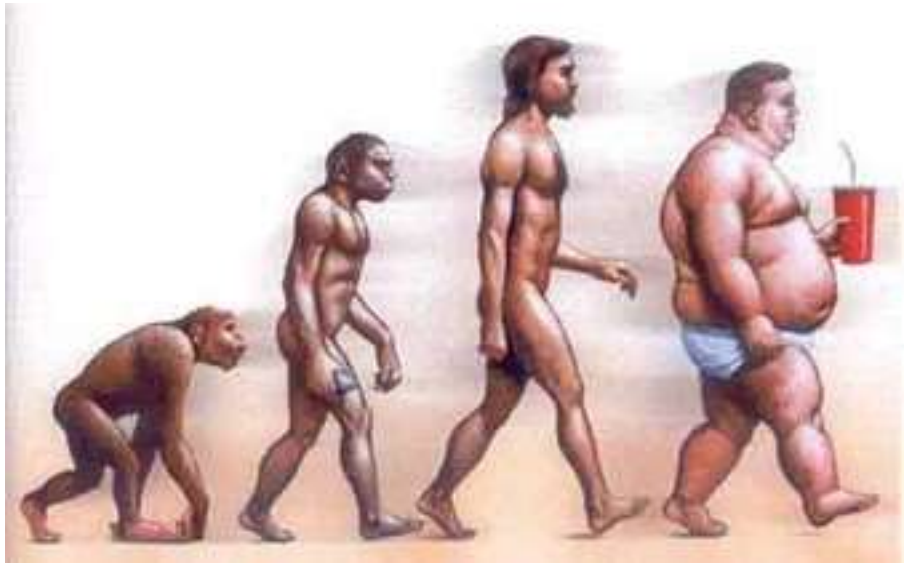
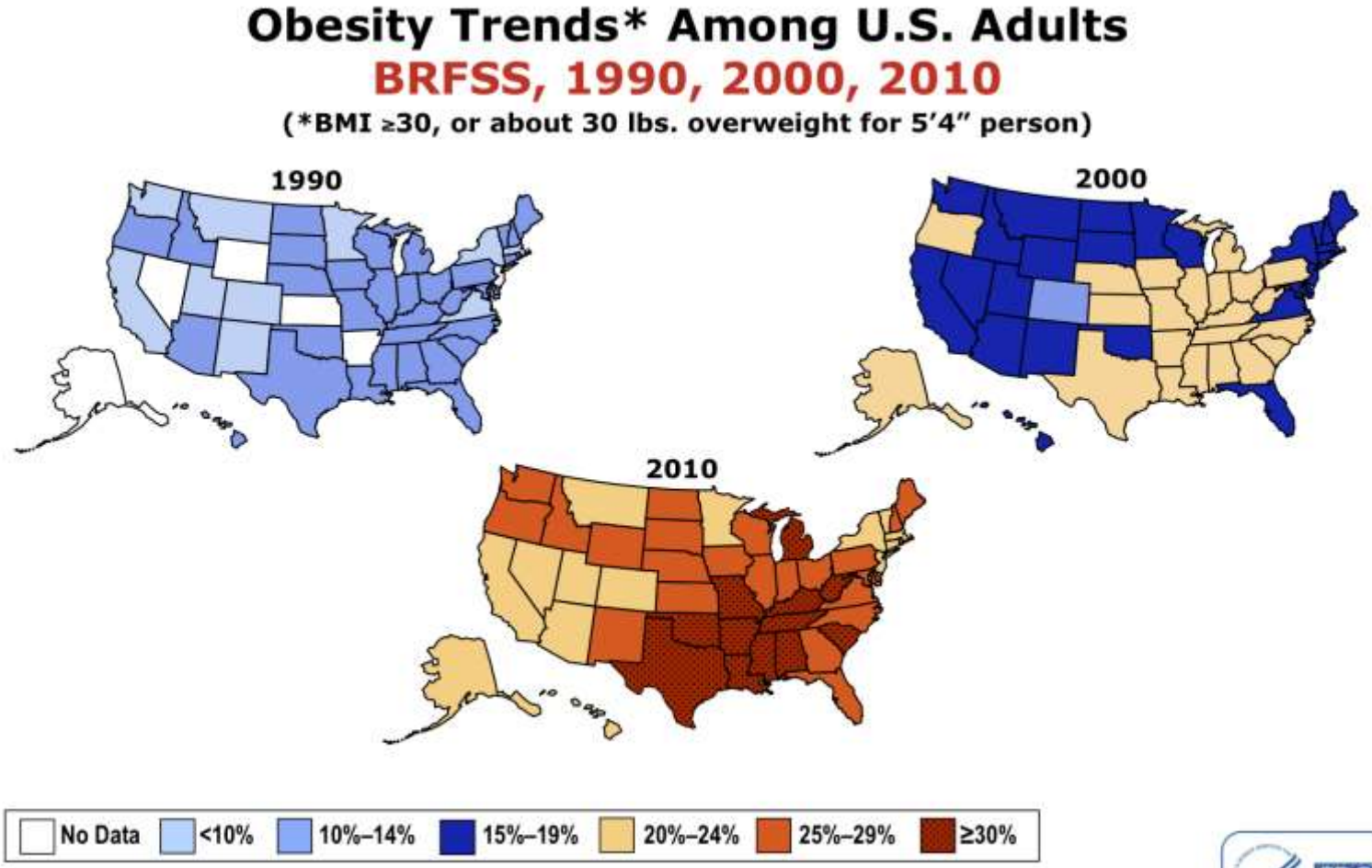
From bariatric to metabolic surgery



Homo Erectus	Homo Sapiens	Homo Diabeticus

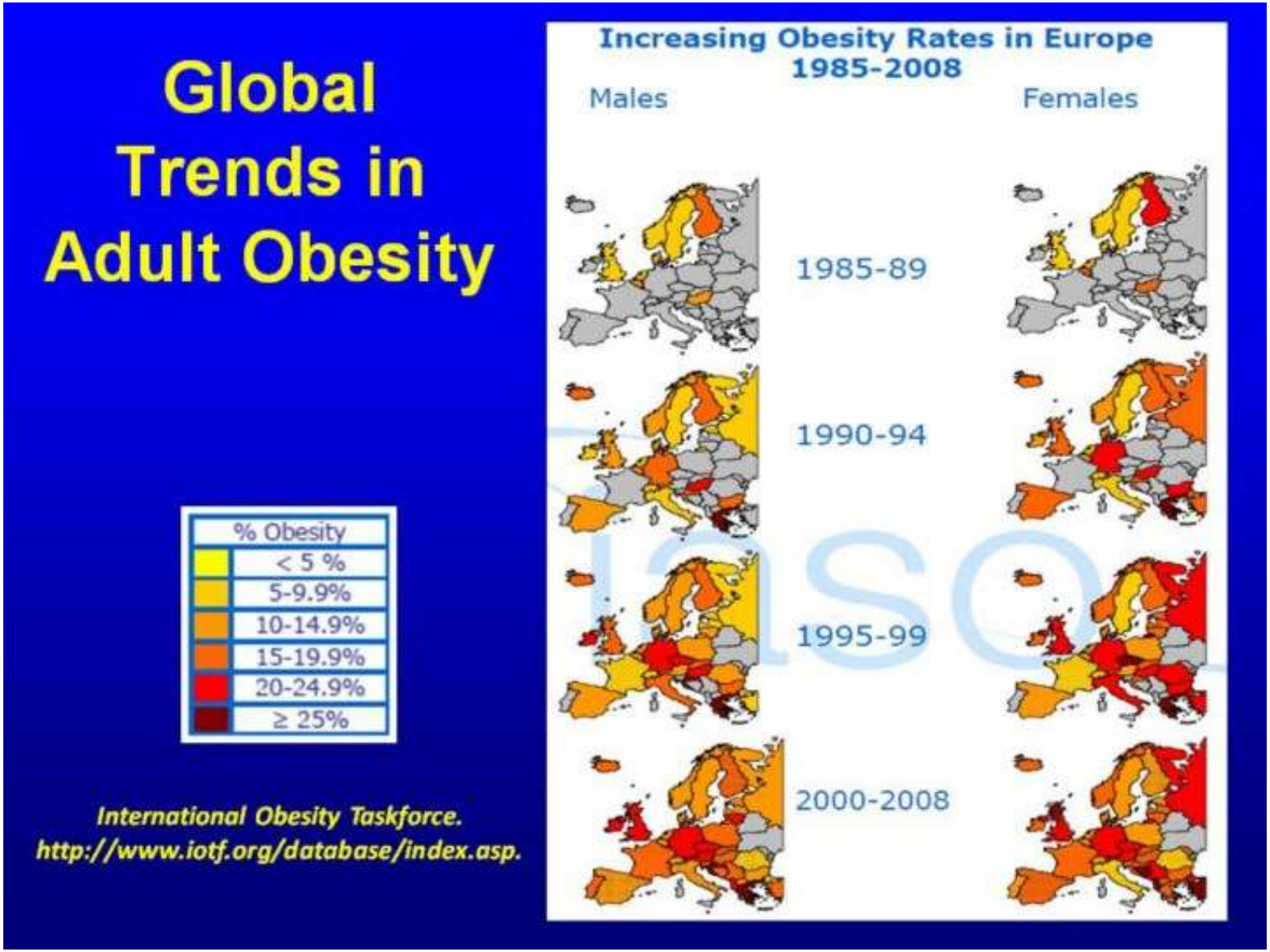
G. Hubens MD PhD
Dept Abdominal Surgery UZ Antwerpen

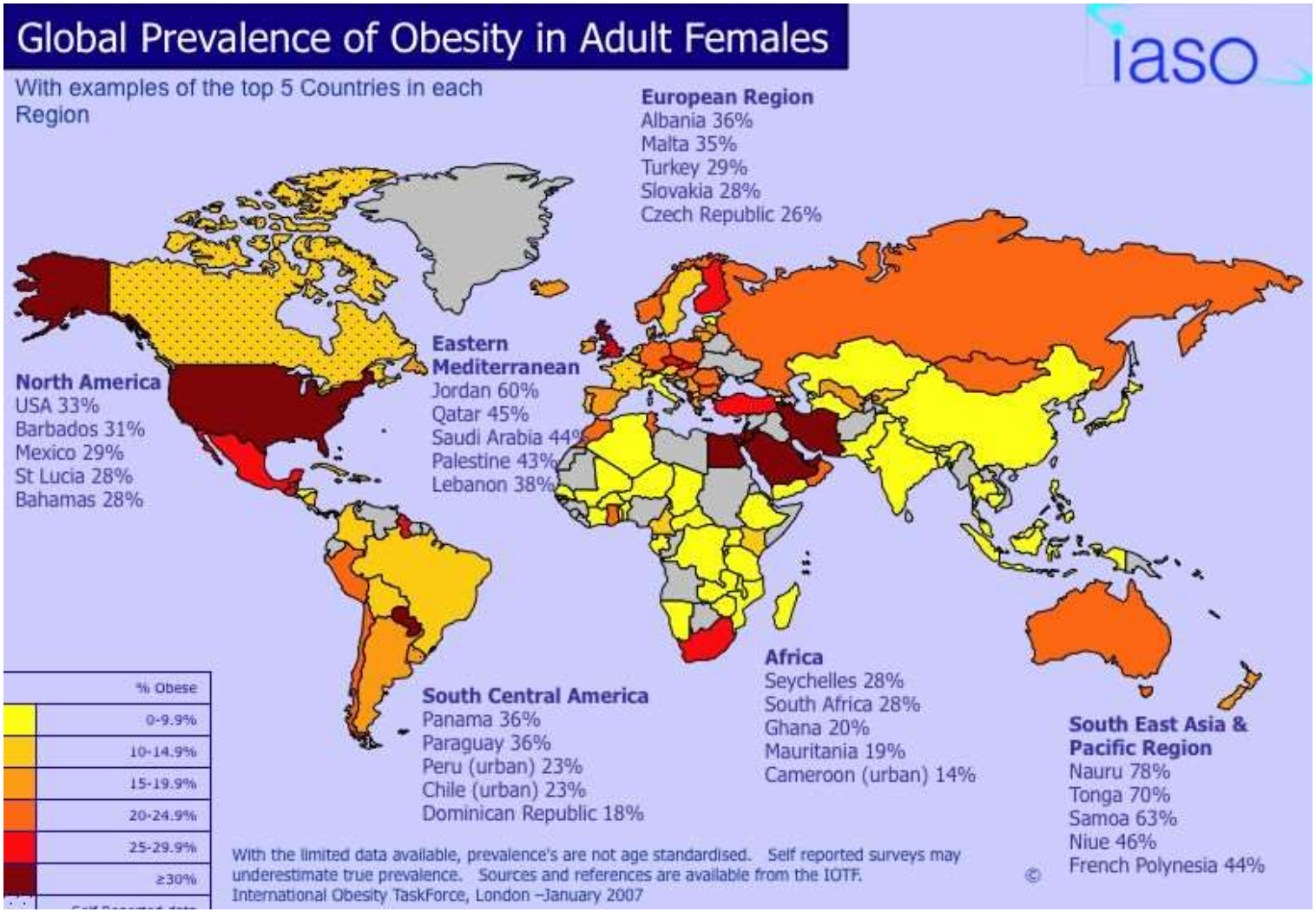

Obesity Trends* Among U.S. Adults
BRFSS, 1990, 2000, 2010
(*BMI ≥30, or about 30 lbs. overweight for 5'4" person)
1990
2000
2010
No Data
<10%
10%–14%
15%–19%
20%–24%
25%–29%
≥30%
Source: Behavioral Risk Factor Surveillance System, CDC.
CDC

the main difference between
Europe and USA

AMERICAN FOOTBALL COACHES
EUROPEAN FOOTBALL COACHES

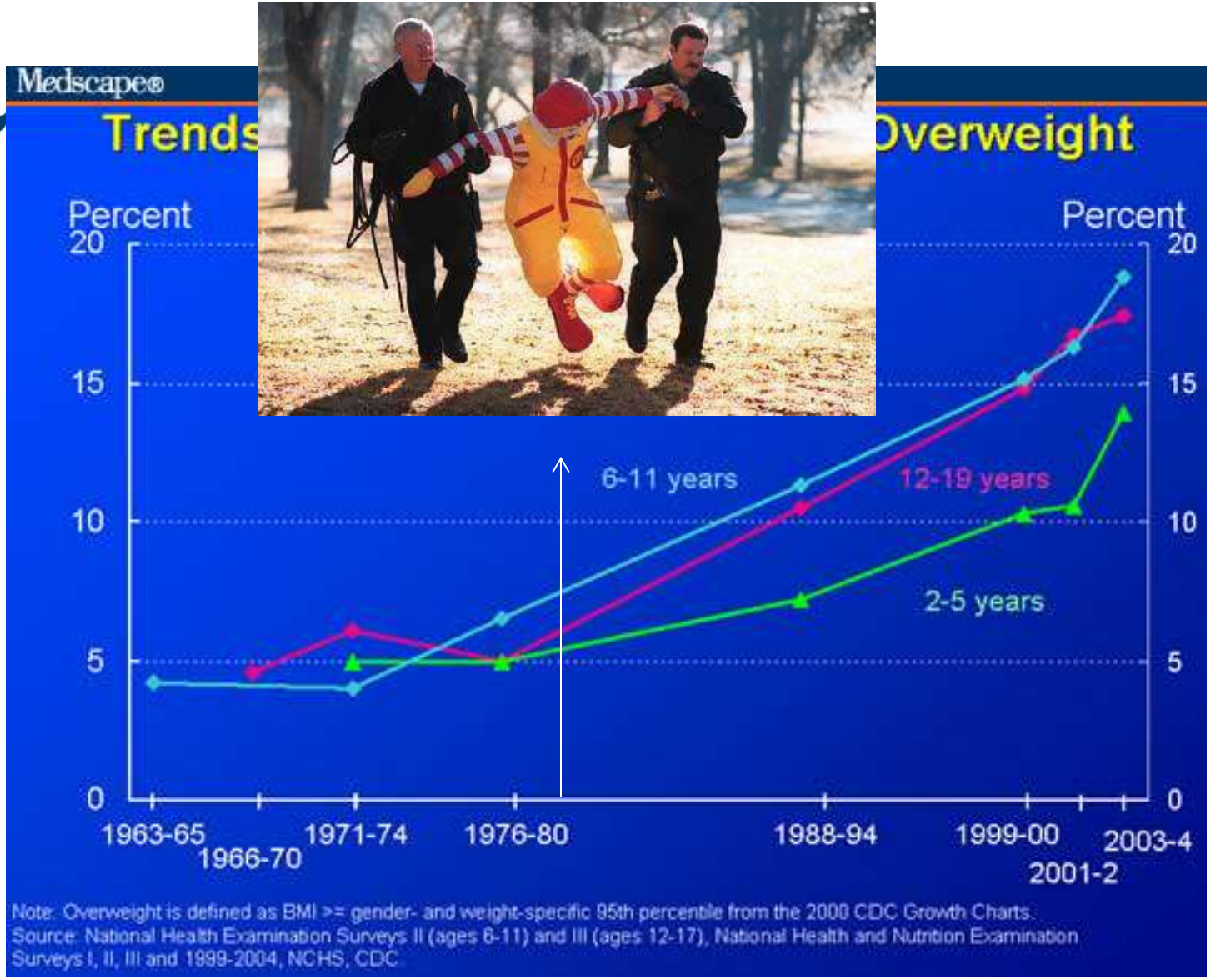
Global Trends in Adult Obesity




Global Prevalence of Obesity in Adult Females
With examples of the top 5 Countries in each Region
iaso
European Region
Albania 36%
Malta 35%
Turkey 29%
Slovakia 28%
Czech Republic 26%
North America
USA 33%
Barbados 31%
Mexico 29%
St Lucia 28%
Bahamas 28%
Eastern Mediterranean
Jordan 60%
Qatar 45%
Saudi Arabia 44%
Palestine 43%
Lebanon 38%
Africa
Seychelles 28%
South Africa 28%
Ghana 20%
Mauritania 19%
Cameroon (urban) 14%
South Central America
Panama 36%
Paraguay 36%
Peru (urban) 23%
Chile (urban) 23%
Dominican Republic 18%
South East Asia & Pacific Region
Nauru 78%
Tonga 70%
Samoa 63%
Niue 46%
French Polynesia 44%
% Obese
0-9.9%
10-14.9%
15-19.9%
20-24.9%
25-29.9%
≥30%
With the limited data available, prevalence's are not age standardised. Self reported surveys may underestimate true prevalence. Sources and references are available from the IOTF.
International Obesity TaskForce, London –January 2007
©

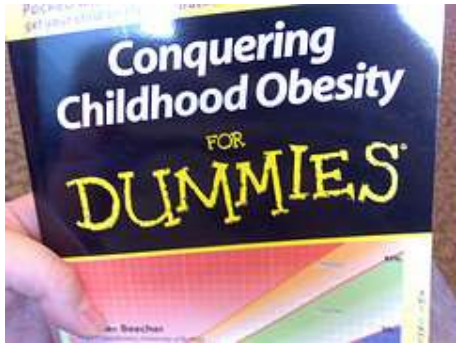
HAS OBAMA SOLD OUT TO THE BANKS?
MAY 14, 2012
Newsweek
When I Grow Up, I'm Going to Weigh 300 Lbs. Help!
P. 32
MELINDA GATES'S BIRTH-CONTROL BOMBSHELL
BILL MAHER REMEMBERS JOHNNY CARSON
THE RAW COURAGE OF CHINA'S BLIND FUGITIVE

fabtoons @ telus.net
caglecartoons.com
GENERATION XXXL
GEN-ERATION X
CHILDHOOD OBESITY EPIDEMIC..

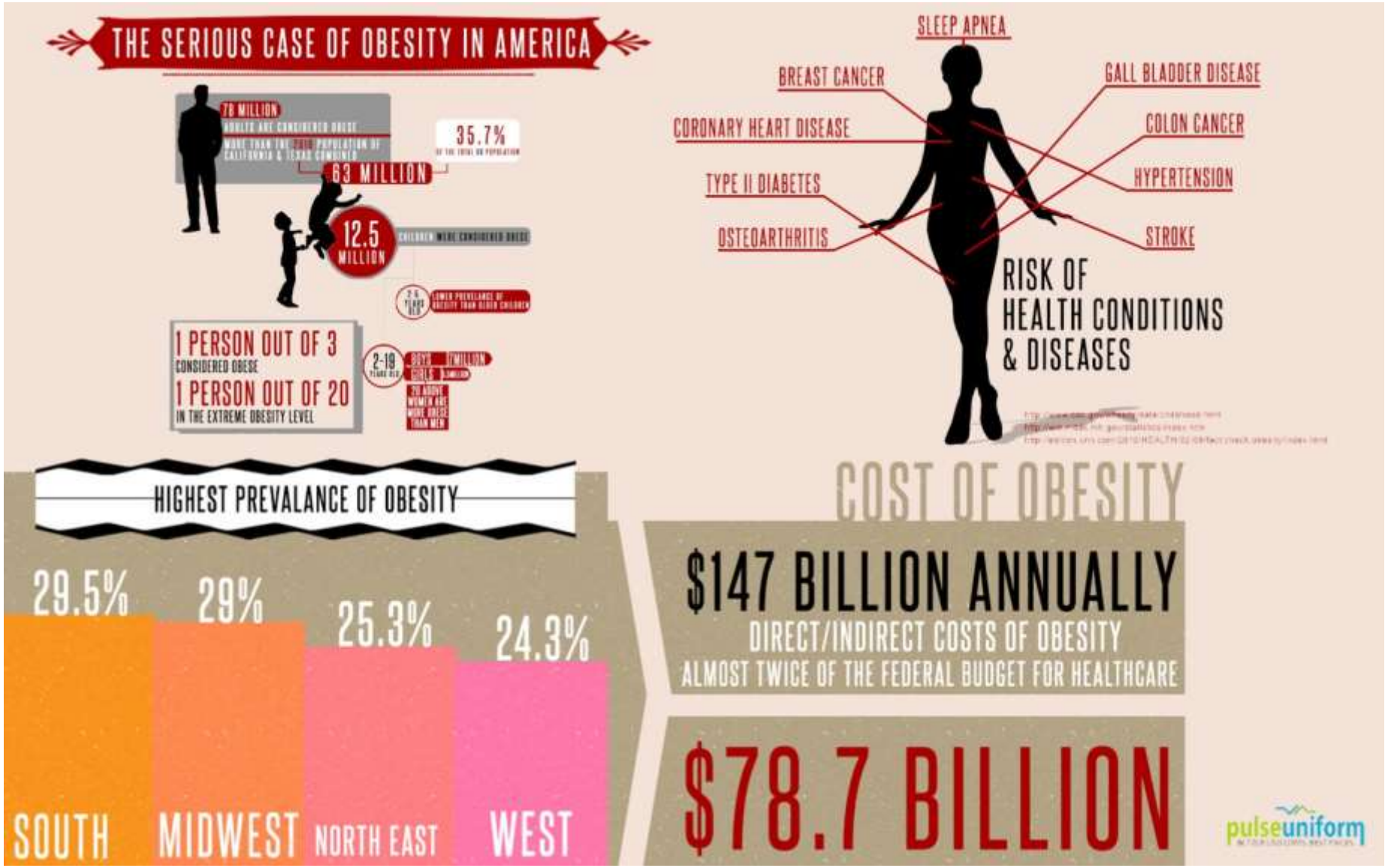

Medscape®
Trends
Overweight
Percent
Percent
20
15
10
5
0
6-11 years
12-19 years
2-5 years
1963-65
1966-70
1971-74
1976-80
1988-94
1999-00
2001-2
2003-4
Note: Overweight is defined as BMI >= gender- and weight-specific 95th percentile from the 2000 CDC Growth Charts.
Source: National Health Examination Surveys II (ages 6-11) and III (ages 12-17), National Health and Nutrition Examination Surveys I, II, III and 1999-2004, NCHS, CDC

THE OBESITY CRISIS

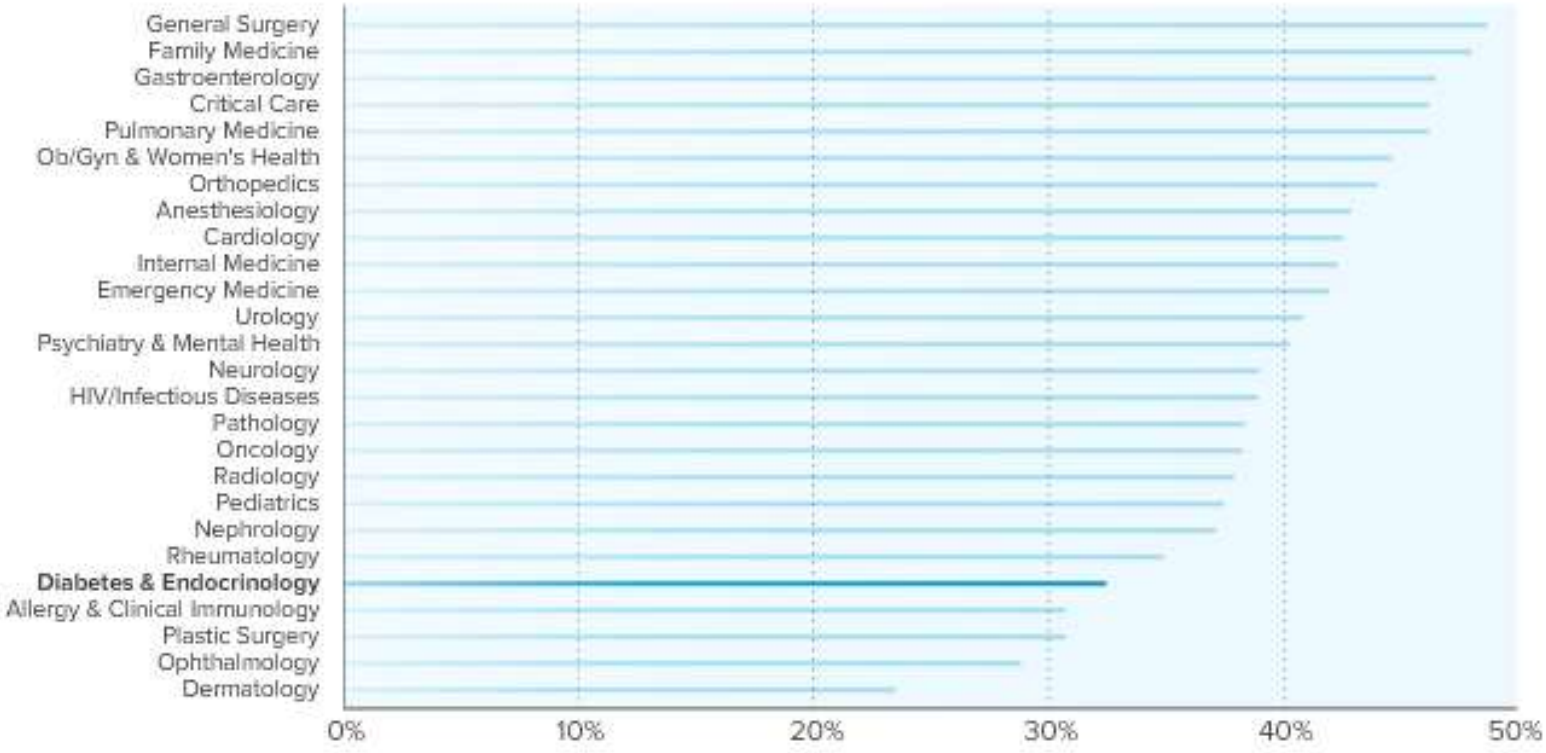
If an answer to this obesity epidemic is not found soon, the present generation of children will not live as long as their parents.



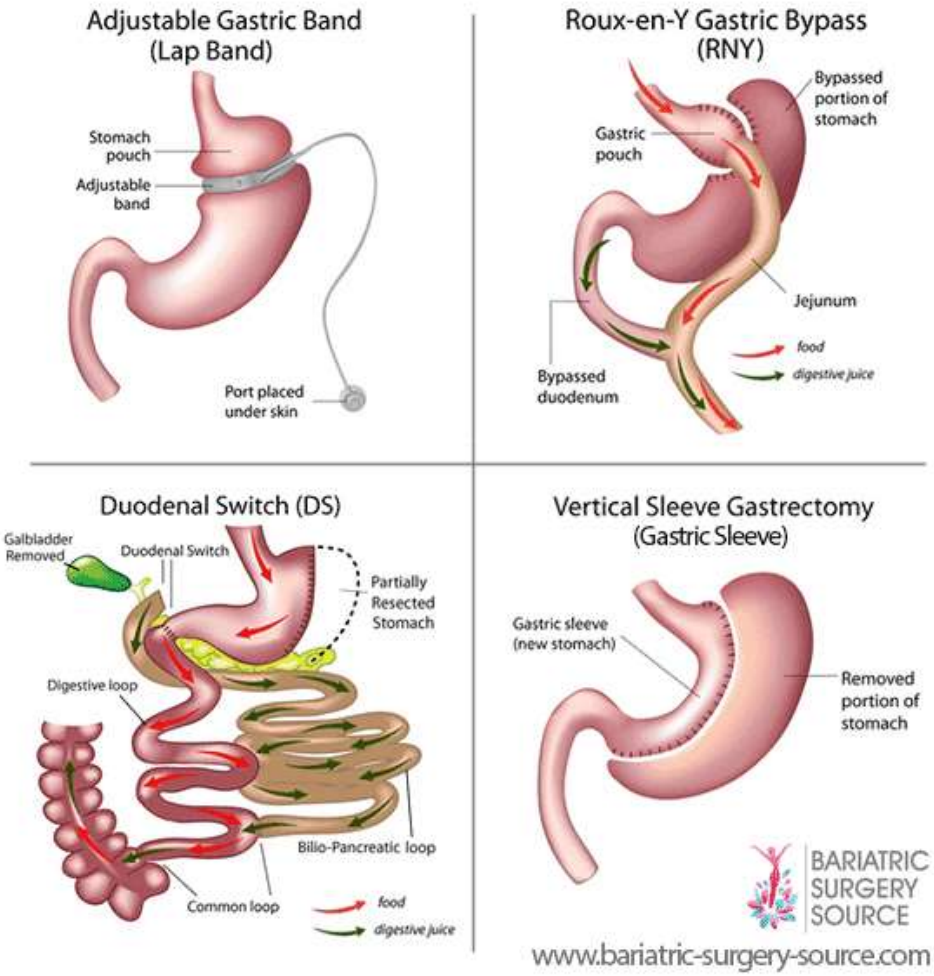
WHO 2002


THE SERIOUS CASE OF OBESITY IN AMERICA
78 MILLION
35.7%
63 MILLION
12.5 MILLION
1 PERSON OUT OF 3
CONSIDERED OBESE
1 PERSON OUT OF 20
IN THE EXTREME OBESITY LEVEL
SLEEP APNEA
BREAST CANCER
GALL BLADDER DISEASE
CORONARY HEART DISEASE
COLON CANCER
TYPE II DIABETES
HYPERTENSION
OSTEOARTHRITIS
STROKE
RISK OF
HEALTH CONDITIONS
& DISEASES
HIGHEST PREVALANCE OF OBESITY
29.5%
29%
25.3%
24.3%
SOUTH
MIDWEST
NORTH EAST
WEST
COST OF OBESITY
$147 BILLION ANNUALLY
DIRECT/INDIRECT COSTS OF OBESITY
ALMOST TWICE OF THE FEDERAL BUDGET FOR HEALTHCARE
$78.7 BILLION
pulseuniform

Which Physicians Are the Most Overweight?



4 Most Common Weight Loss Surgery Procedures in the United States



Roux-en-Y gastric bypass

Figure 1

Figure 2

Figure 3

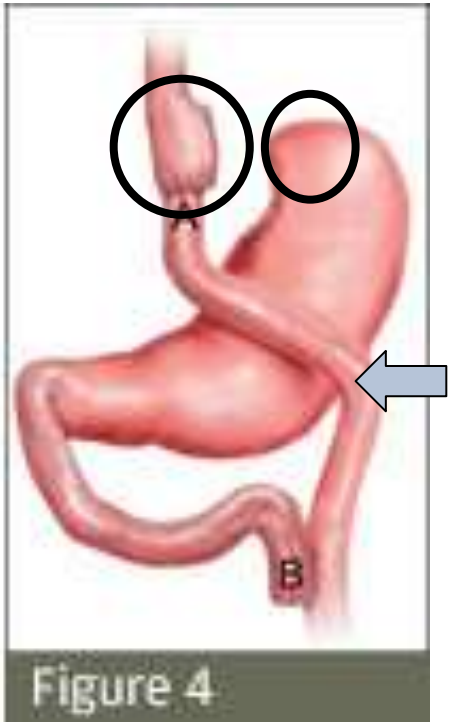
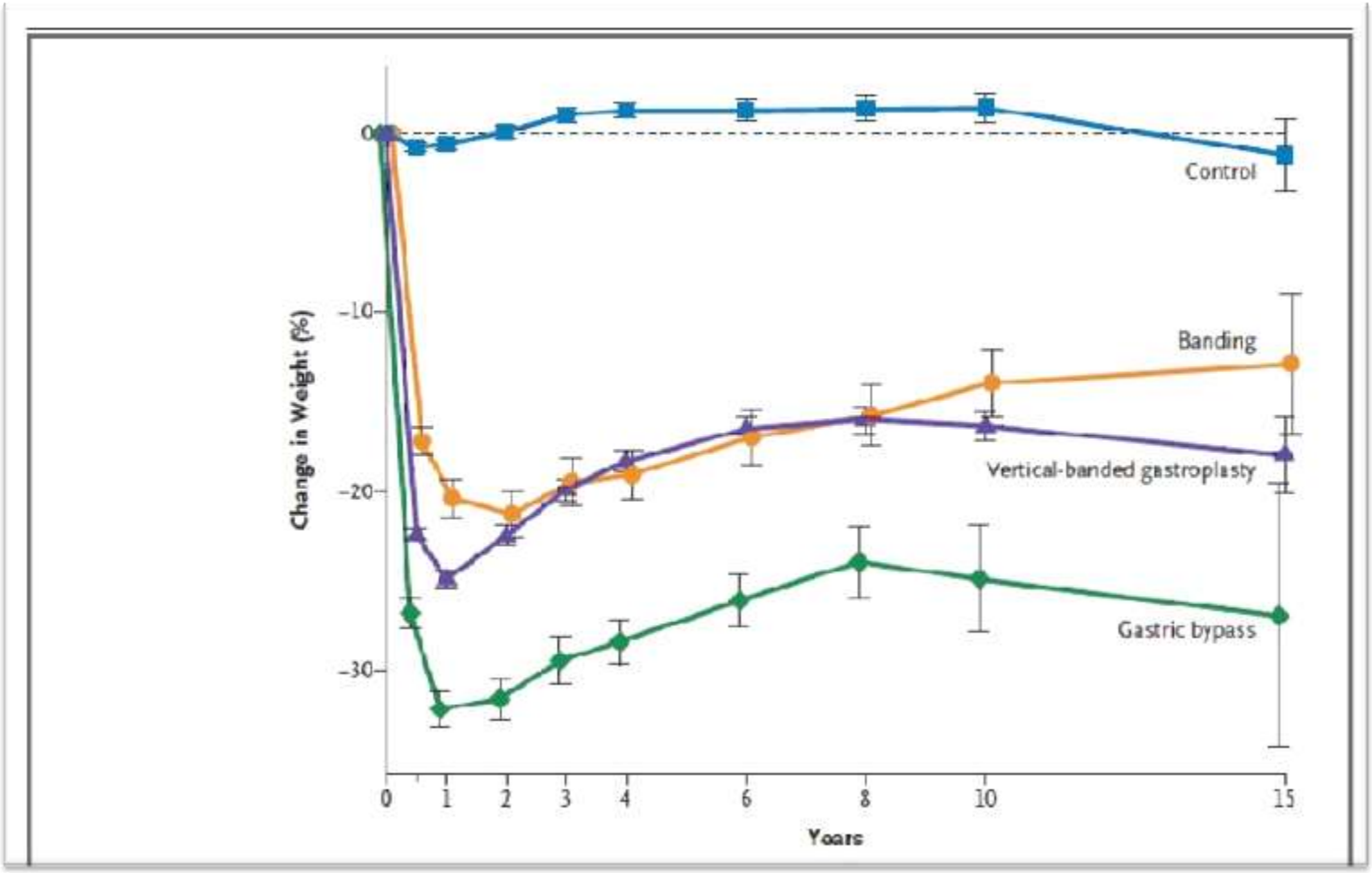
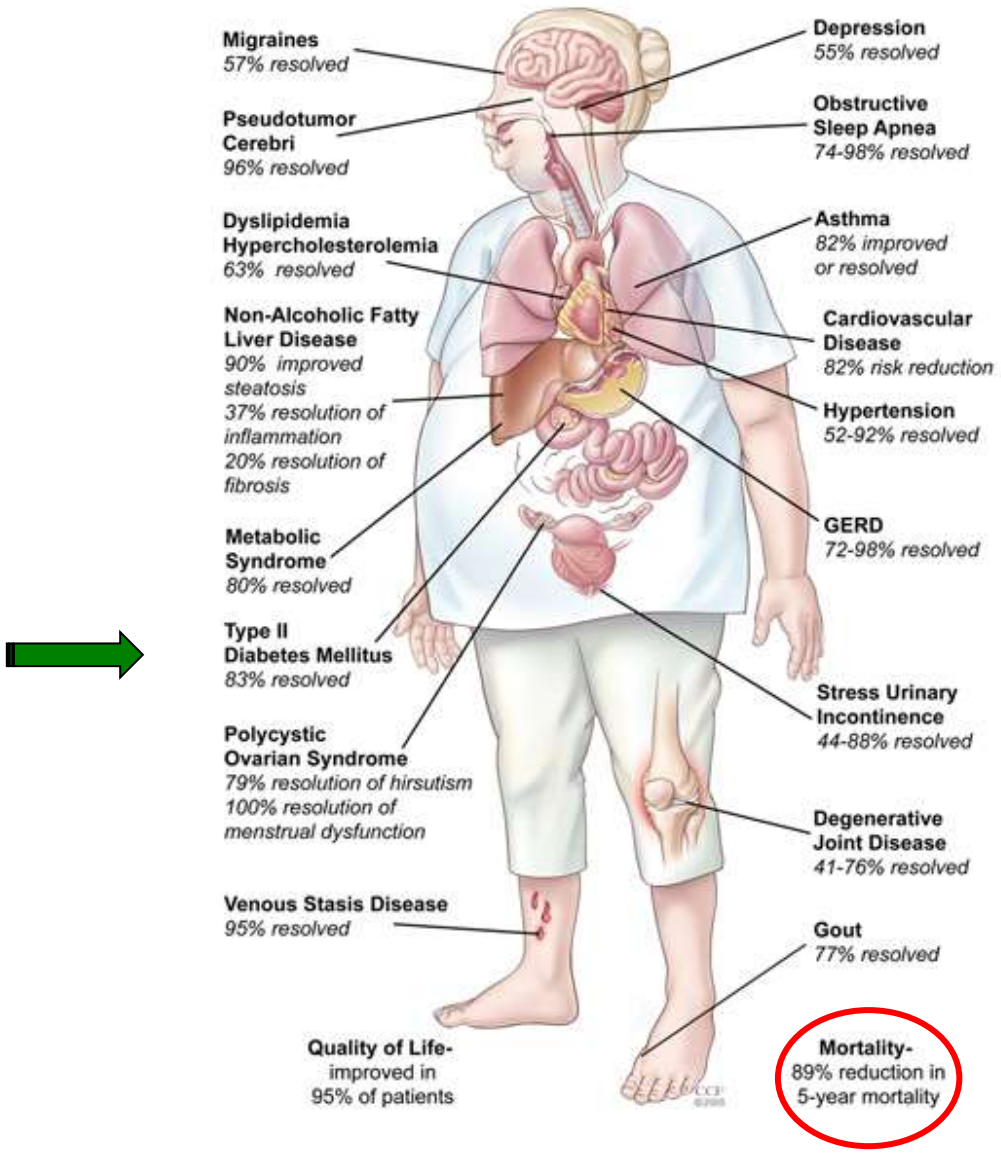


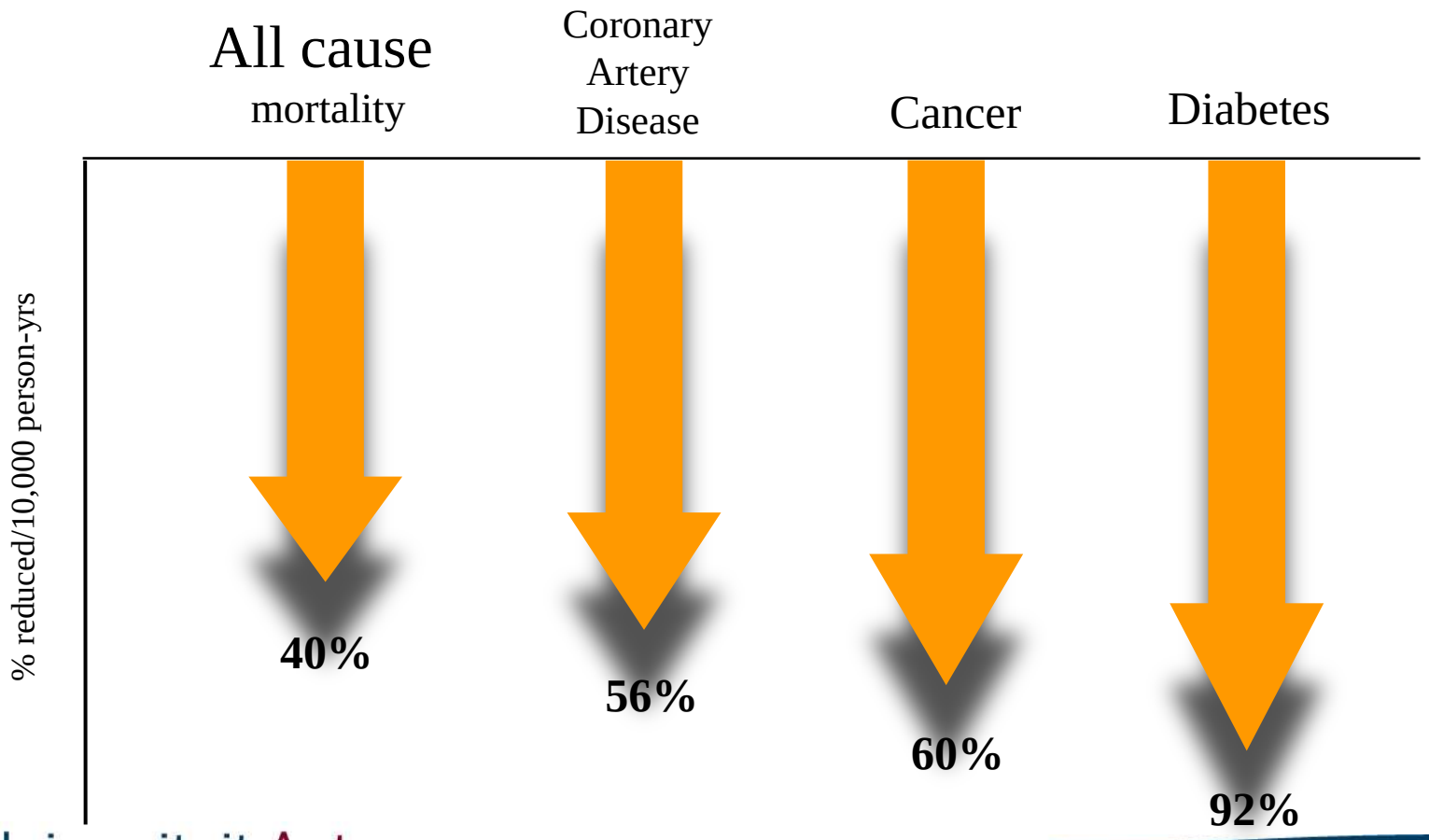
Figure 4



Sjostrom L et al. N Engl J Med 2007; 357:741-752


Migraines
57% resolved
Pseudotumor Cerebri
96% resolved
Dyslipidemia Hypercholesterolemia
63% resolved
Non-Alcoholic Fatty Liver Disease
90% improved steatosis
37% resolution of inflammation
20% resolution of fibrosis
Metabolic Syndrome
80% resolved
Type II Diabetes Mellitus
83% resolved
Polycystic Ovarian Syndrome
79% resolution of hirsutism
100% resolution of menstrual dysfunction
Venous Stasis Disease
95% resolved
Quality of Life-
improved in
95% of patients
Depression
55% resolved
Obstructive Sleep Apnea
74-98% resolved
Asthma
82% improved or resolved
Cardiovascular Disease
82% risk reduction
Hypertension
52-92% resolved
GERD
72-98% resolved
Stress Urinary Incontinence
44-88% resolved
Degenerative Joint Disease
41-76% resolved
Gout
77% resolved
Mortality-
89% reduction in
5-year mortality

Long-Term Mortality After Gastric Bypass Surgery



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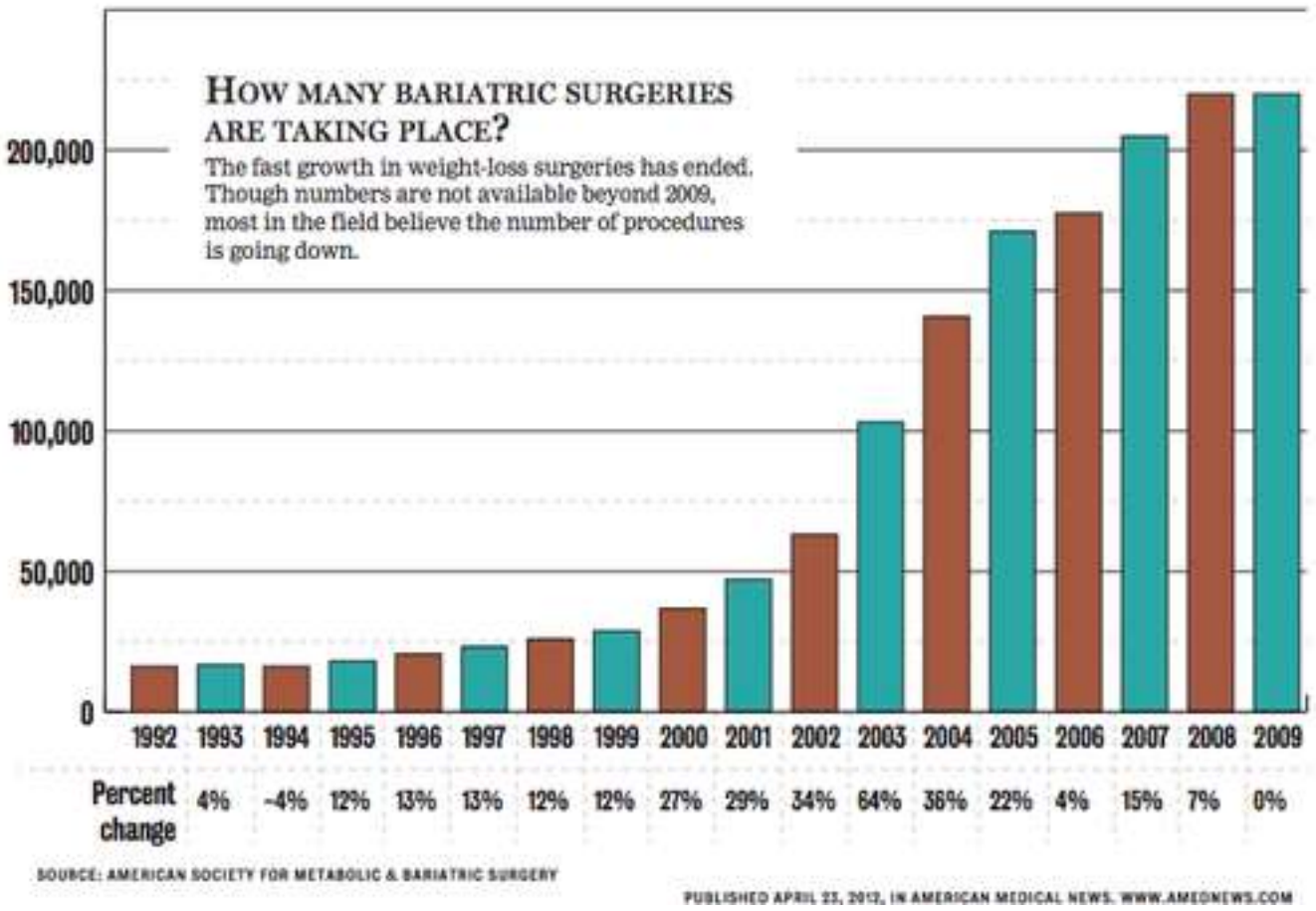
Adams TD, et al. NEJM 2007;357:753

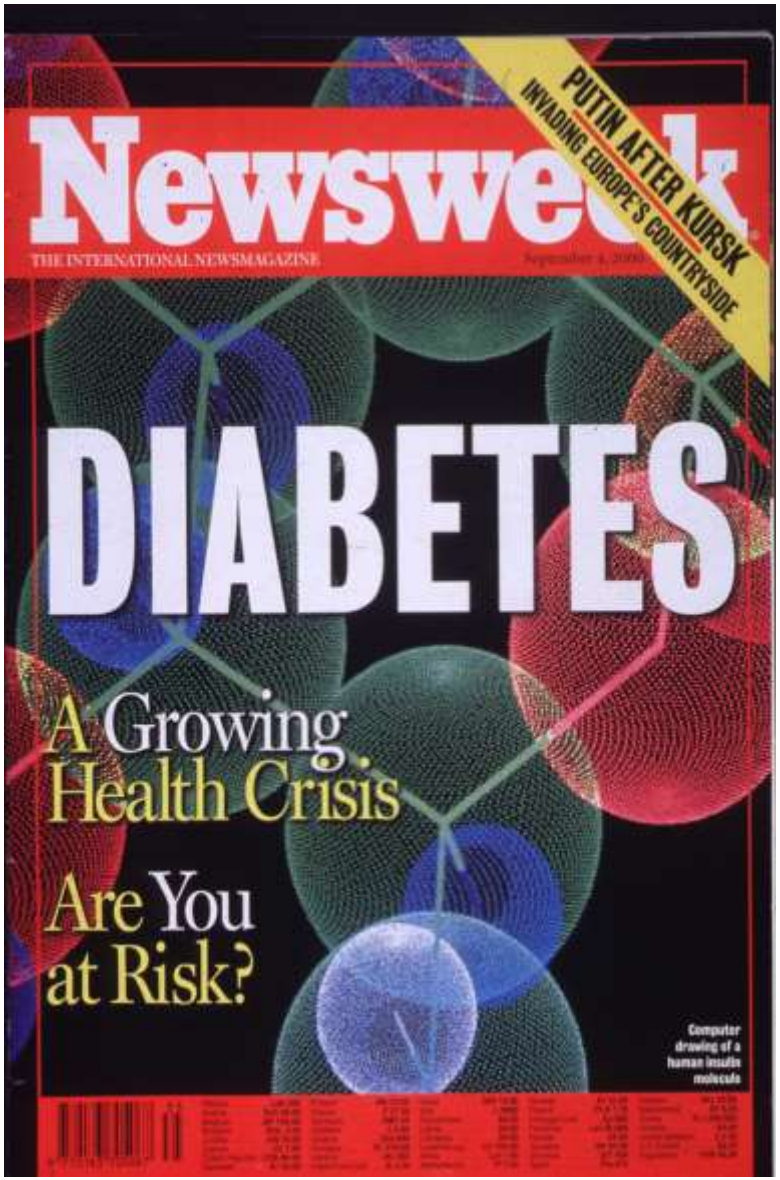
The Risks: Mortality Rates

Mortality rates following common operations in U.S. hospitals [1]				
	Heart bypass	Prostate[2]	Esophageal resection	Hip replacement
National average mortality rate	3.5	0.5	9.1	0.3

1. Dimick JB, Welch HG, Birkmeyer JD. Surgical mortality as an indicator of hospital equality. JAMA 2004; 292:847-51
2. JAMA, Oct 2004 Bariatric Surgery A Systemic Review and Meta-analysis
3. BOLD Data, 2011

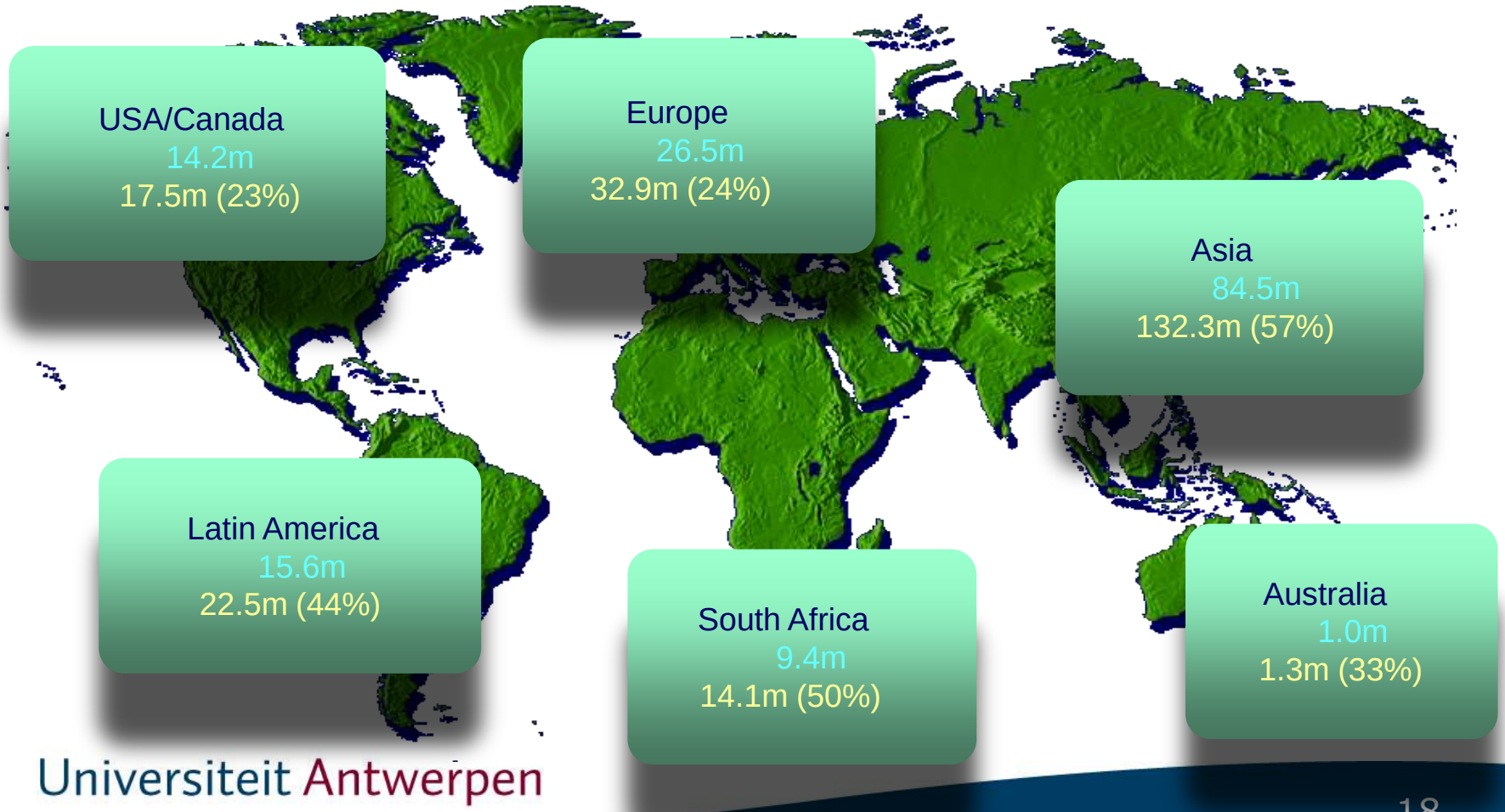
Mortality rates following Weight Loss Surgery [3]


HOW MANY BARIATRIC SURGERIES ARE TAKING PLACE?
The fast growth in weight-loss surgeries has ended. Though numbers are not available beyond 2009, most in the field believe the number of procedures is going down.
200,000
150,000
100,000
50,000
0
1992 1993 1994 1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009
Percent change 4% -4% 12% 13% 13% 12% 12% 27% 29% 34% 64% 36% 22% 4% 15% 7% 0%
SOURCE: AMERICAN SOCIETY FOR METABOLIC & BARIATRIC SURGERY
PUBLISHED APRIL 23, 2012, IN AMERICAN MEDICAL NEWS. WWW.AMEDNEWS.COM


Newsweek
THE INTERNATIONAL NEWSMAGAZINE
PUTIN AFTER KURSK
INVADING EUROPE'S COUNTRYSIDE
DIABETES
A Growing Health Crisis
Are You at Risk?
Computer drawing of a human insulin molecule

The type 2 diabetes epidemic

Number of people with diabetes (million) by region
for 2000 and 2010 (% increase)



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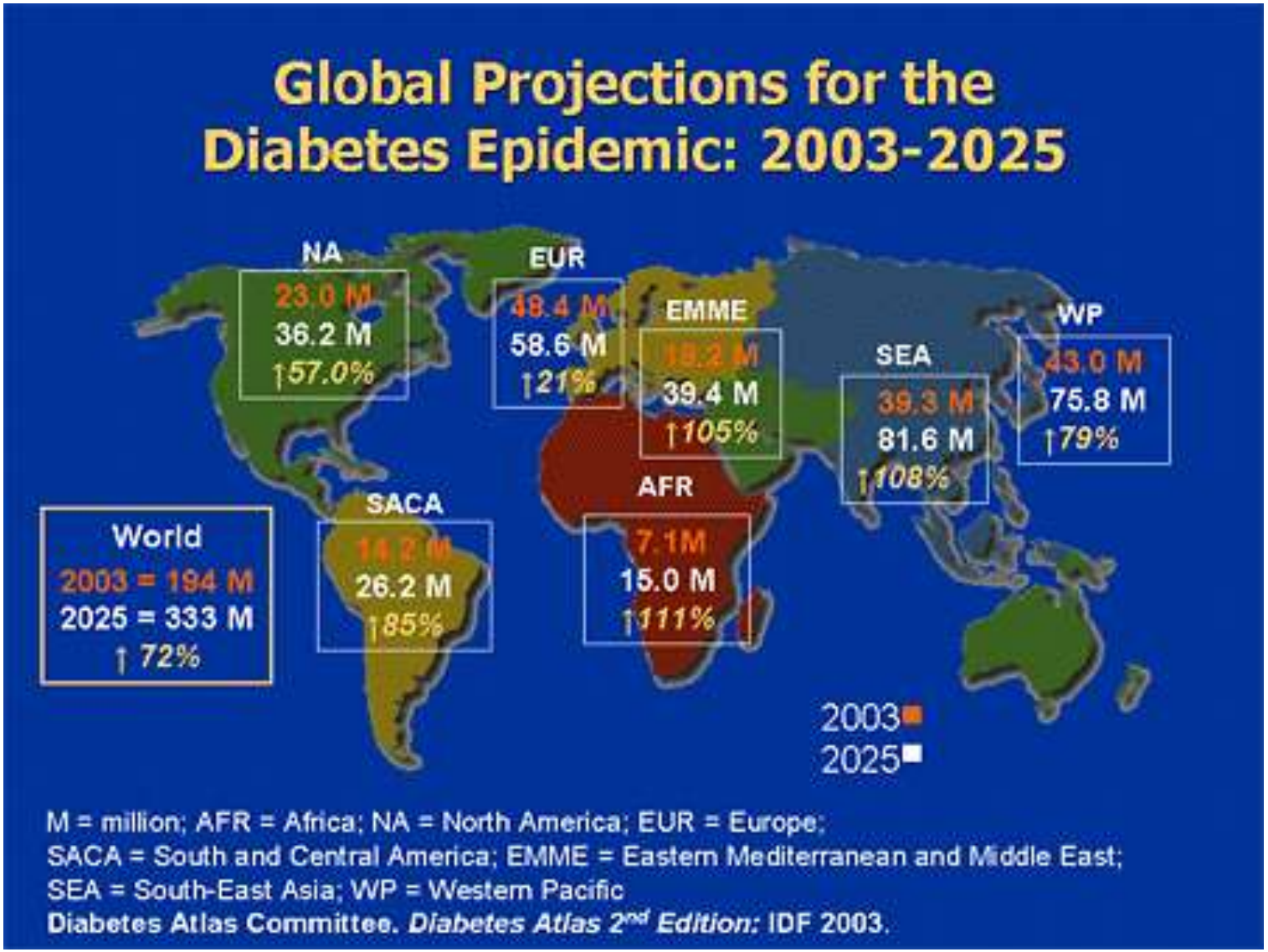
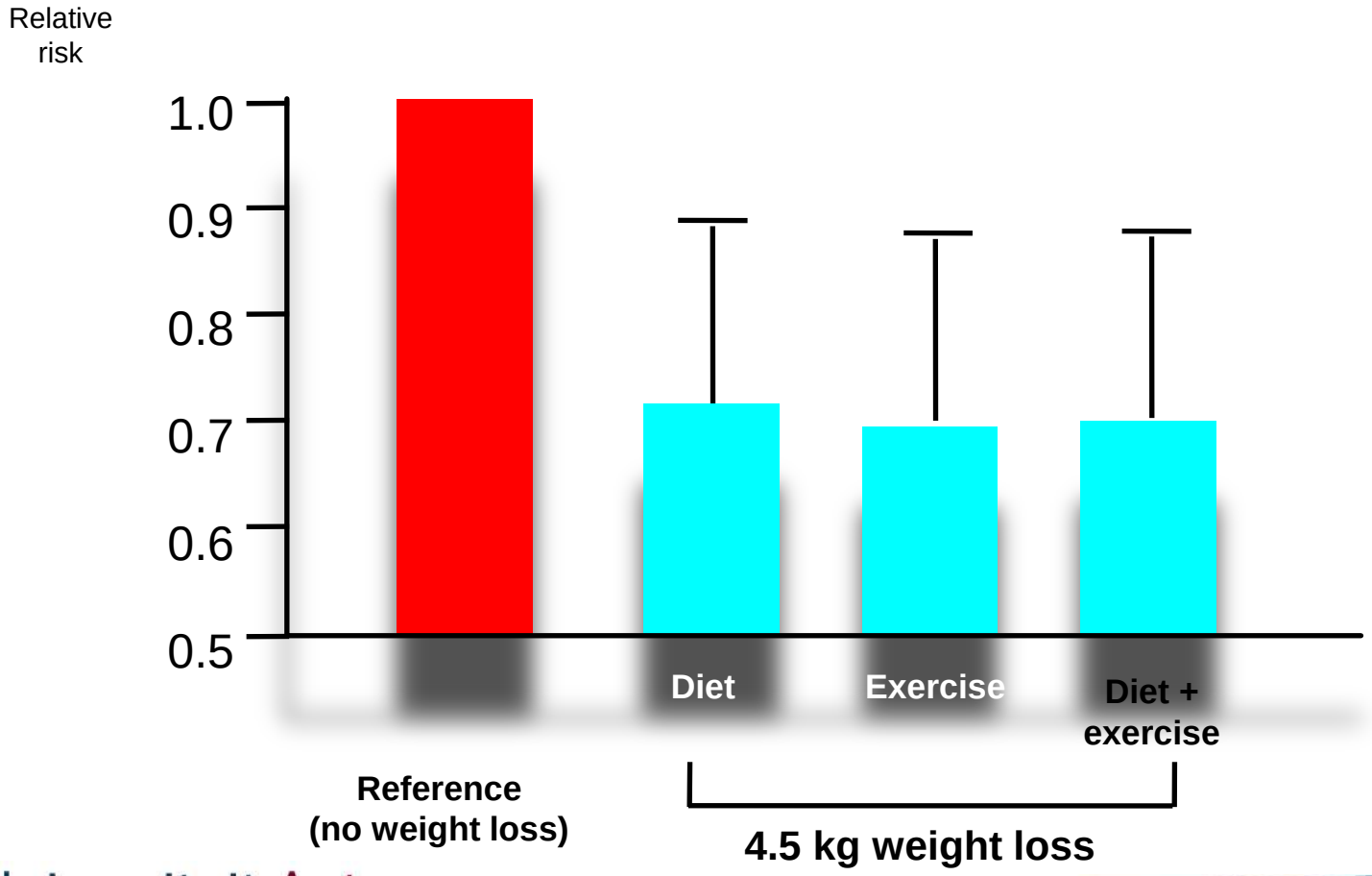

Global Projections for the Diabetes Epidemic: 2003-2025
NA
23.0 M
36.2 M
↑57.0%
EUR
48.4 M
58.6 M
↑21%
EMME
19.2 M
39.4 M
↑105%
SEA
39.3 M
81.6 M
↑108%
WP
43.0 M
75.8 M
↑79%
SACA
14.2 M
26.2 M
↑85%
AFR
7.1M
15.0 M
↑111%
World
2003 = 194 M
2025 = 333 M
↑ 72%
2003
2025
M = million; AFR = Africa; NA = North America; EUR = Europe;
SACA = South and Central America; EMME = Eastern Mediterranean and Middle East;
SEA = South-East Asia; WP = Western Pacific
Diabetes Atlas Committee. Diabetes Atlas 2nd Edition: IDF 2003.

Modest Weight Loss Reduces Risk of Type 2 Diabetes by 30%



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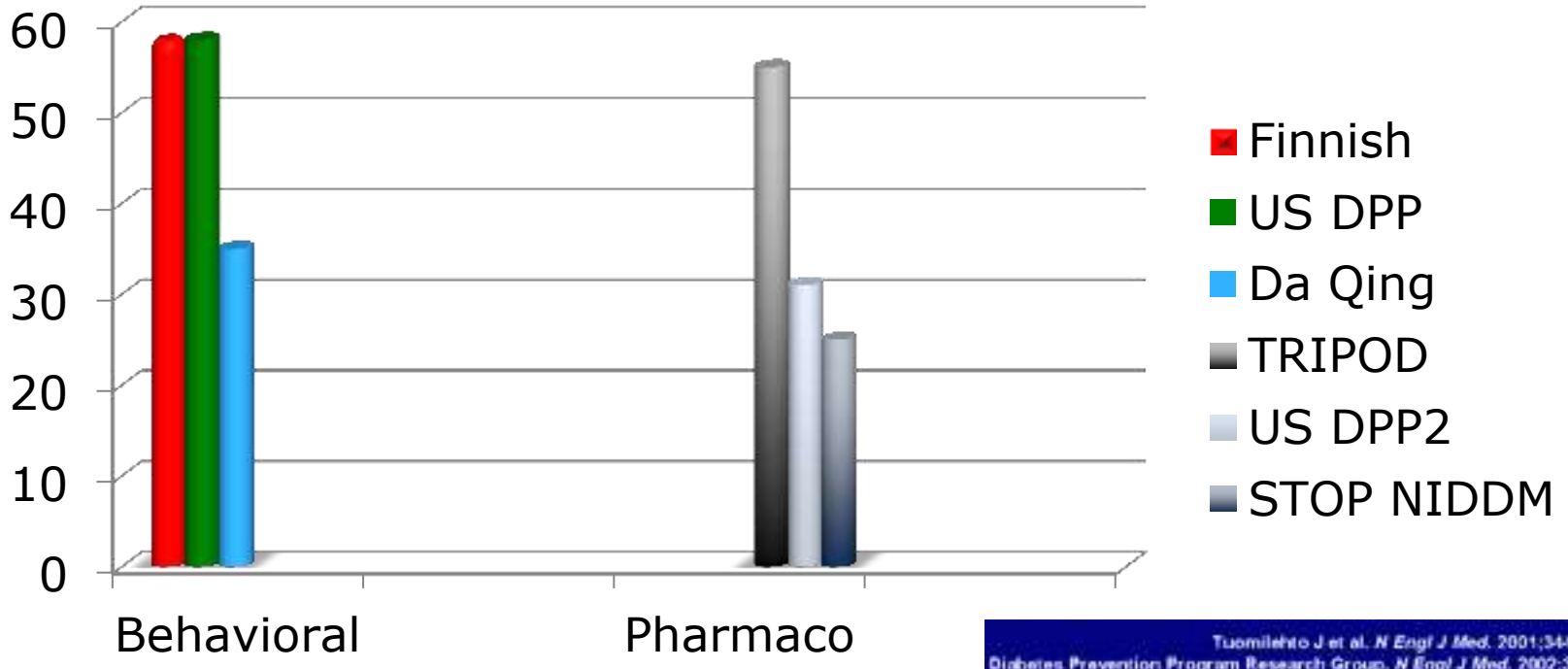
Wing RR et al. Diabetes Care 1998

Wing RR et al. Diabetes Care 1998

Can diabetes type 2 be prevented?



Tuomilehto J et al. *N Engl J Med.* 2001;344:1343-1350.
Diabetes Prevention Program Research Group. *N Engl J Med.* 2002;346:393-403.
Buchanan TA et al. *Diabetes.* 2002;51:2796-2803.
Chiasson JL et al. *Lancet.* 2002;359:2072-2077.

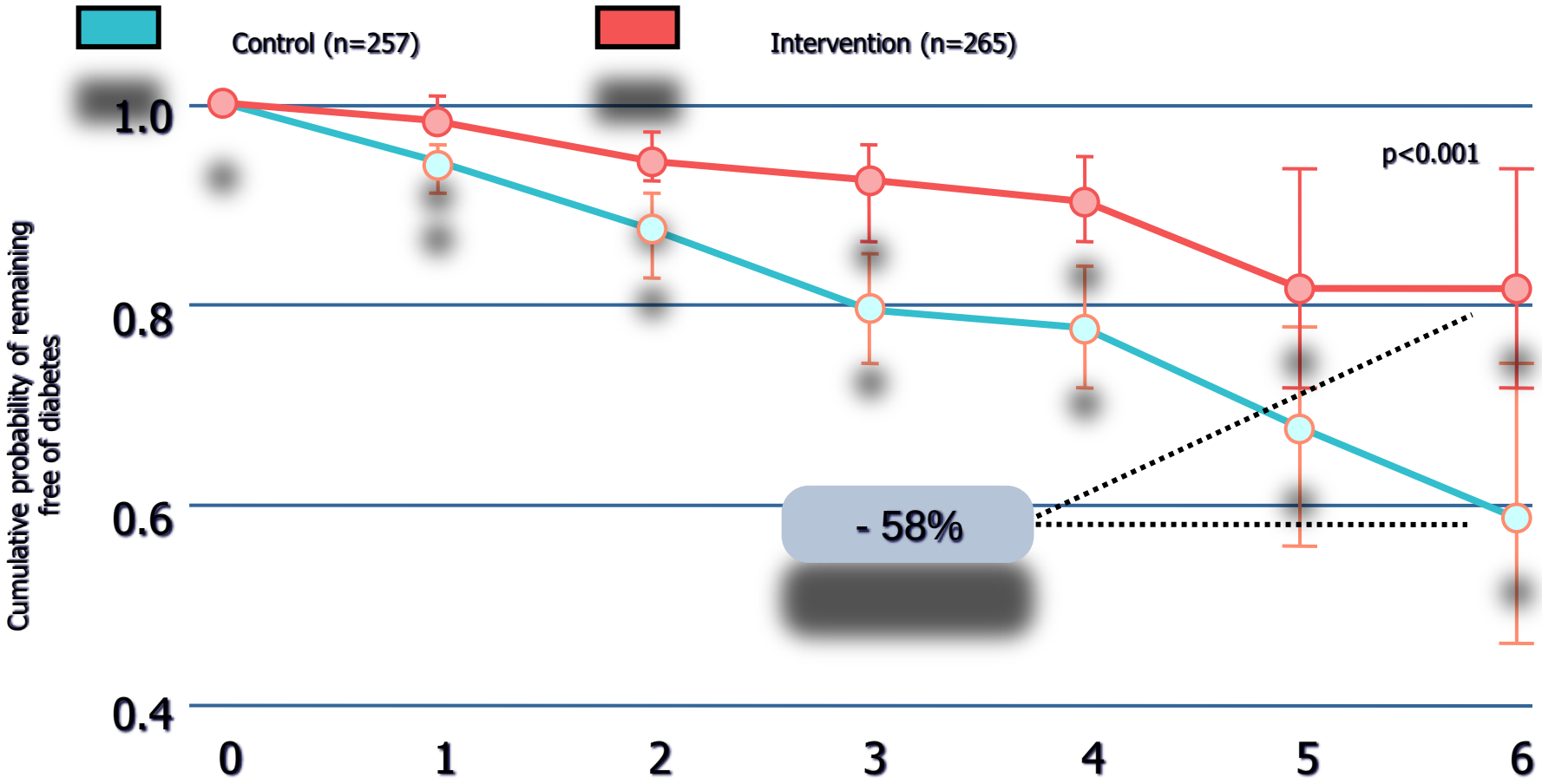
Lifestyle Interventions Finnish Diabetes Prevention Study

- 522 subjects, 40-65 years of age
  - BMI ≥25 kg/m^2; IGT: 2-h PPG 140-200 mg/dL
- Control group: general oral and written information diet and exercise
- Intervention group: individualized
  - Reduce weight ≥5%
  - Decrease fat ≤30%, saturated fat ≤10% energy
  - Increase fiber to at least 15 g/1000 kcal
  - Moderate exercise ≥30 minutes/day
- Primary end point: diagnosis of diabetes

American Diabetes Association.

Tuomilehto J, et al for the Finnish Diabetes Prevention Study Group. *N Engl J Med*. 2001;344:1343-1350.

Finnish Diabetes Prevention Study



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Tuomilehto J, N Engl J Med 2001;344:1343-50

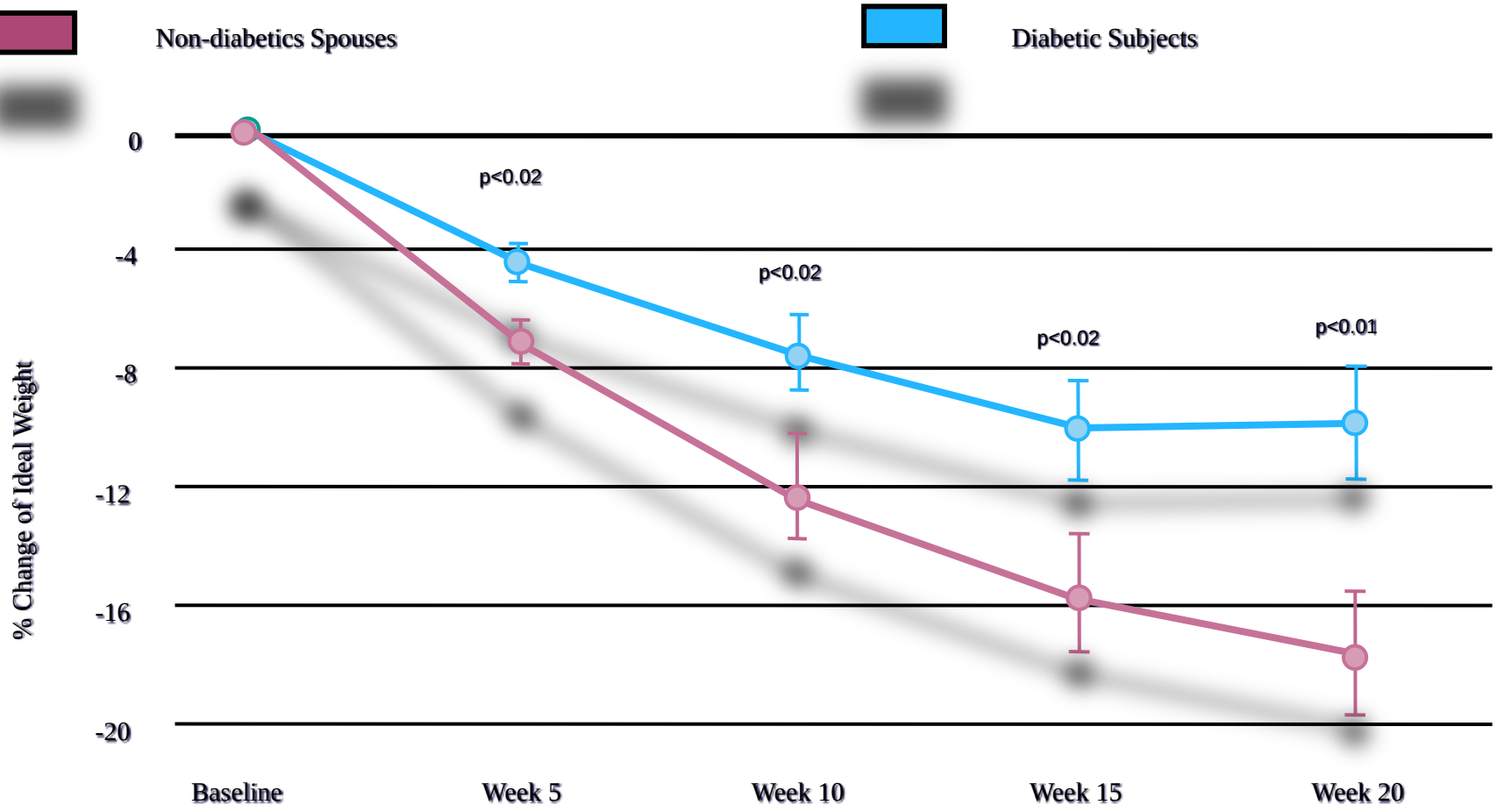
Lifestyle Interventions
Da Qing Study 20-Year Follow-Up

- Combined lifestyle intervention vs control
  - 51% lower incidence of diabetes during active intervention
  - 43% lower incidence over 20 years
  - 3.6 years fewer with diabetes

	Average Annual Incidence	20-Year Cumulative Incidence
Controls	11%	93%
Combined lifestyle intervention	7%	80%

Li G, et al. *Lancet*. 2008;371:1783-1789.

Weight Loss in Overweight Diabetic Subjects and Overweight Non-diabetic Spouses



Adapted from Wing RR. Diabetes Care 1987;10:563-6

ANNALS OF SURGERY
A Monthly Review of Surgical Science Since 1885

Who would have thought it? An operation proves to be the most effective therapy for adult onset diabetes”

W Pories 1995 222: 339-350

KEY POINT: Surgery (RYGBP) is more effective than medical therapy in treating diabetes type 2

83% of type 2 diabetes patients euglycaemic /nl HbA1c

ANNALS OF SURGERY
A Monthly Review of Surgical Science Since 1885

Diabetes and Hypertension in severe obesity and effects of gastric bypass induced weight loss (n> 1000 15% diabetic)

H Sugarman 2003 237 751-758

83% resolution @ 1year
86% resolution @ 5 years

ANNALS OF SURGERY
A Monthly Review of Surgical Science Since 1885

Effect of laparoscopic Roux en Y gastric bypass on type 2 diabetes mellitus

Schauer 2003 238 467-485

treatment	Net reduction
OA usage	80%
OA quantity	84%
Insulin usage	79%
Insulin quantity	90%

30% discontinued medication at discharge of hospital

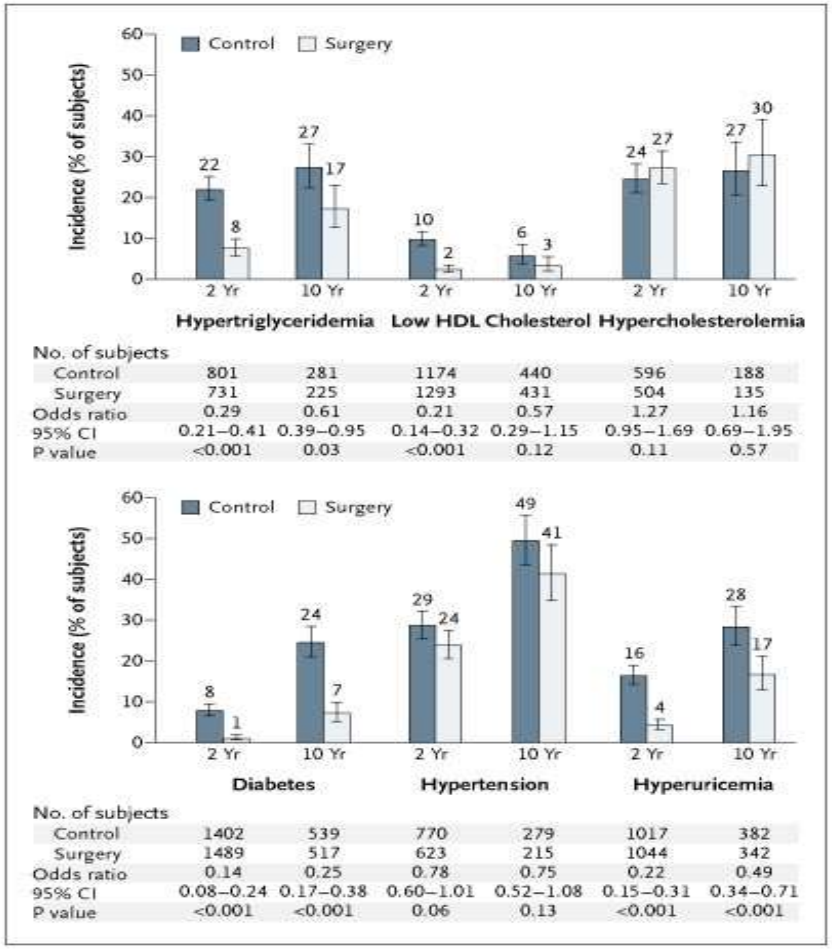
		Improved 33	Resolved 158
Severity			
	IFG	0	100%
	Diet	3%	97%
	Oral	13%	87%
	Insulin	38%	62%

		Improved 33	Resolved 158
Duration			
	<5y	5%	95%
	5-10y	25%	75%
	>10y	46%	54%

Schauer Ann Surg 2003

Is Weight Loss Surgery the Best Currently Available Treatment for Type II Diabetes?

Incidence of Diabetes among Subjects in the SOS Study over 2- and 10-Year Periods



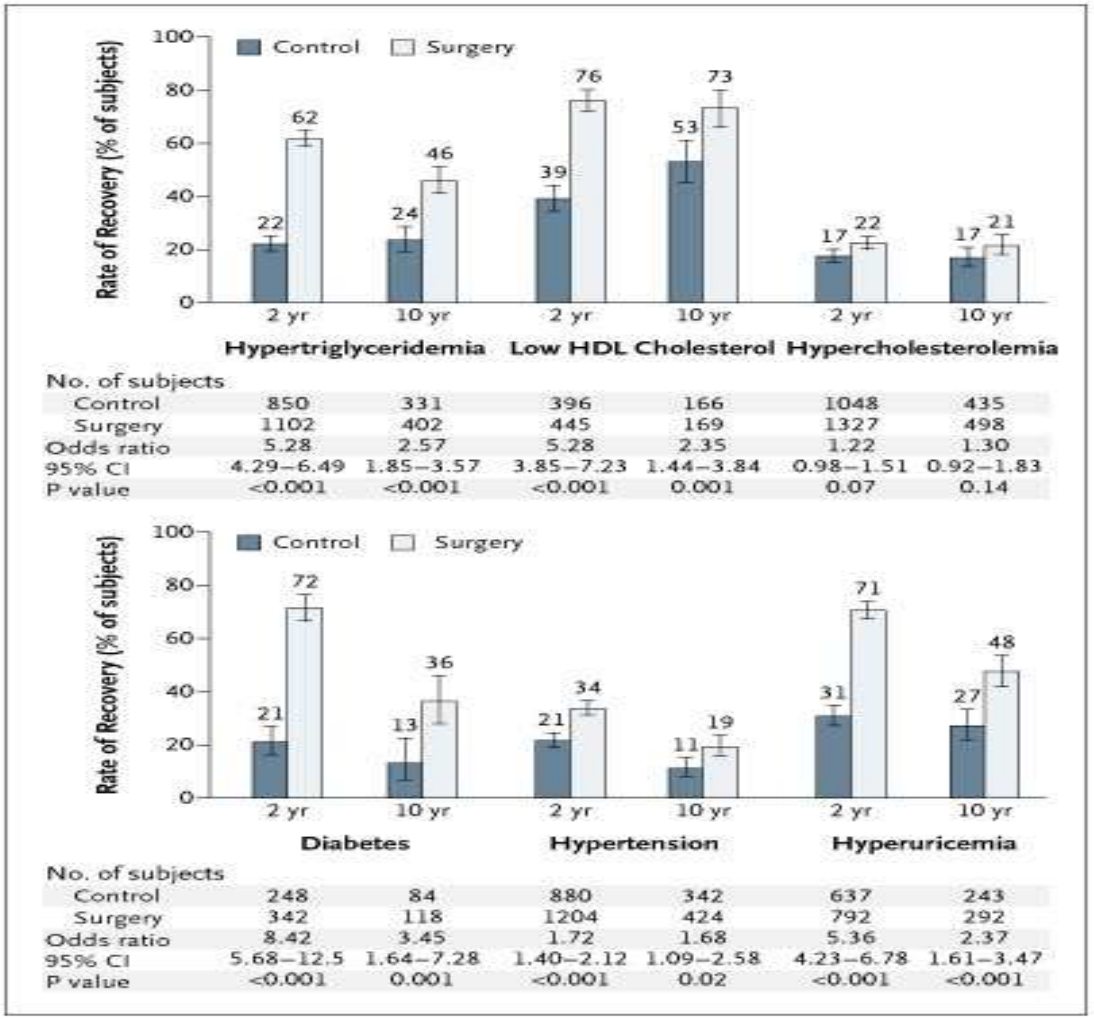
No. of subjects						
Control	801	281	1174	440	596	188
Surgery	731	225	1293	431	504	135
Odds ratio	0.29	0.61	0.21	0.57	1.27	1.16
95% CI	0.21–0.41	0.39–0.95	0.14–0.32	0.29–1.15	0.95–1.69	0.69–1.95
P value	<0.001	0.03	<0.001	0.12	0.11	0.57

No. of subjects						
Control	1402	539	770	279	1017	382
Surgery	1489	517	623	215	1044	342
Odds ratio	0.14	0.25	0.78	0.75	0.22	0.49
95% CI	0.08–0.24	0.17–0.38	0.60–1.01	0.52–1.08	0.15–0.31	0.34–0.71
P value	<0.001	<0.001	0.06	0.13	<0.001	<0.001

The NEW ENGLAND JOURNAL of MEDICINE

Sjostrom L et al. N Engl J Med 2004;351:2683-2693

Recovery from Diabetes over 2 and 10 Years in Surgically Treated Subjects and Their Obese Controls



No. of subjects						
Control	850	331	396	166	1048	435
Surgery	1102	402	445	169	1327	498
Odds ratio	5.28	2.57	5.28	2.35	1.22	1.30
95% CI	4.29–6.49	1.85–3.57	3.85–7.23	1.44–3.84	0.98–1.51	0.92–1.83
P value	<0.001	<0.001	<0.001	0.001	0.07	0.14

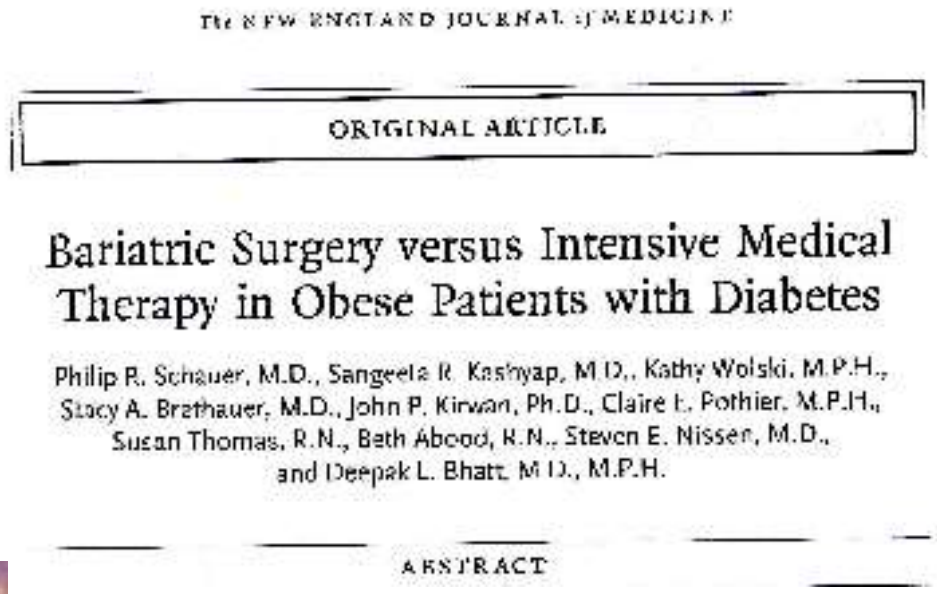
No. of subjects						
Control	248	84	880	342	637	243
Surgery	342	118	1204	424	792	292
Odds ratio	8.42	3.45	1.72	1.68	5.36	2.37
95% CI	5.68–12.5	1.64–7.28	1.40–2.12	1.09–2.58	4.23–6.78	1.61–3.47
P value	<0.001	0.001	<0.001	0.02	<0.001	<0.001

The NEW ENGLAND JOURNAL of MEDICINE

Sjostrom L et al. N Engl J Med 2004;351:2683-2693

RCT comparing medical with surgical therapy for DMT2

Author	Year	Treatment groups	N	FU	Remission rates
Dixon	2009	Meds vs LAGB	30 vs 30	24	13% vs 73%
Mingrone	2012	Meds vs BPD vs RYGBP	20 vs 20 vs 20	24	0% vs 95% vs 75%
Schauer	2014	Meds vs RYGBP vs GS	50 vs 50 vs 50	36	5% vs 38% vs 24%
Ikramuddin	2013	Meds vs RYGBP (+Meds)	60 vs 60	12	19% vs 47%



THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

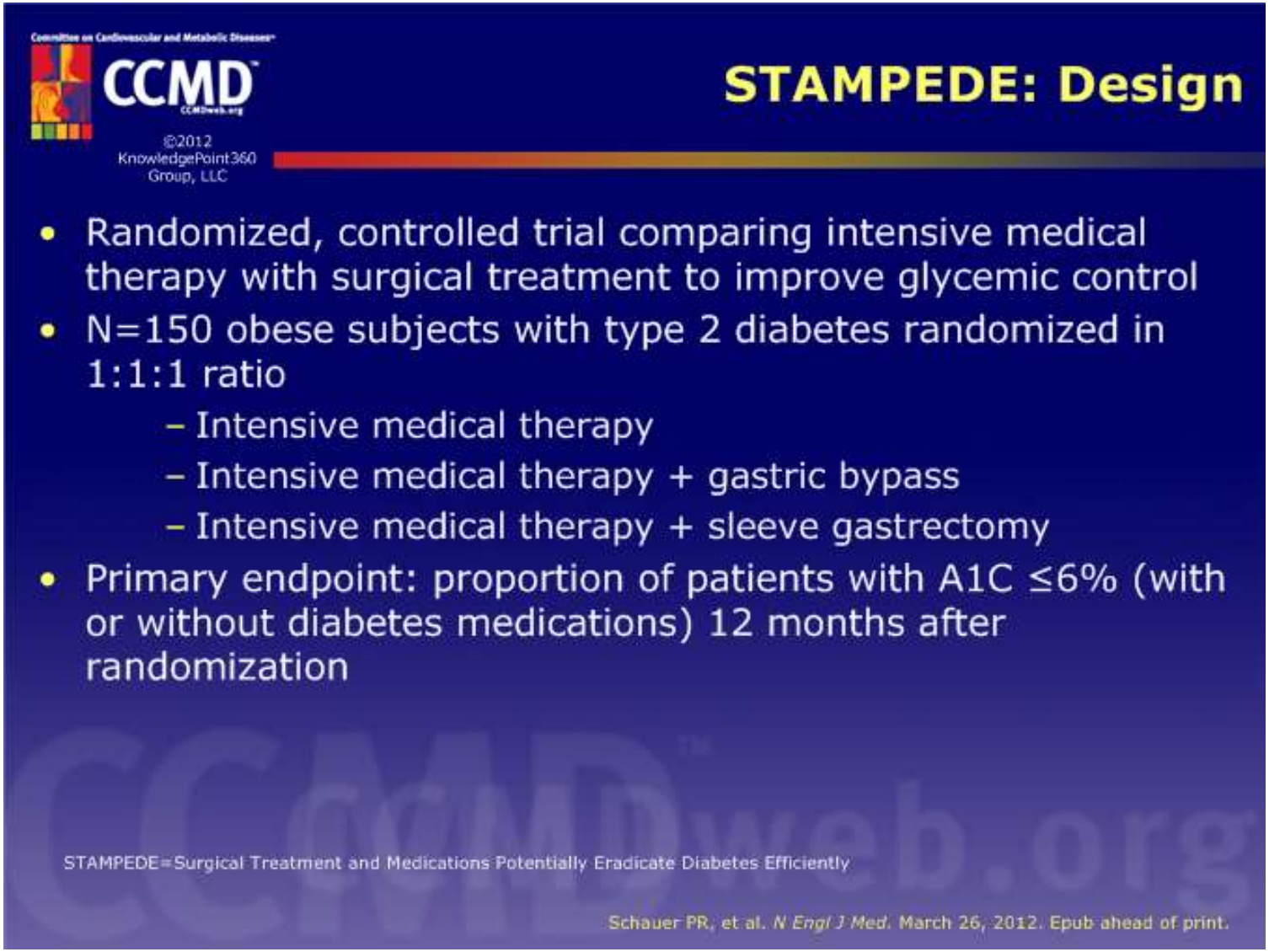
Bariatric Surgery versus Intensive Medical Therapy in Obese Patients with Diabetes

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.

ABSTRACT

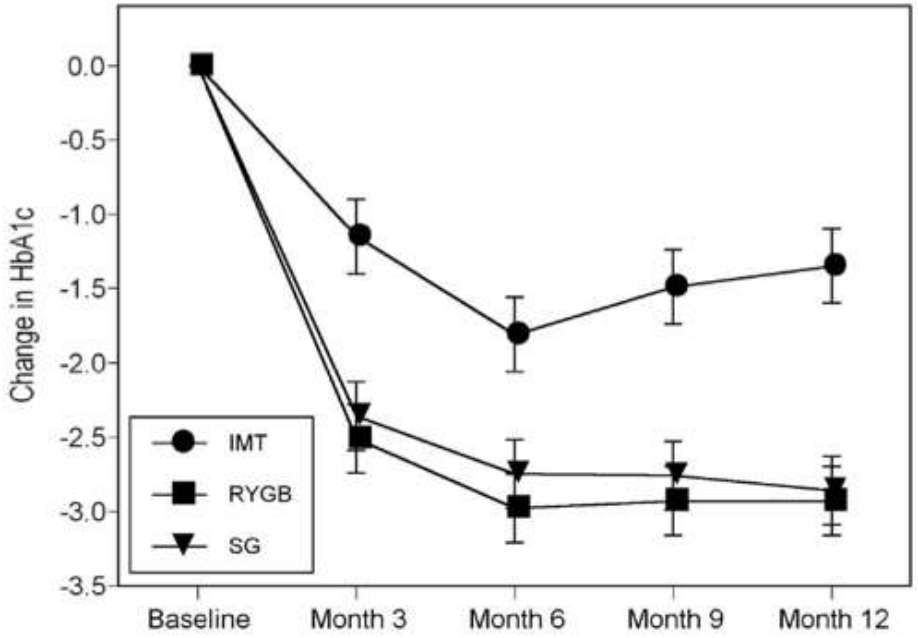
STAMPEDE trial

Surgical **T**reatment **a**nd **M**edications **P**otentially **E**radicate **D**iabetes **E**fficiently


Committee on Cardiovascular and Metabolic Diseases
CCMD
CCMDweb.org
©2012 KnowledgePoint360 Group, LLC
STAMPEDE: Design
• Randomized, controlled trial comparing intensive medical therapy with surgical treatment to improve glycemic control
• N=150 obese subjects with type 2 diabetes randomized in 1:1:1 ratio
– Intensive medical therapy
– Intensive medical therapy + gastric bypass
– Intensive medical therapy + sleeve gastrectomy
• Primary endpoint: proportion of patients with A1C ≤6% (with or without diabetes medications) 12 months after randomization
STAMPEDE=Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently
Schauer PR, et al. N Engl J Med. March 26, 2012. Epub ahead of print.

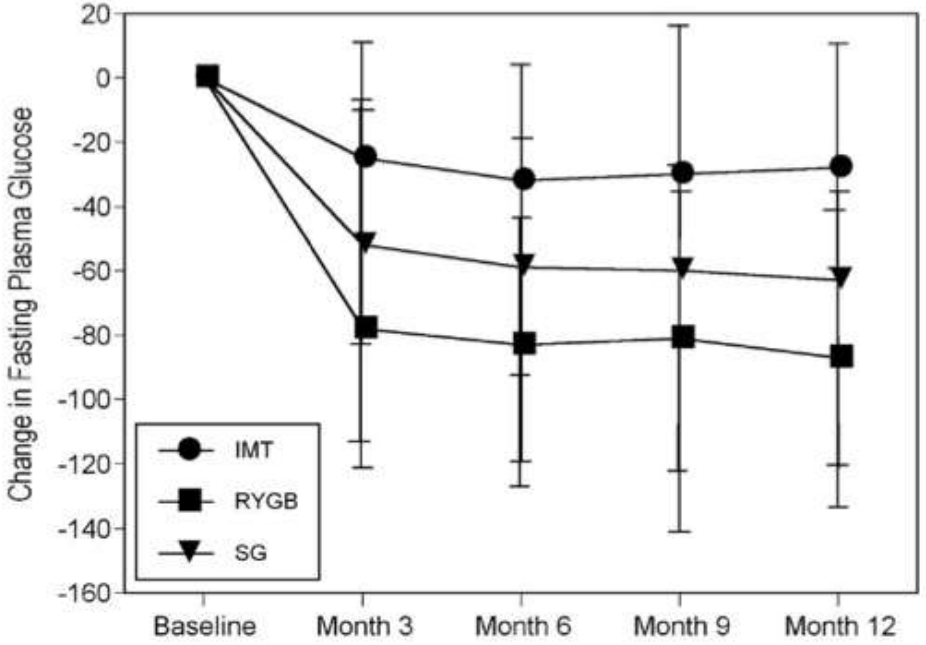
1-year Outcomes, Impact on T2DM Control

A.

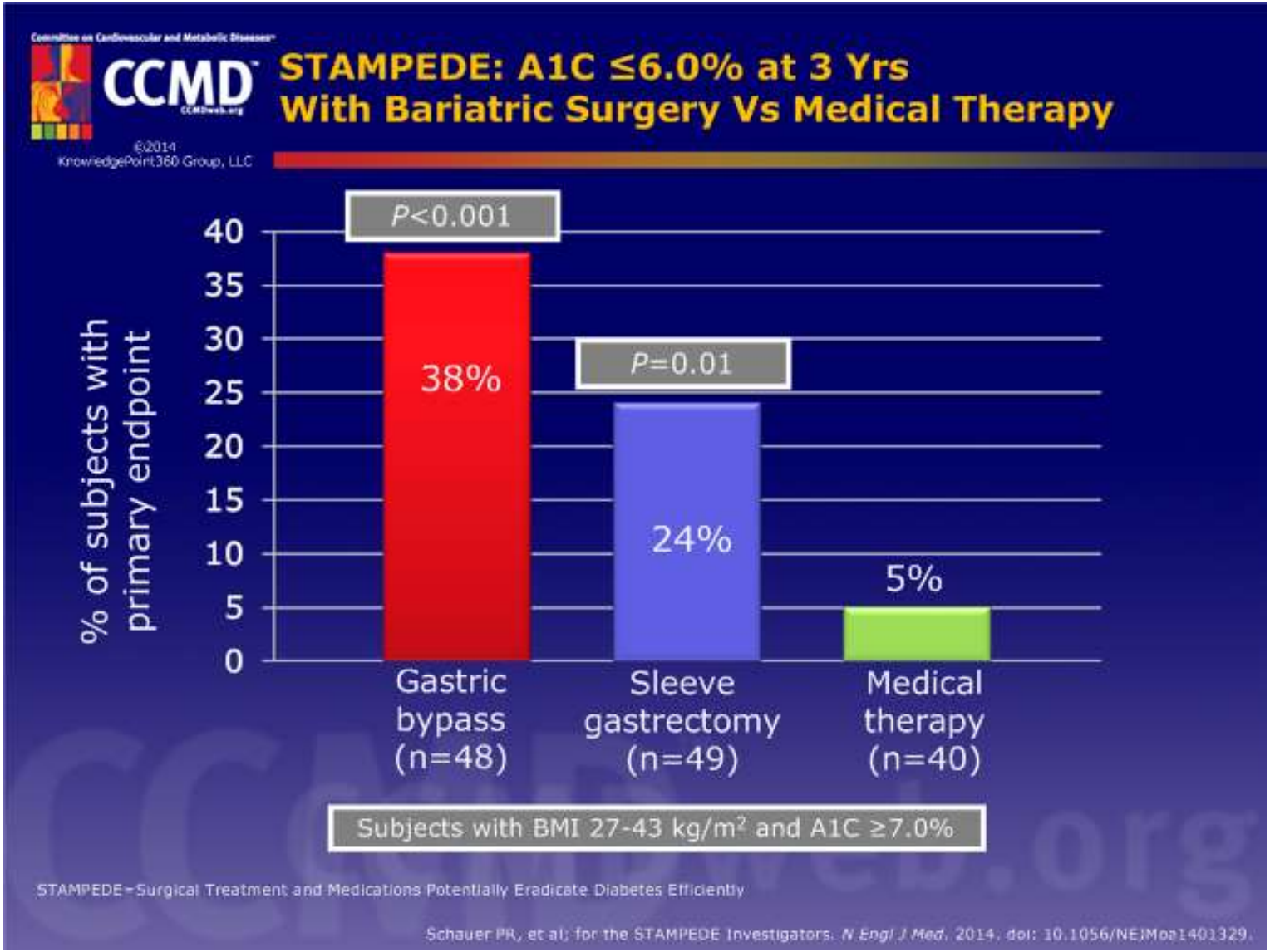


IMT	8.9	7.7	7.1	7.4	7.5
RYGB	9.3	6.8	6.3	6.4	6.4
SG	9.5	7.1	6.7	6.7	6.6

B.



IMT	155	122	113	120	120
RYGB	193	109	96	96	99
SG	164	118	104	102	97


Committee on Cardiovascular and Metabolic Diseases
CCMD
CCMDweb.org
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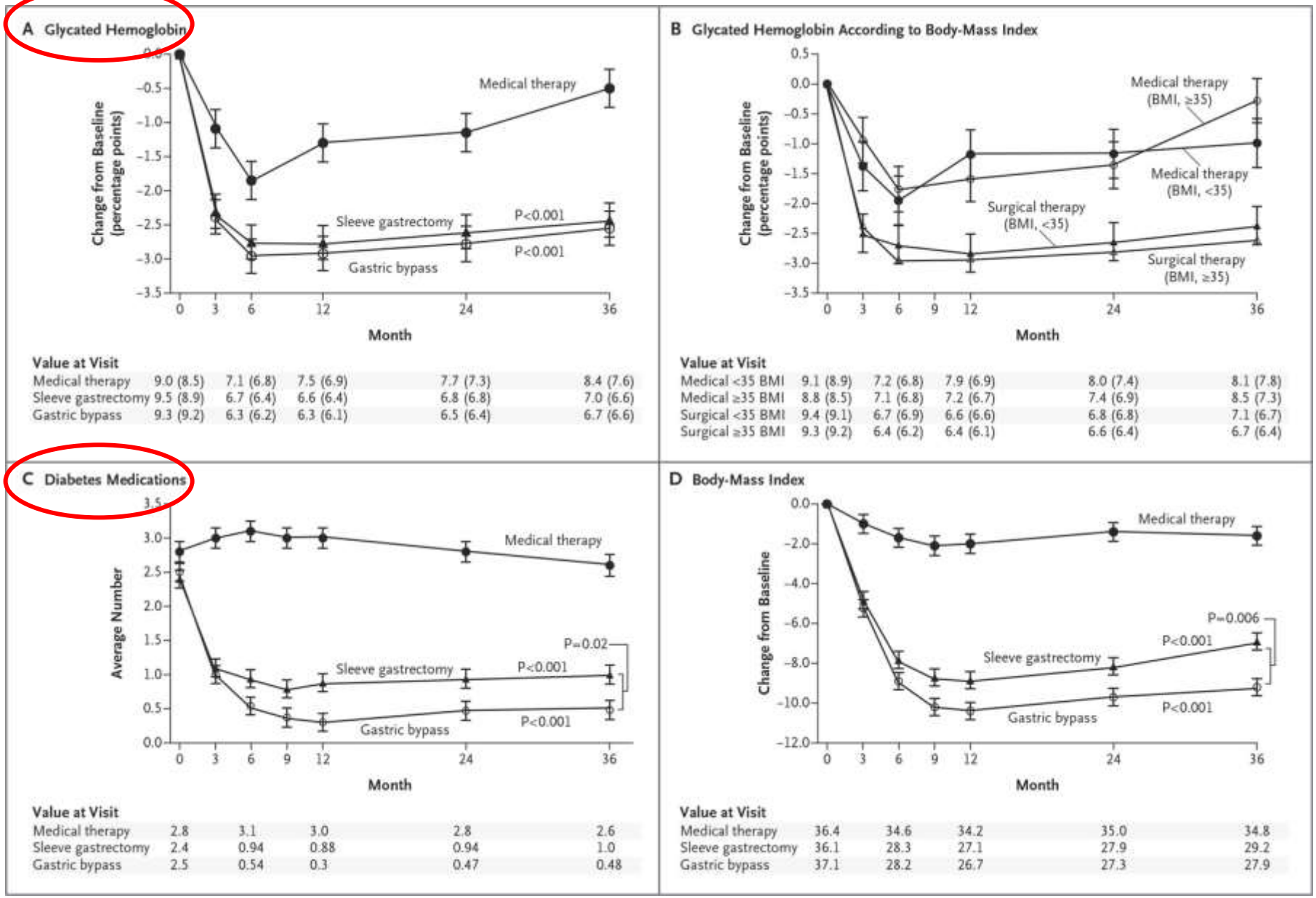
KnowledgePoint360 Group, LLC
STAMPEDE: A1C ≤6.0% at 3 Yrs
With Bariatric Surgery Vs Medical Therapy
% of subjects with primary endpoint
40
35
30
25
20
15
10
5
0
P<0.001
38%
P=0.01
24%
5%
Gastric bypass (n=48)
Sleeve gastrectomy (n=49)
Medical therapy (n=40)
Subjects with BMI 27-43 kg/m² and A1C ≥7.0%
STAMPEDE=Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently
Schauer PR, et al; for the STAMPEDE Investigators. N Engl J Med. 2014; doi: 10.1056/NEJMoa1401329.



Value at Visit

Medical therapy	9.0 (8.5)	7.1 (6.8)	7.5 (6.9)	7.7 (7.3)	8.4 (7.6)
Sleeve gastrectomy	9.5 (8.9)	6.7 (6.4)	6.6 (6.4)	6.8 (6.8)	7.0 (6.6)
Gastric bypass	9.3 (9.2)	6.3 (6.2)	6.3 (6.1)	6.5 (6.4)	6.7 (6.6)

Value at Visit

Medical <35 BMI	9.1 (8.9)	7.2 (6.8)	7.9 (6.9)	8.0 (7.4)	8.1 (7.8)
Medical ≥35 BMI	8.8 (8.5)	7.1 (6.8)	7.2 (6.7)	7.4 (6.9)	8.5 (7.3)
Surgical <35 BMI	9.4 (9.1)	6.7 (6.9)	6.6 (6.6)	6.8 (6.8)	7.1 (6.7)
Surgical ≥35 BMI	9.3 (9.2)	6.4 (6.2)	6.4 (6.1)	6.6 (6.4)	6.7 (6.4)

Value at Visit

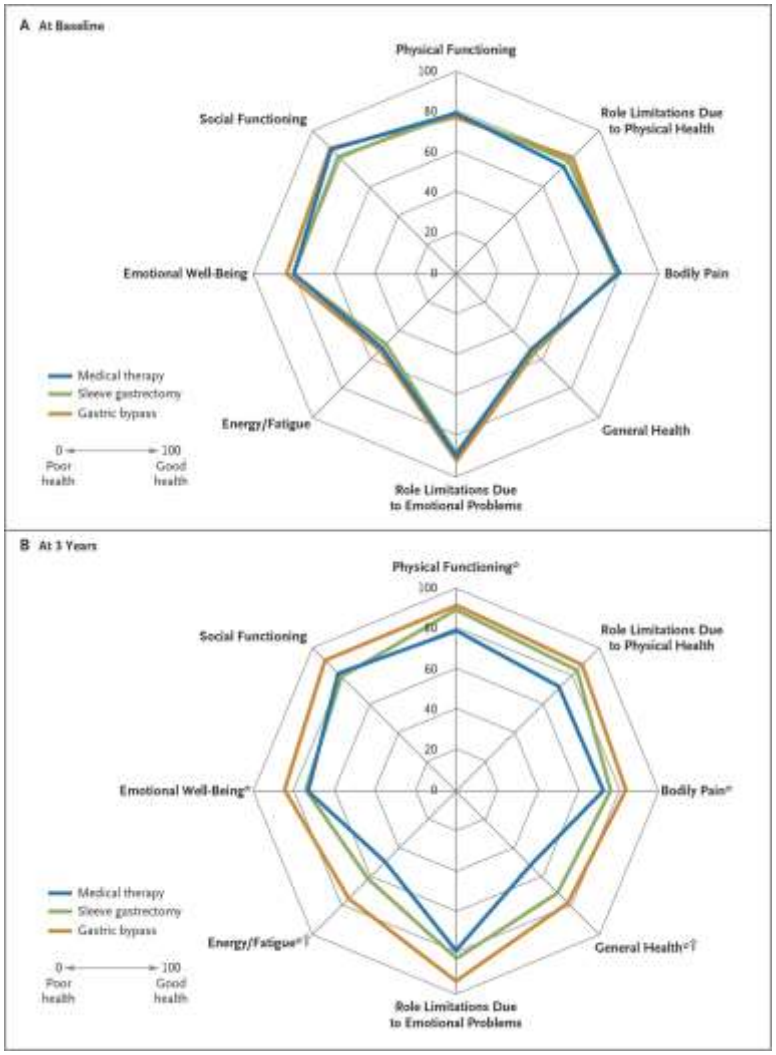
Medical therapy	2.8	3.1	3.0	2.8	2.6
Sleeve gastrectomy	2.4	0.94	0.88	0.94	1.0
Gastric bypass	2.5	0.54	0.3	0.47	0.48

Value at Visit

Medical therapy	36.4	34.6	34.2	35.0	34.8
Sleeve gastrectomy	36.1	28.3	27.1	27.9	29.2
Gastric bypass	37.1	28.2	26.7	27.3	27.9

Schauer PR et al. N Engl J Med 2014;370:2002-2013

Chart of Scores for Quality of Life at Baseline and 3 Years after Randomization.



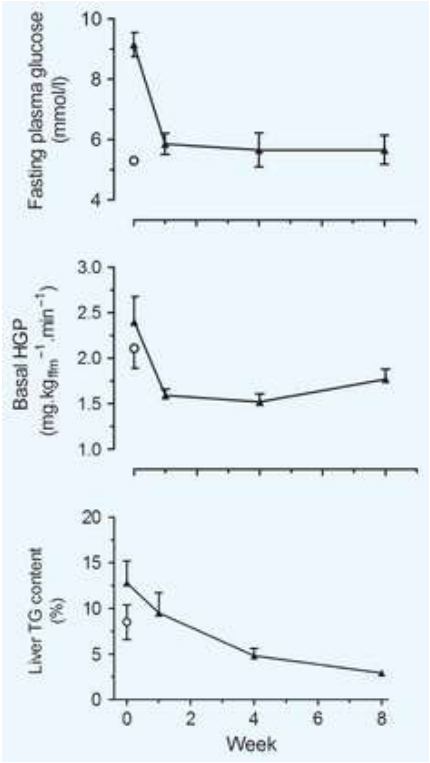
The NEW ENGLAND JOURNAL of MEDICINE

Schauer PR et al. N Engl J Med 2014;370:2002-2013

How does surgery gets the job done ?

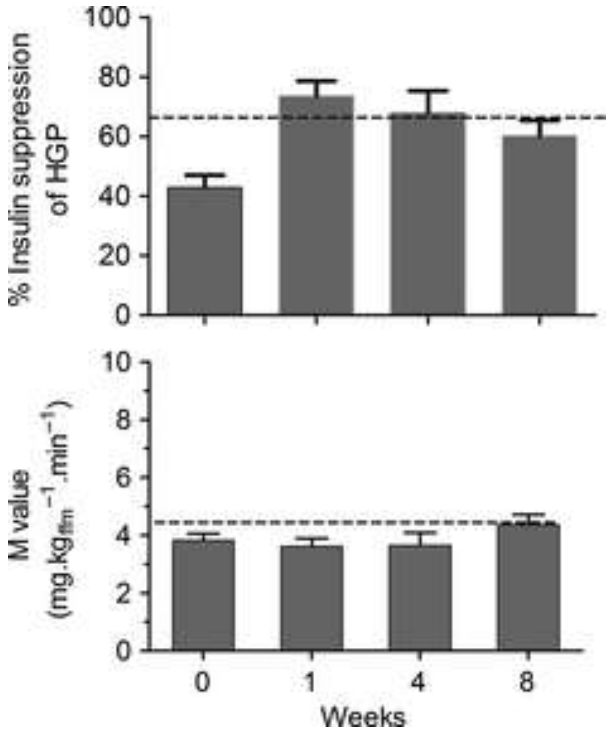
- Weight loss hypothesis
- Caloric restriction hypothesis
- Lower intestinal hypothesis
- Upper intestinal hypothesis
- Ghreline hypothesis
- …

Banting Memorial Lecture 2012 Reversing the twin cycles of Type 2 diabetes



Diabetic Medicine
Volume 30, Issue 3, pages 267–275, 20 FEB 2013 DOI: 10.1111/dme.12039
http://onlinelibrary.wiley.com/doi/10.1111/dme.12039/full#dme12039-fig-0005

Bantin Memorial Lecture 2012 Reversing the twin cycles of Type 2 diabetes



Diabetic Medicine
Volume 30, Issue 3, pages 267–275, 20FEB 2013 DOI: 10.1111/dme.12039
http://onlinelibrary.wiley.com/doi/10.1111/dme.12039/full#dme12039-fig-0006

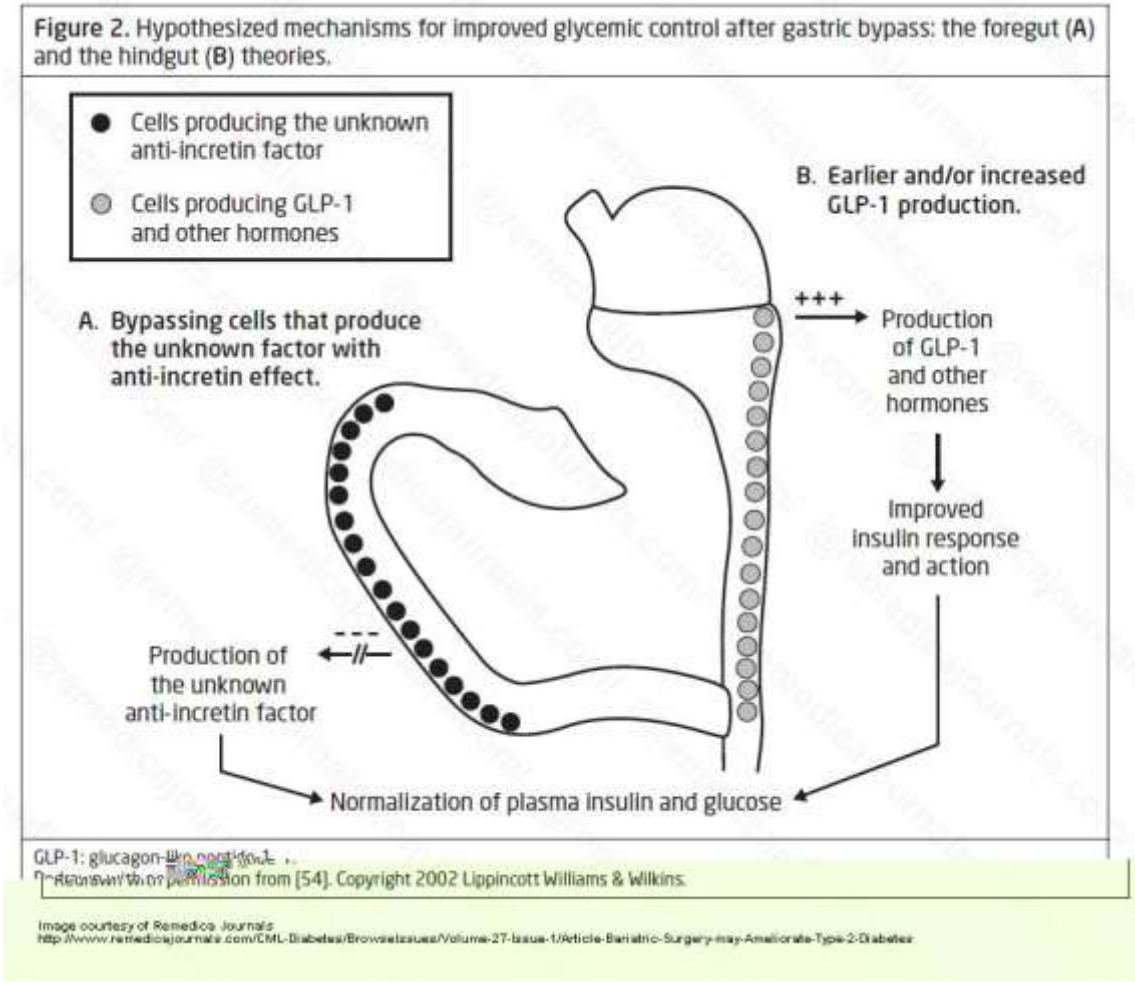


Figure 2. Hypothesized mechanisms for improved glycemic control after gastric bypass: the foregut (A) and the hindgut (B) theories.
Cells producing the unknown anti-incretin factor
Cells producing GLP-1 and other hormones
A. Bypassing cells that produce the unknown factor with anti-incretin effect.
B. Earlier and/or increased GLP-1 production.
+++
Production of GLP-1 and other hormones
Improved insulin response and action
Production of the unknown anti-incretin factor
Normalization of plasma insulin and glucose
GLP-1: glucagon-like peptide-1
Reprinted with permission from [54]. Copyright 2002 Lippincott Williams & Wilkins.
Image courtesy of Remedica Journals
http://www.remedicajournals.com/CML-Diabetes/BrowseIssues/Volume-27-Issue-1/Article-Bariatric-Surgery-may-Ameliorate-Type-2-Diabetes

Rubino et al Ann Surg 2004

Goto –Kakizaki ratten: lean rat model type 2 diabetes

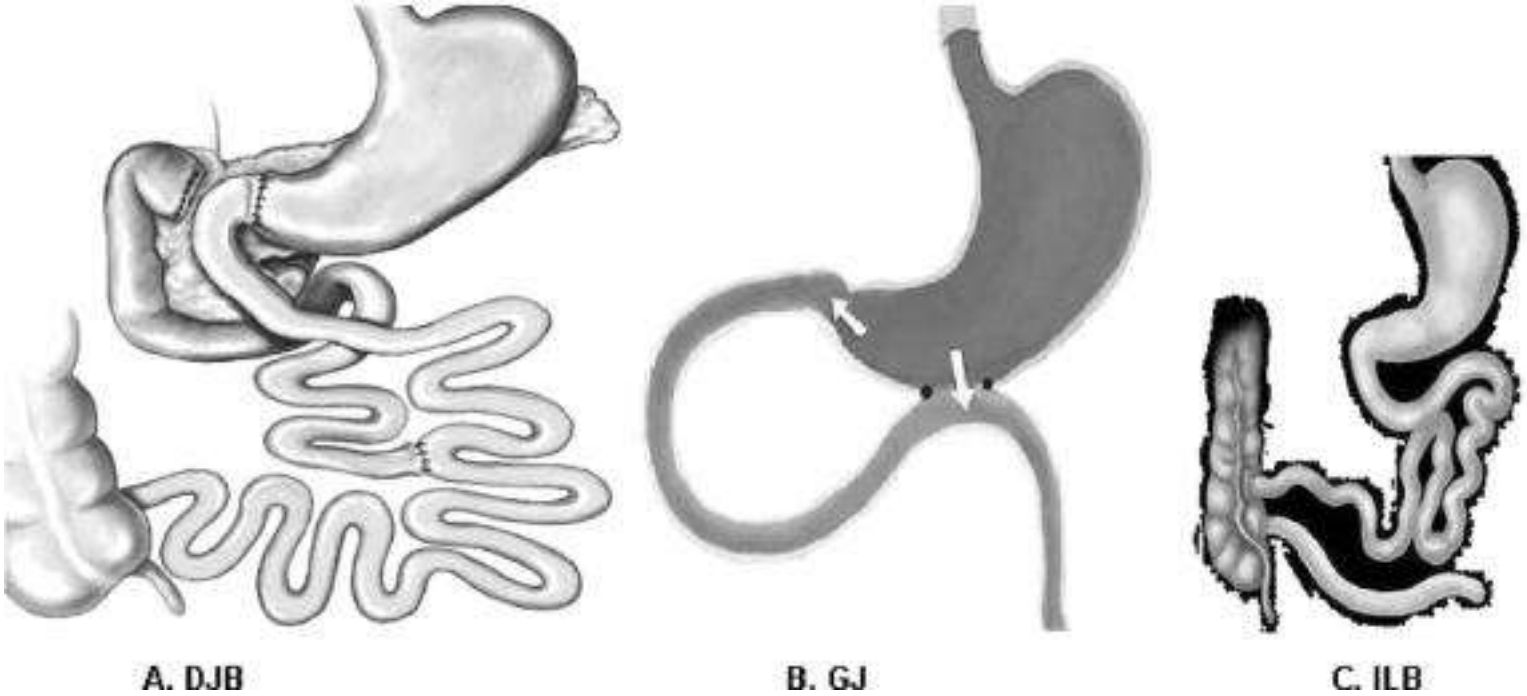
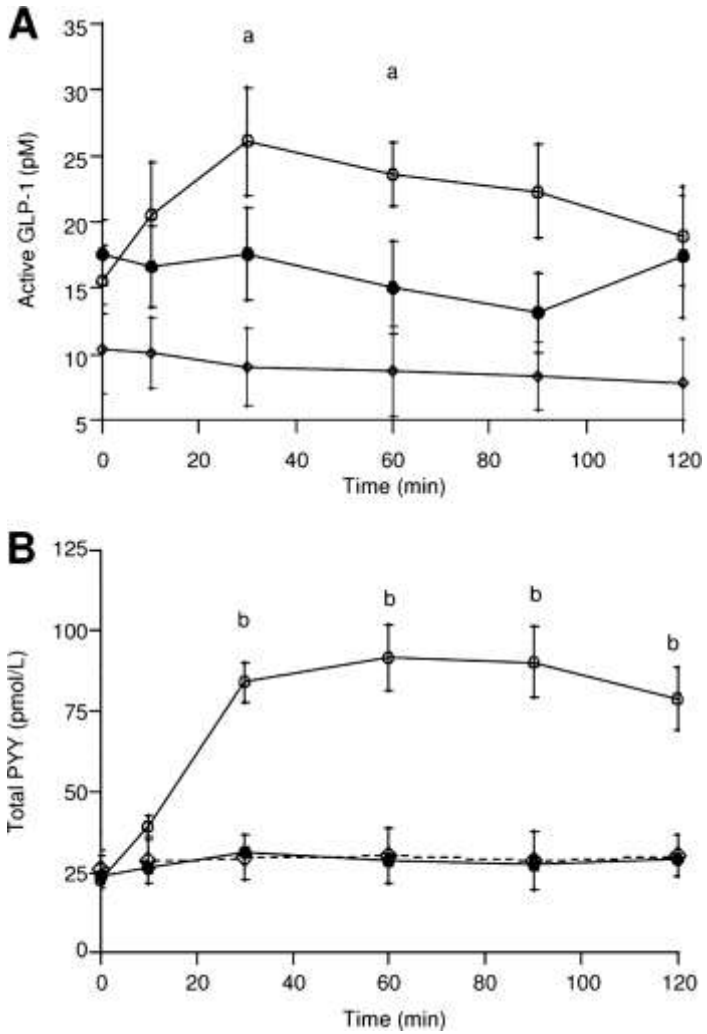


FIG. 1. Active GLP-1 and total PYY in response to a liquid test meal



6wkn na RYGBP

- Obese ptn preop

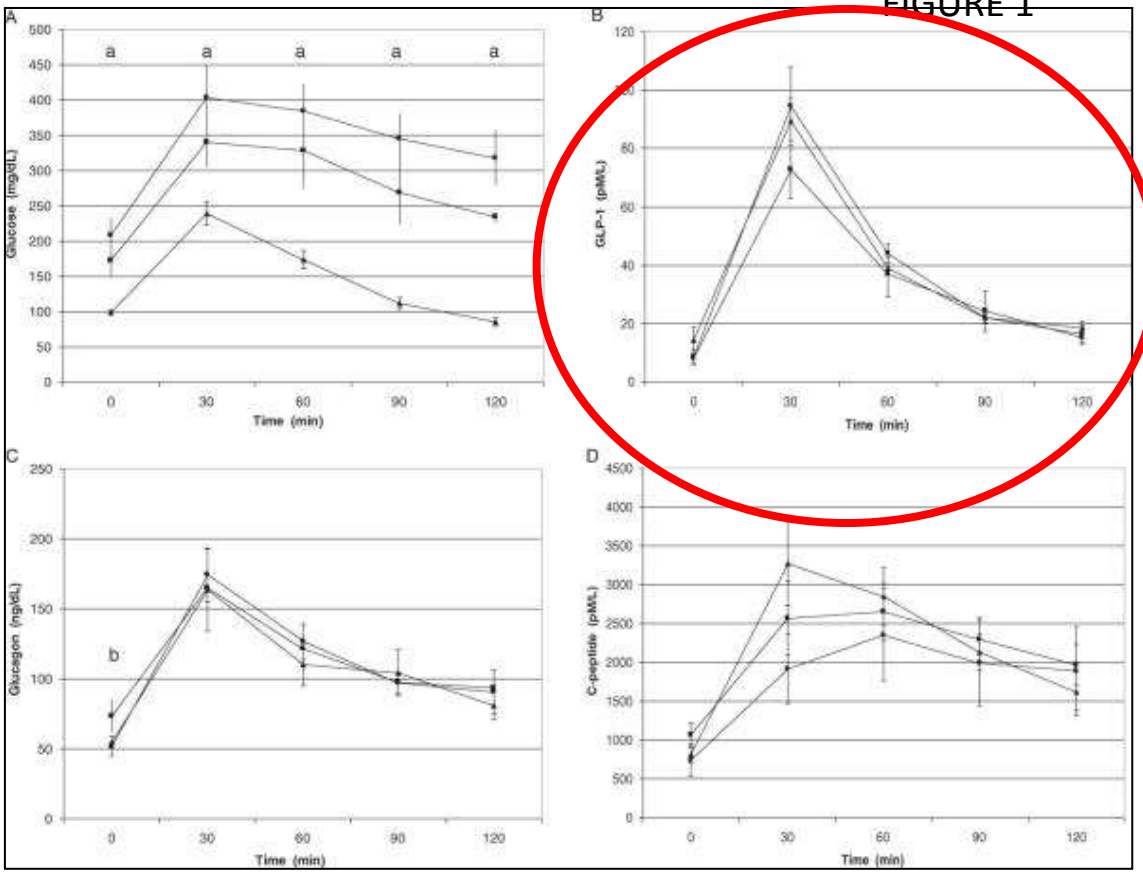
BMI gematchte ptn niet geopereerd

THE JOURNAL OF CLINICAL ENDOCRINOLOGY & METABOLISM

Morinigo, R. et al. J Clin Endocrinol Metab 2006;91:1735-1740

Copyright ©2006 The Endocrine Society

FIGURE 1



GLP-1 and the Long-Term Outcome of Type 2 Diabetes Mellitus After Roux-en-Y Gastric Bypass Surgery in Morbidly Obese Subjects.
Jimenez, Amanda; Casamitjana, Roser; Flores, Lilliam; MD, PhD; Delgado, Salvadora; MD, PhD; Lacy, Antonio; MD, PhD; Vidal, Josep; MD, PhD

Annals of Surgery. 257(5):894-899, May 2013.
DOI: 10.1097/SLA.0b013e31826b8603

Incretin response of diabetic RYGBP 5y after surgery

3 groups:
A.Remission
B. Relapse
C. Never achieved remission

After STM similar levels of GLP-1 in all groups

FIGURE 1 . Time course of plasma glucose (A), GLP-1 (B), glucagon (C), and C-peptide (D) concentrations in response to a STM according to T2DM outcome. Data are expressed as mean +/- standard deviation. Triangles: group 1 (remission); Squares: group 2 (relapse); group 3 (lack of remission). a: P P < 0.05 for the comparison between group 2 and group 1, and group 2 and group 3.

Wolters Kluwer Health | OvidSP

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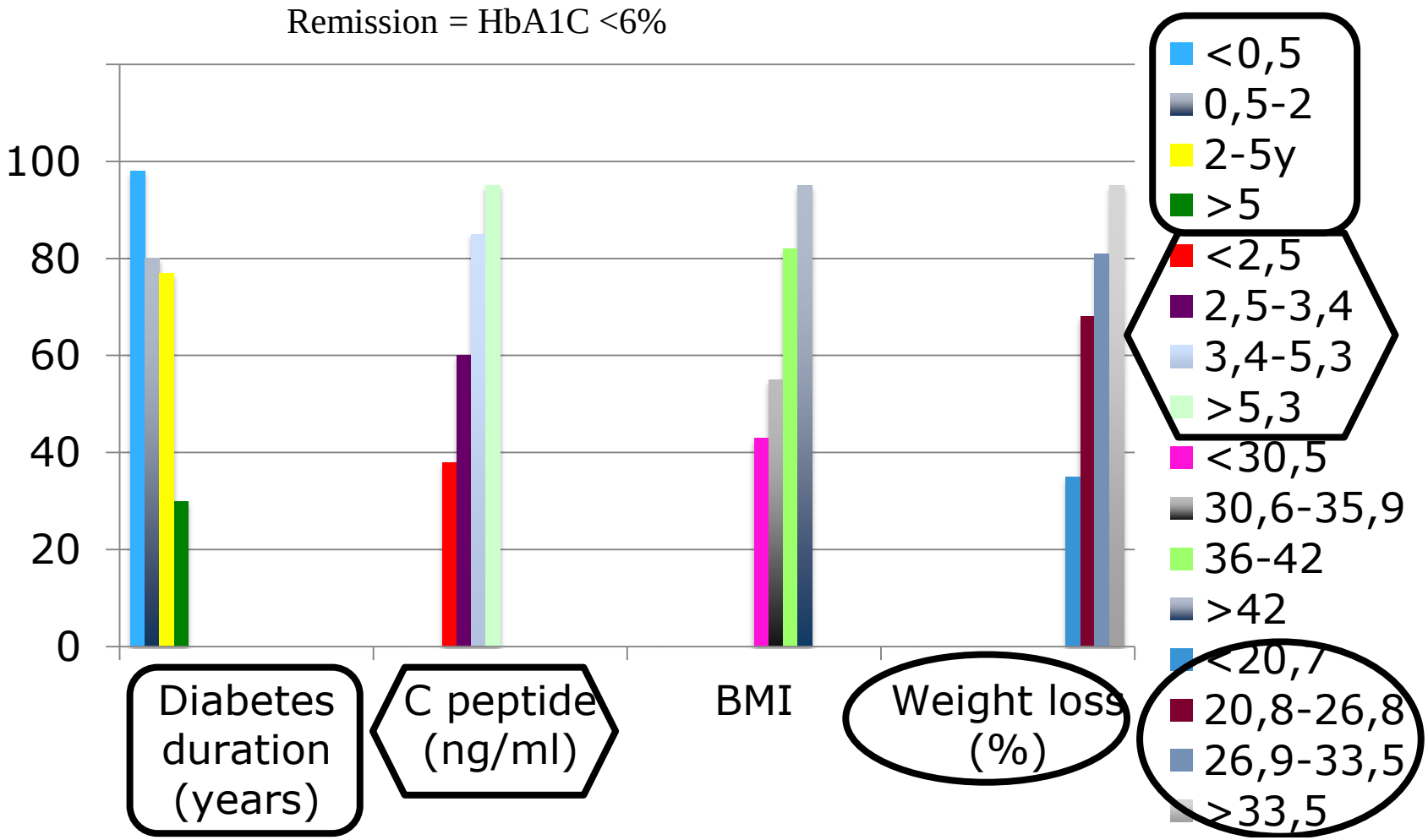
Predictive factors

Dixon et al
Diabetes Care Jan 2013; 36(1)20-26



Prediction factor		Score
Age (years)	If age <40, enter 0 →	2
	If age 40–49, enter 1 →	
	If age 50–59, enter 2 →	
	If age 60+, enter 3 →	
HbA1c (%)	If HbA1c <6.5, enter 0 →	4
	If HbA1c 6.5–6.9, enter 2 →	
	If HbA1c 7.0–8.9, enter 4 →	
	If HbA1c >9, enter 6 →	
Diabetes medication	If not sulfonylureas or ISA*, enter 0 →	3
	If sulfonylureas or ISA*, enter 3 →	
Insulin treatment	If not on insulin, enter 0 →	10
	If on insulin, enter 10 →	
***DiaRem* score (sum) →**		19

*Insulin sensitizing agent other than metformin

DiaRem score	Probability of remission
0–2	88%–99%
3–7	64%–88%
8–12	23%–49%
13–17	11%–33%
18–22	2%–16%

1 million dollar question:

- can we treat low BMI type 2 diabetes patients with bariatric surgical procedures?

World J Surg. 2014 Aug 27.

A Meta-Analysis of Short-Term Outcomes of Patients with Type 2 Diabetes Mellitus and BMI ≤35 kg/m2 Undergoing Roux-en-Y Gastric Bypass.

Rao WS1, Shan CX, Zhang W, Jiang DZ, Qiu M.

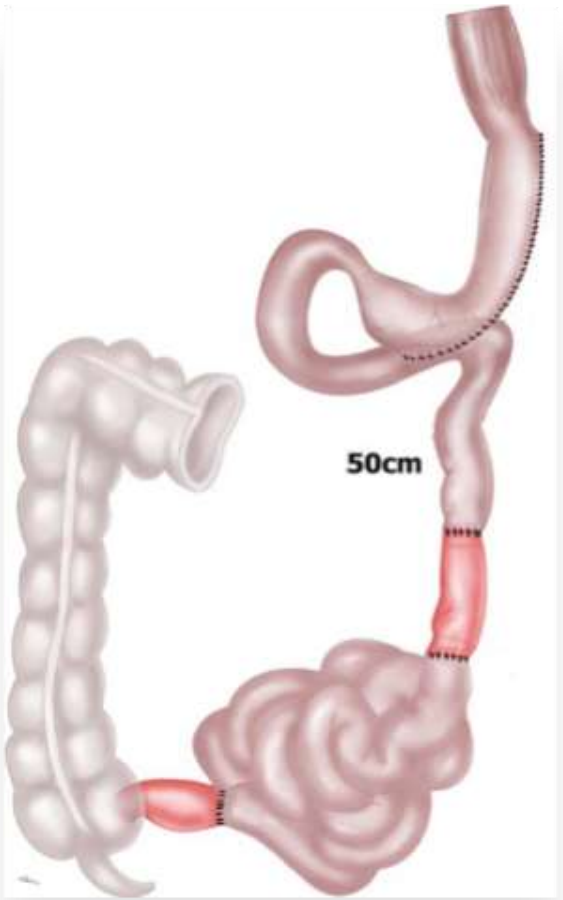
- 9 series
- FU 12 months
- All remission DMT2
- M: 7-26%

New types of interventions?

DePaula Surg Endosc 2008

Laparoscopic treatment of type2 diabetes for patients with a BMI less than 35

- 30 pts
- mean age 50.3y (36-66)
- mean BMI 30.1 (23.4-34.9)
- T2DM for >3y (3-22y)
- stable treatment: oral, insulin (41%) or both >12m
- mean FU 7m (4-16m)



DePaula Surg Endosc 2008

	preop	postop	p value
HbA1c	8.8 (1.7)	6.3 (0.9)	<0.001
Fasting glucose	210.7 (66.6)	116.7 (33.1)	<0.001
Postpr. glucose	259.3 (92.6)	141.7 (56.6)	<0.001
Insulin	15.5 (17.4)	8.9 (8.8)	<0.003

medication use severity disease

	resolution	glycemic control	improv.
oral	54%	37%	9%
insulin	33%	34%	33%
both	38%	46%	16%

duration disease

	resolution	glycemic control	improv.
3-5y	87%	13%	-
5-10y	37%	56%	7%
>10y	36%	36%	28%

DePaula Surg Endosc 2008

morbidity 10.3%
mortality 2.6%

Medical Innovations: 2013
Top 10
Bariatric Surgery for
Control of Diabetes