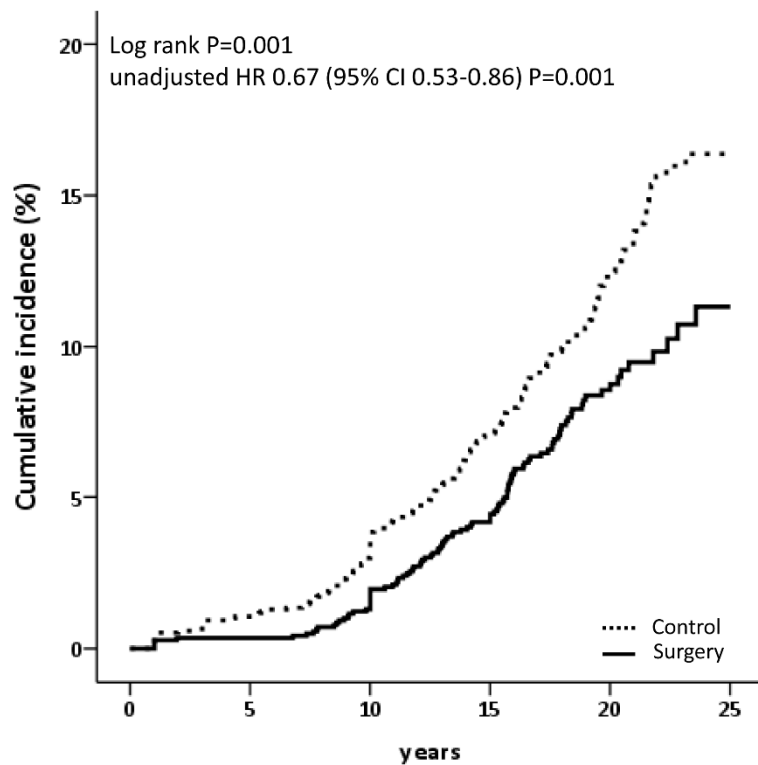
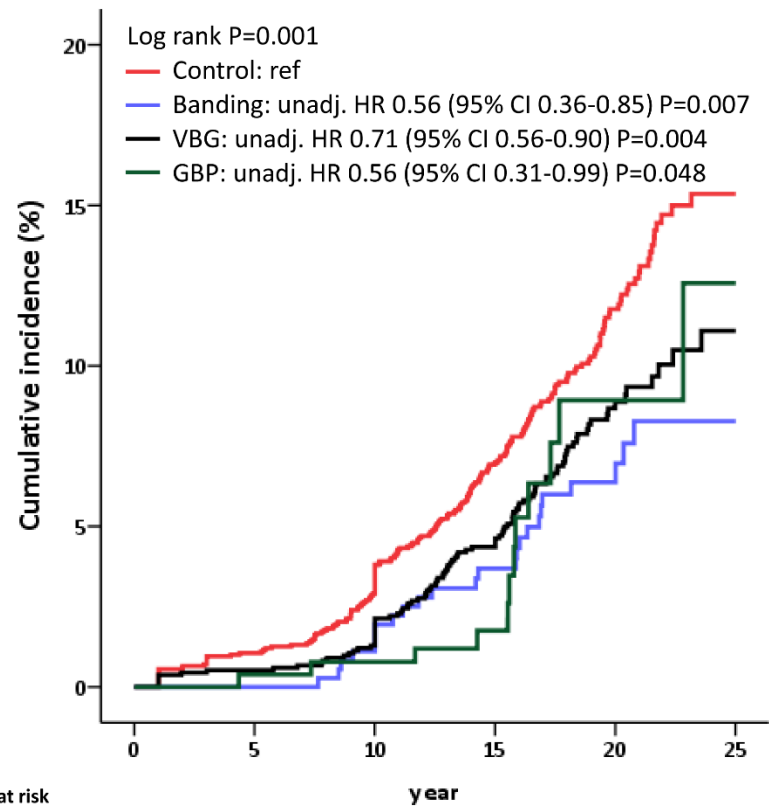


Supplementary Figure 1. Flow scheme of the present report. A, analysis on gout incidence. B, analysis on hyperuricemia incidence. Boxes on the right indicate subjects excluded from the present report.



Number at risk		0	5	10	15	20	25
Control		1715	1671	1582	1257	535	28
Surgery		1426	1394	1341	1086	456	19
Number of events		0	23	69	170	261	285

Supplementary Figure 2. Per Protocol Analysis of Gout Incidence. Kaplan-Meier unadjusted estimates of the cumulative incidence of gout in the bariatric surgery group and in the control group. The analyses were performed after excluding subjects from the control group who underwent bariatric surgery as well as subjects from the surgery group who underwent additional bariatric procedures during follow-up. A total of 181 events occurred in the control group (11%, median follow-up 18.7 years [range 0-26]) as compared to 104 in the surgery group (7%, median follow-up 18.7 years [range 0-26]). Survival distributions in the control and surgery groups were compared by a log rank test. After adjustment (for sex, baseline age, body-mass index, serum creatinine, smoking habit, hypertension, type 2 diabetes, hyperuricemia, previous cardiovascular events, self-reported co-medications associated with gout risk and alcohol intake) results are virtually unchanged: HR 0.60 (95% CI 0.46 to 0.77), $P < 0.001$. The estimated number needed to treat (NNT) with bariatric surgery to prevent one event over the course of 15 years was 35 (95% CI 23 to 73).



	0	5	10	15	20	25
Number at risk						
Control	1999	1952	1857	1465	619	32
Banding	372	362	355	302	159	11
VBG	1347	1319	1278	1087	455	23
GBP	263	257	243	136	40	6
Number of events	0	29	81	205	313	339

Supplementary Figure 3. Cumulative Incidence of Gout Stratified by Surgical Procedure. Kaplan-Meier unadjusted estimates of the cumulative incidence of gout in the bariatric surgery group and in the control group according to intention-to-treat principle. A total of 201 events occurred in the control group (10%, median follow-up 18.6 years [range 0-26]) as compared to 24 in the banding group (6%, median follow-up 19.6 years [range 0-26]), 102 in the vertical banded gastroplasty (VBG) group (8%, median follow-up 18.9 years [range 0-26]), and 12 in the gastric bypass (GBP) group (5%, median follow-up 15.1 years [range 0-26]). Survival distributions in the control and surgery groups were compared by a log rank test. After adjustment (for sex, baseline age, body-mass index, serum creatinine, smoking habit, hypertension, type 2 diabetes, previous cardiovascular events and self-reported co-medications associated with gout risk) the hazard ratios were as follows: banding, HR 0.52 (95% CI 0.34 to 0.80) P=0.003; VBG, HR 0.66 (95% CI 0.51 to 0.85) P=0.001; GBP, HR 0.50 (95% CI 0.28

to 0.90) $P=0.02$. The estimated number needed to treat (NNT) with bariatric surgery to prevent one event over the course of 15 years was 31 (95% CI 21 to 60) for banding, 39 (95% CI 24 to 107) for VBG and 19 (95% CI 14 to 33) for GBP.

Supplementary Table 1. Risk Factor-Treatment Interaction Analyses for Gout Incidence.

Variable, sub-grouping at baseline	Incidence of Gout, IR per 1000 Person-Years*						Relative Treatment Effects			
	No.	Surgery Person- Years	IR (95%CI)	No.	Control Person- Years	IR (95%CI)	Hazard Ratio (95% CI)	P Value for HR	P Value for inter- action†	NNT (95% CI)
Total							0.66 (0.53-0.82)	<0.001	-	32 (22-59)
Age, years										
≤47.7	1093	19925	2.4 (1.8-3.1)	902	16414	3.8 (3.0-4.9)	0.61 (0.42-0.89)	0.01	0.33	53 (28-467)
>47.7	889	15537	5.9 (4.8-7.2)	1097	18337	7.5 (6.4-8.9)	0.76 (0.58-0.98)	0.04		28 (18-81)
Sex										
Men	573	9871	5.7 (4.4-7.4)	568	9511	9.4 (7.6-11.5)	0.60 (0.43-0.84)	0.003	0.47	17 (10-44)
Women	1409	25591	3.2 (2.6-4.0)	1431	25240	4.4 (3.7-5.3)	0.70 (0.53-0.93)	0.01		50 (29-170)
Body-mass index										
≤40.8	787	14165	3.2 (2.-4.3)	1213	21342	5.5 (4.6-6.6)	0.58 (0.41-0.82)	0.002	0.44	32 (20-86)
>40.8	1195	21297	4.3 (3.5-5.3)	786	13409	6.2 (5.0-7.7)	0.67 (0.50-0.90)	0.008		29 (18-90)
Weight, kg										
≤116	874	15893	2.6 (2.0-3.6)	1149	20300	5.3 (4.4-6.4)	0.49 (0.34-0.70)	<0.001	0.98	25 (18-43)
>116	1108	19570	4.9 (4.0-6.0)	850	14451	6.4 (5.3-7.9)	0.74 (0.56-0.99)	0.04		36 (19-245)
Waist, cm										
≤118	896	16472	2.3 (1.7-3.2)	1196	21177	5.0 (4.1-6.1)	0.46 (0.32-0.66)	<0.001	0.21	27 (19-50)
>118	1081	18907	5.2 (4.3-6.3)	803	13573	7.0 (5.7-8.6)	0.72 (0.55-0.96)	0.02		30 (18-110)
Systolic blood pressure, mmHg										
≤140	1002	17908	2.5 (1.8-3.3)	1284	22551	4.6 (3.8-5.5)	0.53 (0.37-0.75)	<0.001	0.19	43 (26-130)
>140	975	17477	5.3 (4.3-6.5)	711	12122	8.0 (6.5-9.7)	0.64 (0.48-0.85)	0.002		19 (12-39)
Diastolic blood pressure, mmHg										
≤88	825	14568	2.5 (1.8-3.4)	1208	20858	4.8 (4.0-5.9)	0.50 (0.34-0.73)	<0.001	0.11	29 (19-69)
>88	1151	20790	4.9 (4.0-5.9)	784	13764	7.2 (5.9-8.8)	0.66 (0.50-0.87)	0.003		26 (16-74)
Hypertension										
No	437	7779	1.3 (0.7-2.4)	732	12928	3.4 (2.5-4.6)	0.37 (0.19-0.74)	0.005	0.16	33 (20-96)

Yes	1545	27684	4.6 (3.9-5.5)	1267	21823	7.2 (6.2-8.4)	0.63 (0.50-0.79)	<0.001		25 (17-49)
Uric acid, mg/dl										
≤5.9	951	17149	1.7 (1.2-2.4)	1062	18991	2.5 (1.9-3.4)	0.66 (0.41-1.04)	0.07	0.67	333 (59-∞)††
>5.9	1026	18229	5.9 (4.9-7.1)	934	15726	9.7 (8.3-11.4)	0.59 (0.46-0.75)	<0.001		15 (11-23)
Uric acid ≥ 6.8 mg/dl										
No	1475	26610	2.2 (1.7-2.8)	1533	27394	3.2 (2.6-4.0)	0.67 (0.48-0.93)	0.02	0.32	100 (44-∞)††
Yes	502	8768	8.9 (7.1-11.1)	463	7323	15.4 (12.8-18.6)	0.56 (0.42-0.74)	<0.001		9 (6-15)
Creatinine, mg/dl										
≤0.78	1048	19220	3.3 (2.6-4.3)	1017	18442	4.3 (3.4-5.3)	0.77 (0.55-1.07)	0.11	0.55	48 (26-242)
>0.78	930	16180	4.4 (3.5-5.6)	980	16281	7.5 (6.3-8.9)	0.58 (0.43-0.77)	<0.001		24 (15-55)
Insulin, mU/l										
≤16.9	844	15349	2.8 (2.1-3.8)	1135	19958	5.1 (4.2-6.2)	0.54 (0.38-0.77)	0.001	0.99	29 (20-58)
>16.9	1129	19967	4.7 (3.8-5.8)	861	14758	6.8 (5.6-8.2)	0.68 (0.51-0.90)	0.008		26 (16-66)
Type 2 diabetes										
No	1641	29682	3.6 (3.0-4.3)	1746	29681	5.1 (4.3-5.9)	0.69 (0.54-0.89)	0.003	0.15	37 (24-86)
Yes	334	5675	5.6 (4.0-8.0)	249	3905	11.3 (8.4-15-1)	0.48 (0.30-0.75)	0.001		14 (8-62)
Total cholesterol, mg/dl										
≤219	891	15769	3.4 (2.6-4.4)	1100	19098	4.5 (3.6-5.6)	0.73 (0.52-1.03)	0.07	0.29	34 (21-91)
>219	1087	19631	4.2 (3.4-5.2)	897	15625	7.4 (6.1-8.8)	0.57 (0.43-0.75)	<0.001		26 (16-62)
Alcohol intake, g/day										
≤2.15	976	17775	3.2 (2.5-4.2)	1014	17886	4.6 (3.7-5.8)	0.67 (0.48-0.94)	0.02	0.81	45 (25-254)
>2.15	1006	17688	4.6 (3.7-5.7)	984	16847	7.0 (5.9-8.4)	0.64 (0.48-0.85)	0.002		23 (15-48)
Previous cardiovascular events										
No	1939	34792	3.9 (3.3-4.6)	1955	34103	5.7 (4.9-6.5)	0.67 (0.54-0.84)	<0.001	0.32	32 (22-59)
Yes	43	670	4.5 (1.4-13.9)	44	648	12.3 (6.2-24.7)	0.35 (0.09-1.34)	0.13		31 (6-∞)
Smoking										
No	1467	26430	4.3 (3.6-5.2)	1572	27537	5.7 (4.9-6.7)	0.74 (0.58-0.94)	0.01	0.10	36 (22-90)
Yes	513	8999	2.7 (1.8-4.0)	417	7076	5.7 (4.1-7.7)	0.46 (0.28-0.77)	0.003		27 (15-141)

Drugs associated with gout risk†††										
No	1549	27816	2.9 (2.4-3.7)	1585	27935	4.5 (3.8-5.4)	0.64 (0.49-0.85)	0.002	0.97	40 (26-92)
Yes	433	7646	7.3 (5.6-9.5)	414	6916	11.0 (8.8-13.8)	0.64 (0.45-0.91)	0.01		17 (10-69)

Risk factor-treatment interaction for gout diagnosis in subgroups and number needed to treat (NNT) by bariatric surgery to prevent one gout event over 15 years. To convert the values for uric acid to micromoles per liter, multiply by 59.48. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for insulin to picomoles per liter, multiply by 6.945. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. CI denotes confidence interval.

* Gout events in high-risk and low-risk subgroups. For continuous variables, subgrouping is based on median baseline values. IR denotes incidence rate.

† For each continuous variable, the test of interaction was calculated using the original continuous variable. Dichotomous variables, including uric acid when dichotomized, could have one of two values (e.g. men/women or uric acid \geq 6.8 mg/dl, yes/no). The interaction P value reflects the difference in relative treatment effect between the indicated high- and low-risk subgroups.

†† Significant difference between the two subgroups with respect to number needed to treat.

††† Drugs associated with gout risk: diuretics, β -blockers, low-dose acetylsalicylic acid, statins, cyclosporine and organic nitrates.

Supplementary Figure 4. Serum Uric Acid Levels (A) and Changes (B) in the Control and Surgery Group during Follow-Up. Serum uric acid levels are shown as mean and standard deviation (A). Serum uric acid changes are shown as mean and 95% confidence interval (B). P values have been calculated by linear regression analysis adjusted for sex and baseline age and body-mass index. Further adjustment for risk factors does not affect the result.

