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Alcohol and other substance use after bariatric surgery: prospective evidence from a U.S. multicenter cohort study

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Abstract

Background: Empirical evidence suggests Roux-en-Y gastric bypass (RYGB) increases risk of developing alcohol use disorder (AUD). However, prospective assessment of substance use disorders (SUD) after bariatric surgery is limited.

Objective: To report SUD-related outcomes after RYGB and laparoscopic adjustable gastric banding (LAGB). To identify factors associated with incident SUD-related outcomes.

Setting: 10 U.S. hospitals

Methods: The Longitudinal Assessment of Bariatric Surgery-2 is an observational cohort study. Participants self-reported past-year AUD symptoms (determined by the Alcohol Use Disorders Identification Test), illicit drug use (cocaine, hallucinogens, inhalants, phencyclidine, amphetamines,

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or marijuana), and SUD treatment (counseling or hospitalization for alcohol or drugs) presurgery and annually postsurgery for up to 7 years through January 2015.

Results: Of 2348 participants who underwent RYGB or LAGB, 2003 completed baseline and follow-up assessments (79.2% women, baseline median age: 47 years, median body mass index 45.6). The year-5 cumulative incidence of postsurgery onset AUD symptoms, illicit drug use, and SUD treatment were 20.8% (95% CI: 18.5–23.3), 7.5% (95% CI: 6.1–9.1), and 3.5% (95% CI: 2.6–4.8), respectively, post-RYGB, and 11.3% (95% CI: 8.5–14.9), 4.9% (95% CI: 3.1–7.6), and .9% (95% CI: .4–2.5) post-LAGB. Undergoing RYGB versus LAGB was associated with higher risk of incident AUD symptoms (adjusted hazard ratio or AHR = 2.08 [95% CI: 1.51–2.85]), illicit drug use (AHR = 1.76 [95% CI: 1.07–2.90]) and SUD treatment (AHR = 3.56 [95% CI: 1.26–10.07]).

Conclusions: Undergoing RYGB versus LAGB was associated with twice the risk of incident AUD symptoms. One-fifth of participants reported incident AUD symptoms within 5 years post-RYGB. AUD education, screening, evaluation, and treatment referral should be incorporated in pre- and postoperative care. (Surg Obes Relat Dis 2017;▮:00–00.)

Keywords: Roux-en-Y gastric bypass; Gastric band; Obese; Substance use; Disorder; Addiction; Abuse; Treatment

Bariatric surgery is the most effective treatment for severe obesity, resulting in substantial and durable weight reduction, and improvement in or remission of obesity-related co-morbidities [1]. However, evidence is mounting that Roux-en-Y gastric bypass (RYGB) increases the risk of developing an alcohol use disorder (AUD) [2–5]. Pharmacokinetic studies provide evidence that RYGB, but not laparoscopic adjustable gastric band (LAGB), is associated with higher peak blood alcohol concentration, which is reached more quickly compared with presurgery status or nonsurgical controls [2,5]. Additionally, rodent models suggest that RYGB increases alcohol reward sensitivity via a neurobiological mechanism, independent of changes in alcohol absorption [2,5]. Hypothesized pathways include changes to the ghrelin system and altered genetic expression in regions of the brain associated with reward circuitry [2,5].

Studies utilizing medical records have documented overrepresentation of prior bariatric surgery, or specifically RYGB, among adults in substance use disorder (SUD) treatment programs [2,5,6]. However, findings from longitudinal studies of AUD-related outcomes before and after bariatric surgery are inconsistent [3–5], and few studies have long-term follow-up or evaluation of nonalcohol SUD [3,4], such that we have little understanding of whether the risk of AUD or nonalcohol SUD changes over time and the proportion of postsurgical patients that are ultimately affected. Recent literature reviews of AUD or SUD and bariatric surgery concluded there is a need for large, prospective, longitudinal studies that extend beyond 2 years, separate alcohol from other drug use, use standardized assessments, account for type of bariatric surgical procedure and identify risk factors for development of postsurgery AUD [3–5]. This study expands our prior work [7] and addresses these gaps in the literature by evaluating alcohol consumption, AUD symptoms, illicit drug use, and SUD treatment for 7 years after RYGB and LAGB, and identifying factors associated with incident SUD-related outcomes.

Materials and methods

Design and patients

The Longitudinal Assessment of Bariatric Surgery-2 (LABS-2) study is a prospective observational cohort study of patients at least 18 years old undergoing a first bariatric surgical procedure as clinical care by participating surgeons at ten hospitals from 6 clinical centers throughout the United States [8]. LABS-2 had a target sample size of 2400 participants based on anticipated loss to follow-up of $\leq$25% and the desire to detect small effect sizes (e.g., odds ratios of at least 2.0 for categorical outcomes) with 90% power. Patients were recruited by clinical research investigators and their research coordinators between February 2006 and February 2009. The institutional review board at each center approved the protocol, and participants gave written informed consent. The study is registered at ClinicalTrials.gov (NCT00465829).

Baseline assessments were conducted by research staff independent of clinical care after clearance for surgery [9]. Criteria for surgery eligibility differed by site and may have included screening for psychiatric disorders, including SUD [10,11]. Participants were informed that their responses were confidential, although informed consent specified that investigators could take steps to prevent serious harm. When participants reported having at least 5 drinks on a typical drinking day or illicit drug use, a safety protocol was triggered to assess the need for referral. Annual follow-up assessments were conducted within 6 months of the surgery anniversary date for 7 years or until January 31, 2015, whichever came first. Participants included in this report completed SUD-related measures at baseline and at least

one assessment after RYGB or LAGB (n = 2003; Fig. 1, supplement).

Measures

The same measures were collected at each assessment, excluding the 6-year assessment, which involved minimal data collection. Study-specific form descriptions have been previously reported [8].

Alcohol consumption and AUD symptoms

The Alcohol Use Disorders Identification Test (AUDIT) [12] is a 10-item test with well-established validity and reliability [11] designed to assess alcohol use and consequences in the prior 12 months. Regular alcohol consumption was defined as drinking ≥ twice per week. An AUDIT score (range: 0–40) ≥ 8 suggests harmful and hazardous alcohol use, and possible dependence [13]. Additionally, subsets of items indicate whether respondents experience symptoms of alcohol dependence (not being able to stop drinking once started, failing to meet normal expectations because of drinking, or needing a drink in the morning to get going), and alcohol-related harm (feeling guilt/remorse, being unable to remember, injuring someone, or eliciting concern due to drinking). Participants were categorized as having AUD symptoms (referred to as "AUD" throughout) if their AUDIT score was ≥8 or they endorsed any symptoms of alcohol dependence or alcohol-related harm.

Illicit drug use

Participants self-reported use of the following substances, "other than as prescribed by a physician," in the past 12 months: marijuana, amphetamines, cocaine, hallucinogens, inhalants, and phencyclidine. Additional names of each substance were provided (e.g., hashish, pot, speed, meth, crack, lysergic acid diethylamide [LSD], sniffing glue, angel dust, phenylcyclohexylpiperidine [PCP]). Illicit drug use was defined as endorsing any such use. Opioid use was not included due to difficulties in differentiating prescribed and nonprescribed use.

SUD treatment

Participants self-reported counseling and hospital admissions for psychiatric or emotional problems in the past 12 months, and if applicable, endorsed reason(s) for treatment, including "alcohol/drug abuse."

Incidence of SUD-related outcomes

Incidence was defined as the absence of the SUD-related outcome at baseline, in reference to the past 12 months, and presence of the SUD-related outcome at follow-up.

Other measures

Anthropometric measurements followed standardized protocols. Sociodemographic characteristics and smoking status were self-reported. Perceived social support was measured using the 12-item Interpersonal Support Evaluation List (ISEL-12) belonging domain score; a higher score (range: 0–12) indicates greater support availability [14]. Mental health was measured using the norm-based mental component scores from the Medical Outcomes Study 36-item Short-Form Health Survey (SF-36); a higher score (range: 0–100) indicates better functioning [15]. Binge eating disorder, loss of control eating, daily antidepressant medication use, current benzodiazepine use, past-year psychiatric counseling, and lifetime history of psychiatric hospitalization were assessed with LABS-2 forms [7,16].

Statistical analyses

Analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA). All reported P values are 2-sided; P values $< .05$ were considered to be statistically significant. The Pearson $\chi 2$ test for categorical variables, the Cochran–Armitage test for ordinal variables, and the Wilcoxon rank sum test for continuous variables were used to compare (1) preoperative characteristics of LABS-2 participants in the analysis sample to those excluded (Table 1, supplement), and (2) baseline characteristics by surgical procedure.

Longitudinal analyses performed with mixed models assumed the unstructured covariance matrix and used all available data, with control for baseline age, smoking status, and site, which were associated with missing follow-up data [17]. Sensitivity analyses were performed to examine the robustness of results with respect to the missing at random assumption (Appendix 1, supplement).

Poisson mixed models with robust error variance were used to estimate and test for trends in prevalence of outcomes over time, by surgical procedure. Observed data are reported online (Tables 2a, supplement).

Further analyses were restricted to participants without the corresponding SUD-related outcome at baseline. Time to event was calculated from surgery date to the first time AUD was reported. The product-limit estimate of cumulative incidence of postsurgery AUD was determined for annual assessments. Those never reporting AUD were treated as censored observations at the end of follow-up. Because relatively few participants remaining at risk by the final time point make estimates less reliable [18] cumulative incidence by surgical procedure is reported through year 5. This analysis was repeated for components of AUD, illicit drug use and its components, and SUD treatment.

Multivariable Cox proportional-hazard models were used to identify baseline factors associated with increased risk of incident AUD, illicit drug use, and SUD treatment. Independent variables were identified in the literature [7,19–27]:

Table 1
Characteristic of adults before bariatric surgery, by surgical procedure

	Total (n = 2003)*	RYGB (n = 1481)*	LAGB (n = 522)*	*P*
Sociodemographic characteristics				
Female, no. (%)	1586 (79.2)	1185 (8.0)	401 (76.8)	.12
Age, median (IQR), years	47 (37,55)	46 (37,54)	48 (38,57)	<.001
Race, no. (%)	(N = 1983)	(N = 1464)	(N = 519)	.12
White	1725 (87.0)	1260 (85.1)	465 (89.1)	
Black	196 (9.9)	154 (1.4)	42 (8.0)	
Other†	62 (3.1)	50 (3.4)	12 (2.3)	
Hispanic ethnicity, no./total no. (%)	92/2001 (4.6)	69/1480 (4.7)	23/521 (4.4)	.82
Relationship status, no. (%)	(N = 1993)	(N = 1472)	(N = 521)	.03
Never married	315 (15.8)	244 (16.6)	71 (13.6)	
Divorced, separated, or widowed	400 (2.1)	309 (21.0)	91 (17.5)	
Married or living as married	1278 (64.1)	919 (62.4)	359 (68.9)	
Education, no. (%)	(N = 1994)	(N = 1475)	(N = 519)	<.001
≤High school	464 (23.3)	352 (23.9)	112 (21.6)	
Some college	803 (4.3)	628 (42.6)	175 (33.7)	
≥College degree	727 (36.5)	495 (33.6)	232 (44.7)	
Employment status, no. (%)	(N = 1987)	(N = 1467)	(N = 520)	<.001
Employed	1355 (68.2)	1006 (68.6)	349 (67.1)	
Unemployed	75 (3.8)	65 (4.4)	10 (1.9)	
Disabled	298 (15.0)	229 (15.6)	69 (13.3)	
Other	259 (13.0)	167 (11.4)	92 (17.7)	
Household income, U.S. $, no. (%)	(N = 1940)	(N = 1434)	(N = 506)	<.001
<25,000	354 (18.2)	290 (2.2)	64 (12.6)	
25,000–49,000	505 (26.0)	403 (28.1)	102 (2.2)	
50,000–74,999	456 (23.5)	331 (23.1)	125 (24.7)	
75,000–99,999	312 (16.1)	218 (15.2)	94 (18.6)	
≥100,000	313 (16.1)	192 (13.4)	121 (23.9)	
Body mass index, median (IQR)‡	45.6 (41.7,51.1)	46.4 (42.4,51.7)	43.7 (4.4,48.2)	<.001
Mental health				
ISEL-12 Belonging score§	(N = 1994)	(N = 1742)	(N = 522)	
Median (IQR)	14 (12,16)	14 (12,16)	14 (12,16)	.60
SF-36 Mental Component Summary score¶	(N = 1966)	(N = 1450)	(N = 516)	
Median (IQR)	51.7 (43.0,57.2)	51.6 (42.8,57.4)	51.9 (44.0,57.0)	.87
Binge eating, no./total no. (%)	313/1968 (15.9)	219/1457 (15.0)	94/511 (18.4)	.07
Loss of control eating, no./total no. (%)	700/1979 (35.4)	498/1462 (34.1)	202/517 (39.1)	.04
Antidepressant medication, no./total no. (%)	746/1941 (38.4)	558/1431 (39.0)	188/510 (36.9)	.40
Benzodiazepine medication, no./total no. (%)	177/1952 (9.1)	136/1442 (9.4)	41/510 (8.0)	.35
Past-year psychiatric counseling, no./total no. (%)	455/1984 (22.9)	339/1468 (23.1)	116/516 (22.5)	.78
Lifetime history of psychiatric hospitalization, no./total no. (%)	198/1989 (1.0)	158/1470 (1.8)	40/519 (7.7)	.047
Substance use, past year				
Smoking, no./total no. (%)	238/2000 (11.9)	194/1478 (13.1)	44/522 (8.4)	<.01
Alcohol consumption, no. (%)	(N = 1995)	(N = 1475)	(N = 520)	<.01
None	821 (41.2)	636 (43.1)	185 (35.6)	
Any	1043 (52.2)	749 (5.8)	294 (56.5)	
Regular (≥2 times/week)	131 (6.6)	90 (6.1)	41 (7.9)	
AUD symptoms, no./total no. (%)	133/1988 (6.7)	97/1469 (6.6)	36/519 (6.9)	.79
Illicit drug use, no./total no. (%)	84/1985 (4.2)	64/1468 (4.4)	20/517 (3.9)	.63
SUD treatment, no./total no. (%)	8/1925 (.4)	7/1424 (.5)	1/501 (.2)	.38

RYGB = Roux-en-Y gastric bypass; LAGB = laparoscopic adjustable gastric banding; IQR = interquartile range; ISEL-12 = 12-item Interpersonal Support Evaluation List; SF-36 = Short-Form 36-item Health Survey; AUD = alcohol use disorder; SUD = Substance Use Disorder.

*Denominators shift between variables because of missing data.

†Racial categories were combined due to small numbers: 4 Asian, 13 Native American, 3 Pacific Islander, 30 multiple races among RYGB; 1 Asian, 1 Native American, 1 Pacific Islander, 9 multiple races among LAGB.

‡Calculated as weight in kilograms divided by height in meters squared.

§A lower score (range: 0–12) indicates less support availability.

¶A lower score (range: 0–100) indicates worse function.

site, surgical procedure, sex, race, baseline age, marital status, education, household income, history of psychiatric hospitalization, smoking status, and alcohol consumption, as well as baseline AUD and illicit drug use, when applicable. Ethnicity, employment status, body mass index, ISEL belonging score, Short-Form-36 mental component

summary score, binge eating, loss of control eating, antidepressant use, benzodiazepine use, and psychiatric counseling were also considered and retained if significant. As a sensitivity analysis, this analysis was repeated after excluding data collected after reversal of the initial bariatric procedure or a new bariatric procedure.

Poisson mixed models were used to determine whether preto postsurgery changes were related to postsurgery AUD, illicit drug use, and SUD treatment, with control for surgical procedure and baseline factors identified in the previous analysis. Percentage total weight loss, change from baseline in the ISEL belonging score and the SF-36 mental component score, with control for baseline values, and postsurgery marital status, employment status, loss of control eating, antidepressant use, benzodiazepine use, psychiatric counseling, smoking, and alcohol consumption, with consideration for baseline status (e.g., divorced versus remained married) were considered and retained if significant. AUD and illicit drug use were also included in models in which they were not the outcome. Postsurgery binge eating and psychiatric hospitalization, and change in education and income were too rare to evaluate as independent variables.

Once independent variables were selected (in both Cox and PMM models), interactions with surgical procedure were evaluated.

Results

Baseline characteristics of the analysis sample (n = 2003) and surgical groups are reported in Table 1. Participants undergoing RYGB versus LAGB differed with respect to age, marital status, education, unemployment, income, body mass index, loss of control eating, history of psychiatric hospitalization, smoking, and alcohol consumption.

SUD-related data were obtained from 78% (1684/2157), 70% (1503/2151), 67% (1434/2145), 66% (1408/2140), 67% (1418/2129), and 68% (1016/1494) of participants eligible for follow-up at years 1, 2, 3, 4, 5, and 7, respectively.

Substance use and SUD over time

Fig. 1 shows the modeled prevalence of regular alcohol consumption, AUD, illicit drug use, and SUD treatment over time, stratified by surgical procedure. These and additional outcomes are reported online (Table 2B, supplement). After RYGB only, presurgery-to-year-7 prevalence of AUD (6.6% [95% CI: 5.3–7.9] to 16.4% [95% CI: 14.1–18.7]; P < .001) and illicit drug use (4.4% [95% CI: 3.3–5.4] to 6.3% [95% CI: 4.7–7.9]; $P < .001$) increased, as did any and regular alcohol consumption, subcomponents of AUD, and marijuana use (P for quadratic trends < .01), but not other drug use ($P = .23$) or SUD treatment ($P = .18$). After LAGB there was a significant increase over time in any and regular alcohol consumption (P for quadratic trends = .01) only.

Incidence of postsurgery SUD

Fig. 2 shows the cumulative incidence of AUD and its subcomponents, illicit drug use, and SUD treatment over

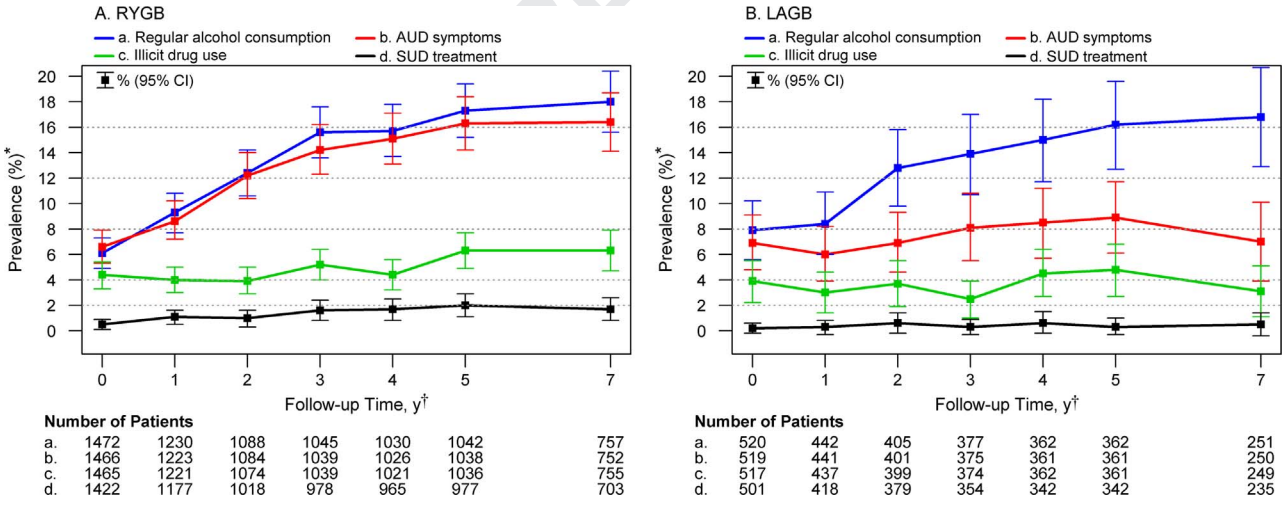

Fig. 1. Modeled prevalence of substance use and indicators of related problems among adults who underwent RYGB or LAGB. (A) Among RYGB participants, there were significant increases over time in prevalence of regular alcohol consumption, AUD, and illicit drug use (quadratic trends; P for all <.001) but not of SUD treatment ($P = .18$). (B) Among LAGB participants, there was a significant increase in prevalence of regular alcohol consumption over time (quadratic trend; $P = .01$). There was not a significant trend in AUD ($P = .09$), illicit drug use ($P = .33$), or SUD treatment ($P = .40$). AUD = alcohol use disorder; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; SUD = substance use disorder. *Annual assessments occurred within 6 months of the surgery anniversary date. Outcomes were not assessed at year 7. Data are based on observations until January 31, 2015; data collection ended before 432 RYGB and 177 LAGB participants were eligible for a 7-year assessment. †Models were adjusted for baseline factors related to missing follow-up data (age, smoking status, and site). Observed and modeled data are reported online in Table 2a and 2b, respectively, supplemental material.

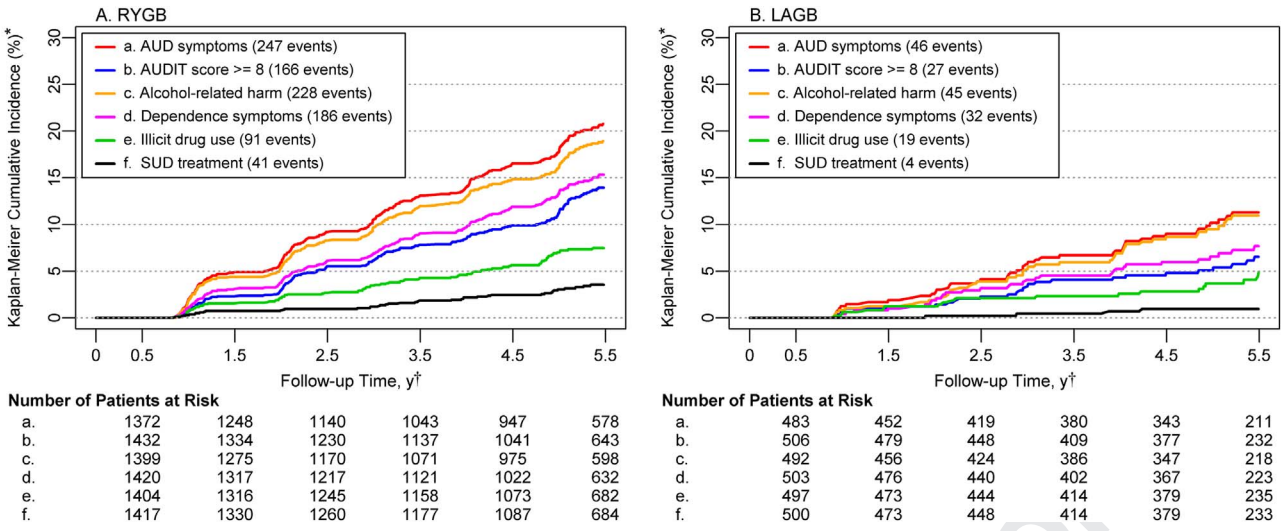

Fig. 2. Cumulative incidence of alcohol use disorder symptoms, its subcomponents, illicit drug use, and substance use disorder treatment among adults who underwent RYGB or LAGB.

Cumulative incidence of postsurgery SUD outcomes, among those without specified SUD outcome in the year presurgery, is shown by surgical procedure, as a function of time since surgery. AUD = alcohol use disorder; AUDIT = Alcohol Use Disorder Identification Test; LAGB = laparoscopic adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; SUD = substance use disorder. *Numbers at risk at each time point are those who had not reported SUD outcome since surgery and were not censored before or at the specified time point. Annual assessments occurred within 6 months of surgery anniversary date. †Modeled cumulative incidence with 95% CI of all SUD-related outcomes are reported in Table 3, supplemental material.

time, among participants who did not report the respective outcome at baseline. These and additional outcomes are reported online (Table 3, supplement). The 5-year cumulative incidence of AUD, illicit drug use, and SUD treatment was 20.8% (95% CI: 18.5–23.3), 7.5% (95% CI: 6.1–9.1), and 3.5% (95% CI: 2.6–4.8), respectively, after RYGB, and 11.3% (95% CI: 8.5–14.9), 4.9% (95% CI: 3.1–7.6), and .9% (95% CI: .4–2.5), respectively, after LAGB.

Baseline factors associated with incident SUD-related outcomes

Male sex, younger age, smoking, and any or regular alcohol consumption (versus none) presurgery were associated with increased risk of developing AUD and illicit drug use postsurgery (Table 2). Lower social support was also associated with increased risk of developing AUD, whereas low income, antidepressant use and a history of psychiatric hospitalization were also associated with increased risk of illicit drug use. Psychiatric counseling, a history of psychiatric hospitalization, smoking and symptoms of AUD presurgery were associated with increased risk of postsurgery SUD treatment. Compared with LAGB, undergoing RYGB was associated with a higher risk of incident AUD (AHR = 2.08 [95% CI: 1.51–2.85]), illicit drug use (AHR = 1.76 [95% CI: 1.07–2.90]) and SUD treatment (AHR = 3.56 [95% CI: 1.26–10.07]). In a sensitivity analysis in which data after reversal of the initial bariatric surgical procedure (n = 62) or new bariatric surgical procedure (n = 64) were excluded, associations between surgical procedure and SUD-related outcomes were similar: RYGB versus LAGB— AHR = 2.36 (95% CI: 1.68–3.33) for AUD, AHR = 1.76 (95% CI: 1.04–2.96) for illicit drug use, and AHR = 3.14 (95% CI: 1.10–8.94) for substance use treatment.

Pre- to postsurgery changes associated with postsurgery SUD

Less improvement/worsening mental health, getting divorced (versus remaining married), starting smoking (versus remaining a nonsmoker), and starting regular drinking (versus remaining a nonregular drinker) postsurgery were independently associated with a higher risk of postsurgery AUD, illicit drug use, and SUD treatment. Starting illicit drug use (versus continuing no use) was also associated with a higher risk of postsurgery AUD, whereas postsurgery onset AUD (versus continuing no AUD) was associated with a higher risk of illicit drug use and SUD treatment (Table 3). Additionally, stopping (versus continuing) regular drinking was associated with a lower risk of postsurgery AUD, and stopping (versus continuing) smoking was associated with a lower risk of illicit drug use.

Discussion

In this observational prospective study of adults with severe obesity, the prevalence of regular drinking doubled in the 7 years after both RYGB and LAGB. In contrast, the prevalence of AUD increased substantially over time after RYGB from approximately 7% presurgery to 16% at year 7,

Table 2
Presurgery predictors of incident postsurgery AUD symptoms, illicit drug use, and SUD treatment

	AUD symptoms (n = 1740)			Illicit drug use (n = 1749)			SUD treatment (n = 1817)		
	No. of Participants	AHR (95% CI)[*]	*P*	No. of participants	AHR (95% CI)[*]	*P*	No. of participants	AHR (95% CI)[*]	*P*
Sex			<.001			<.01			.24
Female	1379	1 [Reference]		1378	1 [Reference]		1429	1 [Reference]	
Male	361	1.74 (1.34–2.24)		371	1.92 (1.26–2.9)		388	1.49 (.77–2.88)	
Age, per 10 yr younger	1736	1.44 (1.29–1.60)	<.001	1749	1.43 (1.2–1.7)	<.001	1817	1.28 (.98–1.68)	.07
Race			.71			.39			.32
White	1515	1 [Reference]		1527	1 [Reference]		1580	1 [Reference]	
Black	173	.99 (.64–1.54)		172	1.33 (.69–2.54)		179	.34 (.08–1.47)	
Other	52	1.30 (.69–2.44)		50	1.56 (.74–3.29)		58	.59 (.08–4.44)	
Marital status[†]			.73			.75			.73
Single	611	1 [Reference]		608	1 [Reference]		649	1 [Reference]	
Married/living like married	1129	.95 (.73–1.24)		1141	1.07 (.71–1.61)		1168	1.11 (.60–2.07)	
Education			.10			.56			.88
≤High school	404	1 [Reference]		386	1 [Reference]		410	1 [Reference]	
Some college	708	.79 (.58–1.08)		707	1.25 (.78–2.02)		734	1.20 (.58–2.48)	
College degree	628	1.05 (.77–1.42)		656	1.04 (.61–1.77)		673	1.11 (.51–2.41)	
Household income[‡]			.54			<.01			.73
≥$25,000	1422	1 [Reference]		1447	1 [Reference]		1506	1 [Reference]	
<$25,000	318	.89 (.63–1.28)		302	2.14 (1.34–3.40)		311	.86 (.38–1.95)	
ISEL-12 Belonging score, per 1 point lower[§]	1740	1.06 (1.01–1.11)	.01			[†]			[†]
Antidepressant medication use			[†]			.049			[†]
No				1081					
Yes				668	1.49 (1.01–2.21)				
Psychiatric counseling			[†]			[†]			.01
No							1432	1 [Reference]	
Yes							385	2.17 (1.18–3.98)	
History of psychiatric hospitalization			.45			.02			<.001
No	1570	1 [Reference]		1586	1 [Reference]		1650	1 [Reference]	
Yes	170	1.16 (.79–1.71)		163	1.76 (1.09–2.85)		167	3.96 (2.06–7.62)	
Smoking			.04			<.01			.04
No	1547	1 [Reference]		1557	1 [Reference]		1608	1 [Reference]	
Yes	193	1.41 (1.02–1.96)		192	2.06 (1.30–3.27)		209	2.07 (1.04–4.12)	
Alcohol consumption			<.001			.03			.37
No consumption	762	1 [Reference]		716	1 [Reference]		733	1 [Reference]	
Some but not regular consumption	900	2.95 (2.17–4.03)		921	1.73 (1.13–2.66)		960	1.02 (.52–1.99)	
Regular consumption (≥2 drinks/wk)	78	12.68 (8.34–19.26)		112	1.99 (.82–4.84)		124	1.98 (.69–5.71)	
AUD			NA			.98			.01
No				1638	1 [Reference]		1693	1 [Reference]	
Yes				111	.99 (.49–2.02)		124	2.80 (1.25–6.28)	

Table 2
Continued.

	AUD symptoms (n = 1740)			Illicit drug use (n = 1749)			SUD treatment (n = 1817)		
	No. of Participants	AHR (95% CI)*	P	No. of participants	AHR (95% CI)*	P	No. of participants	AHR (95% CI)*	P
Illicit drug use			.07			NA			.65
No	1680	1 [Reference]					1743	1 [Reference]	
Yes	60	1.60 (.96–2.66)					74	1.27 (.45–3.60)	
Surgical procedure¶			<.001			.03			.02
LAGB	1284	1 [Reference]		1287	1 [Reference]		1338	1 [Reference]	
RYGB	456	2.08 (1.51–2.85)		462	1.76 (1.07–2.90)		479	3.56 (1.26–1.07)	

AUD = alcohol use disorder; SUD = substance use disorder; AHR = adjusted hazard ratio; ISEL-12, 12-item Interpersonal Support Evaluation List; LAGB = laparoscopic adjustable gastric band; NA = not applicable; RYGB = Roux-en-Y gastric bypass.

*Cox proportional hazards models adjusted for other variables as indicated in this table, as well as site.

†This variable was considered but not retained (P > .05). Ethnicity, employment status, body mass index, SF-36 mental component summary score, binge eating, loss of control eating, and benzodiazepine use were also considered but not retained in any models (P for all > .05).

‡Categories that did not differ with respect to the outcome were collapsed.

§A lower score (range: 0–12) indicates less support availability.

¶There were no significant interactions with surgical procedure.

while remaining stable after LAGB between 6% and 8%. Due to differences in baseline characteristics (e.g., age, income, smoking), the RYGB versus LAGB subgroup appeared to have higher risk for AUD. However, after excluding participants who reported the respective outcome at baseline and controlling for potential confounders, treatment with RYGB versus LAGB was independently associated with approximately twice the risk of incident AUD and illicit drug use and nearly quadruple the risk of incident SUD treatment over 7 years of follow-up. Thus our results strongly suggest that RYGB increases risk of developing AUD, using illicit drugs, and undergoing SUD treatment, and that the prevalence of AUD continues to climb for many years after RYGB.

Very few studies have longitudinally evaluated SUD-related outcomes more than 2 years after bariatric surgery. An exception is the Swedish Obesity Study, which began in 1987 and primarily includes surgical procedures no longer performed [3,19] Consistent with our findings, compared with nonsurgical controls or banding patients, gastric bypass patients (n = 265) had higher risk for incident alcohol abuse diagnoses, medium/high risk alcohol consumption, and self-reported alcohol problems over 8 or more years of follow-up [19]. However, the 6-year cumulative incidence of these outcomes was approximately 4%–5%, whereas in the current report we found that one-fifth of participants without AUD in the year before surgery reported AUD at least once within 5 years after RYGB. Although not all of these participants necessarily met Diagnostic and Statistical Manual of Mental Disorders (Fifth Edition) criteria for AUD [28], most reported symptoms of alcohol dependence and alcohol-related harm.

Similar to previous SUD research [26,27], male sex and younger age were identified as risk factors for incident AUD and illicit drug use, whereas low income (<$25,000/year) was associated with incident illicit drug use only. Different psychiatric variables were predictive of incident AUD (i.e., less social support) and illicit drug use (i.e., antidepressant medication use, history of psychiatric hospitalization), whereas worsening mental quality of life [20,23] and divorce [24] were independently associated with all 3 SUD-related outcomes, as were initiating smoking and initiating regular drinking postsurgery. Initiating AUD or illicit drug use postsurgery was also associated with increased risk of the other, suggesting common causal factors [26]. Contrary to the “addiction transfer” hypothesis [2], binge eating and loss of control eating were not associated with SUD-related outcomes. Weight loss was also not related to any SUD-related outcomes, which is contrary to findings by Reslan et al. in which patients with a lower percentage total weight loss were more likely to endorse substance misuse [22]. Although it was outside the scope of the present study, future research should investigate the role of gut-brain neuroendocrine signaling (e.g., changes in ghrelin, as a risk factor) in risk of developing SUD after bariatric surgery [5].

Table 3
Independent associations of participant characteristics and surgical procedure with postsurgery AUD symptoms, illicit drug use and SUD treatment, among participants without the respective condition in the year before surgery

	AUD symptoms (n = 1703)		Illicit drug use (n = 1578)		SUD treatment (n = 1772)	
	ARR (95% CI)*	*P*	ARR (95% CI)*	*P*	ARR (95% CI)*	*P*
Pre- to postsurgery change						
SF-36 mental component summary score, per 10 points lower†	1.15 (1.07–1.23)	<.001	1.24 (1.10–1.40)	<.001	1.38 (1.15–1.66)	<.001
Pre- and postsurgery status						
Marital status‡		<.01		.01		.048
Got married versus remained single	.66 (.43–1.00)		1.33 (.79–2.24)		.77 (.31–1.92)	
Became single versus remained married	1.60 (1.20–2.13)		2.23 (1.33–3.74)		2.20 (1.19–4.07)	
Single versus married§	1.32 (1.04–1.67)		1.10 (.70–1.73)		.93 (.49–1.77)	
Smoking		<.001		<.001		<.01
Started versus continued not to	1.63 (1.18–2.25)		2.63 (1.43–4.83)		2.88 (1.49–5.55)	
Stopped versus continued	.71 (.48–1.04)		.51 (.27–.98)		.46 (.13–1.69)	
Yes versus no[d]	1.71 (1.26–2.31)		2.76 (1.73–4.42)		2.24 (1.00–5.03)	
Regular alcohol consumption		<.001		.03		<.01
Started versus continued not to	7.39 (5.91–9.23)		1.79 (1.19–2.70)		2.77 (1.63–4.71)	
Stopped versus continued	.30 (.16–.57)		1.51 (.03–3.20)		2.93 (.56–15.47)	
Yes versus no[d]	13.64 (9.74–19.10)		1.14 (.50–2.64)		1.06 (.39–2.90)	
AUD symptoms		NA		<.01		<.001
Started versus continued not to			2.36 (1.46–3.79)		6.51 (3.42–12.39)	
Stopped versus continued			1.00 (.39–2.55)		.21 (.02–2.11)	
Yes versus no§			1.65 (.72–3.78)		6.40 (2.54–16.16)	
Illicit drug use		.02		NA		.78
Started versus continued not to	1.45 (1.08–1.94)				.75 (.31–1.78)	
Stopped versus continued	1.12 (.56–2.26)				.37 (.02–8.25)	
Yes versus no§	1.55 (.83–2.90)				.99 (.25–3.98)	

AUD = alcohol use disorder; SUD = substance use disorder; ARR = adjusted relative risk; SF-36 = Short-Form 36-item Health Survey; NA = not applicable.

*Poisson models with robust error variance assuming the unstructured covariance matrix, adjusted for baseline variables shown in Table 2 and other variables as indicated in this table. The following variables were also considered as independent variable but were not retained because they were not significant ($P > .05$): percentage weight loss from baseline, pre- to postsurgery change in the Interpersonal Support Evaluation List Belonging score, pre/postsurgery status for employment, loss of control eating, antidepressant medication, psychiatric counseling and benzodiazepine medication. There were no significant interactions with surgical procedure.

†A lower score (range: 0–100), indicates worse function.

‡The "married" category includes "married" and "living like married."

§Status pre- and postsurgery.

Incidence of SUD treatment after both procedures was much lower than the incidence of AUD symptoms, indicating treatment may be underutilized. This is troubling given the availability of a wide range of effective treatments for AUD, including brief drinking reduction interventions in medical settings, evidence-based manualized behavioral treatments (e.g., 12-step facilitation, motivational interviewing), and medications (e.g., naltrexone) [29]. In addition to undergoing RYGB, history of psychiatric hospitalization and psychiatric counseling in the year before surgery were strong predictors of incident SUD treatment, possibly reflecting greater medical surveillance or willingness to receive SUD treatment. The increase in the prevalence of regular drinking after both RYGB and LAGB may also have important implications as alcohol consumption may affect weight or induce dumping syndrome, vitamin deficiencies, dehydration, or alcoholic liver disease [11]. Together, our findings strongly support the need for routine pre- and postsurgery alcohol and AUD education, screening, and evaluation, and referral for treatment when appropriate.

Illicit drug use in this study was primarily explained by marijuana use, which increased in popularity across the country during the timeframe of this study [30]. However, not all relevant drugs of abuse (i.e., opioids and benzodiazepine) [31] were assessed. Thus the measured prevalence and cumulative incidence of illicit drug use were likely underestimated. Additionally, determination of illicit drug use was based on self-report of any use rather than symptoms of abuse or dependence or clinical diagnosis. Thus, although RYGB versus LAGB was significantly associated with risk of incident illicit drug use in this study, more work is needed to clarify whether bariatric surgical procedures affect risk of nonalcohol SUD.

Additional study limitations should be considered when interpreting results. First, the study did not have a nonsurgical control group nor did it randomize participants to surgery. To address this source of bias, analysis evaluating

associations with surgical procedure controlled for potential confounders. Still, the findings cannot necessarily be attributed to the surgery itself. Second, although participants were informed that research data were confidential, there was a potential for underreporting of SUD-related outcomes. Underreporting may have differed over time, but should not have differed by surgical procedure. Third, due to the unique criteria used to establish SUD-related outcomes in this study, comparisons with other studies should be made with caution. Fourth, this study excluded the gastric sleeve procedure, which although popular today [1] accounted for <5% of procedures in the LABS-2 cohort [9]. Finally, because we did not measure lifetime history of SUD-related outcomes, incident cases included new-onset and recurrent cases, which might differ with respect to risk factors. Furthermore, we cannot estimate the incidence of new-onset AUD.

Notable strengths of this study are its large, geographically diverse sample, longitudinal design, standardized and detailed data collection, which allowed us to evaluate many potential risk factors, use of a validated and reliable alcohol screening tool, assessment of past-year substance use (i.e., smoking, alcohol, and illicit drugs), which may differ from current use, especially at the baseline assessment, follow-up through 7 years, and high retention. These factors should make the results of our study generalizable to clinical practice. Although missing follow-up data are a concern, the initial sample size and retention rate were adequate to ensure sufficient statistical power for the primary outcome. Additionally, analyses controlled for baseline factors related to missing follow-up data and the sensitivity analysis indicated that the missing data has minimal effect on the results.

Conclusion

Among adults with severe obesity, undergoing RYGB was associated with increased risk of incident AUD symptoms, illicit drug use, and SUD treatment. Several nonsurgical risk factors for postsurgery AUD and illicit drug use were also identified. Patients considering bariatric surgery should be informed of risk factors for postsurgery AUD, including type of procedure. Additionally, alcohol and AUD screening, evaluation, and referral for treatment should be incorporated into pre- and postoperative care.

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Appendix

Supplementary data

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.soard.2017.03.021.

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