

1 **Reported appetite, taste and smell changes following Roux-en-Y gastric bypass**
2 **and sleeve gastrectomy: effect of gender, type 2 diabetes and relationship to**
3 **post-operative weight loss**

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36 **Abstract**

37

38 Reduced energy intake drives weight loss following Roux-en-Y gastric bypass (RYGB) and
39 sleeve gastrectomy (SG) procedures. Post-operative changes in subjective appetite, taste, and
40 smell and food preferences are reported and suggested to contribute to reduced energy
41 intake. We aimed to investigate the prevalence of these changes following RYGB and SG and
42 to evaluate their relationship with weight loss.

43

44 98 patients post-RYGB and 155 post-SG from a single bariatric centre were recruited to a
45 cross-sectional study. Participants completed a questionnaire, previously utilised in post-
46 operative bariatric patients, to assess the prevalence of post-operative food aversions and
47 subjective changes in appetite, taste and smell. Anthropometric data were collected and
48 percentage weight loss (%WL) was calculated. The relationship between food aversions,
49 changes in appetite, taste and smell and %WL was assessed. The influence of time post-
50 surgery, gender and type 2 diabetes (T2D) were evaluated.

51

52 Following RYGB and SG the majority of patients reported food aversions (RYGB=62%,
53 SG=59%), appetite changes (RYGB=91%, SG=91%) and taste changes (RYGB=64%, SG=59%).
54 Smell changes were more common post-RYGB than post-SG (RYGB=41%, SG=28%, $p=0.039$).
55 No temporal effect was observed post-RYGB. In contrast, the prevalence of appetite changes
56 decreased significantly with time following SG.

57

58 Post-operative appetite changes associated with and predicted higher %WL post-SG but not
59 post-RYGB. Taste changes associated with and predicted higher %WL following RYGB but not
60 post-SG. There was no gender effect post-RYGB. Post-SG taste changes were less common in
61 males (female=65%, males=40%, $p=0.008$). T2D status in females did not influence post-
62 operative subjective changes. However, in males with T2D, taste changes were less common
63 post-SG than post-RYGB together with lower %WL (RYGB= 27.5 ± 2.7 , SG= 14.6 ± 2.1 , $p=0.003$).
64 Further research is warranted to define the biology underlying these differences and to
65 individualise treatments.

66

67 **Keywords:** Obesity, Roux-en-Y gastric bypass, sleeve gastrectomy, appetite, taste, smell, food
68 aversions, weight loss.

69

70 Introduction

71

72 Bariatric surgery is the most effective treatment for patients with severe obesity, leading to
73 sustained weight reduction, improved obesity-associated co-morbidities and decreased
74 mortality (Sjostrom, 2013). The most commonly performed bariatric procedures globally are
75 the Roux-en-Y gastric bypass (RYGB) and the sleeve gastrectomy (SG), accounting for 45% and
76 37% respectively of operations undertaken in 2013 (Angrisani et al., 2015). Observational
77 studies and a limited number of randomised controlled studies suggest that RYGB and SG
78 produce comparable health improvements in the short-term (Schauer et al., 2014; Sczepaniak,
79 Owens, Shukla, Perlegos, & Garner, 2015). Other procedures, such as the adjustable gastric
80 banding (AGB) are now less commonly performed (Angrisani et al., 2015).

81

82 Eating behaviour is a key determinant of the pathogenesis of obesity and weight loss achieved
83 following bariatric surgery (Manning, Pucci, & Batterham, 2015; Scott & Batterham, 2011). An
84 energy intake that consistently exceeds energy expenditure leads to weight gain and
85 eventually obesity (Berthoud, 2011). Obese individuals subjectively rate energy-dense foods
86 as more pleasant compared to lean individuals (Rissanen et al., 2002). In addition, weight gain
87 and obesity have been linked to a reduction in taste sensitivity and smell perception (Miras &
88 le Roux, 2010; Patel, DelGaudio, & Wise, 2015; A. C. Shin, Townsend, Patterson, & Berthoud,
89 2011). Furthermore, neuroimaging studies have revealed that obese subjects exhibit altered
90 neural responses within reward regions in response to food cues (Atalayer et al., 2014;
91 Rissanen et al., 2002).

92

93 The gastrointestinal (GI) tract is established as a key regulator of energy and glucose
94 homeostasis and it is now clear that changes in gut-derived signals as a consequence of
95 altered GI anatomy following bariatric surgery play a key role in driving reduced energy intake
96 and weight loss (Dirksen, Damgaard, et al., 2013; Manning et al., 2015; Scott & Batterham,
97 2011). Following RYGB and SG patients report reduced hunger in the fasted state, increased
98 post-meal satiety, changes in subjective taste and altered food preferences (Manning et al.,
99 2015; Scott & Batterham, 2011). For example, a recent prospective study of 30 patients
100 undergoing SG reported a 68% decrease in energy intake 6 months post-surgery sustained at
101 24 months post-surgery. 75% of patients in this study reported reduced preference toward
102 sweet and fatty foods (Coluzzi et al., 2016).

103

104 In order to assess changes in subjective taste following bariatric surgery Tichansky *et al.*
105 developed a questionnaire comprised of 23 questions. They reported that subjective taste
106 changes were more common post-RYGB than following AGB surgery (Tichansky, Boughter, &
107 Madan, 2006). Subsequently, Graham and colleagues used Tichansky's questionnaire in a
108 cross-sectional study to evaluate taste changes following RYGB in patients who were a median
109 19 months post-RYGB (Graham, Murty, & Bowrey, 2014). They added 10 additional questions
110 assessing subjective changes in appetite, smell and food aversions. They found that 93% of
111 patients reported a change in appetite, 73% a change in taste, 42% a change in smell and 73%
112 developed food aversions. Additionally, they reported that patients who developed food
113 aversions achieved higher absolute post-operative weight loss and greater reduction in body
114 mass index (BMI) (Graham et al., 2014). Zerrweck *et al.* using the questionnaire from Graham
115 *et al.*, reported that appetite, taste, smell and food aversions were equally common following
116 RYGB and SG at 10 months post-surgery (Zerrweck et al., 2015). However, it remains unclear

117 whether these subjective changes in appetite, taste and smell are a consequence of weight
118 loss *per se* or if they are mediated by bariatric procedure-dependent physiological changes.
119 The subjective hedonic value of sweet foods has been shown to reduce following RYGB
120 (Ochner et al., 2011; Ochner et al., 2012; Scholtz et al., 2014). This effect was not observed
121 in BMI-matched subjects following AGB, suggesting that post-RYGB hedonic responses to
122 food change independent of weight loss (Scholtz et al., 2014).

123
124 The impact of bariatric surgery on objectively assessed olfaction and taste sensitivity is
125 controversial, in part due to methodological issues. There are reports of improved post-
126 operative taste sensitivity for sweet, salty, sour and bitter (Altun et al., 2016; Holinski,
127 Menenakos, Haber, Olze, & Ordemann, 2015), no taste sensitivity changes (Pepino et al.,
128 2014) and improved olfactory sensitivity (Holinski et al., 2015). There is also a suggestion of a
129 difference between RYGB and SG with improved olfactory sensitivity post-SG but not post-
130 RYGB (Jurowich et al., 2014).

131
132 Taste and smell perception are complex processes, integrating a range of sensory, cognitive
133 and hormonal signals (Cummings, 2015; Miras & le Roux, 2010). Gender, obesity, presence of
134 T2D and nutritional status (vitamin B12 and zinc levels) have all been reported to impact upon
135 gustatory and olfactory function (Bustos-Saldana et al., 2009; Deglaire et al., 2015; Fabian,
136 Beck, Fejerdy, Hermann, & Fabian, 2015; Hwang, Kang, Seo, Han, & Joo, 2016). The tendency
137 to like fatty and salty tasting foods has been shown to have a linear relationship with
138 increasing BMI in both males and females (A. C. Shin et al., 2011). However, a liking for sweet
139 foods is more commonly reported by obese females compared to obese males (Deglaire et
140 al., 2015) and females outperform males in their ability to detect certain odours (Doty &
141 Cameron, 2009). T2D *per se* has been linked to impaired taste sensitivity, particularly for
142 sweet stimuli and to impaired olfaction (Bustos-Saldana et al., 2009). Following RYGB,
143 patients with T2D loose significantly less weight compared to patients who do not have T2D
144 (Courcoulas et al., 2015). However, there are no reports comparing the prevalence of changes
145 in subjective appetite, taste or smell following bariatric surgery in people with T2D compared
146 to people without T2D.

147
148 Following RYGB and SG, circulating gut hormone levels are markedly altered and these
149 changes are suggested to contribute to post-operative appetite changes (Yousseif et al., 2014).
150 Patients with a poor response to surgery experience increased hunger and reduced satiety
151 levels. In addition, an attenuated gut hormone response is seen in poor weight loss
152 responders compared to good weight loss responders (Dirksen, Jorgensen, et al., 2013;
153 Manning et al., 2015). Interestingly, gut hormones are present in saliva and their cognate
154 receptors are found on taste buds and olfactory neurons (Acosta et al., 2011; Cummings,
155 2015; Loch, Breer, & Strotmann, 2015; Y. K. Shin et al., 2008). Hence, it is plausible that gut
156 hormones mediate gustatory and olfactory changes following bariatric surgery through
157 weight-independent mechanisms. Of note, RYGB and SG are anatomically very different and
158 differentially impact upon circulating gut hormone levels (le Roux et al., 2007; Yousseif et al.,
159 2014). These differences may in turn result in post-procedural differences in appetite, taste
160 and smell. Whilst the development of food aversions following SG and RYGB has been linked
161 to increased weight loss, it remains to be established whether subjective change in appetite
162 taste or smell associate with weight loss (Graham et al., 2014).

163

164 We hypothesized that post-operative subjective changes in appetite, taste and smell would
165 differ between SG and RYGB patients and be influenced by gender and the presence of T2D.
166 In addition that appetite, taste and smell changes would associate with post-operative weight
167 loss. Thus, we aimed to investigate prevalence of appetite, taste, smell changes and food
168 aversions following RYGB and SG and their relationship to post-operative percentage weight
169 loss (%WL). We also aimed to evaluate the influence of gender, T2D and time post-surgery
170 upon these changes.

171

172

173 **Methods**

174

175 Patients who attended the University College London Hospitals (UCLH) Bariatric Centre for
176 Weight Management and Metabolic Surgery for follow up appointments after primary RYGB
177 or primary SG were invited to participate. Participation was voluntary and informed consent
178 was obtained in person by a healthcare professional. Ethical approval was obtained from the
179 National Health Service Research Ethics Committee (ID#09/H0715/65) and the study was
180 undertaken in accordance with the Helsinki Declaration. Inclusion criteria were adult patients
181 (18 years or older), following either primary RYGB or SG and proficient in spoken and written
182 English.

183

184 Prior to surgery all patients had been assessed by a multidisciplinary team and fulfilled the
185 criteria outlined by the National Institute for Health and Care Excellence (NICE, 2014). In RYGB
186 stomach size is reduced by the creation of a small gastric pouch (~ 20cm³), ingested nutrients
187 pass rapidly from the gastric pouch directly into the mid-jejunum, bypassing the majority of
188 the stomach, the duodenum and the proximal jejunum (Olbers, Lonroth, Fagevik-Olsen, &
189 Lundell, 2003). In SG, 80-90% of the total stomach volume is removed by transecting along
190 the greater curvature of the stomach (Abu-Jaish & Rosenthal, 2010), the remainder of the GI
191 tract is left intact and nutrient follow the normal anatomical route.

192

193 Weight was measured using a Walkthrough Platform by a trained health professional.
194 Participants completed a 33-question questionnaire, developed by Tichansky *et al.*, and
195 modified by Graham *et al.* (Graham *et al.*, 2014; Tichansky *et al.*, 2006) (appendix). Permission
196 to use the questionnaire was obtained (Graham *et al.*, 2014). Clinical data including height
197 and weight on the day of surgery and presence or absence of T2D and exclusion criteria were
198 obtained from the patients' clinical records. Vitamin B12 and zinc levels were measured by
199 the UCLH Department of Clinical Biochemistry using a competitive immunoassay (Roche) and
200 colorimetric assay (Randox) respectively, as part of routine post-surgical care.

201

202 After RYGB or SG surgery, patients are advised to adhere to a soft diet for the first two post-
203 operative weeks, followed by a soft diet with gradual reintroduction of solid food. Patients
204 start eating meals of normal textured food 7 weeks after surgery. Thus, in order to eliminate
205 the effect of early post-operative dietary restriction and allow for their eating behaviour to
206 be established, patients less than 90 days post-surgery were excluded. Patients with factors
207 affecting gustatory (including low zinc and low vitamin B12 levels) or olfactory function or
208 who suffered a severe or debilitating illness, active malignancy and pregnant women were
209 also excluded.

210

211 Percentage weight loss (%WL) was calculated by the weight difference between the day of
 212 surgery and the day of questionnaire completion and expressed as percentage of the weight
 213 on the day of surgery. Data were analysed using GraphPad Prism version 6 and STATA
 214 statistical software version 13. Mean and standard error of mean (SEM) were calculated.
 215 Continuous data was assessed for normality using D'Angostino and Pearson omnibus
 216 normality test. Parametric (t-test or one-way analysis of variance (ANOVA) and non-
 217 parametric tests (Mann-Whitney tests)) were used as appropriate. Chi-square tests were used
 218 for categorical data. Furthermore, linear regression analyses were performed. Significance
 219 was assumed below the 0.05 level.

220
 221

222 **Results**

223
 224

224 **Patient demographics**

225 253 patients were included in the final analysis, 98 following RYGB and 155 post-SG. 37
 226 patients were excluded from the study due pregnancy (n=8), B12 and/or zinc deficiency (n=4),
 227 symptomatic hypoglycaemia (n=3), conversion of SG to RYGB (n=8), active malignancy (n=4),
 228 previous cranial radiotherapy (n=1), anosmia (n=2), intolerance to solid foods (n=2), severe
 229 illness or reduced mobility (n=4) and inability to read English (n=1). Out of the included
 230 patients, 199 (79%) were female and 54 (20%) male. The patient characteristics are presented
 231 in Table 1. The RYGB and SG groups had a similar age and BMI but %WL and time post-surgery
 232 were significantly greater in the RYGB group.

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234 **Table 1: Patient characteristics**

	Age (years)	BMI (kg/m ²)	%WL	Time post-surgery (days)
RYGB n=98 (M=19, F=79)	46.5 ± 1.1	44.7 ± 0.7	25.6 ± 0.9	769 ± 53
SG n=155 (M=35, F=120)	44.3 ± 1.0	46.1 ± 0.6	21.2 ± 0.8	593 ± 43
p value	0.120	0.260	0.0001	0.001

236 Mean age, Body Mass Index (BMI), percentage weight loss (%WL) and time post-surgery in patients following
 237 Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)

238
 239

239 **Subjective changes in appetite, taste and smell post-surgery**

240 The majority of patients reported post-operative change in appetite (Figure 1A, Question 1).
 241 Changes in taste and to a lesser extent smell were observed following both RYGB and SG, as
 242 were the development of food aversions (Figure 1B, 1C and 1D). While there were no
 243 significant differences in appetite, taste and food aversions between the two groups, smell
 244 changes were significantly more common following RYGB compared to SG (RYGB=41%,
 245 SG=28%, p=0.039).

246

247 In view of evidence regarding difference in taste perception between males and females, we
 248 examined the influence of gender upon the frequency of reported appetite, taste and smell
 249 changes and development of food aversions. No significant differences were found when
 250 comparing responses of female and male patients following RYGB (Table 2). However, within
 251 the SG group, taste and smell changes were significantly more common in female compared
 252 to male patients (Table 2). Furthermore, men post-SG lost significantly less weight compared
 253 to men following RYGB (%WL: RYGB=26.7 ± 2.13, SG=18.7 ± 1.7 p=0.004)

254
 255 (Figure 1 here)

256
 257 **Table 2: Gender differences in the prevalence of subjective appetite, taste, smell changes**
 258 **and food aversions**

	RYGB Group (% of patients/number reporting post-surgery change)			SG Group (% of patients/number reporting post-surgery change)		
	Females	Males	p value	Females	Males	p value
Appetite changes	92.4% (73)	84.2% (16)	0.370	91.7% (110)	88.6% (31)	0.521
Taste changes	62.0% (49)	73.7% (14)	0.341	65% (78)	40% (14)	0.008
Smell changes	41.8% (33)	36.8% (7)	0.695	31.7% (38)	14.3% (5)	0.043
Food aversions	45.7% (49)	66.7% (12)	0.713	62.3% (76)	45.7% (16)	0.062

260 Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)

261
 262 **Influence of time post-surgery upon subjective changes in appetite, taste, smell, food**
 263 **aversions and %WL**

264 In light of the cross-sectional nature of our study, we investigated the effect of time since
 265 surgery on patients reporting perceived changes in appetite, taste and smell (Table 3).
 266 Following RYGB, no differences were found in the frequency of changes in appetite, taste,
 267 smell and food aversions at different time points. In contrast, following SG, the prevalence of
 268 subjective appetite changes decreased after 3 years (Table 3). The prevalence of taste and
 269 smell changes also reduced with time post-SG but these failed to reach significance. Following
 270 RYGB, maximum %WL was achieved at 1-2 years post-surgery and was similar at 2-3 years
 271 and 3-5 years post-RYGB (Table 4). Maximum %WL following SG was also observed at 1-2
 272 years post-surgery and was comparable to that seen in the RYGB group. %WL decreased with
 273 time post-surgery in the SG group (Table 4). Comparison of 2-5 year %WL between the RYGB
 274 and SG groups revealed greater %WL post-RYGB (%WL; RYGB=26.2±1.3, SG=20.8 ±1.9,
 275 p=0.023).

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281 **Table 3: Effect of time post-surgery on the prevalence of food aversions, subjective**
 282 **changes in appetite, taste and smell changes**
 283

RYGB Group				
Time post-surgery	Change in appetite	Change in taste	Change in smell	Food aversions
< 180 days (n=6)	100.0%	50.0%	50.0%	66.7%
180-364 days (n=24)	83.3%	62.5%	45.8%	54.2%
p value	0.468	0.458	0.855	0.709
1-2 years (n=23)	95.7%	73.9%	43.5%	65.2%
p value	0.267	0.289	0.817	0.528
2-3 years (n=16)	100%	62.5%	31.3%	62.5%
p value	0.202	0.795	0.292	0.879
3-5 years (n=29)	86.2%	62.1%	37.9%	65.5%
p value	0.306	0.767	0.706	0.665
SG Group				
Time post-surgery	Change in appetite	Change in taste	Change in smell	Aversions
< 180 days (n=36)	97.2%	75.0%	44.4%	58.5%
180-364 days (n=41)	100.0%	65.9%	24.4%	68.3%
p value	0.283	0.321	0.063	0.879
1-2 years (n=27)	88.9%	48.1%	14.8%	59.3%
p value	0.072	0.065	0.067	0.485
2-3 years (n=19)	84.2%	57.9%	21.1%	52.6%
p value	0.722	0.797	0.499	0.309
3-5 years (n=32)	78.1%	43.8%	28.1%	43.8%
p value	0.001	0.110	0.056	0.068

284 Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG). Fisher's exact correlation, p values represent
 285 comparison of given time interval versus previous data.
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Table 4: Weight loss at different time points following RYGB and SG

Time post-surgery	%WL in RYGB patients	%WL in SG patients
< 180 days	18.8 ± 2.2	17.0 ± 1.0
180-364 days	24.6 ± 1.4	23.1 ± 1.1
1-2 years	27.4 ± 1.9	26.2 ± 1.9
2-3 years	26.1 ± 1.9	19.9 ± 3.3
3-5 years	26.3 ± 1.8	20.3 ± 2.1

297 Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), percentage weight loss (%WL)
298

Relationship between subjective changes in appetite, taste, smell, food aversion and %WL

300 We investigated the relationship between post-operative changes in appetite, taste, smell,
301 food aversions and %WL. In the RYGB group there was significant association between a
302 change in taste and higher %WL (27.8 ± 1.0 vs. 23.1 ± 1.6, p=0.036). In the SG group a
303 significantly higher %WL was detected in patients with a change in appetite (21.9 ± 0.8 vs.
304 13.4 ± 3.1, p=0.006) and food aversions (22.6 ± 1 vs. 19.2 ± 1.3, p=0.032). However, there was
305 no association between subjective taste changes and %WL.

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Table 5: %WL in patients with and without subjective changes in appetite, taste, smell and food aversion post-RYGB

	Appetite	Taste	Smell	Food aversion
Change	25.8 ± 0.9 n=89	27.8 ± 1.0 n=63	26.3 ± 1.5 n=40	26.5 ± 1.1 n=61
No change	23.8 ± 3.2 n=9	23.1 ± 1.6 n=35	25.2 ± 1.1 n=58	24.2 ± 1.2 n=37
p value	0.435	0.036	0.595	0.111

310 Roux-en-Y gastric bypass (RYGB), percentage weight loss (%WL)

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Table 6: %WL in patients with and without subjective changes in appetite, taste, smell and food aversion post-SG

	Appetite	Taste	Smell	Food aversion
Change	21.9 ± 0.8 n=141	21.9 ± 1.0 n=92	21.7 ± 1.8 n=43	22.6 ± 1.0 n=92
No change	13.4 ± 3.1 n=14	20.3 ± 1.3 n=63	21.1 ± 0.9 n=112	19.2 ± 1.3 n=63
p value	0.006	0.520	0.772	0.032

316 Sleeve gastrectomy (SG), percentage weight loss (%WL)

317

Subjective changes in taste towards sweet and salty foods

319 Patients were asked if they had experienced a change in their taste towards sweet and salty
320 foods. They were asked separately if they had experienced an increase or decrease in the

321 taste of sweet or salty tasting foods (Appendix: Questions 9, 10, 12 and 13). 87.8% of RYGB
 322 patients responded that their taste for sweet foods had either increased or decreased
 323 compared to 65.2% of SG patients (p=0.001). Changes in taste towards salty tasting foods
 324 were also significantly more common following RYGB (% of patients reporting change in taste
 325 towards salty tasting foods: RYGB =56.1, SG= 40.6%, p=0.020, Figure 2).

326
 327 Following RYGB, there were no gender differences in subjective taste change towards sweet
 328 foods (females 89% and males 84%, p=0.685). However, post-SG a change in taste towards
 329 sweet foods, either an increase or decrease, was significantly more common in females
 330 compared to males (females 70% and males 45%, p=0.009).

331
 332 **(Figure 2 here)**

333
 334 **Influence of T2D**

335 T2D was present in 92 patients (53 RYGB and 39 SG). No differences were seen in the
 336 prevalence of subjective change in appetite, taste, smell or food aversion between individuals
 337 with and without T2D post-RYGB (appetite change: no T2D=93.3%, T2D=88.7%; taste change:
 338 no T2D=73.3%, T2D=56.6%, smell change: no T2D=40%, T2D=41.5%; food aversions: no
 339 T2D=62.2%, T2D=62.3%; all p > 0.05) or post-SG (appetite change: no T2D=89.7%, T2D=94.9%;
 340 taste change: no T2D=62.1%, T2D=51.3%, smell change: no T2D=26.7%, T2D=30.8%; food
 341 aversions: no T2D=62.1%, T2D=51.3%; all p > 0.05). However, within the SG group, taste
 342 changes were significantly less common in males with T2D compared to females with T2D (%
 343 of patients reporting change in taste: T2D females=61.3%, T2D males=12.5%, p=0.020.
 344 Furthermore, taste changes were less common in males with T2D following SG than post-
 345 RYGB (change in taste prevalence: T2D men RYGB=69.2%, T2D men SG=12.5%, p=0.024).
 346 Moreover, %WL was significantly lower in male T2D patients following SG compared to post-
 347 RYGB (%WL: SG=14.6 ± 2.1, RYGB=27.5 ± 2.7, p=0.003).

348 **Table 7: Frequency of reported appetite, taste, smell changes and food aversions by gender**
 349 **in patients with T2D following RYGB and SG.**

350

	RYGB			SG		
	Females	Males	p value	Females	Males	p value
Appetite	87.5%	92.3%	0.370	96.8%	87.5%	0.372
Taste	52.5%	69.2%	1.0	61.3%	12.5%	0.019
Smell	42.5%	38.5%	1.0	35.5%	12.5%	0.393
Food aversions	65.0%	53.4%	0.522	58.1%	25%	0.123

351 Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG)

352
 353 **Predictors of weight loss**

354 Linear regression analyses were performed in order to correct for characteristics within
 355 groups and identify predictors of %WL. The models for RYGB and SG patients are illustrated
 356 in Table 8. The basic model (M1) adjusted for gender and days since surgery. Subjective taste
 357 changes following surgery were associated with greater %WL post-RYGB, even after adjusting
 358 for gender, age, duration since surgery and the presence of T2D. In contrast, post-SG,

359 subjective taste change was not related to %WL. However, in patients post-SG subjective
 360 change in appetite strongly associated with greater %WL after adjusting for gender, age,
 361 duration since surgery and T2D, which is not observed in RYGB.

362

363 **Table 8: Linear regression model testing %WL by appetite, taste, smell and aversions**

364

RYGB				
Model	Appetite	Taste	Smell	Aversions
	Coefficient (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)	Coefficient (95% CI)
Basic Model (M1)	2.4 (-3.5; 8.4)	4.0 (0.5; 7.5)*	1.3 (-2.2; 4.9)	1.1 (-2.6; 4.8)
M1 + age	2.5 (-3.4; 8.4)	3.6 (0.7; 7.1)*	1.1 (-2.4; 4.5)	0.9 (-2.7; 4.5)
M1 + T2D	2.3 (-3.7; 8.3)	3.8 (0.2; 7.4)*	1.4 (-2.1; 4.9)	1.3 (-2.4; 4.7)
SG				
Model	Appetite	Taste	Smell	Aversions
Basic Model (M1)	8.1 (2.5; 13.7)**	0.9 (-2.5; 4.3)	0.1 (-3.5; 3.7)	3.1 (-0.1; 6.4)
M1 + age	8.7 (3.2; 14.1)**	0.6 (-2.7; 3.9)	0.4 (-3.2; 3.9)	2.8 (-0.5; 5.9)
M1 + T2D	8.9 (3.4; 14.5)**	0.5 (-2.8; 3.9)	0.3 (-3.2; 3.8)	2.8 (-0.4; 6.0)

* p<0.05, ** p<0.01; Basic model adjusts for gender and days since surgery

365 Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), Type 2 diabetes (T2D), M1 (Model 1)

366

367

368 Discussion

369

370 In this cross-sectional study we examined the prevalence of food aversions and subjective
 371 changes in appetite, taste and smell in a cohort of patients 6 months to 5 years following
 372 primary RYGB or SG. Our cohort included the largest SG group examined to date with the
 373 longest duration post-surgery. Our data show that whilst subjective changes in appetite, taste,
 374 smell and food aversions are common following both RYGB and SG they differ in their impact
 375 on subjective changes in smell and taste, durability of changes, influence of gender and
 376 relationship with %WL.

377

378 In the RYGB group the prevalence of changes in appetite, taste, smell and food aversions was
 379 similar across all periods examined, with 86% of patients reporting appetite changes and 64%
 380 taste changes 3-5 years following RYGB. We observed no influence of gender or T2D status
 381 upon changes in appetite, taste or smell. %WL was similar at 1-2, 2-3 and 3-5 years post-
 382 surgery. Linear regression analysis showed that subjective taste changes associated with and
 383 predicted %WL.

384

385 After SG, smell changes were less common than after RYGB, as were also changes in taste
 386 towards sweet and salty tasting foods. The prevalence of changes in appetite significantly
 387 decreased with time post-surgery; the prevalence of changes in taste, smell and food aversion
 388 showed a trend to decrease with time post-surgery. Importantly, following SG the prevalence
 389 of changes in taste and smell was lower in males compared to females particularly in male
 390 patients with T2D. While %WL was comparable between RYGB and SG during the first post-

391 operative 2-year period, between 2-5 years %WL was significantly greater in the RYGB group
392 at 2-5 years post-surgery compared to the SG group. Subjective appetite changes associated
393 with and predicted %WL in the SG group.

394

395 Gender differences in taste sensitivity have been reported in obesity (Doty & Cameron, 2009;
396 Hwang et al., 2016). Similarly, T2D, which is known to impact upon gut hormone profiles, has
397 also been suggested to affect taste sensitivity, particularly toward sweet tasting foods
398 (Bustos-Saldana et al., 2009). However, until now, no data existed with regards to effects of
399 gender or T2D on appetite, taste or smell in patients following bariatric surgery. While no
400 significant gender differences were seen within our RYGB group, there was a marked gender
401 effect following SG. In particular, following SG the prevalence of taste changes was
402 significantly lower in males with T2D compared to females with T2D. Moreover, the
403 prevalence of taste changes and %WL were significantly lower in males with T2D following SG
404 compared to RYGB. Our findings highlight the need for further research into the underlying
405 physiology of these gender differences.

406

407 The role of weight loss in mediating subjective changes in taste and smell remains to be
408 clarified. Interestingly, reduced subjective taste and smell following GI surgery were first
409 reported in normal weight patients as a transient complication following gastrectomy and
410 oesophagectomy for GI malignancies (Harris & Griffin, 2003), suggesting that these changes
411 are not restricted to people with obesity. In our cohort, the prevalence of smell changes was
412 greater in the RYGB group compared to the SG despite comparable %WL during the first two
413 post-operative years, suggesting weight independent processes may be involved. The
414 perception of flavour is thought to be predominantly mediated through smell (Yeomans,
415 2006), thus our findings of much higher prevalence of taste changes compared to smell
416 changes following RYGB and SG is somewhat surprising. However, recent studies have
417 identified gut hormone receptors on taste buds, gut hormones within saliva and postulated a
418 role for saliva gut hormones in taste modulation (Acosta et al., 2011; Y. K. Shin et al., 2008).
419 Circulating levels of gut hormones, in particular ghrelin, GLP-1 and PYY, change post-
420 operatively (Yousseif et al., 2014). Thus, these changes offer not only a plausible biological
421 explanation for appetite changes post-surgery but also for the higher prevalence of taste
422 compared to smell changes. In addition, the differential gut hormone pattern observed
423 following RYGB and SG may underlie the procedural differences in appetite, taste and smell
424 post-surgery (Cummings, 2015; Fabian et al., 2015). Longitudinal studies examining hormone
425 levels in blood and saliva coupled with subjective and objective assessments of appetite, taste
426 and smell in large cohorts of males and females undergoing RYGB and SG are now needed.

427

428 Our study does have limitations. The study was cross-sectional, which resulted in a large
429 variation in time post-surgery. Reported changes in appetite, taste and smell were subjective
430 and no control group was included. In addition, since no data was collected pre-operatively,
431 our data could be subject to recall bias, which is likely to increase with longer duration from
432 surgery. Furthermore, the number of male participants in our study cohort was small.
433 However, this reflects the higher number of females undergoing bariatric surgery in the UK
434 compared to males (Wellbourn R, 2014). Our findings of appetite, taste, smell changes and
435 food aversions include the largest cohort of SG patients to date. Our SG sample size was larger
436 compared to the RYGB group, while the post-RYGB patients had a significantly longer duration
437 since surgery, which reflects the increasing popularity of SG over recent years and the trend

438 to perform a higher number SG (Angrisani et al., 2015). The higher %WL in the RYGB group is
439 in concordance with previous findings from studies that have compared post-operative
440 outcomes between RYGB and SG (Schauer et al., 2014; Szczepaniak et al., 2015). Similarly,
441 weight loss post-RYGB was also higher compared to SG in the study conducted by Zerrweck
442 *et al* (Zerrweck et al., 2015). The higher percentage of T2D in the RYGB population reflects
443 that RYGB remains the preferred procedure in T2D, given the better T2D outcomes post-RYGB
444 in the literature (Schauer et al., 2014). Graham *et al.* and Zerrweck *et al.* reported associations
445 with food aversions and weight loss (Graham et al., 2014; Zerrweck et al., 2015). This effect
446 was observed only following SG in our cohort. However, the wording of the question relating
447 to food aversions did not allow for a clear distinction between true food aversions, and post-
448 ingestive phenomena such as dumping syndrome. This ambiguity needs to be borne in mind
449 when interpreting these results, as food tolerance and GI quality of life may play a role as
450 aversive drivers of eating behaviour (Overs, Freeman, Zarshenas, Walton, & Jorgensen, 2012).
451 Furthermore, feedback from our participants also highlighted the ambiguity of some of the
452 questions, particularly relating to “increase” or “loss” of taste.

453
454 Nevertheless, compared to previous studies, our study design has several strengths and
455 provides novel findings. We obtained consent in person and completed data collection in one
456 visit. Our exclusion criteria allowed for elimination of patients with additional factors that
457 could impact on %WL, including low B12 and zinc. Furthermore, in contrast to previous
458 studies we have used %WL as our outcome for weight loss, in order to avoid for confounding
459 outcomes by pre-operative BMI. Our analysis identified procedure dependent differences in
460 appetite, taste, smell changes and their impact upon %WL. In addition, we investigated the
461 effect of gender and found marked gender differences within the SG group that are
462 exacerbated by the presence of T2D. Finally, we performed linear regression analyses and
463 thereby, for the first time, identified appetite and taste changes as predictors of %WL for SG
464 and RYGB respectively.

465
466 In conclusion, whilst subjective changes in appetite, taste, smell and food aversions are
467 common following both RYGB and SG, marked differences between them exist in relation to
468 the prevalence of changes in smell, taste, durability of changes, influence of gender and %WL.
469 The presence of gender differences highlights the need to study comparable numbers of
470 males and females. Furthermore, correlating gut hormone profiles with appetite and taste
471 changes, will not only aid to further our understanding of the biological mediators for weight
472 loss post-bariatric surgery allowing for personalised procedure allocation but may also lead
473 to novel therapies, such as taste modulation approaches.

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480

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484 **Figure Legends**

485

486 **Figure 1: Frequency of reported appetite, taste, smell changes and food aversions following**
487 **Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)**

488

489 A: Appetite changes (Q1) B: Taste changes (Q2) C: Smell changes (Q3) D: Food aversions (Q4)

490

491 **Figure 2: Change in taste toward sweet and salty foods**

492

493 Reported frequency of increased and decreased taste toward sweet (A) and salty (B) tasting
494 foods in Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) respectively.

495

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Q8. Has your overall taste increased in intensity since your weight loss surgery?

YES/ NO

Q9. Have you experienced an increase in taste for sweet foods?

YES/ NO

Q10. Have you experienced a decrease in taste for sweet foods?

YES/ NO

Q11. If you have had a loss of sweet taste, is that loss:

No loss				Partial				Complete	
1	2	3	4	5	6	7	8	9	10

Q12. Have you experienced an increase in taste for salty foods?

YES/ NO

Q13. Have you experienced a decrease in taste for salty foods?

YES/ NO

Q14. If you have had a loss of salty taste, is that loss:

No loss				Partial				Complete	
1	2	3	4	5	6	7	8	9	10

Q15. Have you experienced an increase in taste for sour foods?

YES/ NO

744 Q16. Have you experienced a decrease in taste for sour foods?

745

746 **YES/ NO**

747

748

749 Q17. If you have had a loss of sour taste, is that loss:

750

751 **No loss**

Partial

Complete

752

753 **1 2 3 4 5 6 7 8 9 10**

754

755

756 Q18. Has this change in taste affected how much you eat?

757

758 **YES/ NO**

759

760

761 Q19. In your opinion, has your change in taste affected your weight loss?

762

763 **YES/ NO**

764

765 Q20. Overall, do you feel that your taste has increased or decreased in intensity
766 since your weight loss surgery?

767

768 **Increased/ Decreased**

769

770

771 Q21. In your opinion, does loss of taste lead to better weight loss?

772

773 **YES/ NO**

774

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776 Q22. Is your postoperative change in taste greater or less than what you expected
777 preoperatively?

778

779 **Greater/ Less**

780

781

782 Q23. How important is taste to the enjoyment of food?

783

784 **Important/ Not important**

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787 Q24. Have you experienced an overall loss in your sense of smell since your weight loss
788 surgery?

789

790 **YES/ NO**

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Q25. If you have had a loss of smell, is that loss:

No loss		Partial						Complete	
1	2	3	4	5	6	7	8	9	10

Q26. Are there any foods that smell differently to you since your weight loss surgery?

YES/ NO

If yes, please state what food?

Q27. In your opinion, has your change in smell affected your weight loss?

YES/ NO

Q28. Overall, do you feel that your smell has increased or decreased in intensity since your weight loss surgery?

Increased/ Decreased

Q29. Is your postoperative change in smell greater or less than what you expected preoperatively?

Greater/ Less

Q30. How important is smell to the enjoyment of food?

Important/ Not important

Q31. Do you eat less food because it does not taste or smell good?

YES/ NO

Q32. Do you eat less food because you are simply not hungry?

YES/ NO

838

839 Q33. Is your postoperative change in appetite greater or less than what you expected
840 preoperatively?

841

842 **Greater/ Less**

843

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845