reversal or improvement in A1C seems to be defined as < 7% - needs some description: with/without medication. Required with standard definitions of reversal (remission) and improvement.	2	Agree. We have changed this to <6.0% without medication (=reversal of diabetes), and also focused on complete remission in the report.
Tom Mala Consultant			Perhaps comment in the discussion how diabetes effect was	2	This is indeed a challenge. The effects on diabetes control (continuous outcome) was

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			evaluated – by hb1ac only or by frequencies of remission. Was this with /without use of antidiabetics. It is a major challenge e evaluating effectiveness across procedures as different definitions of remission is used (for pooled analyses).		evaluated in the NMA in which diabetes control data included in the analysis were based on ranked sequence of outcomes for the SMD for details see p.27-28. In the NMA, the use of antidiabetic drugs were not included as this would have called for a much more complex and time-consuming analysis. We have added a paragraph describing this limitation to the discussion. In the analysis of diabetes remission (dichotomous outcome) both target HbA1c and stopped antidiabetic medication were taken into account. Both were required for complete resolution.However, not all studies reported on diabetes resmission. "One limitation pertaining to the available diabetes data for the NMA was that not all studies reported a change in HbA1c from baseline, or even a measure of post intervention HbA1 c, which according to the expert constitute a reliable measure of diabetes control, but instead reported FBG (or other outcomes). Also, the data on diabetes control included in the

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					SMD calculations were based on ranked sequence of outcomes (for details see p.27-28), in which the use of antidiabetic drugs was not included. However, in the analysis of diabetes remission (dichotomous outcome), both target HbA1c and stopped antidiabetic medication were taken into account, but unfortunately not all studies reported on diabetes remission, and only four EFF studies included solely T2DM patients"
Tom Mala Consultant			Table 3-3 page 54: state AGB is recommended I Norway – this is not correct? Also applies to OAGB?	2	The report cited is a previous report by NIPH which refers to mini-gastric bypass (OAGB): *"The method is not yet widely used in Norway and long-term effects are not well documented."* AGB: *"Laparoscopic band surgery has been widely used internationally, but little in Norway in recent years."* https://www.fhi.no/en/publ/2018/Bariatric-surgery-for-Type-2-Diabetes-and-a-body-mass-index-below-35/ Information on AGB has been removed.
Tom Mala			Figures page 73 and further: SG, B-SG, B-RYGB, SR - RYGB etc:	1	Sorted

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Consultant			abbreviations should be more clearly defined (for instance Fig 5.6)? Confusing with so many variants and needs further description		
Tom Mala Consultant			It would help if the Figure legends to Fig. 5.2, 5.4 etc – would be more descriptive.	2	Sorted
Tom Mala Consultant			The SUCRA plot could include a more informative Figure legend.	2	Sorted
Tom Mala Consultant			Discussion page 105: it is stated that Risstad 2016 only included diabetics – This is not correct.	2	Correted
Tom Mala Consultant			A paragraph (line 35-40) page 105 (discussion) duplicated at page 106 line 41-45. Line 7 and 40 page 107 – the same statement is given.	2	Duplicate section removed
Tom Mala Consultant			Only RCTs included (commented on in the discussion). I would expect the heterogeneity in data and populations make summarizing of data challenging – in part commented on in the report.	2	We have added the following paragraph to the discussion: "Few if any of the included studies assessed differential effects of obesity surgery procedures on different subgroups (e.g. people with class II obesity, super-obesity, people with T2DM or other co-morbidity). Data from people with

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					different obesity class and different comorbidity profile are typically pooled, and with no sub-group analyses it is not possible to discriminate the effect of bariatric surgery on two different patient population: i.e. patients with low BMI 30-35 with "heavy" T2D uncontrolled; patients with BMI > 40 with no or few T2D discriminate. This is problematic as the effect of each technique are maybe not the same on different populations. "
Tom Mala Consultant			It is surprising that the outcome for BPD DS did not come out differently in regard to eight loss and diabetes control.	1	BPD-DS did show superiority in diabetes control, and weight, but not consistently so, but it should be noted that only one study was included at 2 years, and another at 5 years follow up, while in other recent NMAs all follow ups have been pooled together..
Tom Mala Consultant			The varying comorbidity profiles – is a limitation for the comparison between studies. Some include only diabetics etc.	1	We have added a couple of sentences decribing the limitation related to the varying number of people with different co-morbidities across studies-
Tom Mala Consultant			Page 86-94 could perhaps present all the measures for the procedures compared combined (more systematic) – rather than "back and forth" – a bit challenging to take in?	1	Sorry, but this is the way it typically is done. i.e that results ae reported for each comparison searately, and not by outcome.

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Tom Mala Consultant			Discussion page 107: " we did not include placebo controlled studies or studies with no treatment". This is listed as a limitation. For comparisons between surgical procedures this may be less relevant as comparison with no surgical treatment is not the topic here?	2	Agree. We have removed this s entence.
Tom Mala Consultant			Line 24 page 105: important differences = clinically relevant differences?	2	We have removed the word 'clinically'
Tom Mala Consultant			Page 18: it is stated that available evidence for SADI-S and SASI will be included – but not commented on in discussion/conclusion?	2	We've added a sentence to the paragraph summarising the main results staing that no evidence was found for SASI or SADI-S.
			GERD and bone health listed under clinical effectiveness, may better be located to safety/adverse events part?	2	We have moved GERD and micronutrient deficiency under safety.
Safety					
Tom Mala Consultant			Micronutrient deficiencies are explored – but not protein malnutrition? A main potential adverse event for maabsorptive procedures like the BPD DS and D RYGB	2	We have explored protein malnutrition also, but very few studies reported this outcome.
Tom Mala Consultant			For analyses of death these are all RCTs with perhaps incorporated learning curves aspects for experimental procedures and selected patient categories like patients with extra high BMI only diabetes etc. Larger pragmatic every day observational studies may deviate from findings presented in this regard. The reported death rates appears a	1	To address this we have added the following paragraph to the discussion: "It should be noted that since these results are based solely on data from RCTs, which may be affected by learning curve aspects for experimental procedures and selected patient categories (e.g. patients with

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			bit high compared to routine practice (larger observational studies). Comments in this regard may be better stressed in discussion.		extra high BMI only diabetes etc.,), results of larger pragmatic every day observational studies may deviate from our findings. "
Tom Mala Consultant			A large variation in standards of reporting appears to be demonstrated challenging comparisons for several outcome measures. A need for more uniform standards of reporting of outcome could be considered as a comment i the discussion.	2	To address this comment we have added the following paragraph to the discussion: "Due to the large variation in standards of reporting, both for adverse events, but also for other outcomes, there is a need for more uniform standards of reporting of outcomes in bariatric surgery studies."
Tom Mala Consultant			Pge 97 "More well defined types of reoperations ..... are reported in the Morbidity section" page indicating where to find this could be given/specified – highly relevant parameter.	2	We have moved this data under the safety section.

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