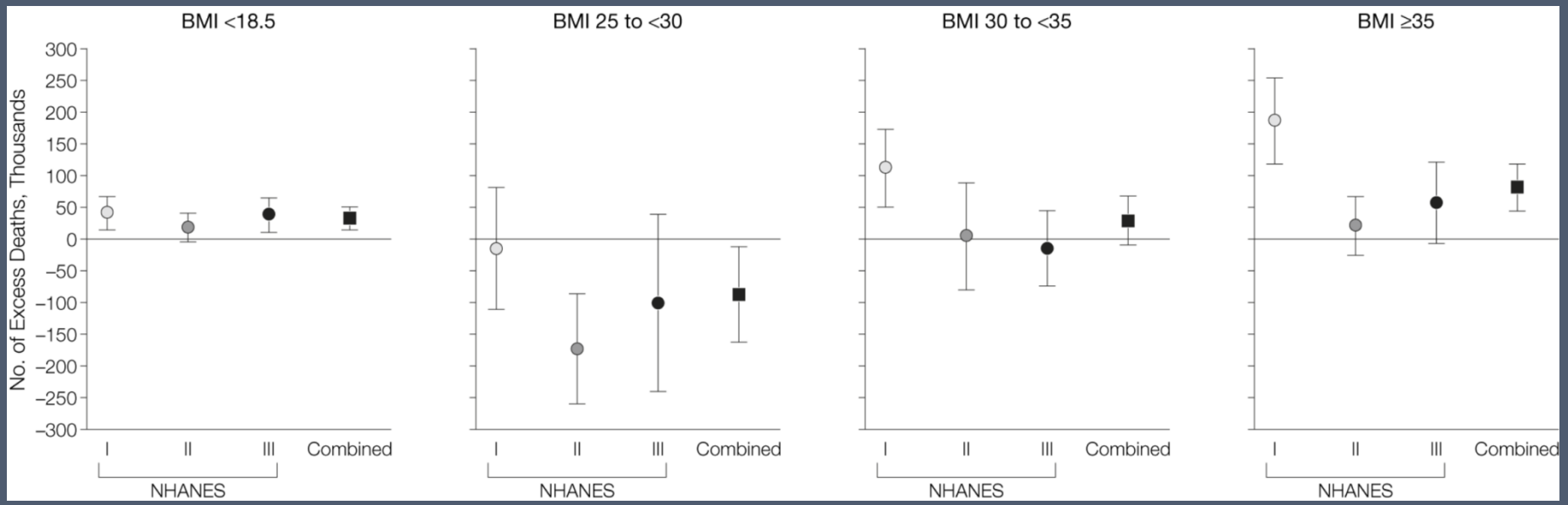
La terapia del diabete tipo 2 con chirurgia bariatrica: evidenze cliniche

Padova 7 marzo 2014

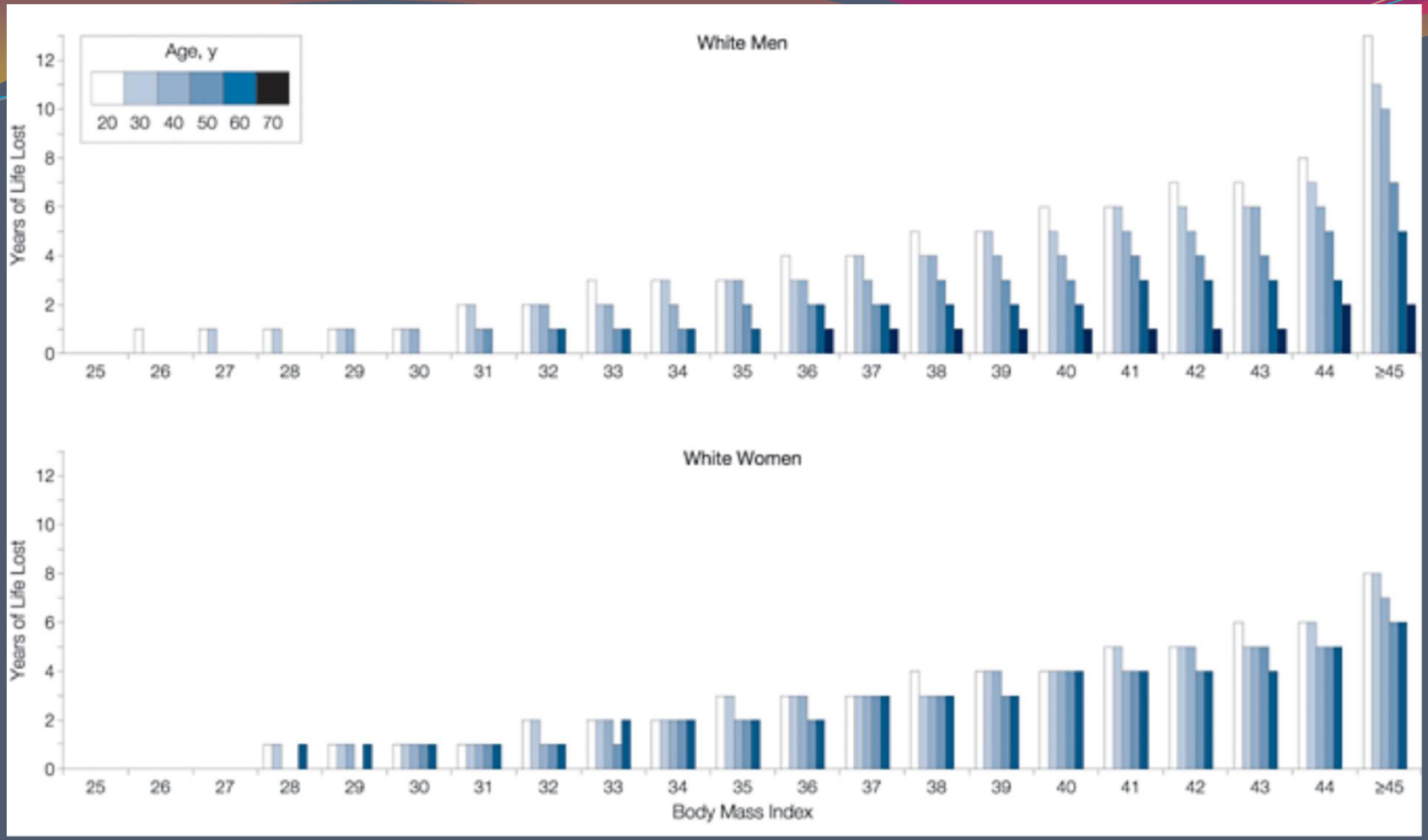
Geltrude Mingrone

Istituto di Clinica Medica
Università Cattolica S. Cuore
Roma



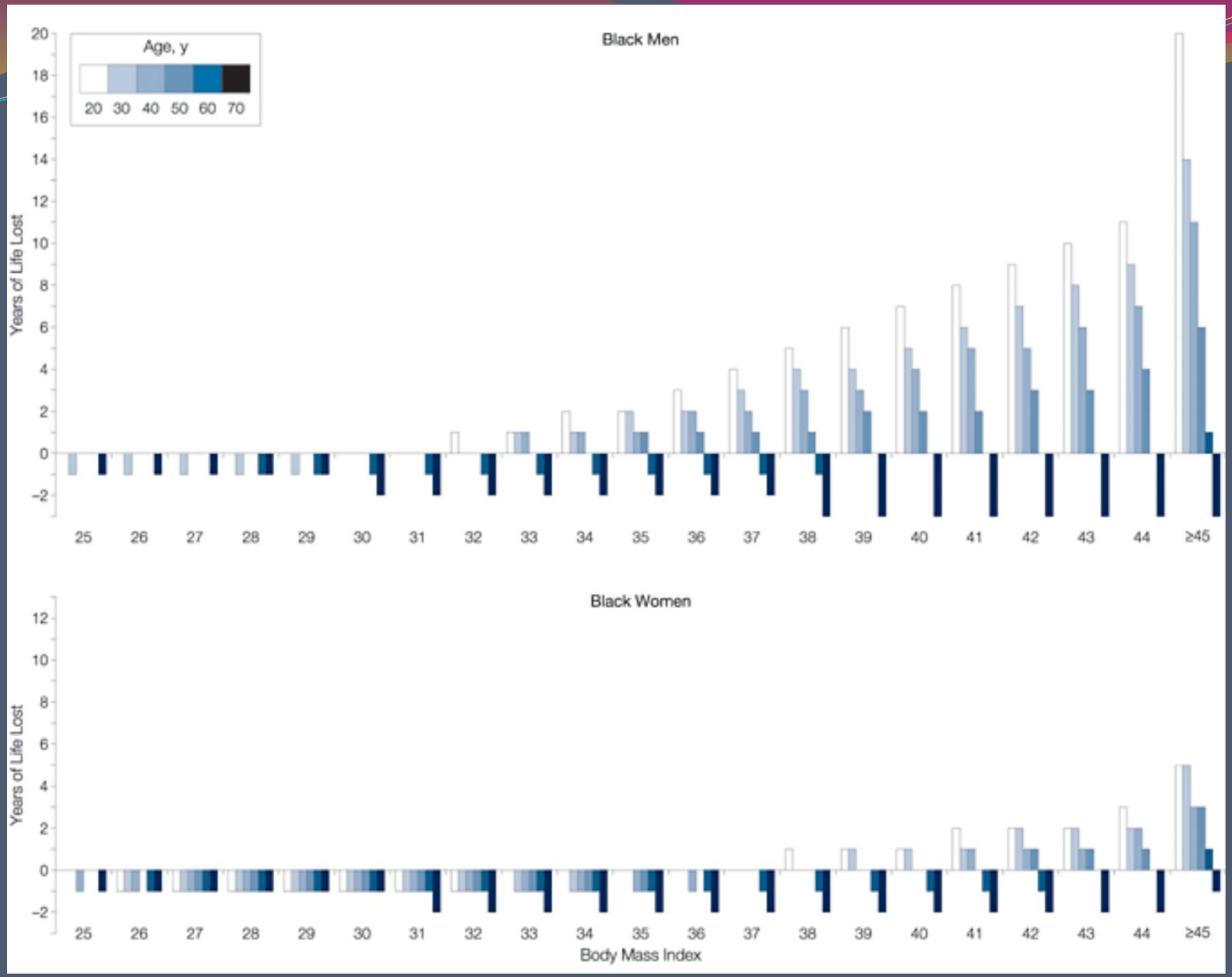
From: **Excess Deaths Associated With Underweight, Overweight, and Obesity**

JAMA. 2005;293(15):1861-1867. doi:10.1001/jama.293.15.1861



From: **Years of Life Lost Due to Obesity**

JAMA. 2003;289(2):187-193. doi:10.1001/jama.289.2.187


Black Men
Age, y
20 30 40 50 60 70
Years of Life Lost
20
18
16
14
12
10
8
6
4
2
0
−2
25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 ≥45
Black Women
Years of Life Lost
12
10
8
6
4
2
0
−2
25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 ≥45
Body Mass Index

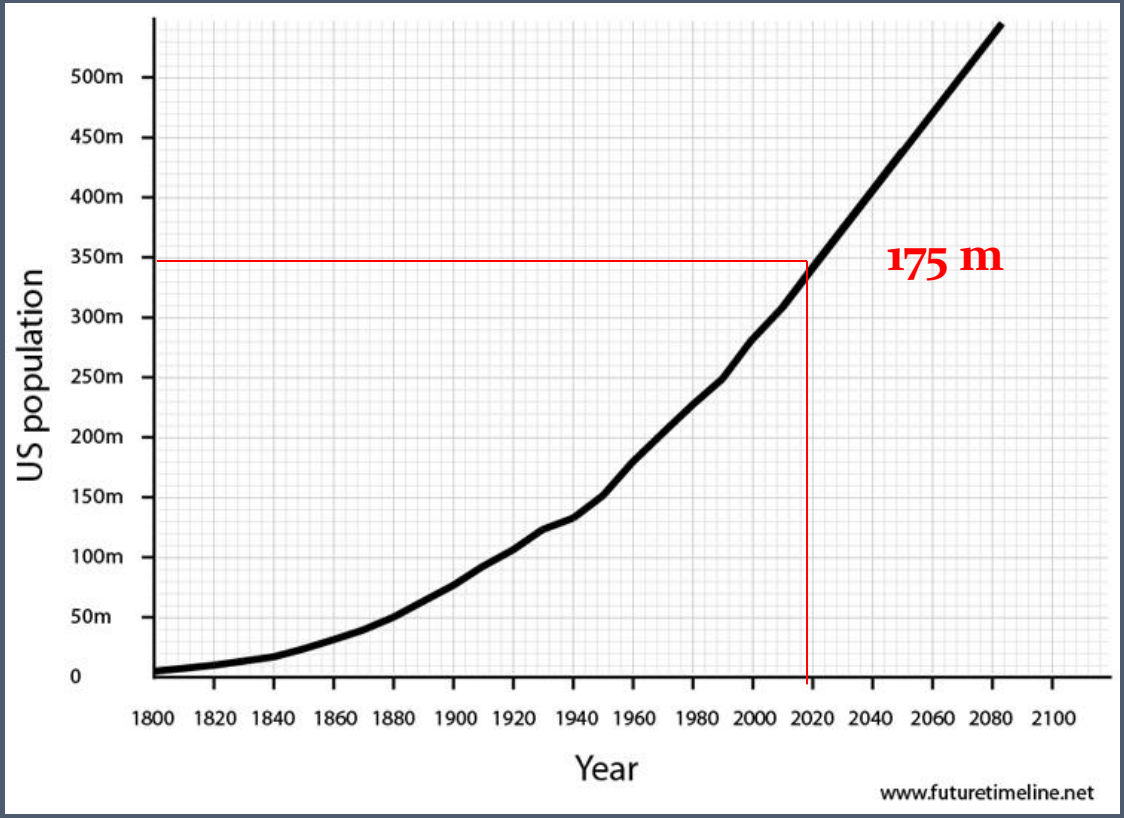
The NEW ENGLAND JOURNAL of MEDICINE

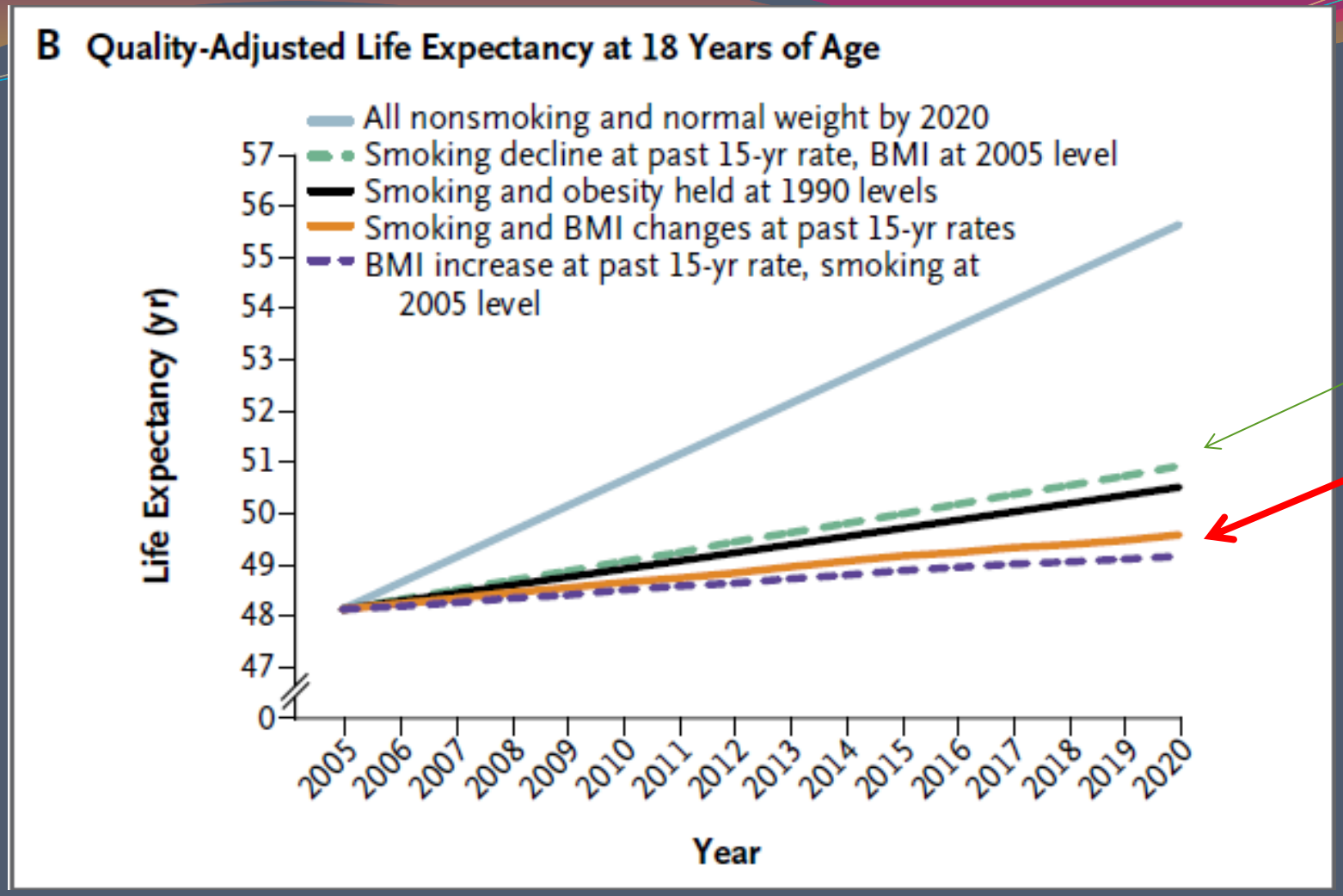
SPECIAL ARTICLE

Forecasting the Effects of Obesity and Smoking on U.S. Life Expectancy

Susan T. Stewart, Ph.D., David M. Cutler, Ph.D., and Allison B. Rosen, M.D., Sc.D.

By 2020 half of the US population will be obese





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Susan T. Stewart, Ph.D., David M. Cutler, Ph.D., and Allison B. Rosen, M.D., Sc.D.

Long-term weight-loss maintenance: a meta-analysis of US studies[1–3]

James W Anderson, Elizabeth C Konz, Robert C Frederich, and Constance L Wood

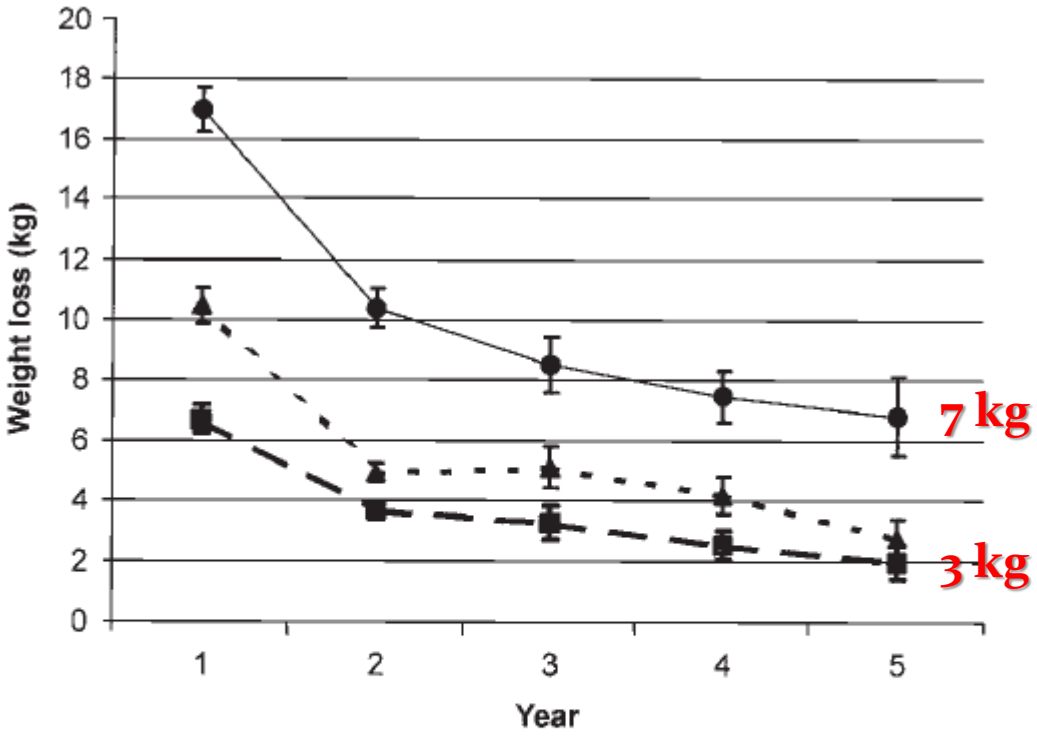
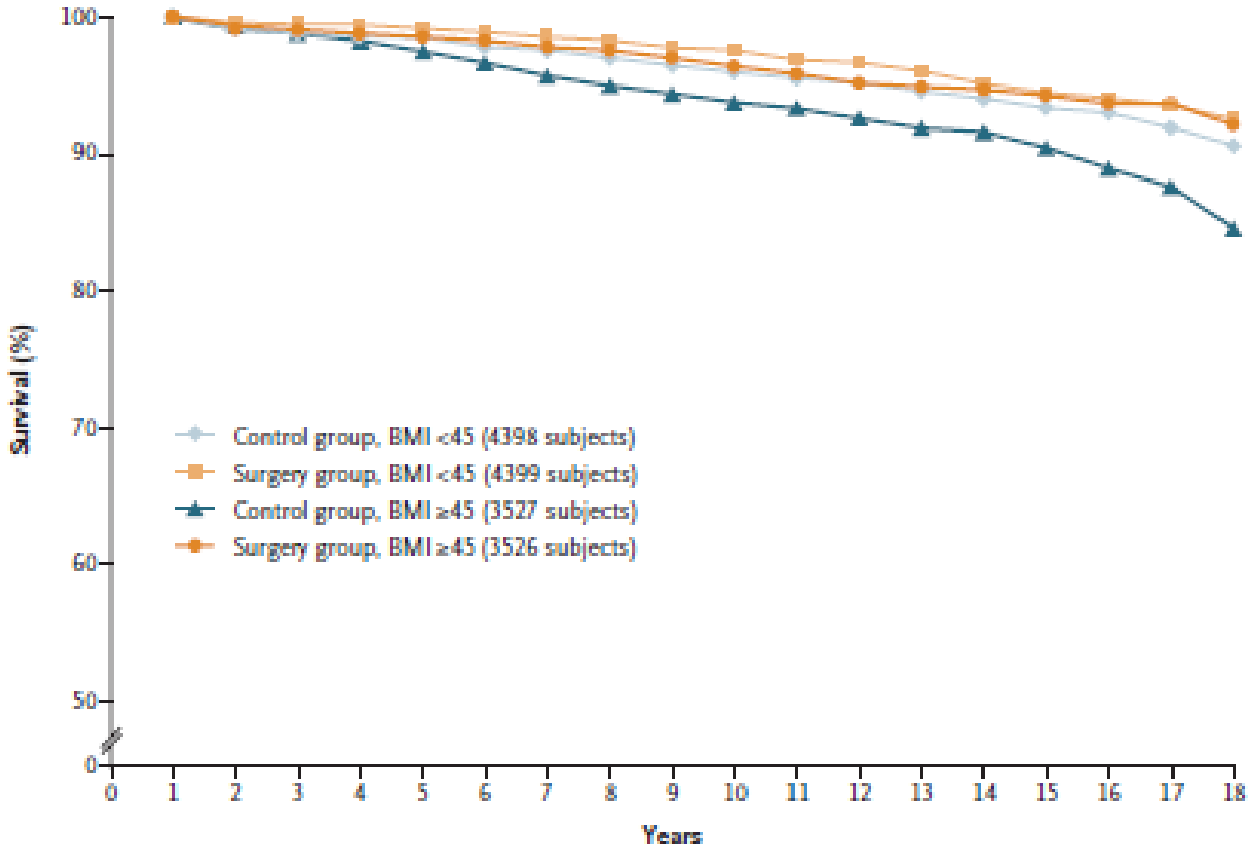


FIGURE 1. Weight reduction maintained over time. Values are weighted means (±95% CIs) for all subjects (▲), subjects consuming very-low-energy diets (●), and subjects consuming hypoenergetic balanced diets (■). In the very-low-energy and hypoenergetic balanced diet groups, respectively, n = 298 and 152 at 1 y, 1307 and 650 at 2 y, 778 and 152 at 3 y, 688 and 152 at 4 y, and 337 and 36 at 5 y.

Am J Clin Nutr 2001;74:579–84.



No. of Deaths																		
Control group	41	66	85	117	153	176	199	219	234	244	259	271	281	294	302	310	318	327
Surgery group	42	54	62	74	86	102	113	132	141	159	169	182	192	202	206	210	213	213

Figure 2. Survival According to BMI in the Surgery Group and the Control Group.

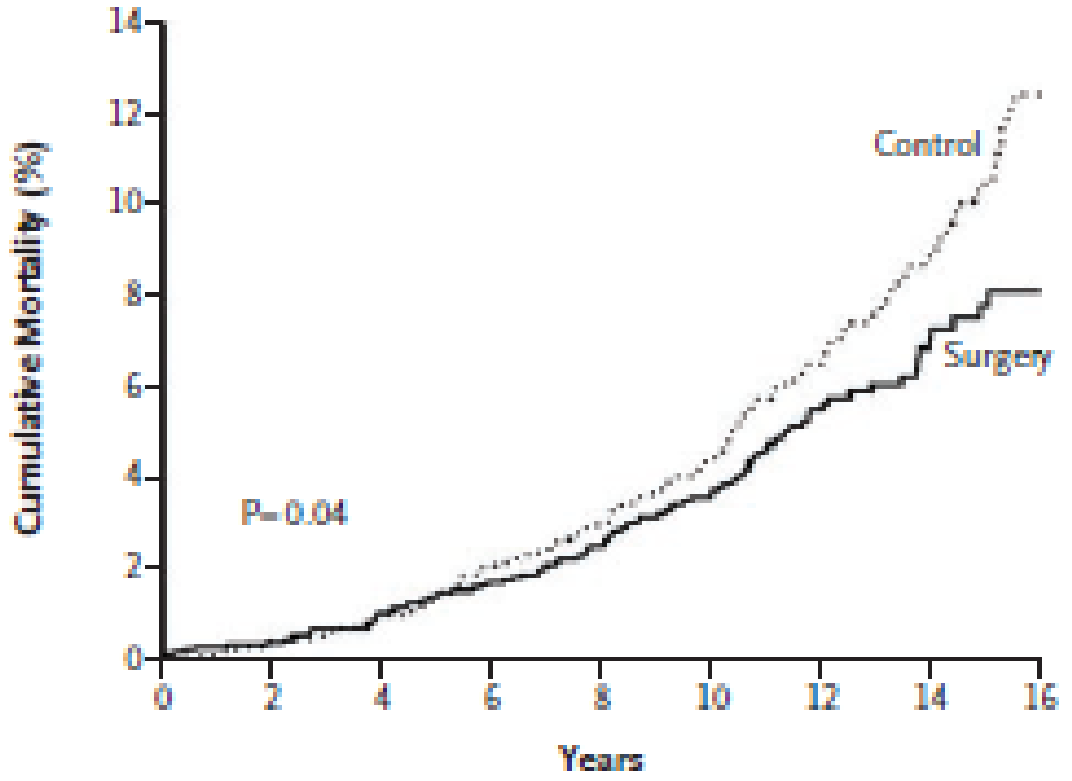
The body-mass index (BMI) is the weight in kilograms divided by the square of the height in meters.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Term Mortality after Gastric Bypass Surgery

Ted D. Adams, Ph.D., M.P.H., Richard E. Gress, M.A., Sherman C. Smith, M.D., R. Chad Halverson, M.D., Steven C. Simper, M.D., Wayne D. Rosamond, Ph.D., Michael J. LaMonte, Ph.D., M.P.H., Antoinette M. Stroup, Ph.D., and Steven C. Hunt, Ph.D.



No. at Risk

Surgery	2010	2001	1987	1821	1590	1260	760	422	169
Control	2037	2027	2016	1842	1455	1174	749	422	156

Figure 2. Unadjusted Cumulative Mortality.

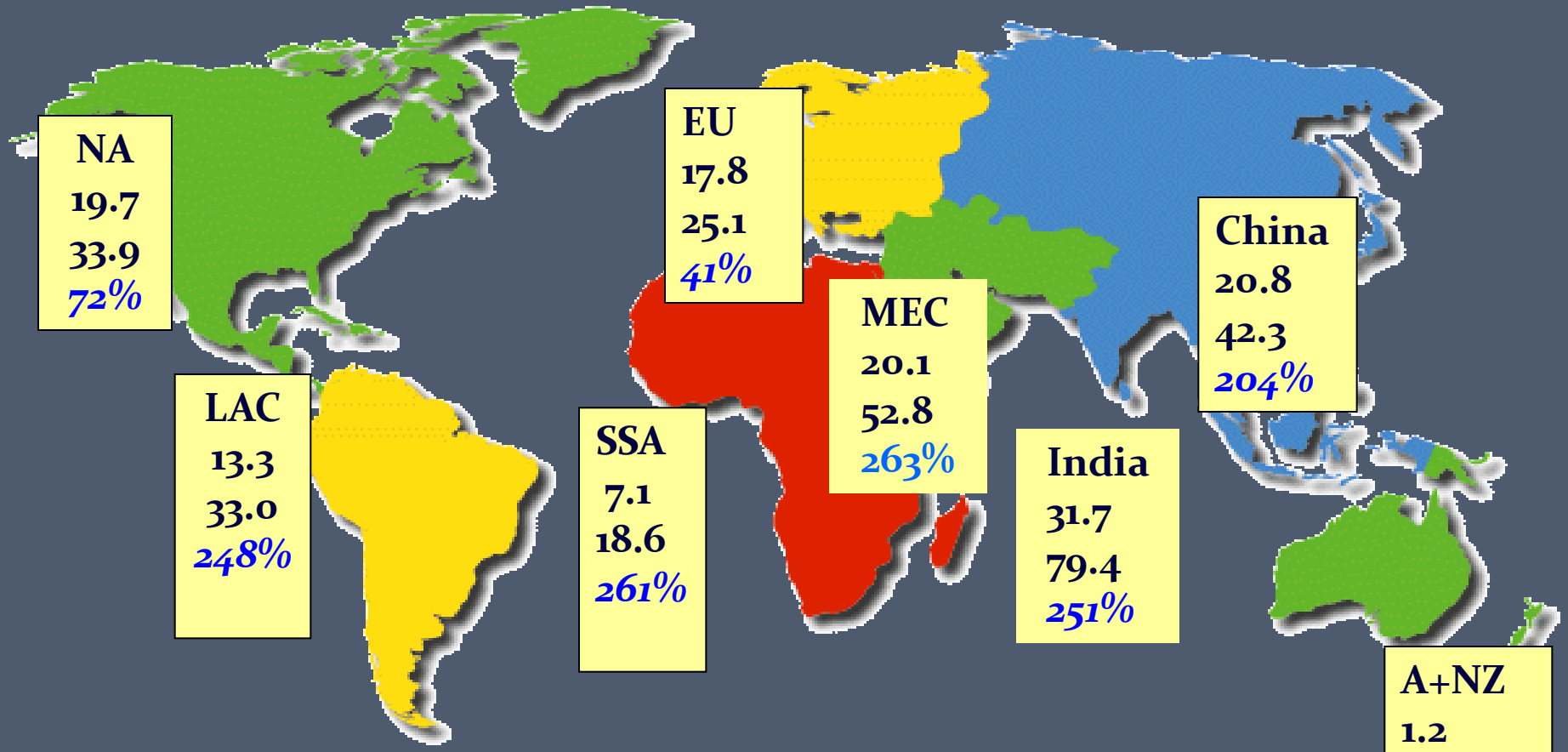
The hazard ratio for subjects who underwent bariatric surgery, as compared with control subjects, was 0.76 (95% confidence interval, 0.59 to 0.99; P= 0.04), with 129 deaths in the control group and 101 in the surgery group.

The NEW ENGLAND JOURNAL of MEDICINE
ESTABLISHED IN 1812 AUGUST 23, 2007 VOL. 357 NO. 8

Effects of Bariatric Surgery on Mortality in Swedish Obese Subjects

Lars Sjöström, M.D., Ph.D., Kristina Narbro, Ph.D., C. David Sjöström, M.D., Ph.D., Kristjan Karason, M.D., Ph.D., Bo Larsson, M.D., Ph.D., Hans Wedel, Ph.D., Ted Lystig, Ph.D., Marianne Sullivan, Ph.D., Claude Bouchard, Ph.D., Björn Carlsson, M.D., Ph.D., Calle Bengtsson, M.D., Ph.D., Sven Dahlgren, M.D., Ph.D., Anders Gummesson, M.D., Peter Jacobson, M.D., Ph.D., Jan Karlsson, Ph.D., Anna-Karin Lindroos, Ph.D., Hans Lönroth, M.D., Ph.D., Ingmar Näslund, M.D., Ph.D., Torsten Olbers, M.D., Ph.D., Kaj Stenlöf, M.D., Ph.D., Jarl Torgerson, M.D., Ph.D., Göran Ågren, M.D., and Lena M.S. Carlsson, M.D., Ph.D., for the Swedish Obese Subjects Study

Global Projections for the Diabetes Epidemic: 2000-2030 (in millions)

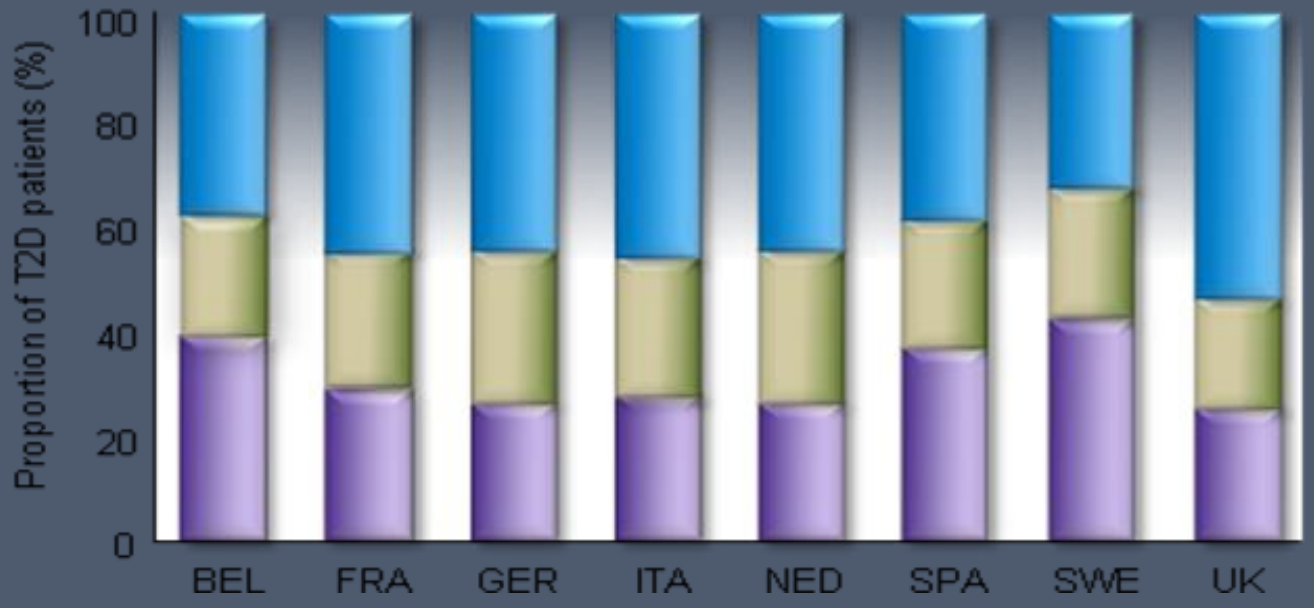


Wild. S et al.: Global prevalence of diabetes: Estimates for 2000 and projections for 2030 Diabetes Care 2004

World
2000 = 171 million
2030 = 366 million
Increase 213%

Diabetes care across Europe reported in 2002 did not deliver glycaemic targets. Purple shows percent of people ≤6.5%; yellow 6.5-7.5%; blue >7.5%.

From Liebl A. et al. Diabetologia. 2002;45:S23-S28.



PRELIMINARY COMMUNICATION

JAMA®

John B. Dixon, MBBS, PhD
Paul E. O'Brien, MD
Julie Playfair, RN
Leon Chapman, MBBS
Linda M. Schachter, MBBS, PhD
Stewart Skinner, MBBS, PhD
Joseph Proietto, MBBS, PhD
Michael Bailey, PhD, MSc(stats)
Margaret Anderson, BHealthMan

Adjustable Gastric Banding and Conventional Therapy for Type 2 Diabetes

A Randomized Controlled Trial

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 APRIL 26, 2012 VOL. 366 NO. 17

Bariatric Surgery versus Intensive Medical Therapy in Obese Patients with Diabetes

Philip R. Schauer, M.D., Sangeeta R. Kashyap, M.D., Kathy Wolski, M.P.H., Stacy A. Brethauer, M.D., John P. Kirwan, Ph.D., Claire E. Pothier, M.P.H., Susan Thomas, R.N., Beth Abood, R.N., Steven E. Nissen, M.D., and Deepak L. Bhatt, M.D., M.P.H.

The NEW ENGLAND JOURNAL of MEDICINE

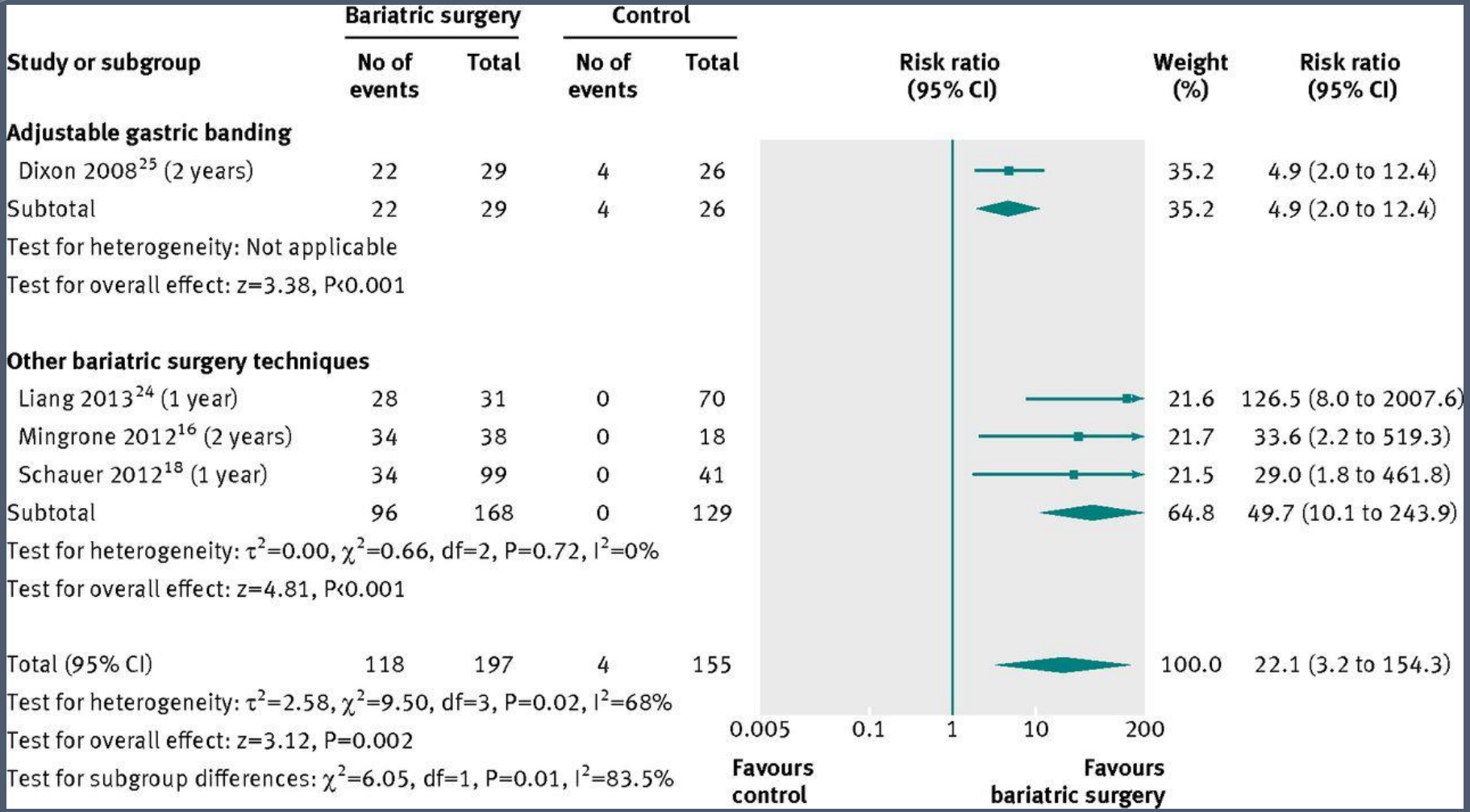
ORIGINAL ARTICLE

Bariatric Surgery versus Conventional Medical Therapy for Type 2 Diabetes

Geltrude Mingrone, M.D., Simona Panunzi, Ph.D., Andrea De Gaetano, M.D., Ph.D., Caterina Guidone, M.D., Amerigo Iaconelli, M.D., Laura Leccesi, M.D., Giuseppe Nanni, M.D., Alfons Pomp, M.D., Marco Castagneto, M.D., Giovanni Ghirlanda, M.D., and Francesco Rubino, M.D.

	Dixon et al. JAMA 2008		Schauer et al. NEJM 2012			Mingrone et al. NEJM 2012		
	LAGB	Medical therapy	RYGB	SG	Intensive medical therapy	RYGB	BPD	Medical therapy
Selection criteria	BMI: 30-40; T2D from 2 years		BMI: 27-43; HbA1c >7%			BMI>35; HbA1c>7%; T2D from more than 5 years		
T2D remission criteria	FPG<126 mg/dl; HbA1c<6.2%; without T2D therapy		HbA1c≤6.0%; with or without T2D therapy			FPG<100 mg/dl; HbA1c<6.5%; without T2D therapy for at least 1 year		
N. Pts	30	30	50	50	50	20	20	20
T2D remission (%)	73	13	42 (no therapy)	37 27% no therapy	12	75	95	0
Weight (kg) Changes (%)	84.6±15.8 -21.1±0.5	104.8±15.3* -1.5±5.4	77.3±13.0 * -29.4±8.9	100.6±16.5 -29.4±8.9	104.4±14.5 -5.4±8.0	84.3±13.4 -33.3±7.9	89.5±17.8* -33.8±10.2	128.1±19.8 -4.7±6.4
HbA1c (%)	6.0±0.8*	7.2±1.4*	6.4±0.9*	6.6±1.0*	7.5±1.8	6.4±1.4*	4.9±0.5*	7.7±0.6
Glycemia (mg/dl)	105.6±30.3	139.6±38.1				102.5±55.3 *	70.1±12.1	141.1±29.9
CH (mg/dl)	205.4±46.6	198.8±59.3				164.9±29.7 *	107.0±31.3*	189.6±33.6

Type 2 diabetes remission after bariatric surgery versus non-surgical treatment (control) for obesity.



Study or subgroup	Bariatric surgery No of events	Bariatric surgery Total	Control No of events	Control Total	Risk ratio (95% CI)	Weight (%)	Risk ratio (95% CI)
Adjustable gastric banding							
Dixon 2008[25] (2 years)	22	29	4	26		35.2	4.9 (2.0 to 12.4)
Subtotal	22	29	4	26		35.2	4.9 (2.0 to 12.4)
Test for heterogeneity: Not applicable							
Test for overall effect: z=3.38, P<0.001							
Other bariatric surgery techniques							
Liang 2013[24] (1 year)	28	31	0	70		21.6	126.5 (8.0 to 2007.6)
Mingrone 2012[16] (2 years)	34	38	0	18		21.7	33.6 (2.2 to 519.3)
Schauer 2012[18] (1 year)	34	99	0	41		21.5	29.0 (1.8 to 461.8)
Subtotal	96	168	0	129		64.8	49.7 (10.1 to 243.9)
Test for heterogeneity: τ^2=0.00, χ^2=0.66, df=2, P=0.72, I^2=0%							
Test for overall effect: z=4.81, P<0.001							
Total (95% CI)	118	197	4	155		100.0	22.1 (3.2 to 154.3)
Test for heterogeneity: τ^2=2.58, χ^2=9.50, df=3, P=0.02, I^2=68%							
Test for overall effect: z=3.12, P=0.002							
Test for subgroup differences: χ^2=6.05, df=1, P=0.01, I^2=83.5%							

Gloy V L et al. BMJ 2013;347:bmj.f5934

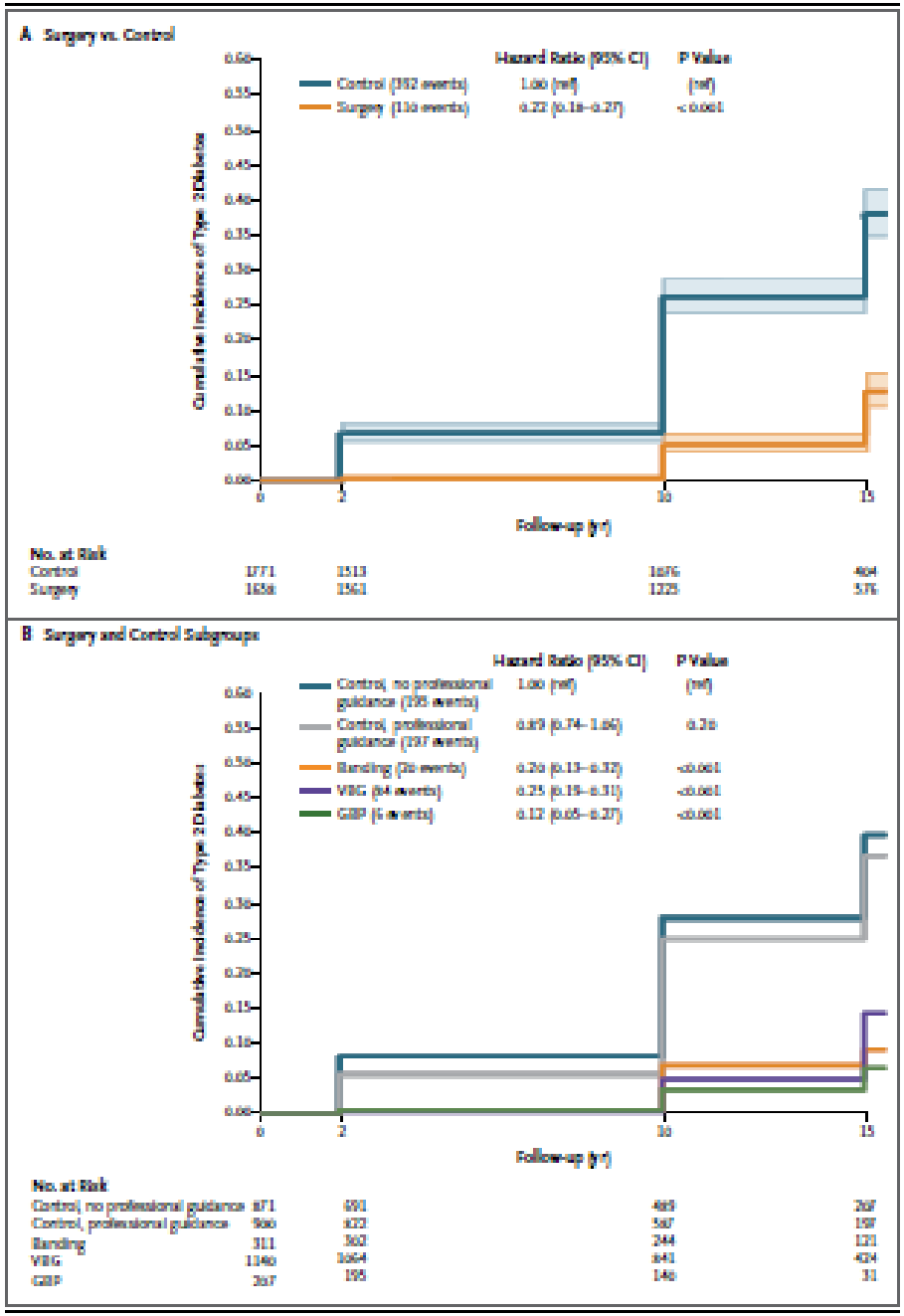
BMJ

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 AUGUST 23, 2012 VOL. 367 NO. 8

Bariatric Surgery and Prevention of Type 2 Diabetes in Swedish Obese Subjects

Lena M.S. Carlsson, M.D., Ph.D., Markku Peltonen, Ph.D., Sofie Ahlin, M.D., Åsa Anveden, M.D., Claude Bouchard, Ph.D., Björn Carlsson, M.D., Ph.D., Peter Jacobson, M.D., Ph.D., Hans Lönroth, M.D., Ph.D., Cristina Maglio, M.D., Ingmar Näslund, M.D., Ph.D., Carlo Pirazzi, M.D., Stefano Romeo, M.D., Ph.D., Kajsa Sjöholm, Ph.D., Elisabeth Sjöström, M.D, Hans Wedel, Ph.D., Per-Arne Svensson, Ph.D., and Lars Sjöström, M.D., Ph.D.



Panel A : Kaplan–Meier unadjusted estimates of the cumulative incidence of type 2 diabetes in the bariatric-surgery group and the control group. The light shading represents the 95% confidence interval. The adjusted hazard ratio with bariatric surgery was 0.17 (95% confidence interval, 0.13 to 0.21). Panel B: Kaplan–Meier unadjusted estimates of the incidence of type 2 diabetes in subgroups defined in the control group according to receipt or no receipt of professional guidance to lose weight and in the surgery group according to the method of bariatric surgery: gastric banding, vertical banded gastroplasty (VBG), or gastric bypass (GBP).

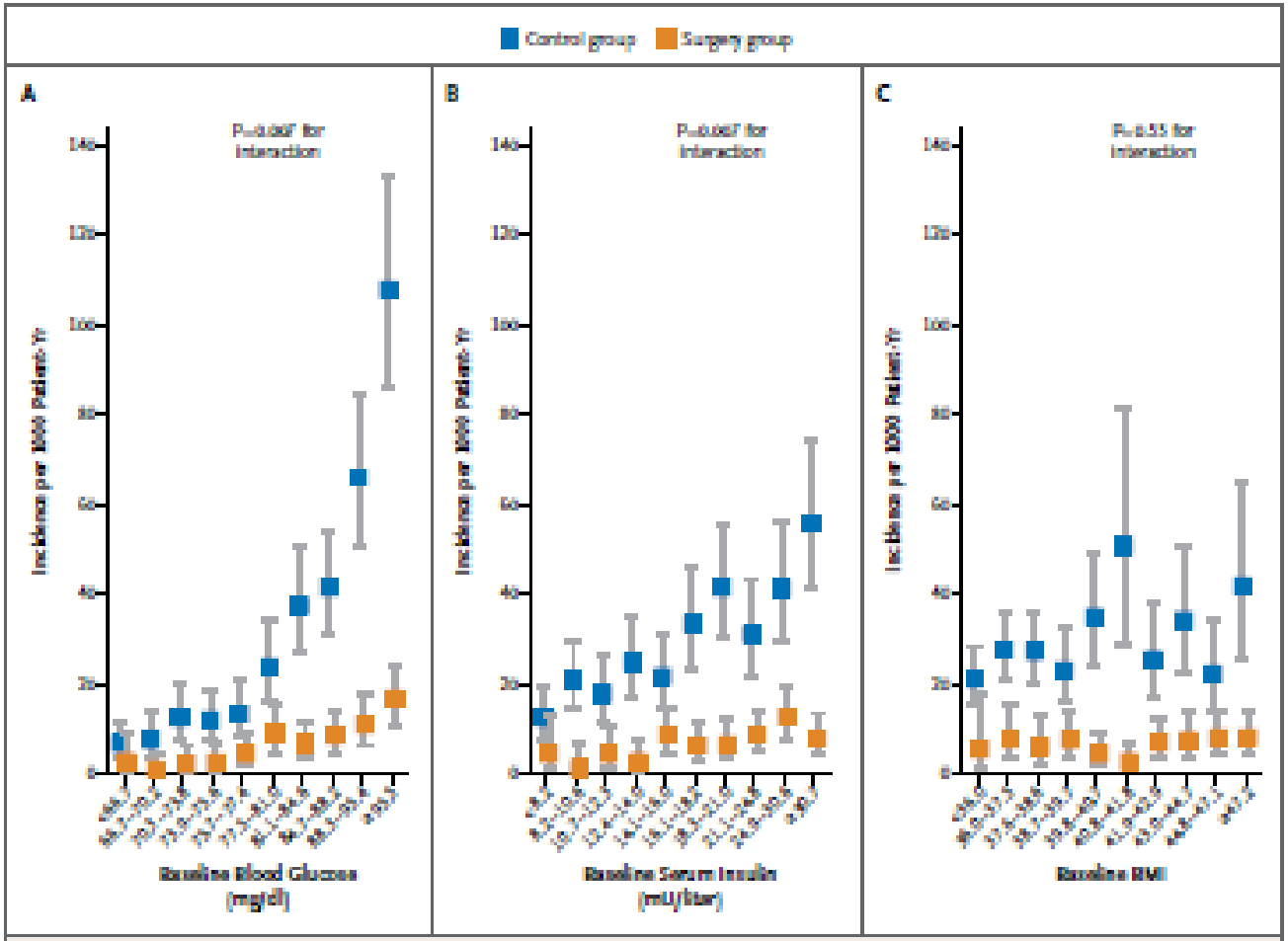


Figure 2. Interaction between Selected Risk Factors and Treatment.

The incidence of type 2 diabetes per 1000 person-years in the bariatric-surgery and control groups is shown according to deciles of baseline blood glucose levels (Panel A), serum insulin levels (Panel B), and body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) (Panel C). In Panel A, $P=0.002$ for the interaction of treatment with the presence or absence of impaired fasting glucose. All incidence rates are adjusted for age and sex. The P values for interaction are unadjusted. For complete information on all calculated P values for interaction, see Table S7 in the Supplementary Appendix. To convert the values for glucose to millimoles per liter, multiply by 0.0551. I bars indicate 95% confidence intervals.

Roux-en-Y Gastric Bypass vs Intensive Medical Management for the Control of Type 2 Diabetes, Hypertension, and Hyperlipidemia

The Diabetes Surgery Study Randomized Clinical Trial

The primary outcome was considered successful if patients achieved the composite of the triple end point: an HbA_{1c} of less than 7.0%, an LDL cholesterol level of less than 100 mg/dL (to convert to millimoles per liter, multiply by 0.0259), and systolic blood pressure less than 130 mm Hg, at the 12-month visit. The triple end

End Points	Lifestyle and Medical Management	Roux-en-Y Gastric Bypass	OR (95% CI)[a]
	Dichotomous Outcomes		
	No. (%) of Patients		
Meets primary outcome triple end point	11 (19)	28 (49)	4.8 (1.9-11.7)
HbA_{1c} <7.0%	18 (32)	43 (75)	6.0 (2.6 to 13.9)
LDL cholesterol <100 mg/dL	38 (70)	45 (79)	1.6 (0.7 to 3.8)
Systolic blood pressure <130 mm Hg	44 (79)	48 (84)	1.7 (0.6 to 4.6)
HbA_{1c} <6.0%	5 (9)	25 (44)	7.9 (2.7 to 23.4)
Fasting glucose <100, mg/dL	7 (14)	25 (44)	5.8 (2.1 to 15.9)
	Continuous Outcomes		
	Mean (SD)		Difference (95% CI)[a]
Glycemia			
HbA_{1c}, %	7.8 (1.5)	6.3 (0.9)	−1.4 (−1.9 to −0.9)
Fasting glucose, mg/mL	153 (59)	111 (34)	−42 (−60 to −24)
Serum lipids, mg/dL			
Cholesterol			
LDL	89 (31)	83 (25)	−5 (−16 to 5)
HDL	42 (9)	50 (14)	7.5 (3 to 12)
Total	162 (40)	153 (32)	−10 (−23 to 4)
Triglycerides	182 (151)	104 (48)	−78 (−119 to −36)
Blood pressure, mm Hg			
Systolic	124 (12)	115 (14)	−9 (−13 to −4)
Diastolic	74 (9)	68 (9)	−6 (−9. to −4)
Weight			
Weight, kg	90.1 (17.0)	73.0 (13.6)	−16.0 (−21.1 to −10.8)
BMI,	31.6 (3.7)	25.8 (3.5)	−5.5 (−6.8 to −4.2)
Percent weight change (%)	−7.9 (7.8)	−26.1 (8.7)	−17.5 (−20.7 to −14.2)
Waist circumference, cm	105 (11)	90 (11)	−15 (−18 to −11)
Other			
Medications for control of glycemia, dyslipidemia and blood pressure (n)	4.8 (2.1)	1.7 (1.8)	−3.0 (−3.6 to −2.3)

[a] ORs, Differences, and their 95% CIs are computed using multiple imputations. Logistic regressions are stratified by site; linear regressions are adjusted for site.

JAMA, June 5, 2013—Vol 309, No. 21

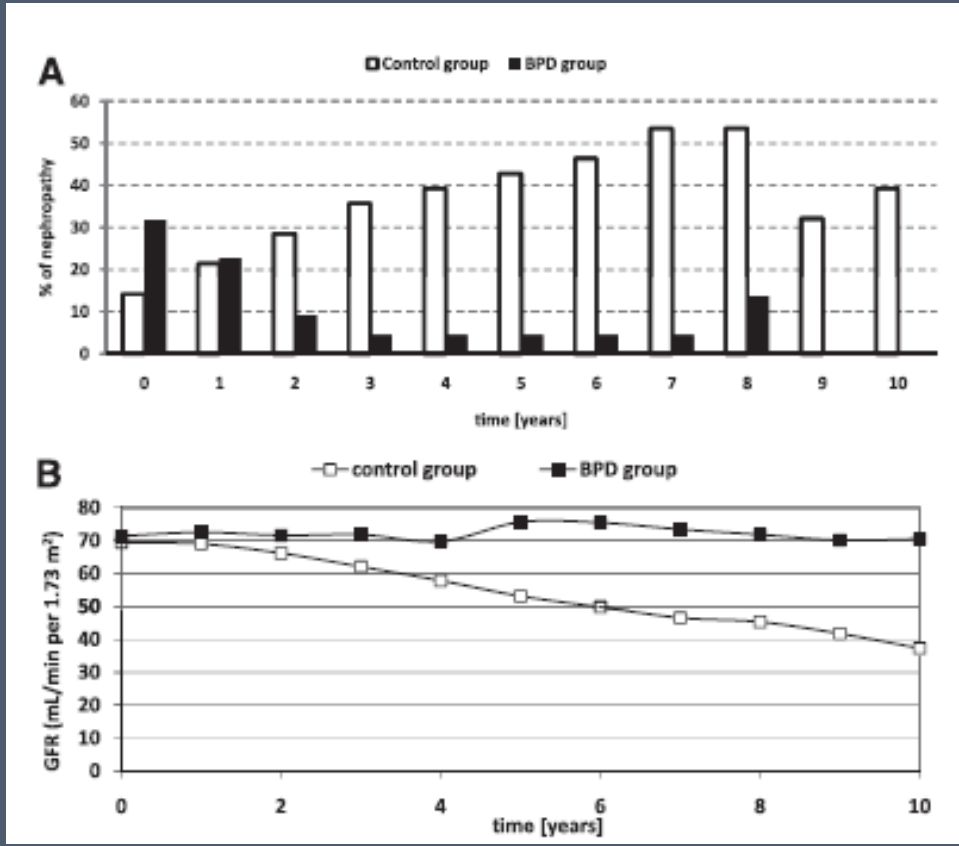
Clinical Care/Education/Nutrition/Psychosocial Research
ORIGINAL ARTICLE

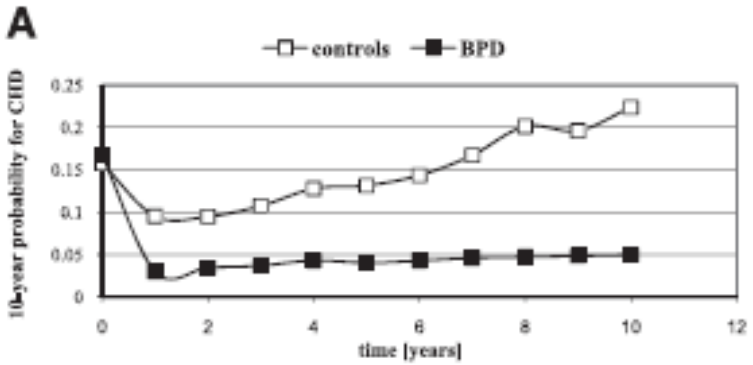
Effects of Bilio-Pancreatic Diversion on Diabetic Complications

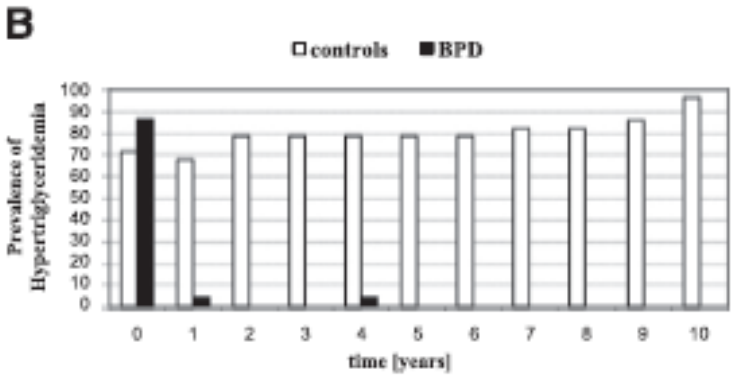
A 10-year follow-up

Amerigo Iaconelli, md[1]
Simona Panunzi, msc, phd[2]
Andrea De Gaetano, md, phd[2]
Melania Manco, md, phd[3]
Caterina Guidone, md[1]
Laura Leccesi, md[1]
Donatella Gniuli, md, phd[1]
Giuseppe Nanni, md[4]
Marco Castagneto, md[4]
Giovanni Ghirlanda, md[1]
Geltrude Mingrone, md, phd[1]

intensive treatment, targeted at attaining normal glycated hemoglobin levels, i.e., <6.0%, not only was found to be ineffective in reducing cardiovascular events but also was found to be associated with significantly higher mortality, leading to the




A
controls
BPD
10-year probability for CHD
0.25
0.2
0.15
0.1
0.05
0
0
2
4
6
8
10
12
time [years]


B
controls
BPD
Prevalence of Hypertriglyceridemia
100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
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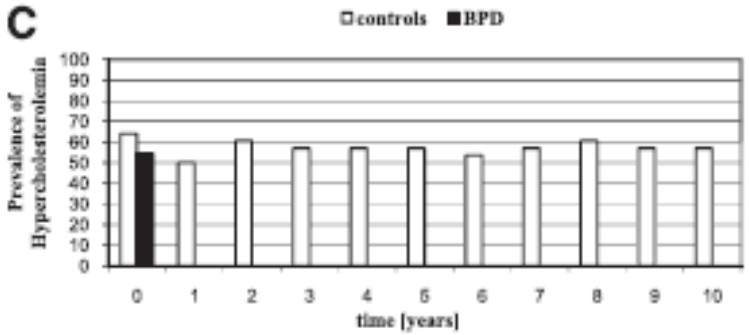
7
8
9
10
time [years]


C
controls
BPD
Prevalence of Hypercholesterolemia
100
90
80
70
60
50
40
30
20
10
0
0
1
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3
4
5
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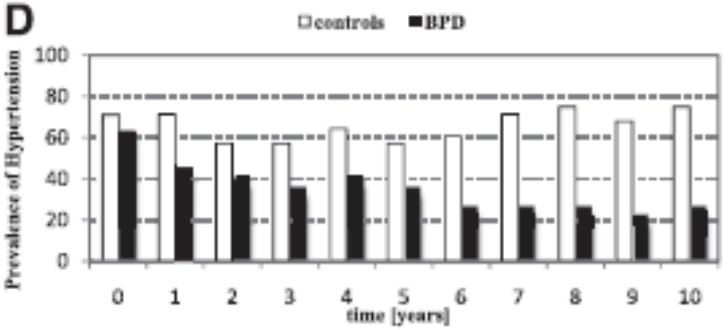
7
8
9
10
time [years]


D
controls
BPD
Prevalence of Hypertension
100
80
60
40
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1
2
3
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5
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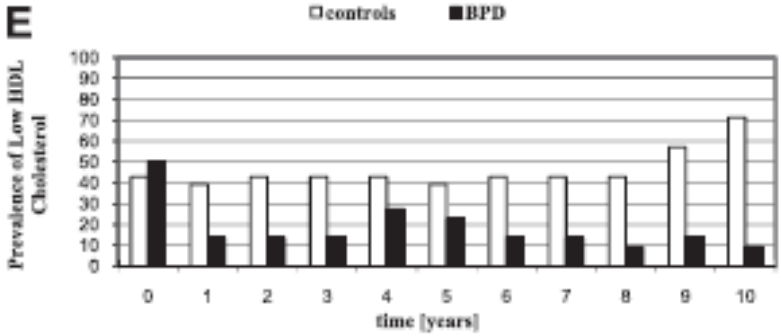
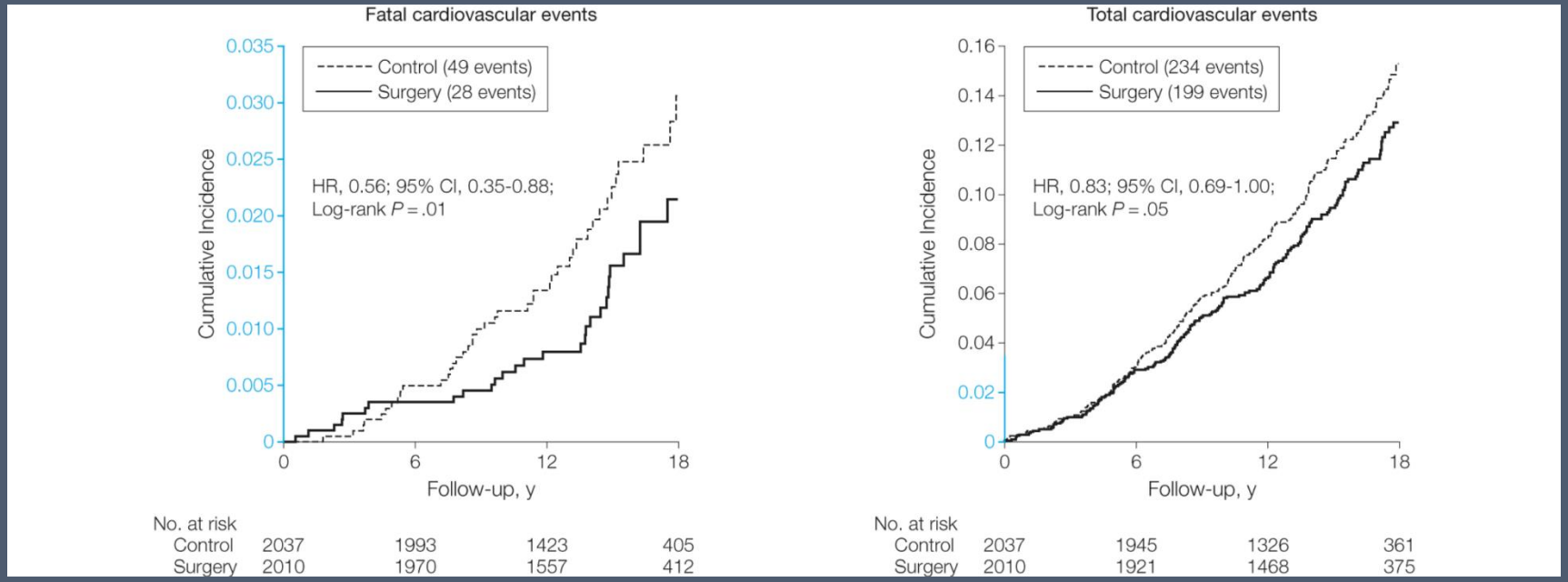
7
8
9
10
time [years]

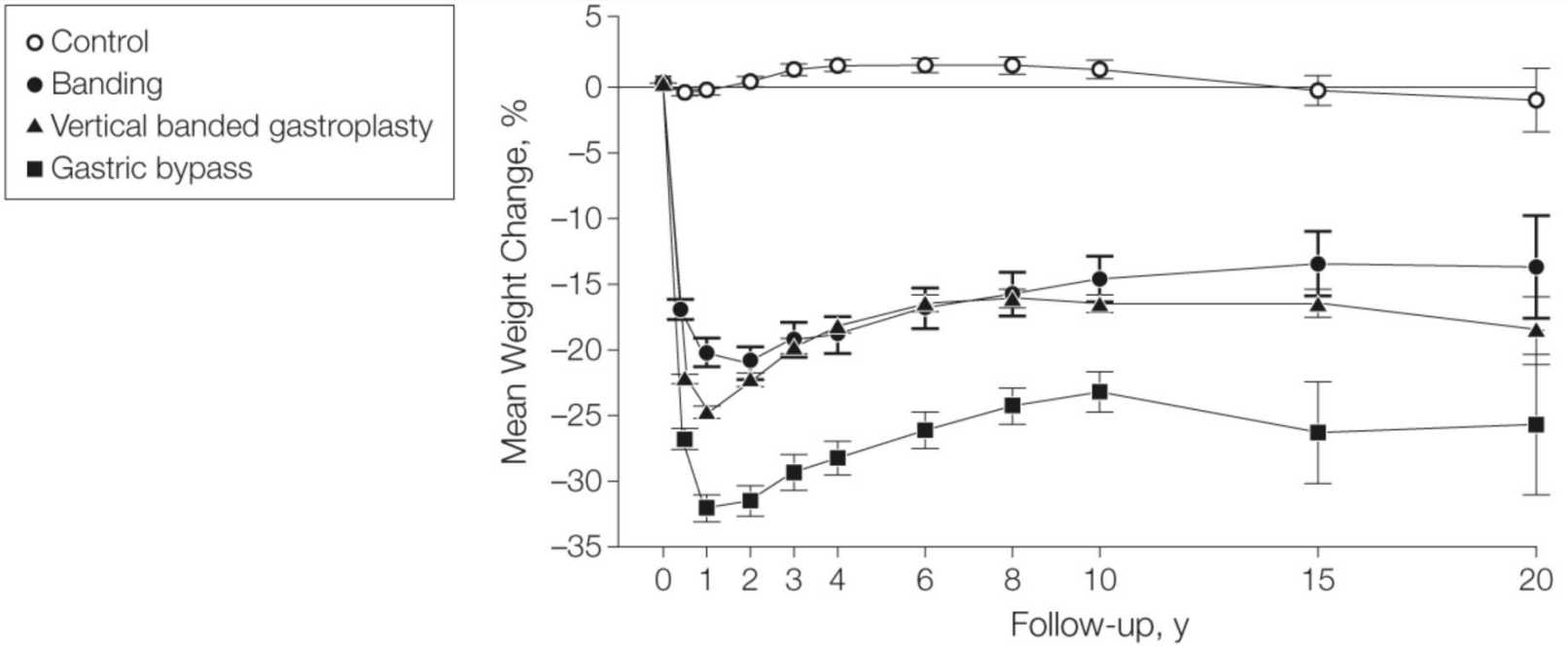

E
controls
BPD
Prevalence of Low HDL Cholesterol
100
90
80
70
60
50
40
30
20
10
0
0
1
2
3
4
5
6
7
8
9
10
time [years]



ORIGINAL CONTRIBUTION

JAMA, January 4, 2012—Vol 307, No. 1

Bariatric Surgery and Long-term Cardiovascular Events



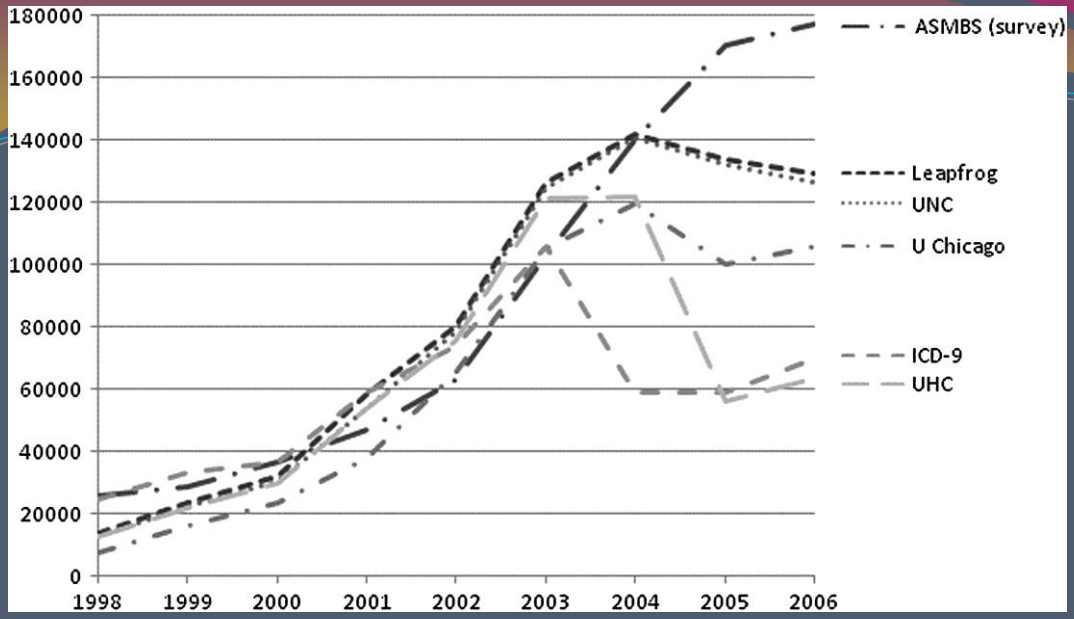
No. of patients						
Control	2037	1490	1242	1267	556	176
Banding	376	333	284	284	150	50
Vertical banded gastroplasty	1369	1086	987	1007	489	82
Gastric bypass	265	209	184	180	37	13

ORIGINAL CONTRIBUTION

JAMA, January 4, 2012—Vol 307, No. 1

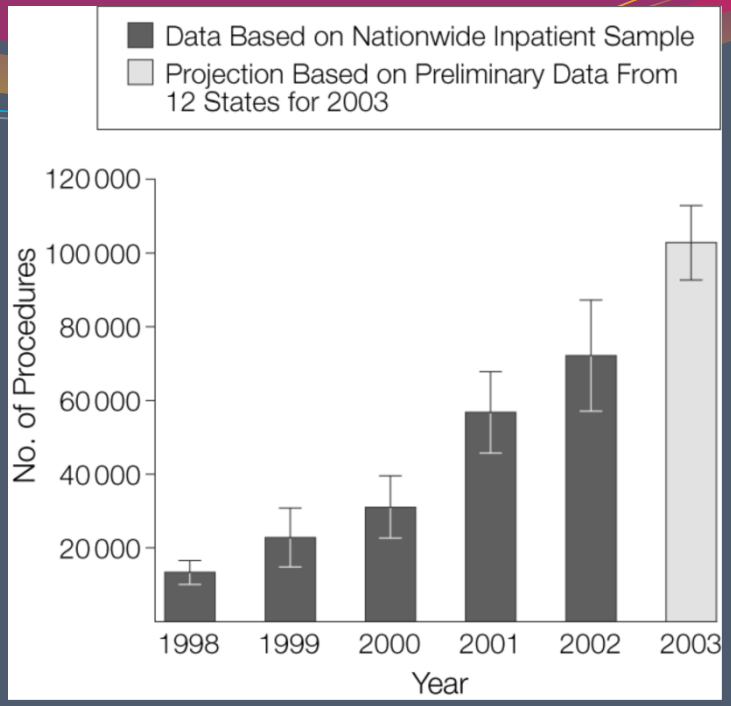
Bariatric Surgery and Long-term Cardiovascular Events

Given that bariatric surgery is associated with both post-operative mortality, ranging from 0.1 to 2% in relation to the type of bariatric operation, and with early and late complications (NEJM 2004), it cannot be extended to totality of obese and diabetic patients.



Annual inpatient and outpatient bariatric case volume.

Geoffrey P. et al.
Recent trends in bariatric surgery case volume in the United StatesS urgery Volume 146, Issue 2 2009 375 - 380



JAMA. 2005;294(15):1909-1917.

< 1% of morbidly obese subjects is operated in the US

CONCLUSIONS

Surgery is more effective than conventional medical treatment in the control of hyperglycemia in patients with severe obesity. While larger, multicenter trials are necessary to investigate the impact of surgery on long-term diabetes complications, available data support the use of surgery in the treatment of type 2 diabetes.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