Swiss Medical Weekly

Formerly: Schweizerische Medizinische Wochenschrift An open access, online journal • www.smw.ch

Systematic review | Published 05 July 2018 | doi:10.4414/smw.2018.14633 **Cite this as:** Swiss Med Wkly. 2018;148:w14633

Comparison of metabolic outcomes in patients undergoing laparoscopic roux-en-Y gastric bypass versus sleeve gastrectomy – a systematic review and meta-analysis of randomised controlled trials

Hayoz Christelle^a, Hermann Thierry^a, Raptis Dimitri Aristotle^{ab}, Brönnimann Alain^c, Peterli Ralph^d, Zuber Markus^a

^a Department of Surgery, Cantonal Hospital Olten, Switzerland

- ^b Department of Surgery and Transplantation, University Hospital Zurich, Switzerland
- ^c Department of Anaesthesia and Intensive Care, Cantonal Hospital Olten, Switzerland

^d Department of Surgery, St. Claraspital, Basel, Switzerland

Summary

BACKGROUND AND OBJECTIVES: Bariatric surgery is the most effective treatment for morbid obesity and is known to have beneficial effects on glycaemic control in patients with type 2 diabetes mellitus (T2DM) and in diabetes prevention. The preferred type of surgery and mechanism of action is, however, unclear. We performed a systematic review and meta-analysis of randomised controlled trials (RCTs) comparing the effects of laparoscopic roux-en-Y gastric bypass (RYGB) with those of sleeve gastrectomy (SG) on metabolic outcome, with a special focus on glycaemic control.

METHODS: A literature search of the Medline, Pubmed, Cochrane, Embase and SCOPUS databases was performed in November 2014 for RCTs comparing RYGB with SG in overweight and obese patients with or without T2DM. The primary outcome was improvement in postoperative glycaemic control. Secondary outcomes included weight-related and lipid metabolism parameters. Synthesis of these data followed established statistical procedures for meta-analysis.

RESULTS: Sixteen RCTs with a total of 1132 patients with overweight or obesity were included in the analysis. When compared with patients who underwent SG, those who underwent RYGB showed no difference after 12 months in mean fasting blood glucose (mean difference [MD] –6.22 mg/dl, 95% confidence interval [CI] –17.27 to 4.83; p <0.001). However, there was a better outcome with RYGB, with lower mean fasting glucose levels at 24 months (MD –16.92 mg/dl, 95% CI –21.67 to –12.18), 36 months (MD –5.97mg/dl, 95% CI –9.32 to –2.62) and at 52 months (MD –15.20 mg/dl, 95% CI –27.35 to –3.05) mg/dl; p = 0.010) and lower mean glycated haemoglobin (HbA1 at 12 months (MD –0.47%, 95% CI –0.73 to –0.20%; p <0.001) and at 36 months postoperatively compared to SG. Fasting insulin levels and HOMA indices showed no differ-

ence at any stage of follow-up. In the subgroup including only diabetic patients HbA1c showed lower levels at 12 months (MD -0.46%, 95% Cl-0.73 to -0.20%). No difference was found for the fasting insulin at baseline and after 12 months. Similarly, when compared to SG, patients that underwent RYGB had lower low-density lipoproteins at 12 months. This effect was lost at 36 months. Patients undergoing RYGB also had lower triglycerides at 12 months and at 52 months, lower cholesterol at 60 months and an improvement of BMI at 52 months postoperatively. BMI values at 12 months and low-density lipoprotein levels at 12 and 36 months were lower for diabetic patients only, as in the overall analysis.

CONCLUSION: Based on this meta-analysis, RYGB is more effective than SG in improving weight loss and shortand mid-term glycaemic and lipid metabolism control in patients with and without T2DM. Therefore, unless contraindicated, RYGB should be the first choice to treat patients with obesity and T2DM and/or dyslipidaemia.

Keywords: gastric bypass, sleeve gastrectomy, glycaemic control, obesity

Introduction

Obesity is a major health issue worldwide and associated with several comorbidities including type 2 diabetes mellitus (T2DM), cardiovascular diseases and cancer. Bariatric surgery is currently the most effective method to induce weight loss in patients with morbid obesity [1]. Worldwide, the most commonly performed bariatric procedures are laparoscopic roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). RYGB was considered to be the gold standard procedure for many years, whereas SG is nowadays the most commonly performed bariatric operation worldwide. Together, both procedures constitute nearly 80% of all bariatric operations worldwide [2].

Author contributions CH and TH share first authorship **Correspondence:**

Markus Zuber, MD, Department of Surgery, Cantonal Hospital Olten, CH-4600 Olten, markus.zuber[at]spital.so.ch Bariatric surgery is superior to medical treatment for T2DM [3]. However, it is unclear whether RYGB or SG offer the greatest benefit for patients with T2DM. Several randomised controlled trials (RCTs) have compared RYGB with SG. However, body weight loss and body mass index (BMI) was chosen as primary endpoint in six RCTs [4], whereas T2DM was primary endpoint in only one, glycated haemoglobin (HbA1c) in five and fasting blood glucose in three. Consequently, most RCTs did not include enough patients with T2DM and thus were not powered to allow a comparison between RYGB and SG in this group. Therefore, it remains unclear which of the two bariatric procedures is superior for optimal metabolic control in general and for optimal glycaemic control specifically after surgery.

The aim of this systematic review and meta-analysis of RCTs was to compare the metabolic effects of RYGB and SG assessed as serum glucose, and other markers for T2DM and dyslipidaemia in order to identify the procedure associated with best metabolic outcomes.

Methods

A systematic review protocol was registered on the international PROSPERO database and can be accessed by the following registration number: CRD42014009837. All units in the meta-analysis were converted to International System of Units (SI units). Glucose values were converted from mmol/l to mg/dl by dividing by 0.555 (mg/dl × 0.555 = mmol/l), high-density lipoprotein, low-density lipoprotein and cholesterol values from mmol/l to mg/dl by dividing by 0.02586 (mg/dl × 0.02586 = mmol/l), and triglyceride values from mmol/l to mg/dl by dividing by 0.0113 (mg/dl × 0.0113 = mmol/l). To convert the standard error of the mean (SEM) into the standard deviation (SD,) the following formula was used: SD = SE \sqrt{n} [5].

Search methods for identification of studies

Electronic searches

A literature search was carried out by a professional librarian, MG in collaboration with DAR. An example of our search strategy is included in appendix 1. Two independent reviewers, TH and CH, [6] screened and extracted the data from the records using a pre-defined electronic protocol available at review-net.com. An official meeting of the investigators resolved discrepancies by specialist group consensus. The same procedure was applied for screening and inclusion/exclusion of articles.

Data extraction and analysis

All RCT reports that included data on the primary and secondary endpoints of this systematic review were included. In six RCTs, changes in fasting blood glucose were reported as the primary endpoint. Specific search terms were used for each database: Medline, Pubmed, Cochrane, Embase and SCOPUS. The search took place on the 21 November 2014 and included publications from 1980 onwards. There were no language restrictions. Additional inclusion criteria were: studies comparing RYGB (including biliopancreatic diversion) with SG, and patient age above 18 years. Studies of banding alone, animal studies, case re-

Published under the copyright license "Attribution – Non-Commercial – No Derivatives 4.0". No commercial reuse without permission. See http://emh.ch/en/services/permissions.html. ports, retrospective or prospective nonrandomised cohort and case control studies were excluded.

For studies where data for the same cohort of patients were reported in more than one publication (follow-up publications), only the most recent data were included. The study of Woelnerhanssen et al. 2011 included the same patient cohort as that of Peterli et al. 2012 and Peterli et al. 2013 [7–9]. The study of Lee et al. July 2011 included the same patient cohort as Lee et al. February 2011 and Lee et al. 2014 [4, 10, 11]. The study of Schauer et al. 2012 [13], Sangeeta [12] and Kashyap et al. [14]. Follow-up studies with same patient cohorts but different endpoints were included in specific analyses.

The data extracted were the following: author's last name, publication year, study design, total number of patients, number of patients in the SG group, number of patients in the RYGB group, age (mean, median, SD, SEM, range, or interquartile range [IQR]), male:female ratio, preoperative BMI (weight and height), preoperative fasting blood glucose, preoperative oral antidiabetic therapy, preoperative insulin administration (units per day), type of operation, operation technique, operating time (mean, median, SD, SEM, range, or IQR), blood loss (mean, median, SD, SEM, range, or IQR), rate of conversion to open surgery, reason for conversion to open surgery, complications, type of complications, postoperative leak, mortality, cause of death, postoperative fasting blood glucose levels, postoperative antidiabetic therapy, postoperative insulin administration (units), length of hospital stay (mean, median, SD, range, or IQR), postoperative weight reduction (BMI), and the level of evidence of each study (Cochrane risk-of-bias assessment).

Primary and secondary outcomes

The primary outcome was improvement in differences in fasting blood glucose levels, insulin resistance and HbA1c in diabetic patients. A subgroup analysis of studies that included only patients with known T2DM preoperatively was performed. Secondary outcomes included weight-related and lipid metabolism endpoints (such as BMI, and low-density lipoprotein, high-density lipoprotein, cholesterol and triglyceride concentrations).

Statistical analysis

A quantitative synthesis was performed if the included studies reported data on the same parameter and at the same time point. A narrative synthesis of the findings from the included studies and summaries of intervention effects for each comparative study by calculating odds ratios (for dichotomous variables) or mean differences (for continuous variables) was created. For the quantitative synthesis, we pooled the results using a fixed-effects meta-analysis, with mean differences (MDs) for continuous variables and odds ratios for binary variables, and calculated 95% confidence intervals (CIs) with the two-sided p-values for each outcome. Heterogeneity between the studies in effect measures were assessed using both the chi-squared test and the I-squared statistic. An I² value greater than 50% was considered indicative of substantial heterogeneity; however, both fixed- and random-effects models are reported. Funnel plots were used and all studies were tested for asymmetry that may reflect selective publication bias or poor

methodology. Statistical analysis was performed using R version 3.3.2 (R Core Team, GNU GPL v2 License), R Studio version 1.0.44 (RStudio, Inc. GNU Affero General Public License v3, Boston, MA, 2016) with the graphical user interface (GUI) rBiostatistics.com alpha version (Cloud Graphical User Interface for R Statistics and eLearning Platform. Zurich, Switzerland, 2016).

Description of the studies

The selection process from the initial results of publication searches to the final included studies is illustrated in figure 1. Initially a total of 879 records were identified, of which 554 were non-duplicates. After the inclusion and exclusion criteria had been applied, 523 records were excluded and an additional 21 records were retrieved. Nine records were excluded after full-text screening (duplicates, statements or abstracts with no full-text available) and four records were added through a manual check of reference lists. Finally, 16 RCT records were included in the meta-analysis (table 1). The focus was on diabetic patients, who were included in eight studies [4, 10, 12–14, 20], including one ongoing study in diabetic patients that was not published at the time of our study [16]. The studies including both diabetic and nondiabetic patients were also analysed, including all 16 RCTs available.

Risk of bias in included studies

The risk-of-bias assessments are described in detail in figures S1a and S1b in appendix 2. Briefly, the assessment of risk of bias was performed by independent reviewers using the updated CBRG criteria [22], including selection, performance, detection, attrition and reporting bias. Disagreements were settled by a third reviewer.



Swiss Medical Weekly · PDF of the online version · www.smw.ch

Results

We first focus on trials including mixed overweight and obese patient populations with and without T2DM. The results from the subgroup analysis of trials including only overweight and obese patients with T2DM are then reported.

Results from randomised trials including both patients with and patients without diabetes mellitus

Patient demographics

Age at baseline, (preoperatively) did not differ between the RYGB and SG groups (MD 0.02 years, 95% CI -1.51 to 1.56) with a pooled mean age of 43 years (range 37–50) for the RYGB and 42 years (range 36–48) for the SG group. Seven RCTs included both female and male patients [9, 11, 13, 15, 17, 18, 20], one study [19] included only female and two studies [16, 21] only male patients. Overall, there was no significant difference in the proportion of female patients in the RYGB and SG groups.

Glucose metabolism

Fasting blood glucose was reported at baseline, 12, 24, 36 and 52 months postoperatively (figs 2a to 2e). Surpris-

Table 1: Summary of the randomised controlled trials included.

ingly, there was a significant difference between the two groups at baseline, with higher fasting blood glucose in the SG group (MD 17.38 mg/dl, 95% CI 12.52 to 22.23; p<0.001; fig. 2a), but with high heterogeneity. However, as illustrated in figure 2b, this difference was lost when the RCT from Schauer et al. [13] was excluded from the analysis (p = 0.738), and this time with zero heterogeneity. Although at 12 months (fig. 2c), there was no significant difference in the fasting blood glucose values between the two groups, at 24 months (fig. 2d) (MD -16.92 mg/dl, 95% CI -21.67 to -12.18; p <0.001) and at 36 months (fig. 2e) (MD -5.97 mg/dl, 95% CI -9.32 to -2.62; p <0.001) there was a significantly better outcome in the RYGB group, with lower fasting blood glucose levels compared with the SG group. The only RCT reporting fasting blood glucose at 52 months (Lee et al. [11]) also showed lower values in the long term in the RYGB group (MD -15.20 mg/dl, 95% CI -27.35 to -3.05; p = 0.010).

Fasting insulin at baseline was reported by three RCTs [8, 12, 16] and significantly lower levels were shown in the SG group (MD 4.76 μ U/l, 95% CI 4.01 to 5.51; p <0.001; fig. 3a). As with the fasting blood glucose results, the difference was due only to the RCT from Schauer et al. [12] (fig. 3b). However, at 12 months, both SG and

Reference	Year of publi- cation	Journal	Time period of trial	Multi- or single centre	Country	City	Total number of patients
Karamanakos et al. [15]	2008	Ann Surg		Single	Greece	Patras	32
Peterli et al. [16]	2009	Ann Surg		Single	Switzerland	Basel	27
Kehagias et al. [17]	2011	Obes Surg	Jan 2005 to Feb 2007	Single	Greece	Patras	60
Lee et al. [10]	2011	Surg Obes Re- lat.	Sept 2007 to Jun 2008	Single	Taiwan	Taoyuan, Taipei,	32
Lee et al. [4]	2011	Arch Surg	Sept 2007 to Jun 2008	Single	Taiwan	Taoyuan, Kaohsiung	60
Woelnerhanssen et al. [7]	2011	Surg Obes Re- lat		Single	Switzerland	Basel	23
Paluszkiewicz et al. [18]	2012	Videosugery	Nov 2008 to Mar 2009	Single	Poland	Warsaw	72
Peterli et al. [8]	2012	Obes Surg		Single	Switzerland	Basel	23
Ramon et al. [19]	2012	J Gastrointest Sur	Apr 2007 to Mar 2008	Single	Spain	Barcelona	15
Schauer et al. [12]	2012	NEJM	Mar 2007 to Jan 2011	Single	USA	Cleveland, Boston	100
Kashyap et al. [14]	2013	Diabetes Care	Mar 2007 to	Single	USA	Cleveland, Boston, Los Angeles,San An- tonio	37
Keidar et al. [20]	2013	Diabetologia	Jun 2008 to Feb 2010	Single	Israel	Jerusalem, Petach Tikva	37
Peterli et al. [9]	2013	Ann Surg	Jan 2007 to Nov 2011	Multi	Switzerland	Basel, Bern, Zürich, St.Gallen	217
Helmiö et al. [21]	2014	Scand J Surg	Apr 2008 to Jun 2010	Multi	Finland	Turku	240
Lee et al. [11]	2014	Obes Surg	Sept 2007 to Jun 2008	Single	Taiwan	Taoyouan	60
Schauer et al. [13]	2014	NEJM	Mar 2007 to Jan 2011	Single	USA	Clevland, Boston	97

Figure 2a: Fasting blood glucose at baseline.

	Experi	mental	Cont	bl			Weight	Weight
Study	Total Mean	SD Total	Mean	D Mean difference	MD	95%-CI	(fixed)	(random)
Lee 2014	30 200.9	76.60 30	230.60 85.3	0	-29.70 [-70.7	72: 11.321	1.4%	13.1%
Peterli 2009	13 102.7	14.41 14	113.51 32.4	0	-10.81 [-29.	52; 7.90]	6.7%	22.2%
Peterli 2012	12 104.5	43.69 11	102.70 59.7	0	1.80 [-41.3	31; 44.91]	1.3%	12.4%
Karamanakos 2008	16 98.0	14.00 16	96.00 12.0	0 -	2.00 [-7.0	03; 11.03]	28.8%	25.8%
Schauer 2014	48 193.0	15.67 49	164.00 15.3	3 🛛 🔤 🛨	29.00 [22.8	33; 35.17]	61.8%	26.5%
Fixed effect model	119	120		-	17.38 [12.5	2; 22.23]	100.0%	
Handom effects mode	$\frac{1}{2}$ 404 7 p (0.01			2.16 [-18.4	0; 22.72]		100.0%
meterogeneity: 1° = 90%, 7	t = 404.7, p <	0.01		-60 -40 -20 0 20 40 60				

Swiss Medical Weekly · PDF of the online version · www.smw.ch

RYGB groups had similar values (fig. 3c). The only RCT reporting fasting insulin at 52 months (Lee et al. [11]) also showed no significant difference between the two groups (MD -0.50μ U/l, 95% CI -1.37 to 0.37; p = 0.260).

HbA1c at baseline (fig. 4a) was similar in both groups. At 12 months, there was a significant difference between the two groups favouring the RYGB group (MD -0.47%, 95% CI -0.73 to -0.20%; p <0.001; fig. 4b). At 36 months, reported by only two RCTs, there was only a trend favouring the RYGB group (p = 0.127; fig. 4c).

The homeostatic model assessment (HOMA) index is a method for assessing β -cell function and insulin resistance from basal fasting blood glucose and insulin concentrations. The HOMA index was reported at baseline, 1 week, and 3, 12, 24 and 52 months postoperatively (figs 5a–5e). At baseline the results were significantly in favour of the SG group (MD 2.96, 95% CI 2.51to3.41; p <0.001; fig. 5a); however this difference was again lost when the study from Schauer et al. [12] was excluded (fig. 5b). At 3 months postoperatively, favourable results were found for the RYGB group (MD –0.64, 95% CI –0.99 to –0.29; p



Study Total Mean SD Total Karamanakos 2008 16 89.00000 8.000000 Peterli 2009* 13 91.90000 16.218000	16 84.00000	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Karamanakos 2008 16 89.00000 8.000000 Peterli 2009* 13 91.90000 16.218000	16 84.00000	8 00000					
Peterli 2009* 13 91,90000 16,218000		0.00000	· · · ·	5.00	[-0.54; 10.54]	55.6%	25.6%
	14 99.11000	30.63400	<u> </u>	-7.21	[-25.52; 11.10]	5.1%	15.6%
Lee 2011 30 99.30000 19.400000	30 140.10000	53.00000 -	11	-40.80	[-61.00; -20.60]	4.2%	14.3%
Woelnerhanssen 2011 12 91.89189 6.241625	11 90.09009	17.91157		1.80	[-9.36; 12.96]	13.7%	21.4%
Kashyap 2013 18 93.00000 13.750000	19 97.00000	14.00000		-4.00	[-12.94; 4.94]	21.4%	23.2%
Fixed effect model 89	90		4	0.10	[-4.04; 4.23]	100.0%	
Random effects model				-6.22	[-17.27; 4.83]		100.0%

Figure 2d: Fasting blood glucose at 24 months.

Study	E) Total	operimo Mean	ental SD	Total	Co Mean	ontrol SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Kashyap 2013 Lee (Surg Obes Relat Dis) 2011	18 16	87.0 106.3	7.5 19.2	19 16	104.0 122.7	8.25 19.40	<u>+</u>	-17.00 -16.40	[-22.08; -11.92] [-29.77; -3.03]	87.4% 12.6%	87.4% 12.6%
Fixed effect model Random effects model Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0$	34 0.93			35			-20 -10 0 10 20	-16.92 -16.92	[-21.67; -12.18] [-21.67; -12.18]	100.0% 	 100.0%

Figure 2e: Fasting blood glucose at 36 months.

	E	xperin	nental		(Control					Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean diffe	rence	MD	95%-CI	(fixed)	(random)
Schauer 2014	48	100.0	9.00	49	106.000	8.330			-6.00	[-9.45; -2.55]	94.2%	94.2%
Peterli 2009*	28	97.3	19.82	26	102.714	30.634 -	•		-5.41	[-19.29; 8.46]	5.8%	5.8%
Fixed effect model	76			75					-5.97	[-9.32;-2.62]	100.0%	-
Random effects mode Heterogeneity: $I^2 = 0\%$, τ^2	$p^2 = 0, p =$	= 0.94							-5.97	[-9.32; -2.62]		100.0%
							-15 -10 -5 0	5 10 15				

Swiss Medical Weekly · PDF of the online version · www.smw.ch

<0.001; fig. 5c). At 12 months, and including the study from Schauer et al. [12], the results favoured the SG group (MD 0.09, 95% CI 0.01 to 0.17; p = 0.036). However, when the study from Schauer et al. [12] was excluded because of the differences at baseline, the results were opposite, favouring the RYGB group (MD –0.61, 95% CI –1.23 to 0.01; p = 0.054; figs 5d and 5e). One RCT reported by Lee et al. [4] also showed favourable results for RYGB at 24 months (MD –0.60, 95% CI –1.16 to –0.04; p = 0.040); however this was lost at 52 months (MD –0.20, 95% CI –0.48 to 0.08; p = 0.160) [11].

Lipid metabolism

Lo-w-density lipoproteins at baseline showed no significant difference between the RYGB and SG groups (fig. S2a in appendix 2). There was a significant difference favouring the RYGB group at 12 months (MD –17.74 mg/dl, 95% CI –25.61 to –9.88; p <0.001; fig. S2b). At 24 months postoperatively, only the RCT from Kashyap et al. [14] showed a significant difference, also favouring the RYGB group (MD –18.60 mg/dl, 95% CI –35.91 to –1.29; p = 0.040). Two RCTs reported results at 36 moths with trends favouring the RYGB group (MD –8.63 mg/dl, 95% CI –19.33 to 2.06; p = 0.113, fig. S2c). The RCT from

	E	xperin	nental		C	ontrol							Weight	Weigh
Study	Total	Mean	SD	Total	Mean	SD	Mean	diffe	rence	MD	95	%-CI	(fixed)	(random
Peterli 2009	13	28.3	13.30	14	37.0	26.10 -			-	-8.70	[-24.17;	6.77]	0.2%	13.7%
Peterli 2012	12	30.0	16.90	11	28.2	16.50		-		1.80	[-11.86; 1	5.46]	0.3%	16.7%
Schauer 2012	50	18.4	2.35	50	13.6	1.35				4.80	[4.05;	5.55]	99.5%	69.6%
Fixed effect model	75			75					b	4.76	[4.01;	5.51]	100.0%	<u> </u>
Random effects model								-	>	2.45	1-3.93:	8.83		100.0%

Figure 3b: Insulin at baseline without Schauer et al. 2012 [12].

	E	perim	ental		Co	ntrol									Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mean	diffe	rence		MD	9	5%-CI	(fixed)	(random)
Peterli 2009	13	28.3	13.3	14	37.0	26.1			1	_		-8.70	[-24.17;	6.77]	43.8%	43.8%
Peterli 2012	12	30.0	16.9	11	28.2	16.5			1		-	1.80	[-11.86;	15.46]	56.2%	56.2%
Fixed effect model	25			25				\sim	1	-		-2.80	[-13.04;	7.44]	100.0%	
Random effects model									-	~		-2.80	[-13.04;	7.44]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	= 0.32						1	1	1						
							-20	-10	0	10	20					

Figure 3c: Insulin at 12 months.

	E	xperin	nental		C	ontrol								Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mear	n diffe	rence		MD	95%-CI	(fixed)	(random)
Woelnerhanssen 2011	12	13.1	4.157	11	14.8	3.317			-	_		-1.70	[-4.76; 1.36]	0.9%	0.9%
Schauer 2012	50	5.3	0.683	50	5.4	0.817						-0.10	[-0.40; 0.20]	96.1%	96.1%
Lee (Arch Surg) 2011	30	4.9	3.800	30	4.7	2.700		13 <u>-</u>		-		0.20	[-1.47; 1.87]	3.0%	3.0%
Fixed effect model	92			91					4			-0.11	[-0.39; 0.18]	100.0%	
Random effects model									\$			-0.11	[-0.39; 0.18]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	= 0.56					r	1	1	1	1		• • •		
and an and a state of the second state of the							-4	-2	0	2	4				

Figure 4a: Glycated haemoglobin (HbA1c) at baseline.

	Exp	erimental		Cont	rol				Weight	Weight
Study	Total	Mean SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Keidar 2013	19	7.7 1.3	18	8.34	1.8		-0.64	[-1.66; 0.38]	5.4%	5.4%
Peterli 2009	13	5.7 0.3	14	6.10	1.3		-0.40	[-1.10; 0.30]	11.5%	11.5%
Schauer 2014	48	9.3 1.4	49	9.50	1.7		-0.20	[-0.82; 0.42]	14.7%	14.7%
Ramón 2012	7	5.7 0.3	8	5.70	0.6		0.00	[-0.47; 0.47]	25.3%	25.3%
Woelnerhanssen 2011	12	5.7 0.3	11	5.70	0.6		0.00	[-0.39; 0.39]	36.4%	36.4%
Lee 2014	30	10.0 1.8	30	9.90	1.8		0.10	[-0.81; 1.01]	6.8%	6.8%
Fixed effect model	129		130				-0.10	[-0.34; 0.13]	100.0%	
Random effects model Heterogeneity: $l^2 = 0\% \tau^2$	= 0 <i>p</i> =	0.78					-0.10	[-0.34; 0.13]		100.0%
,	-, -				1	.5 -1 -0.5 0 0.5 1 1.5				

Swiss Medical Weekly · PDF of the online version · www.smw.ch

Lee et al. [11] with long term results showed a significant difference favouring the RYGB group (MD -30.60 mg/dl 95% CI -48.84 to -12.36; p <0.001).

For high-density lipoproteins, there was a significant difference between the two groups disfavouring the SG group at baseline (MD 2.69 mg/dl, 95% CI 0.22to5.17; p = 0.030; fig. S3a). However, at 12 months (p = 0.066) and at 36 months (p = 0.810) there was no significant difference found (figs S3b and S3c). The only RCT (Lee et al. [11]) reporting data at 60 months postoperatively also showed no significant difference between the two groups (MD -1.10 mg/dl, 95% CI -4.64 to 2.44; p = 0.540).

Cholesterol showed no significant difference between the groups at baseline (fig. S4a). There was a significant difference between the two groups favouring the RYGB group at 12 months (MD –16.29 mg/dl, 95% CI –26.69 to –5.90; p <0.001; fig. S4b). The only RCT reporting cholesterol values at 24 months was that of Kashyap et al. [14], which also showed results favouring the RYGB group (MD –23.20 mg/dl, 95% CI –42.29 to –4.11; p = 0.020). Similarly, the only RCT reporting cholesterol values at 60 months was



Figure 4c: Glycated haemoglobin (HbA1c) at 36 months.

	Exp	erimer	ntal		Con	trol									Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mean	h diffe	rence		MD	95	%-Cl	(fixed)	(random)
Schauer 2014	48	6.7	1.3	49	7.0	1.3		i.	4			-0.30	[-0.82;	0.22]	67.8%	67.8%
Peterli 2009*	28	6.1	1.0	26	6.5	1.7	-	10				-0.40	[-1.15;	0.35]	32.2%	32.2%
Fixed effect model	76			75				_				-0.33	[-0.76;	0.09]	100.0%	
Random effects mode	el							-	\rightarrow			-0.33	[-0.76;	0.09]		100.0%
Heterogeneity: / ² = 0%, τ	$^{2} = 0, p =$	= 0.83						1	1				5 - S			
							-1	-0.5	0	0.5	1					

Figure 5a: HOMA index at baseline.

	Exp	perimental		Co	ntrol				Weight	Weight
Study	Total M	lean SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Lee (Surg Obes Relat Dis) 2011	16	7.9 3.200	16	10.1	6.50 -		-2.20	[-5.75; 1.35]	1.6%	21.2%
Peterli 2009	13	9.1 1.200	14	9.1	1.70		0.00	[-1.10; 1.10]	16.6%	29.8%
Peterli 2012	12	8.0 5.100	11	7.5	5.50		0.50	[-3.85; 4.85]	1.1%	18.2%
Schauer 2012	50	8.9 1.533	50	5.2	0.95		3.70	[3.20; 4.20]	80.8%	30.8%
Fixed effect model	91		91			\$	2.96	[2.51; 3.41]	100.0%	
Random effects model Heterogeneity: $I^2 = 93\%$, $\tau^2 = 6.962$	2, p < 0.01	Ľ					0.77	[-2.12; 3.65]		100.0%
						-4 -2 0 2 4				

Figure 5b: HOMA index at baseline without Schauer et al. 2012 [12].

Study	Exp Total	Derimen Mean	tal SD ⁻	Total	Con Mean	trol SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Lee (Surg Obes Relat Dis) 2011	16	7.9	3.2	16	10.1	6.5 -		-2.20	[-5.75; 1.35]	8.3%	8.3%
Peterli 2009	12	8.0	5.1	11	7.5	5.5		0.00	[-3.85; 4.85]	5.6%	5.6%
Fixed effect model Random effects model Heterogeneity: $J^2 = 0\%$, $\tau^2 = 0$, $p = 0$	41 0.49			41			-4 -2 0 2 4	-0.16 -0.16	[-1.18; 0.87] [-1.18; 0.87]	100.0% 	 100.0%

Swiss Medical Weekly · PDF of the online version · www.smw.ch

the one from Lee et al. [11], which also showed results favouring the RYGB group (MD -43.30 mg/dl, 95% CI -61.10 to -25.50; p <0.001).

Triglyceride levels differed significantly between the SG and RYGB groups, favouring SG at baseline (MD 17.46 mg/dl, 95% CI 10.13to24.83; p <0.001; figs S5a and S5b) purely due to the inclusion of the RCT from Schauer et al. [13]. Despite this, at 12 months there was a significant difference between the two groups favouring the RYGB group (MD -5.60 mg/dl, 95% CI -8.98 to -2.22; p = 0.001; figs S5c and S5d). The only study reporting triglyceride levels at 52 months postoperatively was that of Lee et al. [11], which showed a significant difference favouring the RYGB group (MD -36.60 mg/dl, 95% CI -48.46 to -24.74; p <0.001).

Body mass index

BMI was reported at baseline and at 3, 6, 12, 24 and 52 months postoperatively (figs 6a–6e). There was no significant difference between BMI at baseline, at 3 months, at 12 months and at 24 months. However, two RCTs reporting BMI at 6 months postoperatively showed a significant difference in BMI favouring the SG group (MD 1.88 kg/m², 95% CI 0.38 to 3.38; p = 0.014; fig. 6c). The only study reporting BMI at 52 months (Lee et al. [11]) favoured RYGB (MD -1.80 kg/m², 95% CI-2.92 to -0.68; p = 0.002). Thus, although BMI did not differ between the groups dur-

ing short- and mid-term follow up, there was a clear difference favouring the RYGB over the SG group in the long term, with BMI reductions of nearly -2 up to -3 kg/m².

Results obtained from randomised trials including diabetic patients only

Eight RCTs [4, 10–14, 20] investigated only obese patients with diabetes. The separate analyses for these RCTs is described below.

Demographics

Age was reported by four RCTs including only patients with T2DM. At baseline (preoperatively) there was no significant difference between the SG and RYGB groups (MD -0.11 years, 95% CI -2.32 to 2.10) with a pooled mean age of 48 years (range 39–57) in the RYGB groups and 47 years (range range) in the SG group. This indicates that patients with T2DM were older than the overall analysis group. The gender distribution between the two groups was also comparable.

Glucose metabolism

Baseline levels for fasting blood glucose were reported in three of the studies including only diabetic patients. There was a significant difference, disfavouring the SG group, with higher fasting blood glucose levels at baseline (MD 26.45 mg/dl, 95% CI 20.46to32.44; p < 0.001; fig. S6c in

	E	perim	ental		С	ontrol				Weight	Weigh
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(randon
Woelnerhanssen 2011	12	3.4	1.04	11	5.1	2.985		-1.70	[-3.56; 0.16]	3.5%	14.2
Peterli 2009	13	3.4	0.30	14	4.0	0.600		-0.60	[-0.95; -0.25]	96.5%	85.89
Fixed effect model	25			25				-0.64	[-0.99; -0.29]	100.0%	
Random effects model							-	-0.76	[-1.51: 0.00]		100.09

Figure 5d: HOMA index at 12 months.

	E	Experin	nental		C	ontrol									Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mear	diffe	rence		MD	9	5%-CI	(fixed)	(random)
Lee (Arch Surg) 2011	30	1.2	1.200	30	2.5	3.400 -		,	+ -			-1.30	[-2.59;	-0.01]	0.4%	17.2%
Woelnerhanssen 2011	12	2.9	0.693	11	3.3	0.995			+++-			-0.40	[-1.11;	0.31]	1.3%	32.1%
Schauer 2012	50	1.4	0.133	50	1.3	0.267			<u>.</u>			0.10	[0.02;	0.18]	98.3%	50.6%
Fixed effect model	92			91					-0			0.09	[0.01;	0.17]	100.0%	-
Random effects model								\triangleleft	\rightarrow			-0.30	[-0.96;	0.36]		100.0%
Heterogeneity: $I^2 = 69\%$, τ	$^{2} = 0.22$	211, p =	0.04					1								
ಹಾ ಬೆ		3(8 5)					-2	-1	0	1	2					

Figure 5e: HOMA index at 12 months without Schauer et al. 2012 [12].

	E	Experin	nental		C	ontrol							Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mea	n diffe	rence	MD	9	5%-CI	(fixed)	(random)
Lee (Arch Surg) 2011	30	1.2	1.200	30	2.5	3.400		<u> </u>		-1.30	[-2.59;	-0.01]	23.1%	31.3%
Woelnerhanssen 2011	12	2.9	0.693	11	3.3	0.995	-			-0.40	[-1.11;	0.31]	76.9%	68.7%
Fixed effect model	42			41			\langle			-0.61	[-1.23;	0.01]	100.0%	
Random effects model Heterogeneity: $I^2 = 30\%$, τ^2	² = 0.12	233, p =	0.23						1	-0.68	[-1.50;	0.14]		100.0%

Swiss Medical Weekly · PDF of the online version · www.smw.ch

appendix 2). However, after the RCT from Schauer et al. [13] was excluded, this difference was lost (fig. S6d). The fasting blood glucose values at 12 months were reported in three studies including only diabetic patients and were significantly higher in the SG group (MD -9.25 mg/dl, 95% CI -16.21 to -2.30; p = 0.009; fig. 7a). When the random effect instead of the fixed effect model were used because

of high heterogeneity, the difference lost statistical significance (MD –15.26 mg/dl, 95% CI –33.37 to 2.86). At 24 months, only two studies reported fasting blood glucose values and there was a significant difference between the two groups, again favouring the RYGB group (MD –16.92 mg/dl; 95% CI –21.67 to –12.18; p <0.001; fig. 7b).Two studies reported fasting blood glucose data at 36 months

	E	perime	ental		Co	ntrol					Weight	Weigh
Study	Total	Mean	SD	Total	Mean	SD	Mean differen	ce N	ID	95%-CI	(fixed)	(random)
1 0014	20	20.0	0.00	20	01.0	0.00		0	00 T	0 07. 0 471	04 49/	04.00/
Lee 2014	30	30.2	2.20	30	31.0	2.80		-0.	80 [-	2.07; 0.47]	24.4%	24.0%
Keidar 2013	19	42.0	4.80	18	42.5	5.20		0.	50 [-	3.73; 2.73]	3.8%	3.9%
Peterli 2013	110	44.2	5.30	107	43.6	5.30		0.	60 [-	0.81; 2.01]	19.9%	19.8%
Ramón 2012	7	44.2	2.00	8	43.5	3.00		- 0.	70 [-	1.85; 3.25]	6.1%	6.2%
Kehagias 2011	30	45.8	3.70	30	44.9	3.40		- 0.	90 [-	0.90; 2.70]	12.2%	12.3%
Schauer 2014	48	37.1	3.39	49	36.1	3.91		1.	-] 00	0.46; 2.46]	18.7%	18.6%
Peterli 2009	13	47.0	6.40	14	45.7	6.70		1.	30 [-	3.64; 6.24]	1.6%	1.7%
Karamanakos 2008	16	46.6	3.70	26	45.1	3.60		— 1.	50 [-	0.78; 3.78]	7.6%	7.7%
Paluszkiewicz 2012	36	48.6	5.40	36	46.1	5.90	+	⊢ 2.	50 [-	0.11; 5.11]	5.8%	5.9%
Fixed effect model	309			318				0.	52 [-(0.10: 1.151	100.0%	-
Pandam affaata mad	al						-	0	52 1	11. 1 171		100 0%

Figure 6b: Body mass index (BMI) at 3 months.

Study	Exp Total	erimenta Mean S	ıl D Total	Control Mean SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
1. TO								. ,	, ,
Keidar 2013	19	34.9 4.	5 18	33.9 4.6		1.00	[-1.93; 3.93]	31.7%	31.7%
Peterli 2012	12	39.8 5.	8 11	38.8 4.8		- 1.00	[-3.34; 5.34]	14.5%	14.5%
Karamanakos 2008	16	38.0 3.	1 16	36.8 3.4	-	1.20	[-1.05; 3.45]	53.7%	53.7%
Fixed effect model	47		45			1.11	[-0.55; 2.76]	100.0%	
Random effects mode	1					1.11	[-0.55; 2.76]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	= 0.99							
	-11-				-4 -2 0 2 4				

Figure 6c: Body mass index (BMI) at 6 months.

Study	Exp Total	erime Mean	ntal SD	Total	Con Mean	trol SD		Mean	differ	ence	ME) 95%-CI	Weight (fixed)	Weight (random)
Paluszkiewicz 2012	36	36.0	4.8	36	34.7	5.2			_		- 1.30	[-1.01; 3.61]	42.2%	42.2%
Karamanakos 2008	16	34.3	2.8	16	32.0	2.9			-		- 2.30	0 [0.32; 4.28]	57.8%	57.8%
Fixed effect model	52			52					-	$ \rightarrow $	1.8	8 [0.38; 3.38]	100.0%	
Random effects model									-	$\dot{\frown}$	1.88	8 [0.38; 3.38]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	0.52						1		1				
	2.567						-4	-2	0	2	4			

Figure 6d: Body mass index (BMI) at 12 months.

Study	Exp Total	erimer Mean	ntal SD	Total	Con Mean	sc sc	1	1	Mean	diffe	erence	Ð		MD	9	5%-CI	Weight (fixed)	Weight (random)
Peterli 2009*	28	30.8	4.7	26	32.9	5.4	4	-						-2.10	[-4.81:	0.611	7.7%	12.4%
Lee (Arch Surg) 2011	30	22.8	2.2	30	24.4	2.4	4			÷1				-1.60	[-2.77:	-0.431	41.6%	22.7%
Kashyap 2013	18	26.7	2.5	19	27.6	2.5	5		-	4				-0.90	[-2.51;	0.71]	21.7%	19.4%
Peterli 2012	12	31.1	7.5	11	32.0	5.0) —							-0.90	[-6.07;	4.271	2.1%	5.0%
Keidar 2013	19	31.4	4.2	18	30.4	3.8	3		-	11		_		1.00	[-1.58;	3.58]	8.5%	13.1%
Paluszkiewicz 2012	36	33.8	5.4	36	32.8	5.6	3		-		*			1.00	[-1.54;	3.54]	8.7%	13.3%
Karamanakos 2008	16	31.5	3.4	16	28.9	3.6	5			-	*	-		2.60	[0.17;	5.03]	9.6%	14.0%
Fixed effect model	159			156					<					-0.62	[-1.37;	0.13]	100.0%	
Random effects model									<	\Rightarrow	-			-0.22	[-1.50;	1.07]		100.0%
Heterogeneity: $I^2 = 57\%$, τ^2	² = 1.53	8, p = 0	.03				L.	1							•	-		
		10.01					-6	-4	-2	0	2	4	6					

Swiss Medical Weekly · PDF of the online version · www.smw.ch

postoperatively with similar results, favouring the RYGB group (MD –5.97 mg/dl, 95% CI –9.32 to –2.61; p <0.001; fig. 7c). The only study (Lee et al. [11]) reporting values on fasting blood glucose at 52 months in patients with diabetes clearly showed results favouring the RYGB group (MD –15.20 mg/dl, 95% CI –27.35 to –3.05; p = 0.010). Fasting insulin values at baseline were reported only by Schauer et al. [12] and there were significantly higher levels in the SG group (MD 4.80 μ U/ml, 95% CI 4.05to5.55; p <0.001). The only study reporting fasting insulin values 3 months postoperatively was that of Peterli et al. [16],

which showed significantly lower levels in the RYGB group (MD –9.31 μ U/ml, 95% CI –13.63 to –4.99; p <0.001). At 12 months, fasting insulin levels were no longer different between the RYGB and the SG groups (fig. S6e). The only study reporting results on fasting insulin at 52 months was the one from Lee et al [11], which also showed no significant difference between the two groups (MD –0.50 μ U/ml, 95% CI –1.37 to 0.37; p = 0.260).

Baseline data on HbA1c were reported by four studies. There was no significant difference between the two

	Exp	oerime	ntal		Con	trol				Weight	Weigh
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random
Lee 2011	16	23.0	2.7	16	24.4	2.7		-1.40	[-3.27; 0.47]	46.0%	46.0%
Kashyap 2013	18	27.4	2.9	19	28.2	3.1		-0.80	[-2.73; 1.13]	43.1%	43.1%
Peterli 2009*	28	32.5	5.1	26	30.9	8.7		- 1.60	[-2.24; 5.44]	10.9%	10.9%
Fixed effect model	62			61				-0.81	[-2.08; 0.45]	100.0%	-
Random effects model							\sim	-0.81	[-2.08: 0.45]		100.0%

Figure 7a: Fasting blood glucose at 12 months diabetic only (analysis of studies including only patients with type 2 diabetes).

Study	Exp Total	erimental Mean SD	Total	Control Mean SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Peterli 2009*	28	30.8 4.7	26	32.9 5.4		-2.10	[-4.81; 0.61]	9.7%	12.4%
Lee (Arch Surg) 2011	30	22.8 2.2	30	24.4 2.4		-1.60	[-2.77; -0.43]	52.3%	45.0%
Kashyap 2013	18	26.7 2.5	19	27.6 2.5		-0.90	[-2.51; 0.71]	27.3%	29.1%
Keidar 2013	19	31.4 4.2	18	30.4 3.8		1.00	[-1.58; 3.58]	10.7%	13.5%
Fixed effect model	95		93			-1.18	[-2.02; -0.34]	100.0%	
Random effects mode Heterogeneity: $l^2 = 21\%$,	$\tau^2 = 0.23$	56, p = 0.28	1			-1.11	[-2.12; -0.10]		100.0%
5 K		8			-4 -2 0 2 4				

Figure 7b: Fasting blood glucose at 24 months (analysis of studies including only patients with type 2 diabetes).

Study	E Total	xperin Mean	nental SD	Total	C Mean	ontrol SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Lee (Arch Sura) 2011	30	99.3	19 40	30	140 10	53.00	i :	-40 80	[-61 00: -20 60]	11.9%	27.6%
Peterli 2009*	28	91.9	16.21	26	99.11	30.63		-7.21	[-20.43: 6.01]	27.7%	34.3%
Kashyap 2013	18	93.0	13.75	19	97.00	14.00		-4.00	[-12.94; 4.94]	60.5%	38.1%
Fixed effect model	76			75				-9.25	[-16.21; -2.30]	100.0%	
Heterogeneity: $I^2 = 81\%$, τ^2	² = 203	.5, p < 0	0.01					-15.26	[-33.37; 2.86]		100.0%
						-	60 -40 -20 0 20 40	60			

Figure 7c: Fasting blood glucose at 36 months (analysis of studies including only patients with type 2 diabetes).

	Ex	perim	ental		C	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Kashyap 2013 Lee (Surg Obes Relat Dis) 2011	18 16	87.0 106.3	7.5 19.2	19 16	104.0 122.7	8.25 19.40 -	+	-17.00 -16.40	[-22.08; -11.92] [-29.77; -3.03]	87.4% 12.6%	87.4% 12.6%
Fixed effect model Random effects model Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p = 0$	34).93			35				-16.92 -16.92	[-21.67; -12.18] [-21.67; -12.18]	100.0% 	 100.0%

Swiss Medical Weekly · PDF of the online version · www.smw.ch

groups (fig. S6f), although with high heterogeneity ($I^2 =$ 88%). Excluding the data of Peterli et al. 2009 [16] had no effect on the mean difference (-0.21 µU/ml, 95% CI -0.67 to 0.24) but without heterogeneity ($I^2 = 0\%$). We suspect a data reporting error (HbA1c at baseline for the SG group). HbA1c values at 12 months were reported by four studies and there was a significant difference in favour of the RYGB group. (MD -0.46 µU/ml, 95% CI -0.73 to -0.20; p < 0.001; fig. 7d). Only one RCT (Lee et al. [10] with available data for mean and SD) reported HbA1c values at 24 months, and that showed a clear difference favouring the RYGB group (MD –1.50 $\mu U/ml,~95\%$ CI –2.14 to -0.86; p <0.001). At 36 months, another study from Lee et al. [11] showed no significant difference between the two groups (MD –0.30 $\mu U/ml,\,95\%$ CI –0.82 to 0.22; p = 0.260). However, the same RCT [11] showed clearly significant differences favouring the RYGB group at 52 months of follow up (MD $-1.00~\mu\text{U/ml},\,95\%$ CI -1.50 to -0.50; p <0.001).

Baseline data on the HOMA index were reported by two studies and there was a significant difference between the two groups favouring the SG group due to the data of Schauer et al. [12] (fig. S6g). The two studies reporting the HOMA index at 12 months favoured the SG group (MD 0.09, 95% CI 0.01to0.18; p = 0.030) and this was again clearly due to the inclusion of the Schauer et al. data [12] (fig. S6h), as by excluding it from the analysis, the results were completely opposite, favouring the RYGB group [4] (MD -1.30 (-2.59 to -0.01; p = 0.050).

Lipid metabolism

Three studies reported data on low-density lipoproteins at baseline and showed consistent differences between the two groups (MD -10.41 mg/dl, 95% CI -20.77 to -0.06; p = 0.050; fig. S6i in appendix 2) without any heterogeneity, and favouring the RYGB group. Data available on low-density lipoproteins at 12 months from two studies showed significant differences also favouring this group (MD -23.85 mg/dl, 95% CI -33.23 to -14.48; p < 0.001; fig. S6j). Two studies reported low-density lipoproteins at 36 months, with no significant difference between the two groups (fig. S6k). The only study reporting long-term results on low-density lipoproteins, at 60 months postoperatively, was that of Lee et al. [11], which clearly favoured the RYGB group (MD -30.60 mg/dl, 95% CI -48.84 to -12.36; p = 0.001).

Three studies reported levels of high-density lipoprotein at baseline and there were no significant differences between the two groups (fig. S6l). Two studies reported high-density lipoprotein at 12 months and there was a significant difference favouring the SG group (MD 3.56 mg/dl, 95%)

CI 0.22 to 6.90; p = 0.039; fig. S6m) with low heterogeneity (I² = 21%). Excluding Lee et al. [11] from the analysis shifted the mean difference to 0.55 mg/dl (95% CI –3.33 to 4.43 I² = 0%). High-density lipoprotein data at 36 months were available from two studies and there was no longer a significant difference between the two groups (fig. S6n). Similarly, the only RCT (Lee et al. [11]) reporting longterm results at 60 months postoperatively showed no significant results between the two groups (MD –1.10 mg/dl, 95% CI –4.64 to 2.44; p = 0.540).

Two studies reported cholesterol at baseline and there was no significant difference between the two groups. Two studies reported data on cholesterol levels at 12 months and there was a significant difference between the two groups favouring the RYGB group (MD -21.56 mg/dl. 95% CI -33.98 to -9.14; p <0.001; fig. S6o). One study, from Kashyap et al. [14] and reporting data at 36 months postoperatively, showed significant results favouring the RYGB group (MD -23.20 mg/dl, 95% CI -42.29 to -4.11; p = 0.020). Similarly, the only study (Lee et al. [11]) reporting long term results on cholesterol, at 60 months postoperatively, showed a significant difference favouring the RYGB group (MD -43.30 mg/dl, 95% CI -61.10 to -25.50; p <0.001).

Two studies reported triglyceride levels at baseline, showing a significant difference favouring the SG group (MD 18.09 mg/dl, 95% CI 10.57to25.61; p < 0.001; fig. S6p), again due to the inclusion of the data from Schauer et al. [13]. Despite the initial differences, the results at 12 months were completely opposite, favouring the RYGB group (MD –6.43 mg/dl, 95% CI –9.89 to –2.96; p < 0.001; fig. S6q). The only RCT reporting long-term results at 52 months postoperatively was that of Lee et al. [11], which showed a clear difference in favour of the RYGB group (MD –36.60 mg/dl, 95% CI –48.46 to –24.74; p < 0.001).

Body mass index

BMI at baseline was reported in four studies including only patients with T2DM (fig. S6a in appendix 2). There was no significant difference between the two groups at baseline. Four studies reported BMI after 12 months (fig. 7e) and there was a significant difference favouring RYGB group (MD –1.18 kg/m², 95% CI –2.02 to –0.34; p = 0.006). At 24 months there were three studies reporting the BMI (fig. S6b) with only a trend favouring the RYGB group. The only RCT in diabetic patients reporting BMI at 52 months was that of Lee et al. [11], which clearly favoured the RYGB group (MD –1.80 kg/m², 95% CI –2.92 to –0.68; p = 0.002).

Figure 7d: Glycated haemoglobin (HbA1c) at 12 months (analysis of studies including only patients with type 2 diabetes).



Swiss Medical Weekly · PDF of the online version · www.smw.ch

Discussion

The most commonly performed procedures for bariatric surgery are laparoscopic sleeve gastrectomy (SG) and roux-en-Y gastric bypass (RYGB). SG nowadays represents the most commonly performed bariatric operation worldwide, and both procedures together account for nearly 80% of all bariatric operations performed worldwide [2]. Despite a vast amount of literature, there are only three meta-analyses [23-25] comparing outcome parameters, including glycaemic control, T2DM, triglycerides and cholesterol, for these two procedures. However, all three studies included not only randomised controlled trials (RCTs), but also prospective and retrospective cohort studies. In this meta-analysis we included and analysed only RCTs, and report data derived from 16 RCTs comparing effects of RYGB with SG on metabolic outcomes such as fasting blood glucose, HbA1c levels, insulin resistance measured with the HOMA index, and low- and high-density lipoprotein, triglyceride and cholesterol levels.

Two analyses were performed, one including overweight and obese patients with or without T2DM, and a second including only patients with T2DM. For weight loss adjusted by the BMI, the latter analysis revealed a superiority of RYGB over SG at 12, 24 and 52 months for patients with T2DM. At 6 months, analysis revealed a superiority of RYGB over SG for weight loss in patients with and without T2DM. The former analysis further showed a similar BMI at 3 months for both groups. Interestingly, there was a lower BMI in the SG group 6 six months postoperatively, whereas patients in the RYGB group were found to have a lower BMI at 12 months, but the differences were not significant. As only one RCT reported BMI data at 52 months after surgery, a meta-analysis to compare long-term BMI changes could not be performed. However, a recent metaanalysis focusing on long-term weight loss revealed no difference between RYGB and SG [23].

In accordance with previous meta-analyses, RYGB was found to be superior in terms of fasting blood glucose at 24, 36 and 52 months postoperatively [23]. These results were obtained in both analyses. Only at 12 months was there no difference when patients with and without T2DM were analysed together. However, for diabetic patients only, RYGB was found to be superior in terms of fasting blood glucose at 12 months. Further, favourable HBA1c levels at 12 months were found in the RYGB group, and there was no difference in baseline HbA1c in both analyses, which is also concordant with previous reports [24]. However, there was no difference in HbA1c levels between the two groups 36 months postoperatively with only trends favouring the RYGB group.

Interestingly, there were significant differences in the baseline data for the HOMA index, fasting blood glucose, fasting insulin and triglycerides, which favoured the SG group; this difference was eliminated when one RCT was excluded from the analysis. This study evaluated the efficacy of intensive medical therapy alone versus medical therapy plus RYGB or SG and was not powered to detect differences between the two surgical procedures [12]. Given the randomised study design, it remains surprising that the HOMA index differed at baseline between the two groups in this study. This particular RCT did not report data on the HOMA index at early postoperative time points. However, in our analysis it was found that there was no difference in the HOMA index at 1 week postoperatively, whereas the RYGB group showed a significantly better HOMA index at 3 months postoperatively. In contrast, the SG group showed favourable HOMA indices at 12 months after the surgery when compared with the RYGB group in both types of analysis.

The present meta-analysis failed to detect a clear superiority of one procedure over the other in terms of the HOMA index, but other authors also did not find differences between RYGB and SG in the correction of insulin resistance [26]. In contrast, a recently published meta-analysis reported a significantly lower HOMA index after RYGB when compared with SG, but the analysis was based on the studies of Woelnerhanssen et al. 2011 [7] and Lee et al. 2011 [10], without including the study of Schauer et al. [12].

The effects of RYGB and SG on dyslipidaemia were also analysed. Here, a significant superiority of RYGB, with lower low-density lipoprotein levels 12 months after surgery, was found in both types of analysis. Differences were absent at 36 months after the surgery, which is in accordance with previous reports [27].

In contrast, baseline high-density lipoprotein levels significantly differed between the two groups, with higher levels in the SG group. Such baseline differences may indicate of problems in the randomisation process in the included studies. Alternatively, they may suggest presence of patient selection bias, as patients with a higher cardiovascular and thus surgical risk may be more likely to receive a SG, which many consider as a less invasive and potentially safer operation than RYGB. Differences between the groups were still detected at 12 months postoperatively, both groups showed similar high-density lipoprotein levels at 36 months after surgery. This was true both for both types of analysis.

Figure 7e: Body mass index (BMI) at 12 months (analysis of studies including only patients with type 2 diabetes).

Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
							20			8	
Lee (Arch Surg) 2011	30	5.70	0.50	30	7.20	1.50		-1.50	[-2.07; -0.93]	22.2%	24.7%
Kashyap 2013	18	6.30	0.78	19	6.90	1.11		-0.60	[-1.22; 0.02]	18.8%	24.0%
Peterli 2009*	28	5.80	0.80	26	6.10	1.00		-0.30	[-0.79; 0.19]	30.2%	25.7%
Keidar 2013	19	6.22	0.50	18	5.97	0.96		0.25	[-0.25; 0.75]	28.8%	25.6%
Fixed effect model	95			93			\diamond	-0.46	[-0.73; -0.20]	100.0%	
Random effects model								-0.53	[-1.25; 0.19]		100.0%
Heterogeneity: $I^2 = 86\%$, τ^2	2 = 0.46	05. p <	0.01				1 1 1		•		

Swiss Medical Weekly · PDF of the online version · www.smw.ch

In contrast to the high-density lipoprotein levels, cholesterol levels at baseline were similar between the two groups. Further, there was a significant trend towards superiority of the RYGB group at 12 months postoperatively if patients with and without T2DM were included in the analysis. If RCTs that only included patients with T2DM were analysed, the differences became significant, indicating superiority of the RYGB group.

Although there was a significant difference in triglyceride levels at baseline between the two groups, the analysis revealed a superiority of the RYGB group at 12 months after surgery when compared with the SG group in both types of analysis.

In summary, the data obtained from this meta-analysis indicate a superiority of RYGB over SG in short-, mid- and, in some instances, long-term metabolic outcome. However, most of the early differences were not analysed in the long term. Only BMI was reported at 52 months [11]. The underlying physiological mechanisms that could potentially explain the observed differences in metabolic efficacy of the two procedures remain unclear and are the object of intensive research efforts worldwide. They may be related to early, weight-loss independent differences in gastrointestinal hormone levels, gut microbiota or bile acid metabolism [28] [29]. In the longer term, however, the most important mechanism might be weight loss, which was favoured by RYGB.

Limitations

Every meta-analysis heavily relies on the quality of the included studies. Here, one important limitation is the shortness follow-up in the included studies, with only a few [11, 13, 16] reporting 36-, 52- and 60-month follow-up data, which questions the durability of the observed differences. Further, differences in baseline data for key metabolic parameters might be indicative of a problematic randomisation process in some, but not all RCTs included in this meta-analysis, and not for all parameters. Unfortunately not all studies reported baseline-data and therefore we were unable to investigate this problem by calculating differences between baseline and follow-up in each arm. Moreover and unfortunately for general practitioners, we are unable to present absolute values because results in the included studies were not paired and no paired t-test statistics for mean differences were reported. Blinding of participants and personnel as well as blinding of outcome assessment were the major areas for risk of bias of the included RCTs. Overall, in our bias assessment the risk level in most areas remained unclear. Moreover, it remains unclear whether the observed superiority of RYGB over SG in improving glucose homeostasis translates into a reduced incidence of end-organ complications such as diabetic retinopathy, nephropathy and neuropathy. Similarly, our meta-analysis does not answer the question of whether the advantages of the RYGB in ameliorating dyslipidaemia translates into a mortality benefit over SG. Further clarification will require larger trials with longer follow-up.

Conclusion

This systematic review suggests that RYGB is more effective in short-, mid- to long-term metabolic outcome when compared with SG. Changes in body weight, lipid levels, and glucose homeostasis after RYGB were superior to those reported after SG. The superiority of RYGB over SG on hard clinical end-points, such as myocardial infarction, stroke, renal failure, blindness and death, as suggested in nonrandomised trials, can only be adequately assessed through larger, multicentre trials addressing these specific questions. Of note, data must be interpreted with caution as the follow-up period of most included RCT may be too short to justify long term conclusions. However, based on the currently available reported data, and contrary to the global trend, the authors prefer RYGB, unless contraindicated, over SG to treat patients with obesity and T2DM and/or dyslipidaemia.

Acknowledgments

We are very grateful to Dr Martina Gostelli for performing the literature search at the main library of the University of Zurich.

Disclosure statement

No financial support and no other potential conflict of interest relevant to this article was reported.

References

- Colquitt J, Clegg A, Sidhu M, Royle P. Surgery for morbid obesity. Cochrane Database Syst Rev. 2003;(2):CD003641. PubMed.
- 2 Angrisani L, Santonicola A, Iovino P, Formisano G, Buchwald H, Scopinaro N. Bariatric Surgery Worldwide 2013. Obes Surg. 2015;25(10):1822–32. doi: http://dx.doi.org/10.1007/ s11695-015-1657-z. PubMed.
- 3 Mingrone G, Panunzi S, De Gaetano A, Guidone C, Iaconelli A, Nanni G, et al. Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial. Lancet. 2015;386(9997):964–73. doi: http://dx.doi.org/10.1016/S0140-6736(15)00075-6. PubMed.
- 4 Lee WJ, Chong K, Ser KH, Lee YC, Chen SC, Chen JC, et al. Gastric bypass vs sleeve gastrectomy for type 2 diabetes mellitus: a randomized controlled trial. Arch Surg. 2011;146(2):143–8. doi: http://dx.doi.org/ 10.1001/archsurg.2010.326. PubMed.
- 5 Hozo SP, Djulbegovic B, Hozo I. Estimating the mean and variance from the median, range, and the size of a sample. BMC Med Res Methodol. 2005;5(1):13. doi: http://dx.doi.org/10.1186/1471-2288-5-13. PubMed.
- 6 Raptis DA, Mettler T, Fischer MA, Patak M, Lesurtel M, Eshmuminov D, et al. Managing multicentre clinical trials with open source. Inform Health Soc Care. 2014;39(2):67–80. doi: http://dx.doi.org/10.3109/17538157.2013.812647. PubMed.
- 7 Woelnerhanssen B, Peterli R, Steinert RE, Peters T, Borbély Y, Beglinger C. Effects of postbariatric surgery weight loss on adipokines and metabolic parameters: comparison of laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy--a prospective randomized trial. Surg Obes Relat Dis. 2011;7(5):561–8. doi: http://dx.doi.org/ 10.1016/j.soard.2011.01.044. PubMed.
- 8 Peterli R, Steinert RE, Woelnerhanssen B, Peters T, Christoffel-Courtin C, Gass M, et al. Metabolic and hormonal changes after laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy: a randomized, prospective trial. Obes Surg. 2012;22(5):740–8. doi: http://dx.doi.org/ 10.1007/s11695-012-0622-3. PubMed.
- 9 Peterli R, Borbély Y, Kern B, Gass M, Peters T, Thurnheer M, et al. Early results of the Swiss Multicentre Bypass or Sleeve Study (SM-BOSS): a prospective randomized trial comparing laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass. Ann Surg. 2013;258(5):690–4, discussion 695. doi: http://dx.doi.org/10.1097/ SLA.0b013e3182a67426. PubMed.
- 10 Lee WJ, Chen CY, Chong K, Lee YC, Chen SC, Lee SD. Changes in postprandial gut hormones after metabolic surgery: a comparison of gastric bypass and sleeve gastrectomy. Surg Obes Relat Dis. 2011;7(6):683–90. doi: http://dx.doi.org/10.1016/j.soard.2011.07.009. PubMed.
- 11 Lee WJ, Chong K, Lin YH, Wei JH, Chen SC. Laparoscopic sleeve gastrectomy versus single anastomosis (mini-) gastric bypass for the treatment of type 2 diabetes mellitus: 5-year results of a randomized trial and study of incretin effect. Obes Surg. 2014;24(9):1552–62. doi: http://dx.doi.org/10.1007/s11695-014-1344-5. PubMed.

Swiss Medical Weekly · PDF of the online version · www.smw.ch

- 12 Schauer PR, Kashyap SR, Wolski K, Brethauer SA, Kirwan JP, Pothier CE, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med. 2012;366(17):1567–76. doi: http://dx.doi.org/10.1056/NEJMoa1200225. PubMed.
- 13 Schauer PR, Bhatt DL, Kirwan JP, Wolski K, Brethauer SA, Navaneethan SD, et al.; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes--3-year outcomes. N Engl J Med. 2014;370(21):2002–13. doi: http://dx.doi.org/10.1056/NEJ-Moa1401329. PubMed.
- 14 Kashyap SR, Bhatt DL, Wolski K, Watanabe RM, Abdul-Ghani M, Abood B, et al. Metabolic effects of bariatric surgery in patients with moderate obesity and type 2 diabetes: analysis of a randomized control trial comparing surgery with intensive medical treatment. Diabetes Care. 2013;36(8):2175–82. doi: http://dx.doi.org/10.2337/dc12-1596. PubMed.
- 15 Karamanakos SN, Vagenas K, Kalfarentzos F, Alexandrides TK. Weight loss, appetite suppression, and changes in fasting and postprandial ghrelin and peptide-YY levels after Roux-en-Y gastric bypass and sleeve gastrectomy: a prospective, double blind study. Ann Surg. 2008;247(3):401–7. doi: http://dx.doi.org/10.1097/ SLA.0b013e318156f012. PubMed.
- 16 Peterli R, Wölnerhanssen B, Peters T, Devaux N, Kern B, Christoffel-Courtin C, et al. Improvement in glucose metabolism after bariatric surgery: comparison of laparoscopic Roux-en-Y gastric bypass and laparoscopic sleeve gastrectomy: a prospective randomized trial. Ann Surg. 2009;250(2):234–41. doi: http://dx.doi.org/10.1097/ SLA.0b013e3181ae32e3. PubMed.
- 17 Kehagias I, Karamanakos SN, Argentou M, Kalfarentzos F. Randomized clinical trial of laparoscopic Roux-en-Y gastric bypass versus laparoscopic sleeve gastrectomy for the management of patients with BMI < 50 kg/m2. Obes Surg. 2011;21(11):1650–6. doi: http://dx.doi.org/ 10.1007/s11695-011-0479-x. PubMed.
- 18 Paluszkiewicz R, Kalinowski P, Wróblewski T, Bartoszewicz Z, Białobrzeska-Paluszkiewicz J, Ziarkiewicz-Wróblewska B, et al. Prospective randomized clinical trial of laparoscopic sleeve gastrectomy versus open Roux-en-Y gastric bypass for the management of patients with morbid obesity. Wideochir Inne Tech Malo Inwazyjne. 2012;7(4):225–32. doi: http://dx.doi.org/10.5114/wiitm.2012.32384. PubMed.
- 19 Ramón JM, Salvans S, Crous X, Puig S, Goday A, Benaiges D, et al. Effect of Roux-en-Y gastric bypass vs sleeve gastrectomy on glucose and gut hormones: a prospective randomised trial. J Gastrointest Surg. 2012;16(6):1116–22. doi: http://dx.doi.org/10.1007/s11605-012-1855-0. PubMed.
- 20 Keidar A, Hershkop KJ, Marko L, Schweiger C, Hecht L, Bartov N, et al. Roux-en-Y gastric bypass vs sleeve gastrectomy for obese patients with type 2 diabetes: a randomised trial. Diabetologia. 2013;56(9):1914–8. doi: http://dx.doi.org/10.1007/s00125-013-2965-2. PubMed.

- 21 Helmiö M, Victorzon M, Ovaska J, Leivonen M, Juuti A, Peromaa-Haavisto P, et al. Comparison of short-term outcome of laparoscopic sleeve gastrectomy and gastric bypass in the treatment of morbid obesity: A prospective randomized controlled multicenter SLEEVEPASS study with 6-month follow-up. Scand J Surg. 2014;103(3):175–81. doi: http://dx.doi.org/10.1177/1457496913509984. PubMed.
- 22 Higgins JP, Altman DG, Gøtzsche PC, Jüni P, Moher D, Oxman AD, et al.; Cochrane Bias Methods Group; Cochrane Statistical Methods Group. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343(oct18 2):d5928. doi: http://dx.doi.org/ 10.1136/bmj.d5928. PubMed.
- 23 Li JF, Lai DD, Lin ZH, Jiang TY, Zhang AM, Dai JF. Comparison of the long-term results of Roux-en-Y gastric bypass and sleeve gastrectomy for morbid obesity: a systematic review and meta-analysis of randomized and nonrandomized trials. Surg Laparosc Endosc Percutan Tech. 2014;24(1):1–11. doi: http://dx.doi.org/10.1097/ SLE.0000000000000041. PubMed.
- 24 Yip S, Plank LD, Murphy R. Gastric bypass and sleeve gastrectomy for type 2 diabetes: a systematic review and meta-analysis of outcomes. Obes Surg. 2013;23(12):1994–2003. doi: http://dx.doi.org/10.1007/ s11695-013-1030-z. PubMed.
- 25 Li JF, Lai DD, Ni B, Sun KX. Comparison of laparoscopic Roux-en-Y gastric bypass with laparoscopic sleeve gastrectomy for morbid obesity or type 2 diabetes mellitus: a meta-analysis of randomized controlled trials. Can J Surg. 2013;56(6):E158–64. doi: http://dx.doi.org/10.1503/ cjs.026912. PubMed.
- 26 Benaiges D, Flores Le-Roux JA, Pedro-Botet J, Chillarón JJ, Renard M, Parri A, et al. Sleeve gastrectomy and Roux-en-Y gastric bypass are equally effective in correcting insulin resistance. Int J Surg. 2013;11(4):309–13. doi: http://dx.doi.org/10.1016/j.ijsu.2013.02.007. PubMed.
- 27 Milone M, Lupoli R, Maietta P, Di Minno A, Bianco P, Ambrosino P, et al. Lipid profile changes in patients undergoing bariatric surgery: a comparative study between sleeve gastrectomy and mini-gastric bypass. Int J Surg. 2015;14:28–32. doi: http://dx.doi.org/10.1016/j.ijsu.2014.12.025. PubMed.
- 28 Lutz TA, Bueter M. The physiology underlying Roux-en-Y gastric bypass: a status report. Am J Physiol Regul Integr Comp Physiol. 2014;307(11):R1275–91. doi: http://dx.doi.org/10.1152/ ajpregu.00185.2014. PubMed.
- 29 le Roux CW, Aylwin SJ, Batterham RL, Borg CM, Coyle F, Prasad V, et al. Gut hormone profiles following bariatric surgery favor an anorectic state, facilitate weight loss, and improve metabolic parameters. Ann Surg. 2006;243(1):108–14. doi: http://dx.doi.org/10.1097/ 01.sla.0000183349.16877.84. PubMed.

Appendix 1

Example search strategy (Medline)

This appendix is available as a separate file for downloading at https://smw.ch/en/article/doi/smw.2018.14633/.

Appendix 2

Supplementary figures



Figure S1b: Bias assessment II.



Figure S2a: Low-density lipoprotein at baseline.

		Experin	nental		C	ontrol								Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mear	n differ	ence		MD	95%-CI	(fixed)	(random)
Karamanakos 2008	16	134.00	34.00	16	111.00	23.00				- 21		23.00	[2.89; 43.11]	18.8%	20.6%
Woelnerhanssen 2011	12	123.70	26.80	11	123.70	38.50		-	-			0.00	[-27.34; 27.34]	10.2%	14.9%
Lee 2014	30	137.30	37.80	30	142.90	44.60			B			-5.60	[-26.52; 15.32]	17.4%	19.9%
Schauer 2014	48	92.40	29.00	49	105.80	39.50						-13.40	[-27.17; 0.37]	40.1%	27.2%
Peterli 2009*	28	115.98	42.52	26	115.98	46.39			1			0.00	[-23.79; 23.79]	13.5%	17.4%
Fixed effect model	134			132				-	4			-2.03	[-10.75; 6.70]	100.0%	
Random effects model								-	\Leftrightarrow	>		-0.02	[-13.55; 13.51]		100.0%
Heterogeneity: $I^2 = 54\%$, τ^2	2 = 125.	9, p = 0.	07					1	ſ	1	1				
						1	-40	-20	0	20	40				

Figure S2b: Low-density lipoprotein at 12 months.

Study	Experimental Total Mean SD	Control Total Mean SD	Mean difference	MD 95%-0	Weight Weight Cl (fixed) (random)
Karamanakos 2008 Woelnerhanssen 2011 Lee (Arch Surg) 2011 Schauer 2012	16 111.0 26.0 12 100.5 26.8 30 96.9 21.5 50 93.7 27.1	16 108.0 23.0 11 119.9 38.5 30 136.6 40.8 50 110.0 30.9		3.00 [-14.01; 20.0 ⁻ -19.40 [-46.74; 7.94 -39.70 [-56.20; -23.20 -16.30 [-27.69; -4.9 ⁻	1] 21.4% 25.7% 4] 8.3% 18.5% 0] 22.7% 26.1% 1] 47.6% 29.7%
Fixed effect model Random effects model Heterogeneity: $I^2 = 76\%$, τ	108 ² = 230.8, <i>p</i> < 0.01	107	-40 -20 0 20 40	-17.74 [-25.61; -9.88 -18.01 [-35.40; -0.63	3] 100.0% 3] 100.0%

Figure S2c: Low-density lipoprotein at 36 months.

Study	Total	Experin Mean	nental SD	Total	Co Mean	ontrol SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Schauer 2014 Peterli 2009*	48 28	96.300 112.114	27.20 38.66	49 26	108.100 112.114	35.20 38.66		-11.80 0.00	[-24.30; 0.70] [-20.64; 20.64]	73.1% 26.9%	73.1% 26.9%
Fixed effect model Random effects model Heterogeneity: $l^2 = 0\%$, τ^2	76 = 0, p =	0.34		75			-20 -10 0 10 20	-8.63 -8.63	[-19.33; 2.06] [-19.33; 2.06]	100.0% 	 100.0%

Figure S3a: High-density lipoprotein at baseline.

		Experi	mental		(Control									Weight	Weight	
Study	Total	Mean	SD	Total	Mean	SD		Mear	n differe	nce		MD	9	5%-CI	(fixed)	(random)	
Peterli 2009*	28	38.66	11.598	26	38.66	11.598			+ +			0.00	[-6.19;	6.19]	16.0%	16.0%	
Woelnerhanssen 2011	12	30.90	13.400	11	30.90	12.800			-+ i			0.00	[-10.71;	10.71]	5.3%	5.3%	
Schauer 2014	48	45.40	13.000	49	44.50	12.000		-	-	<u> </u>		0.90	[-4.08;	5.88]	24.7%	24.7%	
Karamanakos 2008	16	46.50	9.000	16	43.00	8.000		2				3.50	[-2.40;	9.40]	17.6%	17.6%	
Lee 2014	30	47.90	9.600	30	42.80	6.300					-	5.10	[0.99;	9.21]	36.3%	36.3%	
Fixed effect model	134			132						>		2.69	[0.22;	5.17]	100.0%		
Random effects model									\langle	\geq		2.69	0.22;	5.17]		100.0%	
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	0.58											-	-			
- ,							-10	-5	0	5	10						

Swiss Medical Weekly \cdot PDF of the online version \cdot www.smw.ch

Figure S3b: High-density lipoprotein at 12 months.

	Ex	perim	ental		Co	ntrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Karamanakos 2008	16	51.0	10.0	16	53.0	12.0		-2.00	[-9.65; 5.65]	14.8%	14.8%
Woelnerhanssen 2011	12	46.4	13.4	11	42.5	12.8		- 3.90	[-6.81; 14.61]	7.6%	7.6%
Lee (Arch Surg) 2011	30	49.3	7.7	30	45.4	7.9		3.90	[-0.05; 7.85]	55.6%	55.6%
Schauer 2012	50	58.8	18.0	50	56.1	13.7		2.70	[-3.57; 8.97]	22.0%	22.0%
Fixed effect model	108			107				2.76	[-0.18; 5.71]	100.0%	
Random effects model							-	2.76	[-0.18; 5.71]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	0.60									
							-10 -5 0 5 10				

Figure S3c: High-density lipoprotein at 36 months.

Study	E Total	xperin Mean	nental SD	Total	Co Mean	ontrol SD	Ме	an d	iffer	ence		MD	95%-CI	Weight (fixed)	Weight (random)
Schauer 2014	48	60.00	19.10	49	59.20	17.20			+		-	0.80	[-6.44; 8.04]	67.0%	67.0%
Peterli 2009*	28	54.12	19.33	26	57.99	19.33 -		10	F	- 11		-3.87	[-14.19; 6.45]	33.0%	33.0%
Fixed effect model	76			75			_			_		-0.74	[-6.67; 5.19]	100.0%	
Random effects model								-	-	-		-0.74	[-6.67; 5.19]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, p =	= 0.47							1	I.					
							-10 -	5	0	5	10				

Figure S4a: Cholesterol at baseline.

Study	Experimenta Total Mean SE	Control Total Mean SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Lee 2014	30 200.90 76.60	30 230.60 85.30		-29.70	[-70.72: 11.32]	10.8%	14.8%
Woelnerhanssen 2011	12 177.90 40.20	11 185.60 51.30		-7.70	[-45.60; 30.20]	12.7%	16.4%
Peterli 2009	13 185.57 34.79	14 208.76 50.26		-23.19	[-55.61; 9.23]	17.4%	19.5%
Kashyap 2013	18 175.10 50.80	19 166.00 35.80		9.10	[-19.36; 37.56]	22.5%	22.2%
Karamanakos 2008	16 198.00 36.00	16 177.00 28.00		21.00	[-1.35; 43.35]	36.5%	27.1%
Fixed effect model	89	90		1.50	[-12.01; 15.01]	100.0%	
Random effects model Heterogeneity: $I^2 = 49\%$, τ	l ² = 243.1, p = 0.10			-2.49	[-22.18; 17.20]		100.0%
	2		-60 -40 -20 0 20 40 60				

Figure S4b: Cholesterol at 12 months.

Ex	perime	ental	Total	Co	ntrol	Maan differense	MD	05% 01	Weight	Weight
TOTAL	wean	50	Total	mean	50	mean difference	WD	95%-01	(lixed)	(random)
16	179.0	35.0	16	176.0	31.0	÷	3.00	[-19.91; 25.91]	20.6%	25.6%
30	162.2	26.6	30	207.8	67.0		-45.60	[-71.40; -19.80]	16.2%	23.2%
12	166.3	26.8	11	185.6	51.3		-19.30	[-53.20; 14.60]	9.4%	17.5%
50	173.6	35.3	50	187.9	37.0		-14.30	[-28.47; -0.13]	53.8%	33.7%
108			107				-16.29	[-26.69; -5.90]	100.0%	
							-18.00	[-36.53; 0.54]		100.0%
= 212.	7, p = 0	.05								
						-60 -40 -20 0 20 40 60				
	Ex Total 16 30 12 50 108 = 212.	Experime Total Mean 16 179.0 30 162.2 12 166.3 50 173.6 108 = 212.7, p = 0	Experimental Total Mean SD 16 179.0 35.0 30 162.2 26.6 12 166.3 26.8 50 173.6 35.3 108 = 212.7, p = 0.05	Experimental Total Mean SD Total 16 179.0 35.0 16 30 162.2 26.6 30 12 166.3 26.8 11 50 173.6 35.3 50 108 107 = 212.7, p = 0.05 105	Experimental Total Mean SD Control Mean 16 179.0 35.0 16 176.0 30 162.2 26.6 30 207.8 12 166.3 26.8 11 185.6 50 173.6 35.3 50 187.9 108 107	Experimental Total Mean Control SD Control Total Mean Control SD 16 179.0 35.0 16 176.0 31.0 30 162.2 26.6 30 207.8 67.0 12 166.3 26.8 11 185.6 51.3 50 173.6 35.3 50 187.9 37.0 108 107 = 212.7, p = 0.05 50 187.9 10.0	Experimental Control Total Mean SD 16 179.0 35.0 16 176.0 31.0 30 162.2 26.6 30 207.8 67.0 12 166.3 26.8 11 185.6 51.3 50 173.6 35.3 50 187.9 37.0 108 107	Experimental Total Mean SD Control Total Mean SD Mean difference MD 16 179.0 35.0 16 176.0 31.0 -45.60 12 166.3 26.8 11 185.6 51.3 -19.30 50 173.6 35.3 50 187.9 37.0 -14.30 108 107 -60 -40 -20 0 20 40 60	Experimental Total Mean Control SD Mean SD Mean SD Mean difference MD 95%-Cl 16 179.0 35.0 16 176.0 31.0 3.00 [-19.91; 25.91] 30 162.2 26.6 30 207.8 67.0 -45.60 [-71.40; -19.80] 12 166.3 26.8 11 185.6 51.3 -45.60 [-71.40; -19.80] 50 173.6 35.3 50 187.9 37.0 -44.30 [-28.47; -0.13] 108 107	Experimental Total Mean Control SD Mean SD Mean difference MD 95%-Cl Weight (fixed) 16 179.0 35.0 16 176.0 31.0 3.00 [-19.91; 25.91] 20.6% 30 162.2 26.6 30 207.8 67.0 -45.60 [-71.40; -19.80] 16.2% 12 166.3 26.8 11 185.6 51.3 -19.30 [-53.20; 14.60] 9.4% 50 173.6 35.3 50 187.9 37.0 -14.30 [-28.47; -0.13] 53.8% 108 107

Swiss Medical Weekly \cdot PDF of the online version \cdot www.smw.ch

Figure S5a: Triglycerides at baseline.

	Ex	perim	nental		C	ontrol				Weight	Weight
Study	Total I	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Lee 2014	30	195.2	128.3	30	262.2	158.8		-67.00	[-140.05: 6.05]	1.0%	13.2%
Woelnerhanssen 2011	12	141.6	30.7	11	194.7	146.8 -		-53.10	[-141.57: 35.37]	0.7%	10.0%
Peterli 2009	13	155.8	70.8	14	173.5	132.7		-17.70	[-97.15: 61.75]	0.9%	11.8%
Schauer 2014	48	179.0	22.1	49	160.0	15.2	<u>e</u>	19.00	[11.44; 26.56]	94.6%	41.5%
Karamanakos 2008	16	136.1	84.0	30	111.0	44.0		25.10	[-18.97; 69.17]	2.8%	23.5%
Fixed effect model	119			134			\$	17.48	[10.13; 24.84]	100.0%	
Random effects model								-2.48	[-34.50; 29.55]		100.0%
Heterogeneity: $I^2 = 54\%$, τ	² = 629.1	, p = 0	.07						•		
							-100 -50 0 50 100				



	Experimental	Control		Weight Weight
Study	Total Mean SD T	otal Mean SD	Mean difference	MD 95%-Cl (fixed) (random)
Lee 2014	30 195.2 128.3	30 262.2 158.8 -		-67.00 [-140.05: 6.05] 19.0% 23.5%
Woelnerhanssen 2011	12 141.6 30.7	11 194.7 146.8 -		-53.10 [-141.57; 35.37] 12.9% 18.7%
Peterli 2009	13 155.8 70.8	14 173.5 132.7		-17.70 [-97.15; 61.75] 16.0% 21.3%
Karamanakos 2008	16 136.1 84.0	30 111.0 44.0		25.10 [-18.97; 69.17] 52.1% 36.5%
Fixed effect model	71	85		-9.32 [-41.13; 22.48] 100.0%
Random effects model				-20.30 [-67.75; 27.15] 100.0%
Heterogeneity: $I^2 = 48\%$, τ	$c^2 = 1102, p = 0.13$			
			-100 -50 0 50 100	

Figure S5c: Triglycerides at 12 months.

	E	xperin	nental		С	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Lee 2014	30	195.2	128.3	30	262.2	158.8		-67.00	[-140.05; 6.05]	1.0%	13.2%
Woelnerhanssen 2011	12	141.6	30.7	11	194.7	146.8 -		-53.10	[-141.57; 35.37]	0.7%	10.0%
Peterli 2009	13	155.8	70.8	14	173.5	132.7		-17.70	[-97.15: 61.75]	0.9%	11.8%
Schauer 2014	48	179.0	22.1	49	160.0	15.2		19.00	[11.44: 26.56]	94.6%	41.5%
Karamanakos 2008	16	136.1	84.0	30	111.0	44.0		25.10	[-18.97; 69.17]	2.8%	23.5%
Fixed effect model	119			134			-	17.48	[10.13; 24.84]	100.0%	
Random effects model Heterogeneity: $l^2 = 54\%$, τ	² = 629.	1. p = (0.07					-2.48	[-34.50; 29.55]		100.0%
3,,,,,,		- F					-100 -50 0 50 100				

Figure S5d: Triglycerides at 12 months without Schauer et al. 2014 [13].

	E	Experin	nental		C	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Lee 2014	30	195.2	128.3	30	262.2	158.8		-67.00	[-140.05; 6.05]	19.0%	23.5%
Woelnerhanssen 2011	12	141.6	30.7	11	194.7	146.8 -		-53.10	[-141.57: 35.37]	12.9%	18.7%
Peterli 2009	13	155.8	70.8	14	173.5	132.7		-17.70	[-97.15: 61.75]	16.0%	21.3%
Karamanakos 2008	16	136.1	84.0	30	111.0	44.0		25.10	[-18.97; 69.17]	52.1%	36.5%
Fixed effect model	71			85				-9.32	[-41.13; 22.48]	100.0%	
Random effects model								-20.30	[-67.75; 27.15]		100.0%
Heterogeneity: $I^2 = 48\%$, τ	² = 1102	2, p = 0	.13								
							-100 -50 0 50 100				

Figure S6a: Body mass index (BMI) at baseline (analysis of studies including only patients with type 2 diabetes).

	Ex	perime	ental		Co	ntrol								Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mear	differ	ence		MD	95%-CI	(fixed)	(random)
Peterli 2009*	28	44.2	5.50	26	45.3	6.20	-					-1.10	[-4.24; 2.04]	7.9%	10.5%
Lee 2014	30	30.2	2.20	30	31.0	2.80		-				-0.80	[-2.07; 0.47]	47.9%	43.3%
Keidar 2013	19	42.0	4.80	18	42.5	5.20	-					-0.50	[-3.73; 2.73]	7.5%	9.9%
Schauer 2014	48	37.1	3.39	49	36.1	3.91			-			1.00	[-0.46; 2.46]	36.7%	36.4%
Fixed effect model	125			123				6	$ \rightarrow $			-0.14	[-1.02; 0.74]	100.0%	
Random effects mode	el							-	\Rightarrow			-0.15	[-1.21; 0.92]		100.0%
Heterogeneity: I ² = 21%,	$\tau^2 = 0.25$	82, p =	0.28							1			-		
							-4	-2	0	2	4				

Figure S6b: Body mass index (BMI) at 24 months (analysis of studies including only patients with type 2 diabetes).

Study	Exp Total	perimental Mean SD	Total	Contro Mean S	D	Mean diffe	erence		MD	95%-CI	Weight (fixed)	Weight (random)
Lee (Surg Obes Relat Dis) 2011	16	23.0 2.7	16	24.4 2	7 -				-1.40	[-3.27; 0.47]	46.0%	46.0%
Kashyap 2013	18	27.4 2.9	19	28.2 3	1	- 10	-		-0.80	[-2.73; 1.13]	43.1%	43.1%
Peterli 2009*	28	32.5 5.1	26	30.9 8	7		*		- 1.60	[-2.24; 5.44]	10.9%	10.9%
Fixed effect model	62		61			\rightarrow			-0.81	[-2.08; 0.45]	100.0%	
Random effects model									-0.81	[-2.08; 0.45]		100.0%
Heterogeneity: $I^2 = 0\%$, $\tau^2 = 0$, $p =$	0.39					1						
 Construction of the second se Second second sec second second sec					-4	-2 0	2	4				

Figure S6c: Fasting blood glucose at baseline (analysis of studies including only patients with type 2 diabetes).

	Exp	erimental		c	Control				Weight	Weight
Study	Total Me	an SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Lee 2014 Peterli 2009* Schauer 2014	30 200 28 120 48 193	.90 76.60 .73 43.24 .00 15.67	30 26 49	230.60 126.14 164.00	85.300 68.470 15.333		-29.70 -5.41 29.00	[-70.72; 11.32] [-36.22; 25.40] [22.83; 35.17]	2.1% 3.8% 94.1%	27.1% 31.9% 41.0%
Fixed effect model Random effects model Heterogeneity: $I^2 = 83\%$, τ^2	106 = 824.2, <i>p</i>	< 0.01	105				26.45 2.12	[20.46; 32.44] [-34.13; 38.36]	100.0% 	 100.0%

Figure S6d: Fasting blood glucose at baseline without Schauer et al. 2014 [13] (analysis of studies including only patients with type 2 diabetes).

		Experin	nental		C	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Lee 2014	30	200.90	76.60	30	230.60	85.30		-29.70	[-70.72; 11.32]	36.1%	36.1%
Peterli 2009*	28	120.73	43.24	26	126.14	68.47		-5.41	[-36.22; 25.40]	63.9%	63.9%
Fixed effect model	58			56				-14.17	[-38.80; 10.47]	100.0%	
Random effects model								-14.17	[-38.80; 10.47]		100.0%
Heterogeneity: $I^{e} = 0\%$, τ^{e}	= 0, p =	= 0.35					60 40 20 0 20 40 60				
							-00 -40 -20 0 20 40 00				

Swiss Medical Weekly · PDF of the online version · www.smw.ch

Figure S6e: Insulin at 12 months (analysis of studies including only patients with type 2 diabetes).

	E	xperin	nental		Co	ontrol				Weight	Weight
Study T	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Schauer 2012	50	5.3	0.683	50	5.4	0.817		-0.10	[-0.40; 0.20]	97.0%	97.0%
Lee (Arch Surg) 2011	30	4.9	3.800	30	4.7	2.700		- 0.20	[-1.47; 1.87]	3.0%	3.0%
Fixed effect model	80			80				-0.09	[-0.38; 0.20]	100.0%	
Random effects model							\	-0.09	[-0.38; 0.20]		100.0%

Figure S6f: Glycated haemoglobin (HbA1c) at baseline (analysis of studies including only patients with type 2 diabetes).

	Exp	erimental		Contro				Weight	Weight
Study	Total	Mean SD	Total	Mean SD	Mean difference	MD	95%-CI	(fixed)	(random)
Keidar 2013	19	7713	18	83418	1	-0 64	[-1 66: 0 38]	16.8%	24 2%
Schauer 2014	48	9.3 1.4	49	9.50 1.7		-0.20	[-0.82; 0.42]	45.3%	26.7%
Lee 2014	30	10.0 1.8	30	9.90 1.8		0.10	[-0.81; 1.01]	20.9%	24.9%
Peterli 2009*	28	7.2 1.9	26	4.60 1.9		2.60	[1.59; 3.61]	16.9%	24.2%
Fixed effect model	125		123		~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~	0.26	[-0.15; 0.68]	100.0%	-
Random effects mode	el 🛛					0.45	[-0.83; 1.72]		100.0%
Heterogeneity: $I^2 = 88\%$,	$\tau^2 = 1.48$, p < 0.01							
		20 0			-3 -2 -1 0 1 2 3				

Figure S6g: HOMA index at baseline (analysis of studies including only patients with type 2 diabetes).

Study	Ex Total M	kperim Mean	nental SD	Total	Co Mean	ntrol SD		Mean	diffe	erence	e	MD	95%-CI	Weight (fixed)	Weight (random)
Lee (Surg Obes Relat Dis) 2011 Schauer 2012	16 50	7.9 8.9	3.200 1.533	16 50	10.1 5.2	6.50 0.95			-	-	1	-2.20 3.70	[-5.75; 1.35] [3.20; 4.20]	1.9% 98.1%	45.4% 54.6%
Fixed effect model Random effects model Heterogeneity: $I^2 = 90\%$, $\tau^2 = 15.73$	66 , p < 0.0)1		66			-4	-2	0	1	- ↓ 4	3.59 1 .02	[3.09; 4.08] [-4.73; 6.78]	100.0% 	 100.0%

Figure S6h: HOMA index at 12 months (analysis of studies including only patients with type 2 diabetes).

	E	xperin	nental		C	ontrol									Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD		Mear	diffe	rence		MD	9	5%-CI	(fixed)	(random)
Lee (Arch Surg) 2011	30	1.2	1.200	30	2.5	3.400	5		-			-1.30	[-2.59]	-0.01]	0.4%	39.0%
Schauer 2012	50	1.4	0.133	50	1.3	0.267						0.10	[0.02	0.18]	99.6%	61.0%
Fixed effect model	80			80					-0			0.09	[0.01;	0.18]	100.0%	
Random effects mode	2 0 76	04	0.02				_	-	+	_	_	-0.45	[-1.78;	0.89]		100.0%
Heterogeneity. 7 = 70%, 1	= 0.70	24, p =	0.03				-2	-1	0	1	2					

Figure S6i: Low-density lipoprotein at baseline (analysis of studies including only patients with type 2 diabetes).

Study	Total	Experin Mean	nental SD	Total	Co Mean	ontrol SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Lee 2014 Schauer 2014 Peterli 2009*	30 48 28	137.30 92.40 115.98	37.80 29.00 42.53	30 49 26	142.90 105.80 123.71	44.60 39.50 46.39		-5.60 -13.40 -7.73	[-26.52; 15.32] [-27.17; 0.37] [-31.52; 16.06]	24.5% 56.6% 18.9%	24.5% 56.6% 18.9%
Fixed effect model Random effects mode Heterogeneity: $I^2 = 0\%$, τ^2	106 I = 0, <i>p</i> =	= 0.81		105			30 -20 -10 0 10 20 3	-10.41 -10.41	[-20.77; -0.06] [-20.77; -0.06]	100.0% 	 100.0%

Figure S6j: Low-density lipoprotein at 12 months (analysis of studies including only patients with type 2 diabetes).

Ohudu	Ex	perim	ental	Tetal	Co	ntrol	Manager	МР	05% 01	Weight	Weight
Study	Total	mean	50	Iotal	mean	50	Mean difference	MD	95%-CI	(fixea)	(random)
Lee (Arch Surg) 2011	30	96.9	21.5	30	136.6	40.8		-39.70	[-56.20; -23.20]	32.3%	46.6%
Schauer 2012	50	93.7	27.1	50	110.0	30.9		-16.30	[-27.69; -4.91]	67.7%	53.4%
Fixed effect model	80			80			-	-23.85	[-33.23; -14.48]	100.0%	
Random effects model Heterogeneity: $l^2 = 81\%$, τ	² = 221.	4. p = (0.02					-27.21	[-50.09; -4.33]		100.0%
inerer genergin a er reg							-40 -20 0 20 40				

Figure S6k: Low-density lipoprotein at 36 months (analysis of studies including only patients with type 2 diabetes).

		Experin	nental		C	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Schauer 2014 Peterli 2009*	48 28	96.30 112.11	27.20 38.66	49 26	108.10 112.11	35.20 38.66		-11.80 0.00	[-24.30; 0.70] [-20.64; 20.64]	73.1% 26.9%	73.1% 26.9%
Fixed effect model Random effects model Heterogeneity: $l^2 = 0\%$, τ^2	76 = 0, p =	= 0.34		75			-20 -10 0 10 20	-8.63 -8.63	[-19.33; 2.06] [-19.33; 2.06]	100.0% 	 100.0%

Figure S61: High-density lipoprotein at baseline (analysis of studies including only patients with type 2 diabetes).

	E	perime	ental		Co	ntrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Schauer 2014	48	45.40	13.0	49	44.50	12.0		0.90	[-4.08; 5.88]	32.1%	32.9%
Lee 2014	30	47.90	9.6	30	42.80	6.3		- 5.10	[0.99; 9.21]	47.2%	44.0%
Peterli 2009*	28	38.66	11.6	26	38.66	11.6		0.00	[-6.19; 6.19]	20.8%	23.1%
Fixed effect model	106			105				2.69	[-0.13; 5.52]	100.0%	
Random effects mode	el							2.54	[-0.69; 5.77]		100.0%
Heterogeneity: $I^2 = 21\%$,	$\tau^2 = 1.78$	B, p = 0.3	28						-		
, ,		999 - CO					-5 0 5				

Figure S6m: High-density lipoprotein at 12 months (analysis of studies including only patients with type 2 diabetes).

	Ex	perim	ental		Co	ntrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
ee (Arch Surg) 2011	30	49.3	7.7	30	45.4	7.9		3.90	[-0.05; 7.85]	71.6%	71.6%
Schauer 2012	50	58.8	18.0	50	56.1	13.7		- 2.70	[-3.57; 8.97]	28.4%	28.4%
Fixed effect model	80			80				3.56	[0.22; 6.90]	100.0%	
Random effects mode deterogeneity: $I^2 = 0\%$, τ^2	 = 0 p =	0.75						3.56	[0.22; 6.90]		100.0%

Figure S6n: High-density lipoprotein at 36 months (analysis of studies including only patients with type 2 diabetes).

	E	xperin	nental		C	ontrol				Weight	Weight
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random)
Schauer 2014	48	60.00	19.10	49	59.2	17.20		0.80	[-6.44; 8.04]	67.0%	67.0%
Peterli 2009*	28	54.12	19.33	26	58.0	19.33 -		-3.88	[-14.20; 6.44]	33.0%	33.0%
Fixed effect model	76			75				-0.74	[-6.67; 5.18]	100.0%	
Random effects model Heterogeneity: $l^2 = 0\%$, τ^2	= 0, p =	0.47						-0.74	[-6.67; 5.18]		100.0%
Heterogeneity: $I^2 = 0\%$, τ^2	= 0, <i>p</i> =	= 0.47					-10 -5 0 5 10				

Figure S60: Cholesterol at 12 months (analysis of studies including only patients with type 2 diabetes).

Study	E) Total	perim Mean	ental SD	Total	Con Mean	trol SD	Mean difference	MD	95%-CI	Weight (fixed)	Weight (random)
Lee (Arch Surg) 2011	30	162.2	26.6	30	207.8	67		-45.60	[-71.40; -19.80]	23.2%	43.8%
Schauer 2012	50	173.6	35.3	50	187.9	37		-14.30	[-28.47; -0.13]	76.8%	56.2%
Fixed effect model	80			80				-21.56	[-33.98; -9.14]	100.0%	
Random effects model								-28.02	[-58.46; 2.42]		100.0%
Heterogeneity: $I^2 = 77\%$, τ^2	2 = 377.	1, p = 0	0.04								
							-60 -40 -20 0 20 40 60				

Figure S6p: Triglycerides at baseline (analysis of studies including only patients with type 2 diabetes).

Study	E	Experin	nental	Total	C	ontrol	Moon difference	мр	05% CI	Weight	Weight
Sludy	Total	wear	50	Total	wean	30	Mean difference	WD	95%-01	(lixed)	(random)
Schauer 2014	48	179.0	22.1	49	160.0	15.2	1.0	19.00	[11.44; 26.56]	98.9%	59.3%
Lee 2014	30	195.2	128.3	30	262.2	158.8 -		-67.00	[-140.05; 6.05]	1.1%	40.7%
Fixed effect model	78			79			\$	18.09	[10.57; 25.61]	100.0%	
Random effects model Heterogeneity: $I^2 = 81\%$, τ^2	² = 299	6. p = 0	.02					-16.01	[-98.82; 66.80]		100.0%
		-,,, -					-100 -50 0 50 100				

	Exp	perime	ntal		Co	ntrol				Weight	Weigh
Study	Total	Mean	SD	Total	Mean	SD	Mean difference	MD	95%-CI	(fixed)	(random
Lee (Arch Surg) 2011	30	104.9	62	30	144.2	58.9		-39.30	[-69.90; -8.70]	1.3%	39.2%
Schauer 2012	50	95.0	9	50	101.0	8.8	p.	-6.00	[-9.49; -2.51]	98.7%	60.8%
Fixed effect model	80			80			\$	-6.43	[-9.89; -2.96]	100.0%	
Random effects mode	I							-19.04	[-50.89; 12.82]		100.0%