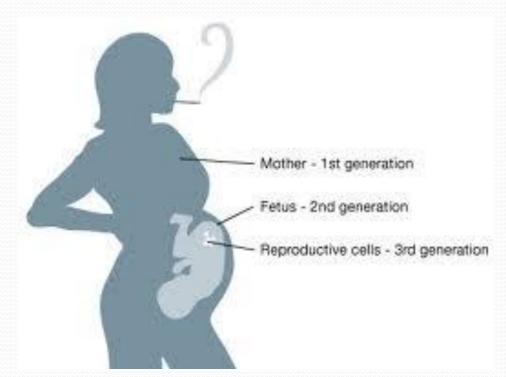


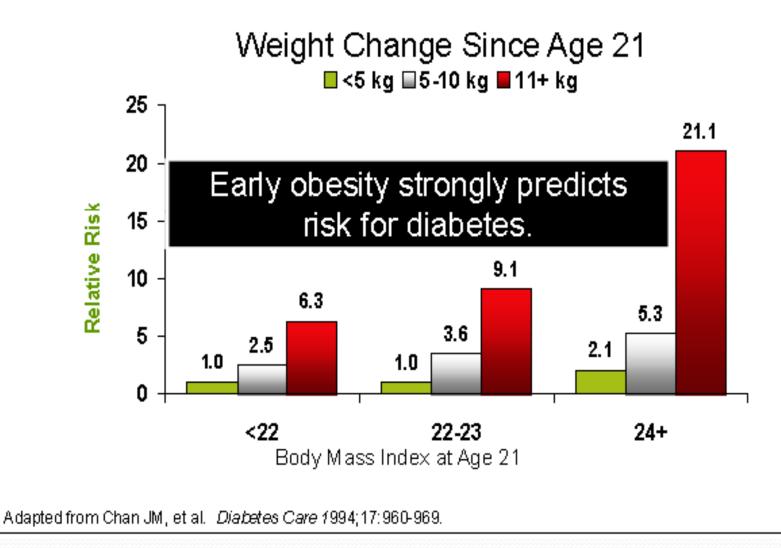
- Some genes are dictators (brown eyes, etc.)
- Others are Committees (genes for DM, etc.) whose recommendations you can ignore
- Genes for DM are like cactus seeds on the desert floor, waiting for a good rain to bloom
  - Neal Barnard

## **Personal History**

- Environment in the womb:
  - Famine
  - Maternal obesity/GDM /excessive weight gain
  - IUGR



#### Weight Gain and Diabetes Risk



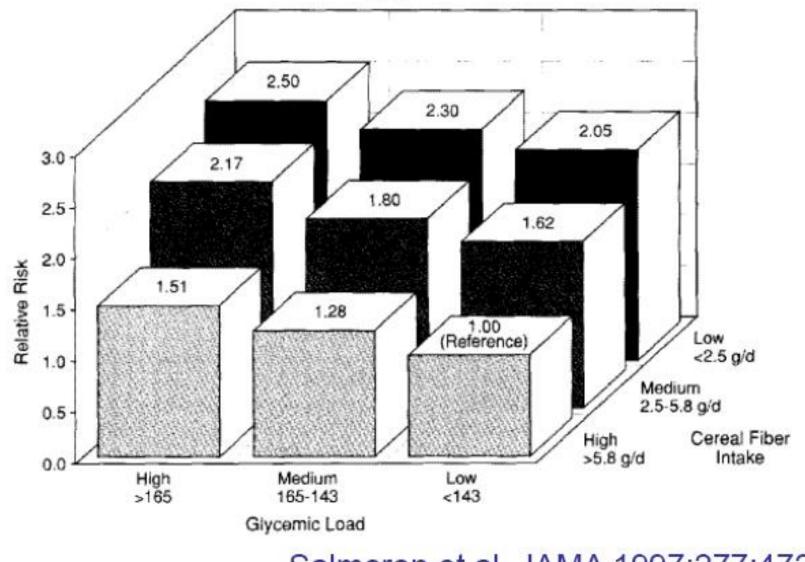
## **Precursor Syndromes**

- Women
  - PCOS
  - Decreased fertility
  - GDM
  - Baby > 9 lb even in absence of GDM
- Men
  - Hypogonadism

## **Behavioral Risk Factors**

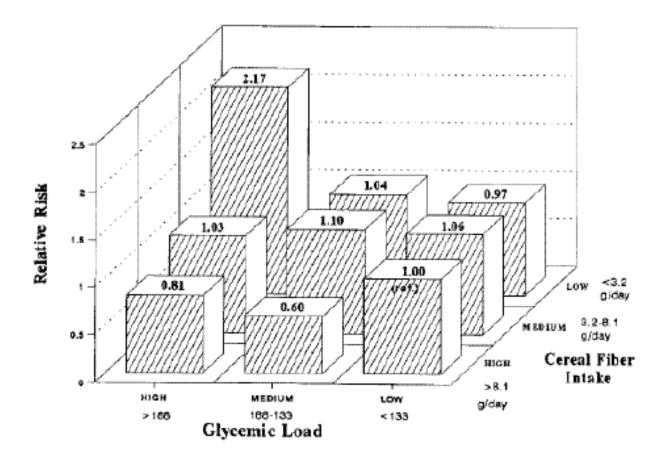
- Lifestyle history
  - Nutrition
  - Exercise/ physical activity

#### Glycemic Load and Cereal Fiber Intake in Women And Risk of Type II Diabetes



Salmeron et al. JAMA 1997;277:472-7

#### Glycemic Load and Cereal Fiber Intake in Men and Risk of Type II Diabetes



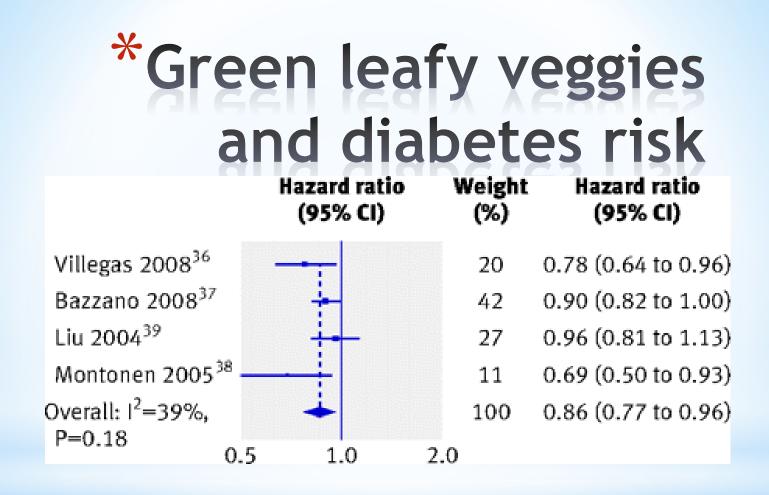
Salmeron et al. Diabetes Care 1997;20:545-50

# \*Dietary fat and risk of DM2 in women

	Quintile					P for
	1	2	3	4	5	trend
Total fat	1	0.87	1.01	0.97	0.97	0.96
Animal fat	1	0.90	1.08	1.17	1.25	<0.0001
Vegetable fat	1	0.88	0.71	0.71	0.68	<0.0001
Trans fat (adjusting for other fats)	1	1.12	1.18	1.14	1.31	0.02

14 yr prospective study Authors estimate 40% decreased risk of DM2 with substitution of 2% of energy from trans fat to PUFA

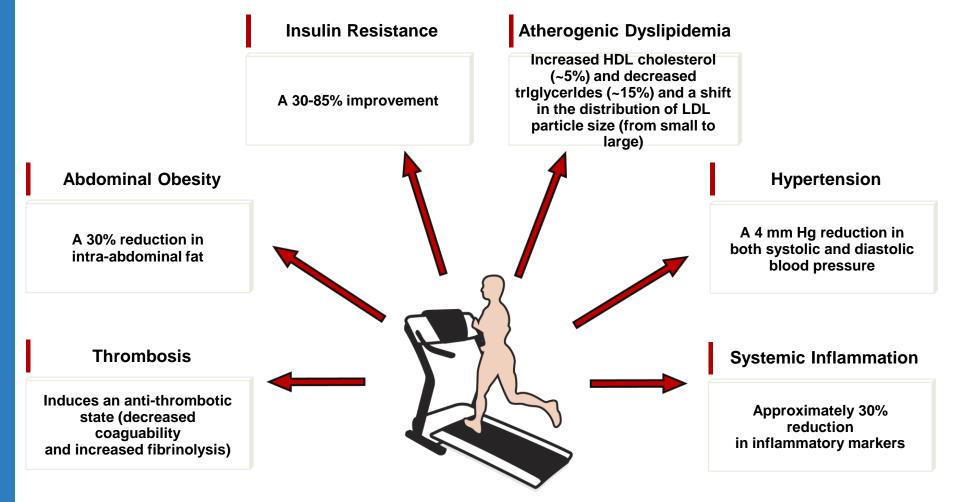
Multivariate adjusted Am J Clin Nutr June 1, 2001 vol. 73 no. 6 1019-1026



\*BMJ2010;341:c4229



#### IMPROVEMENTS IN CARDIOMETABOLIC RISK FACTORS INDUCED BY REGULAR EXERCISE



#### Moderate intensity endurance exercise on most days of the week



Source: www.myhealthywaist.org

# Additional Risk Factors • Stress

- Poverty
  - A Randomized Trial A Social Experiment: Moving from higher to lower poverty community associated with 13 to 21% reductions in obesity and diabetes. NEJM October 20, 2011
- PTSD Diabetes Care 33:1771-1777, 2010
- Work stress mixed studies, metaanalysis says no

Occup Med 2012 Apr;62(3):167-73

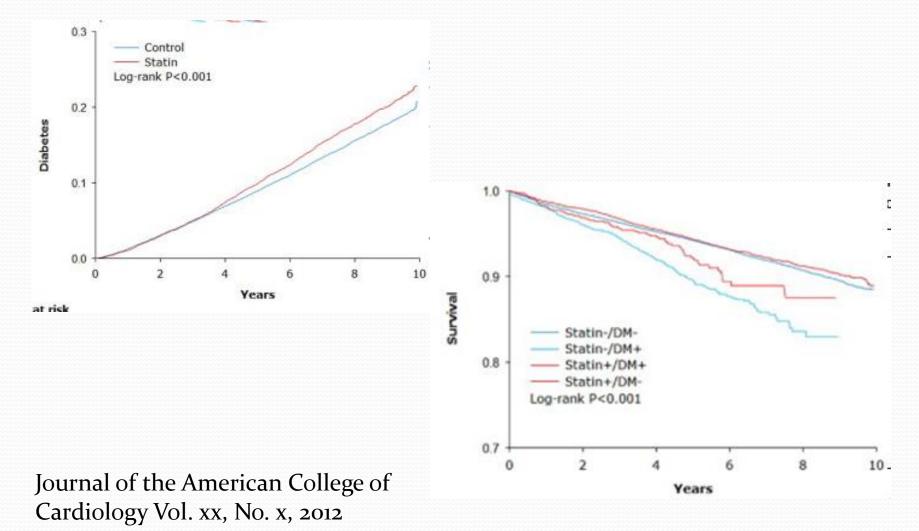
- Stressful life events
  - 46% MetS with 8 or more stressful life events
  - 23.4% with < 8 stressors <u>Metab Syndr Relat Disord.</u> 2010 Dec;8(6):483-7
- Mechanisms:
  - Sleep deprivation Internal Medicine 50(21):2499-2502, 2011 Elevated cortisol
  - Stress-related unhealthy behaviors

## **Additional Risk Factors**

#### Toxin exposure

- Smoking
- Alcohol (>1/d women, 2/d men)
- Medications
  - Statins
    - 47% increase incidence of type 2 diabetes in postmenopausal women Arch Intern Med 2012; 172: 144-52
  - Antipsychotics least for ziprasidone, aripiprazole
  - Beta blockers Am J Cardiology 100(8):1254-1262, 2007
  - Diuretics
- Iron overload

#### Statins – still worth it in high risk populations

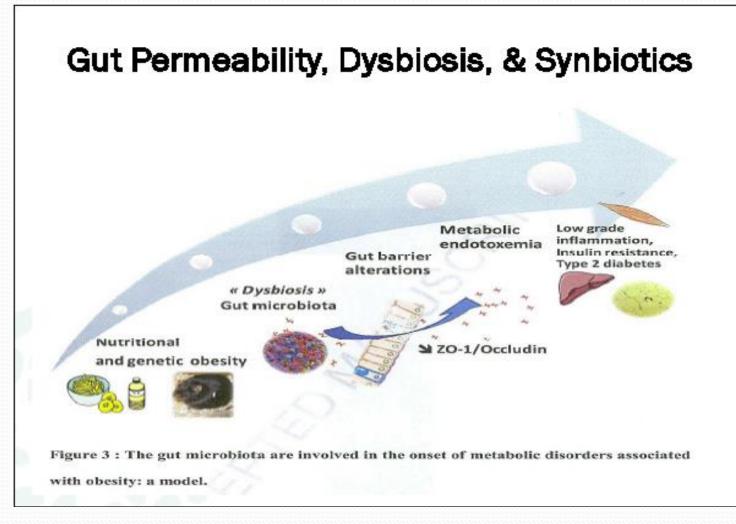


## **Toxins continued**

- Persistent organic pollutants (POPs)
  - Phthalates
  - BPA
  - Arsenic
  - Atrazine
  - Others...

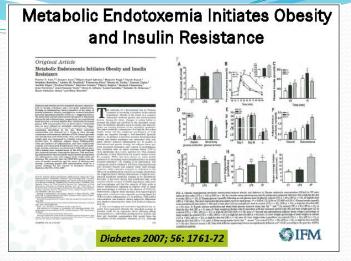
#### (next talk)

## **Additional Risk Factors**



#### Allergies/Adverse food reactions

• Endotoxemia



- Low-grade endotoxemia may contribute to the postprandial inflammatory state and could represent a novel potential contributor to endothelial activation and the development of atherosclerosis". *Am J Clin Nutr* 2007; 86:1286-92
- Periodontal Disease
  - Friedewald VE, Kornman KS, et al, Am J Cardiol. 2009 Jul 1;104(1):59-68

## Today:

- Definitions
- Assessment
- Risk factors: standard and additional
- Treatment Recommendations
- Monitoring

## Acute vs. Chronic Disease

#### Cellulitis

- Diagnose
- Rx Treatment
- Prevention
- Behavior change

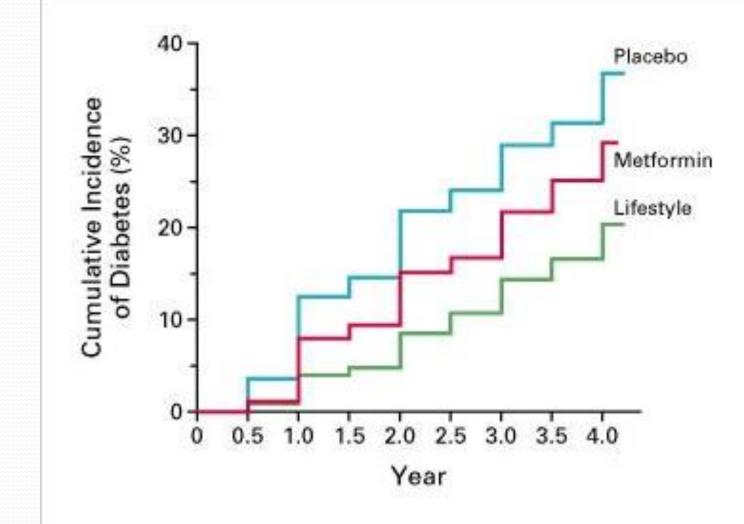
#### **Cardiometabolic Syndrome**

- Diagnose
- Rx Treatment
- Create
   Partnership
- Promote Behavior
   Change

- Assess global risk
- Multifactorial risk reduction strategy
  - target each risk factor
  - emphasize lifestyle & pharmacologic therapy

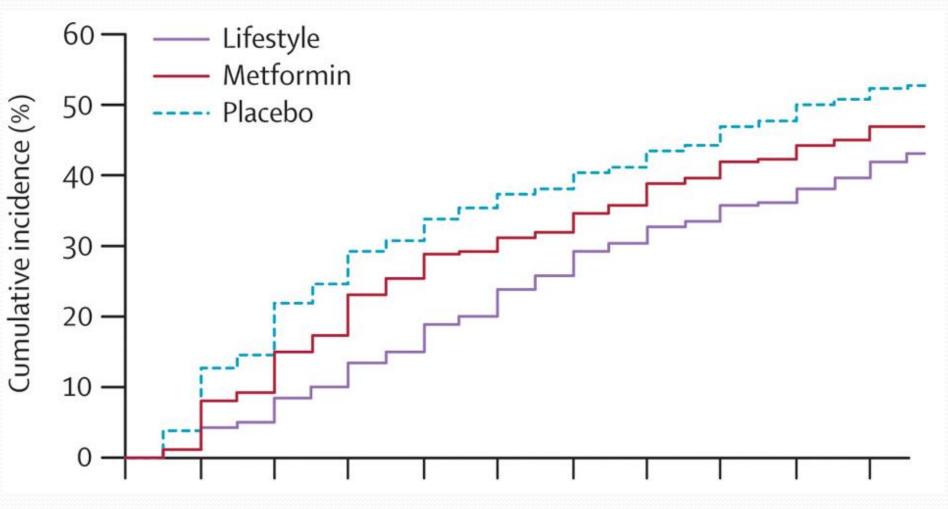
 Consensus Statement from the American Diabetes Association and the American College of Cardiology Foundation, April 2008

#### **Diabetes Prevention Program**



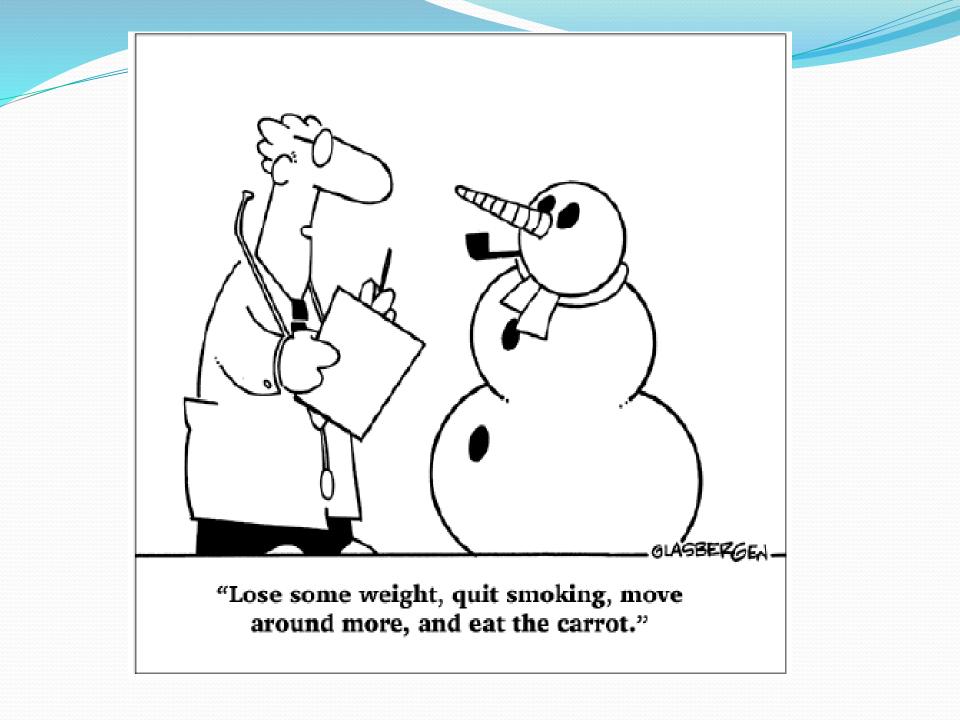
N Engl J Med 2002; 346:393-403

## **Diabetes Prevention Program**



Years since randomization

Lancet 374(9702):1677-1686, 2009



## Shorthand: .dmpreven

For diabetes prevention, the main things you can do are:

1. Eat low glycemic index (see handout or <u>http://www.mendosa.com/gilists.htm</u>)

- 2. Increase fiber in the diet
- 3. Increase fruits and vegetables to 5-9 servings per day, especially dark green leafy vegetables

4. Increase exercise (30 minutes 5 days per week) - include muscle building as well as aerobic

5. Avoid trans fats (hydrogenated oils in baked goods, fried foods)

6. Avoid environmental endocrine disruptors (like PCB's, phthalates, BPA, PFOAs, etc.) - learn more at healthychild.org

Increasing nuts in the diet may be helpful, and eating cinnamon, about  $\frac{1}{2}$  tsp per day, may also be helpful, as may the medication metformin.

Embedded polls only work in PowerPoint for Windows

#### This object is the poll's placeholder

# To view the poll live, enter slideshow mode by pressing F5

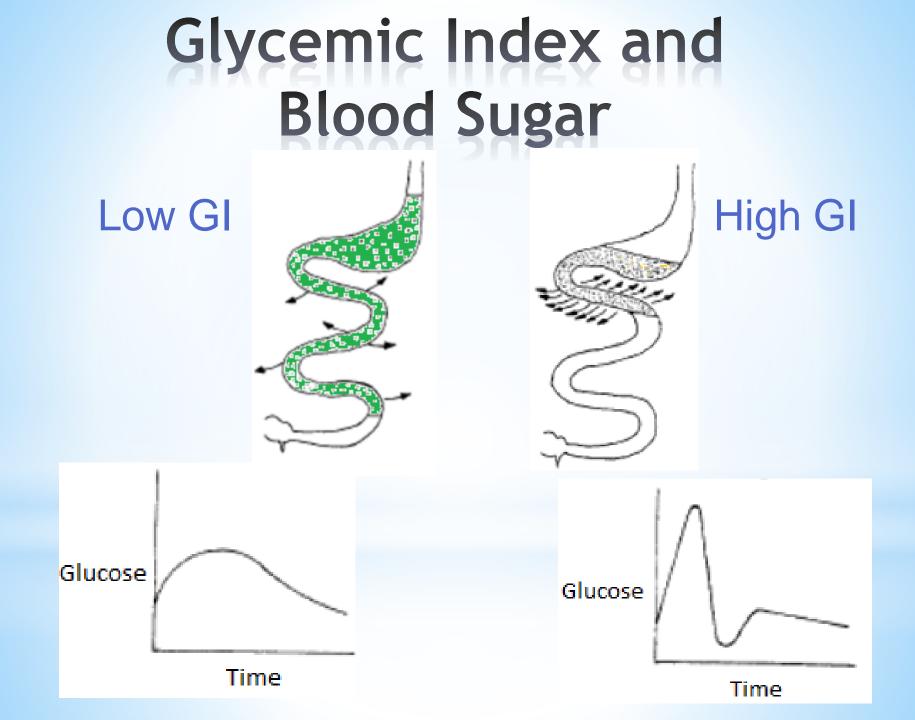
## **Glycemic Index**

#### Not All Carbs are Created Equal

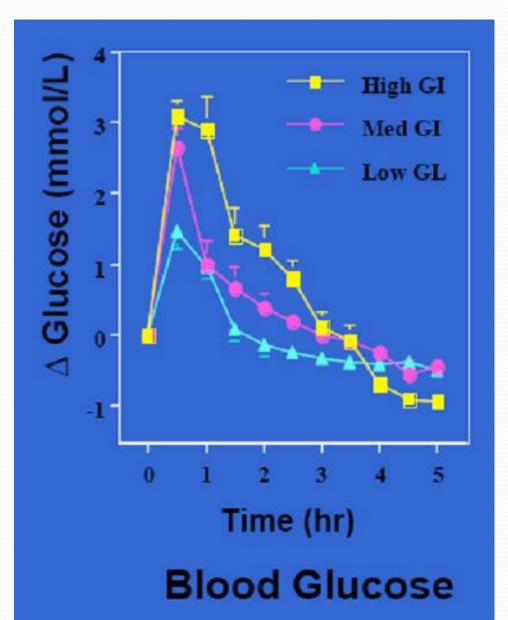
Cola and chips snack vs. Raisins and peanuts (Equal calories from sugar)

75% more insulin mobilized over two hours (p<.001)

Oettle GJ et al. Am J Clin Nutr 1987; 45:86



#### The Overshoot



## **Glycemic Index -**Why do we care?

- \*Long-term health effects
  - \*Diabetes risk
  - \*Cancer risk
- \*Medium term effects
  - \*Weight loss, fat loss
- \*Immediate effects
  - \*Hunger and snacking
  - \*Ability to think straight
  - \*Mood, Irritability

## **Glycemic Index and Snacking**

High-GI breakfast (instant oatmeal) vs. Low-GI breakfast (eggs, fruit) equal calories

81% more snacking in next 5 hours

Ludwig DS et al. Pediatrics 1999; 103:E26

## GI & Regulation of Food Intake

#### Low GL

55 g whole egg 45 g egg white 40 g lowfat cheese 200 g spinach 30 g tomato 185 g grapefruit 115 g apple slices

#### Medium Gl

63.9 g steel-cut oats 160 g 2% milk 15 g H & H cream 16.0 g fructose 0.0 g saccharine 397 g water

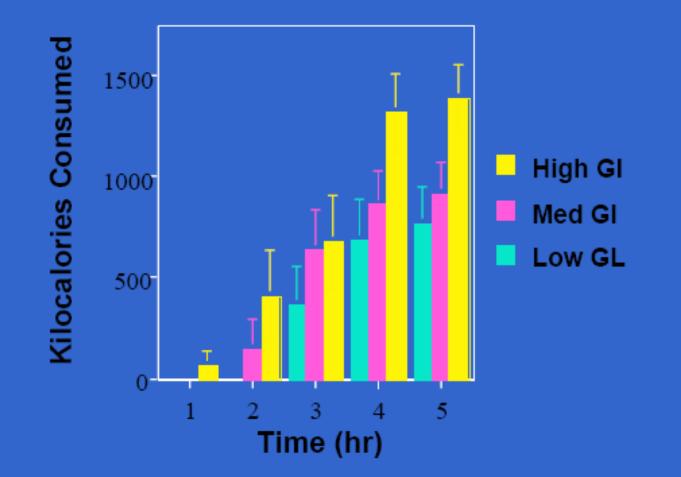
#### High Gl

60.9 g instant oatmeal 160 g 2% milk 15 g H & H cream 19.0 g dextrose 0.2 g saccharine 397 g water

#### Macronutrients (% carbohydrate/protein/fat):

40/30/30	64/16/20	64/16/20
Energy density (KJ/g):		
2.46	2.52	2.52

#### **GI & Regulation of Food Intake**



Ludwig. Pediatrics 1999, 103:e261-6

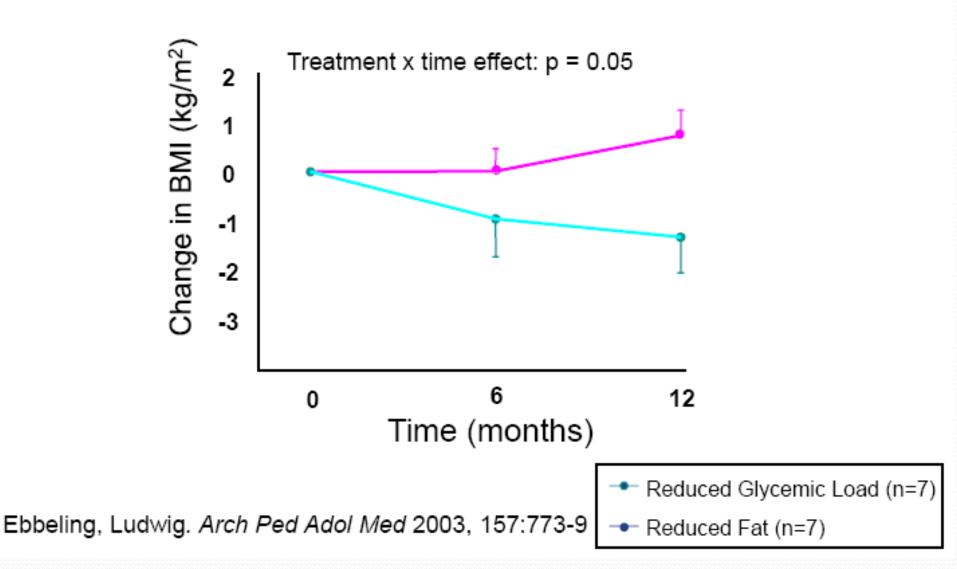
Effects of Glycemic Load on Body Weight A 12-month Pilot Study

#### Methods

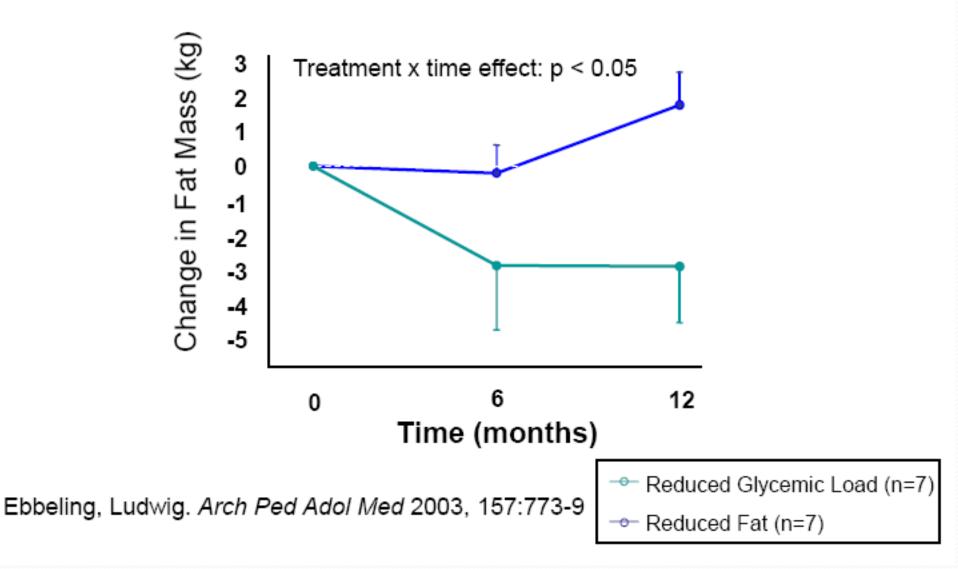
- 16 obese adolescents, age 13 21 years
- Intervention:
  - Ad lib low GL vs energy-restricted reduced-fat diet
  - Total of 14 treatment visits with a dietitian
- Treatment intensity, behavioral approaches, physical activity prescription identical between groups
- Changes in diet assessed by 3 and 7 day food records
- > 85% completion rate at 12 months (7 of 8 per group)

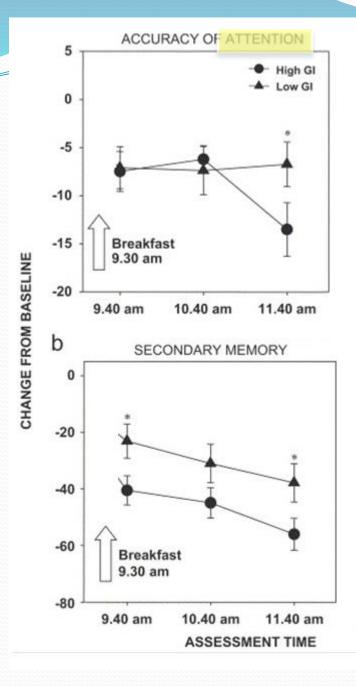
Ebbeling, Ludwig. Arch Ped Adol Med 2003, 157:773-9

## Change in BMI

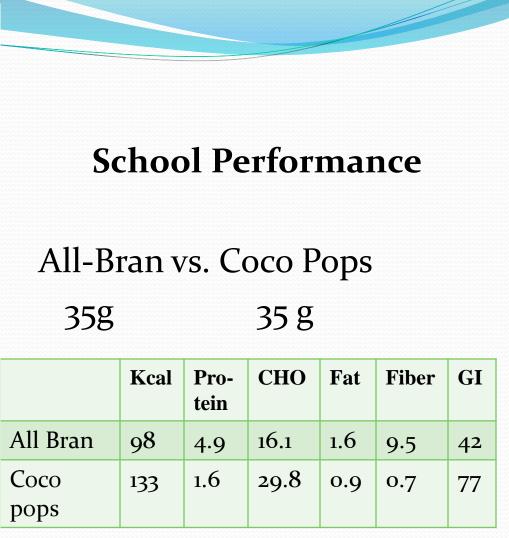


## Change in Fat Mass by Dexa Scan

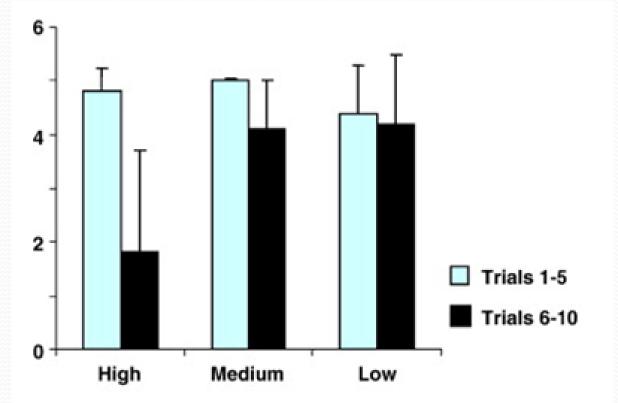




Appetite 49(1):240-244 2007



## Persistence with Frustrating Task Medium, or Low



GL breakfast

**High**: 39 cornflakes, waffle

**Medium:** 14.8 scrambled egg, toast and jam, yogurt

Low: 5.9 Ham, cheese, Burgen bread (soy, flax)

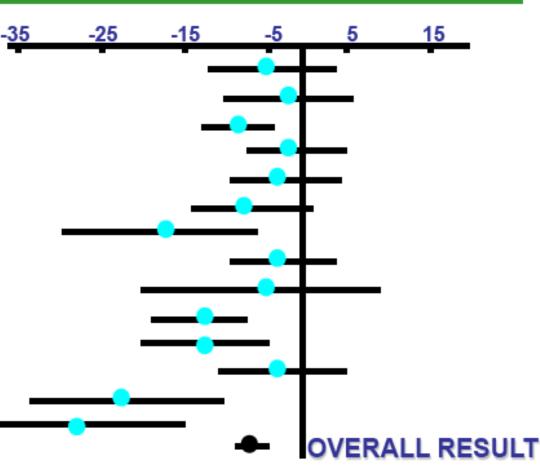
Kids age 6-7 Also imp verbal memory, fewer lapses in attention

Physiology & Behavior 92(4):717-724, 2007

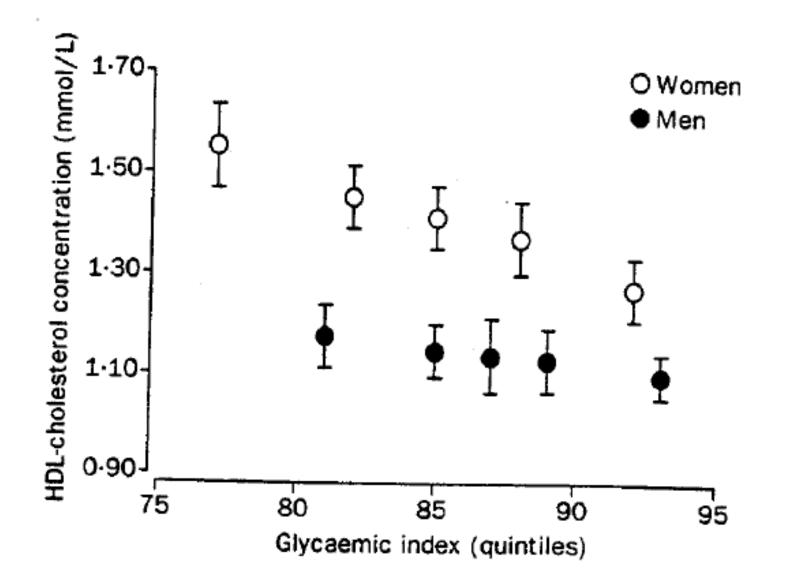
#### Low vs High GI Diet: a Meta-Analysis % Difference in Glycated Proteins

Gilbertson et al. 2001 Komindr et al. 2001 Giacco et al 2000 Luscombe et al 1999 Jarvi et al 1999 Lafrance et al 1998 Frost et al 1993 Wolever et al 1992 Wolever et al 1992 Fontvieille et al 1992 Brand et al 1991 Jenkins et al 1991 Fontvieille et al 1988 Collier et al 1988

%

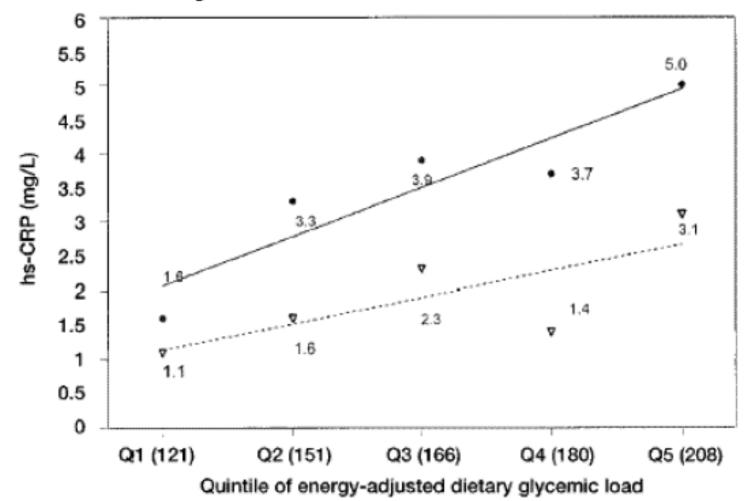


Mean %difference in 14 studies = -7.4% (Cl -8.8 to -6.0%) Brand-Miller et al, Diabetes Care 2003;26:2261-67



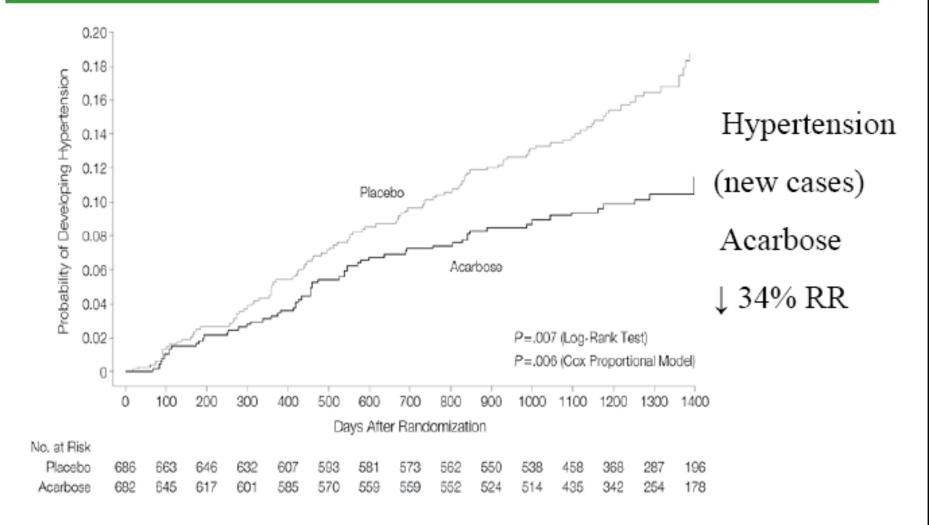
Relation between HDL-cholesterol concentration and glycaemic index in men and women

#### Glycemic Load and CRP



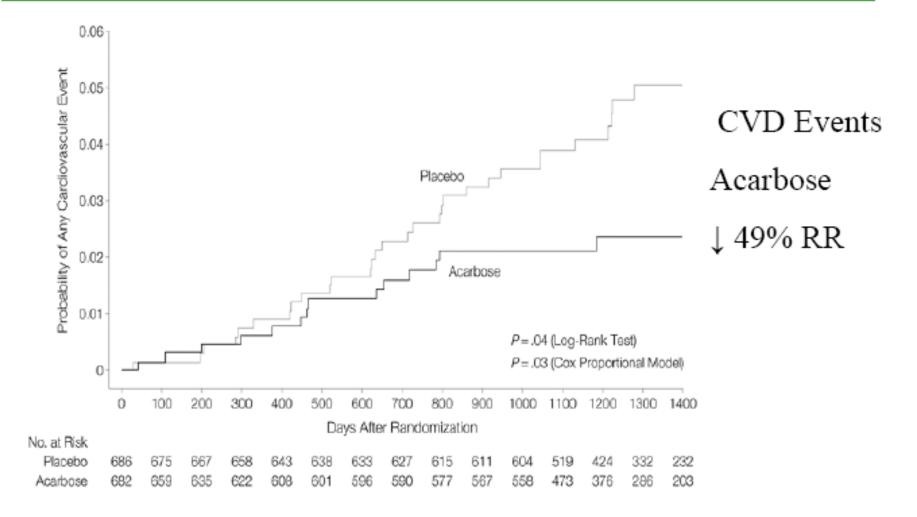
Liu et al. Am J Clin Nutr 2002;75:492-8

## **STOP-NIDDM** Trial



Chiasson J-L, Josse RG, Hanefeld M, et al. JAMA 2003;346:393

## **STOP-NIDDM** Trial



Chiasson J-L, Josse RG, Hanefeld M, et al. JAMA 2003;346:393

### What Affects Glycemic Index/Load

- Eating Pattern (Nibbling vs. Meals)
- Food Composition and Preparation

## Sipping

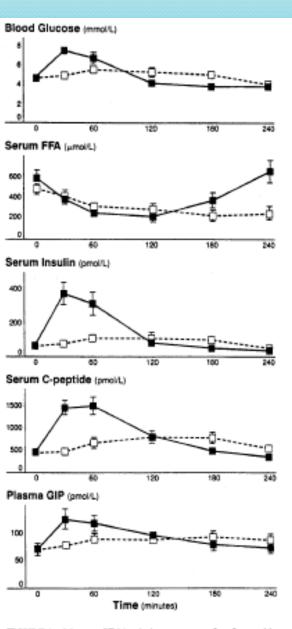
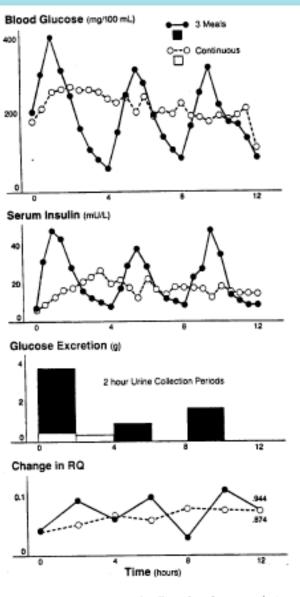
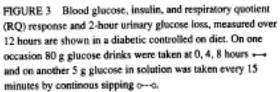


FIGURE 1 Mean ± SE blood glucose; serum free fatty acid (FFA), insulin, and C-peptide; and plasma gastric inhibitory polypeptide (GIP) after taking bolus of glucose solution over 5 minutes (50 g in 700 ml water) at time 0 (□) or sipping same solution over 0-3.5 hours at even rate (■).

## **Bolus vs. Grazing**





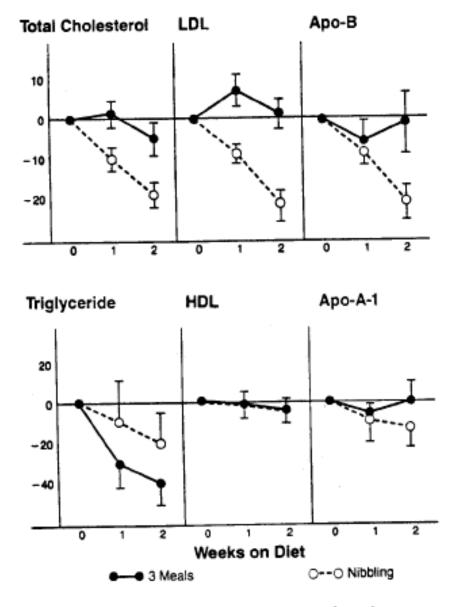


FIGURE 4 Mean ( $\pm$ SE) percentage change from time zero in serum lipid and apolipoprotein (Ap0) concentrations in seven men during the nibbling diet and the three-meal diet.

#### Nibbling vs. 3 Meals

### What Affects Glycemic Index/Load

- Eating Pattern (Nibbling vs. Meals)
- Food Composition and Preparation

## Glycemic Index –

### What Makes it High or Low?

Yogurt, lowfat,	14	Orange	43
unsweetened, plain		Corn	49
Lentils	29	Spaghetti, durum	55
Black beans	30	Rice, white	59
Apple	36	Ice Cream	61
Spaghetti, ww	37	Macaroni & cheese	64
Tortilla, corn	38	Grape-nuts cereal	67
All-bran cereal	42	French baguette	95

## Think Primitive!

#### "Whole wheat flour" ≠ Whole grain

Reference	Study subjects	Disrupted structure	<i>Gl</i> <sup>a</sup>	Intact structure	GI
Jenkins et al (1986)	Diabetics ( $n = 15 - 17$ )	Wholemeal wheat bread	$96\pm5$	Wheat kernels	63±6*
Jenkins et al (1986)	Diabetics $(n = 15 - 17)$	Wholemeal wheat bread	$96 \pm 5$	Cracked wheat kernels	65±4*
Jenkins et al (1986)	Diabetics $(n = 14)$	Wholemeal rye bread	89±6	Rye kernels	47±5*
Jenkins et al (1988)	Diabetics $(n = 6 - 8)$	Wholemeal wheat bread	92 (11)	75% cracked wheat bread	69 (4)*
Jenkins et al (1988)	Diabetics $(n = 6 - 8)$	Barley flour bread	96 (6)	75% barley kernel bread	39 (7)*
Liljeberg et al (1992)	Non-diabetics	80% Wholemeal barley flour bread	94.9±15.1	80% barley kernel bread	57.1±10.3
Granfeldt et al (1994)	Non-diabetics ( $n = 9 - 10$ )	Barley flour porridge	65±9**	Barley kernels	35±8*
Granfeldt et al (1995)	Non-diabetics $(n=9)$	Rolled oat porridge	93±7	Oat kernel porridge	60±7*

Table 3 Comparison of glycaemic index between grains with intact or disrupted structures

<sup>a</sup>GI with reference to white wheat bread (GI = 100); mean $\pm$  s.d., mean (s.e.).

\*Significantly different from GI of food with disrupted structure.

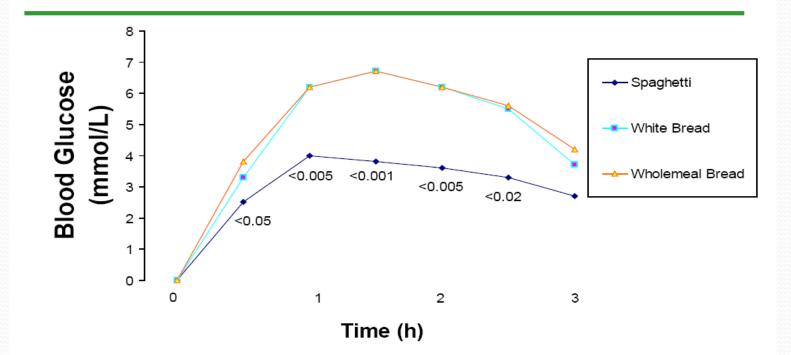
\*\*Significantly different from white wheat bread.

European Journal of Clinical Nutrition (2004) 58, 1443–1461.

## Surface area exposed to enzymes will raise the GI (i.e. grinding flour)

Lack of fat, protein, fiber will raise the GI

# Blood Glucose Increments After Spaghetti vs. Bread



Jenkins et al. Diab Care 1983;6:155-9

## **Glycemic Load**

- Some High-GI foods have so little carbohydrate in an average serving, their impact will be low.
- Examples include
  - Watermelon
  - Popcorn

#### Glycemic Index vs Glycemic Load Carrots GI 47

40g carb - 62/3 cups carrots

40g carb = 1 C cooked noodles



1 cup carrots (1 large carrot) Glycemic Load 3 1 Cup Spaghetti Glycemic Load 18

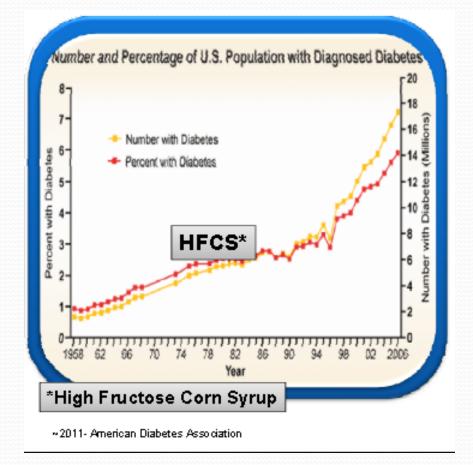


## **Resources for Patients**

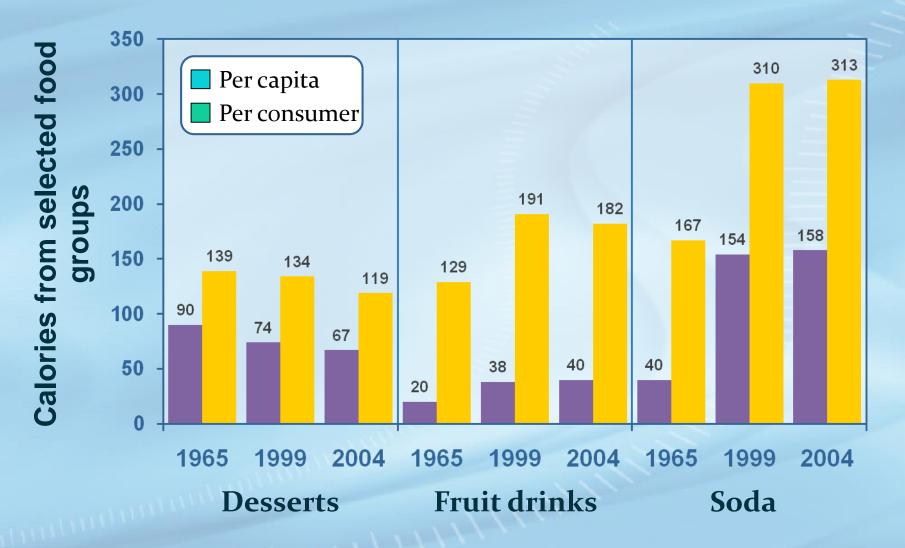
<u>http://mendosa.com/gi.htm</u>

• The GI Diet by Rick Gallup

## **Beverage Choices**



#### Steepest Increase in Calories of Added Sugar From Soda, per 🗘 Capita and Consumer Estimates



Adapted from Duffey KJ and Popkin BM Am J Clin Nutr 2008; 88:1722S-32S

Source: International Chair on Cardiometabolic Risk www.cardiometabolic-risk.org

#### The A to Z Study: The Relationship of Water Intake With Adjusted Mean Daily Total Energy Intake



Adapted from Stookey JD et al. Obesity 2007; 15: 3013-22

Source: International Chair on Cardiometabolic Risk www.cardiometabolic-risk.org

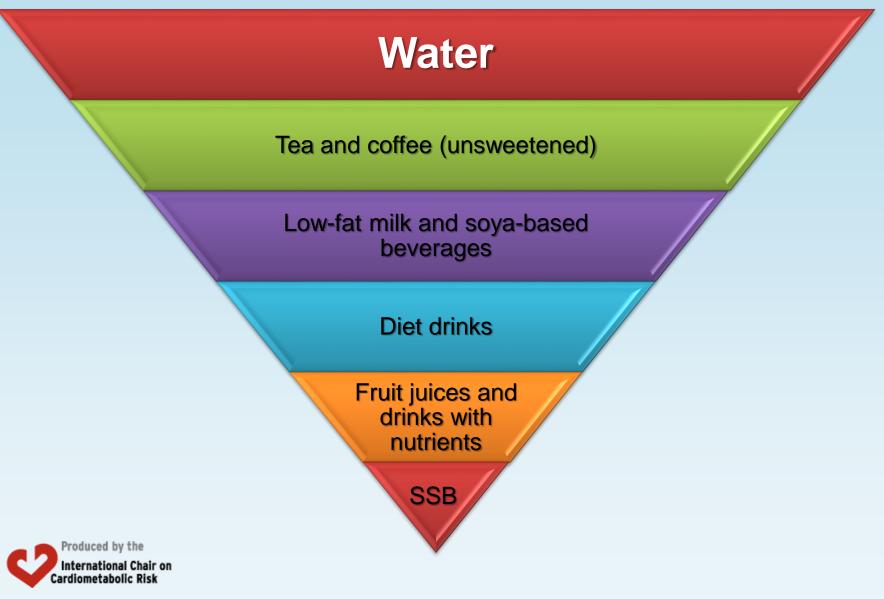
#### The A to Z Study: The Relationship of Water Intake With Mean Body Weight



Adapted from Stookey JD et al. Obesity 2008; 16: 2481-8

Source: International Chair on Cardiometabolic Risk www.cardiometabolic-risk.org





## "Diet" Beverages

	Qı	Q2	Q3	Q4	<i>P</i> for trend
Sugar-sweetened beverages					
Servings	Never	2/mo	1-4/wk	4.5/wk to 7.5/d	
Multivariate adjusted <sup>2</sup>	1.00	1.01 (0.90, 1.13)	1.03 (0.92, 1.15)	1.21 (1.08, 1.36)	<0.01
Previous weight change and low-calorie diet	1.00	1.07 (0.95, 1.20)	1.07 (0.95, 1.20)	1.25 (1.12, 1.40)	<0.01
Artificially sweetened beverages					
Quartile range (servings)	Never	2/mo	1-4/wk	4.5/wk to 18/d	
Multivariate adjusted <sup>2</sup>	1.00	1.21 (1.06, 1.37)	1.29 (1.16, 1.44)	1.94 (1.75, 2.14)	<0.01
Previous weight change and low frage in the first sune 1	1.00 , 2011 vo	<sup>1.13</sup> bl. <sup>(1</sup> 93°rl∂. <sup>9</sup> 6 13	1.10 3 <b>29</b> .9 <b>9327</b> 3)	1.35 (1.22, 1.50)	<0.01

## **Increasing Water**

- Instant Lemon
- Cucumber Slices
- Celestial Seasonings teas
- Your ideas?

## Shorthand: .dmpreven

For diabetes prevention, the main things you can do are:

1. Eat low glycemic index (see handout or <u>http://www.mendosa.com/gilists.htm</u>)

- 2. Increase fiber in the diet
- 3. Increase fruits and vegetables to 5-9 servings per day, especially dark green leafy vegetables

4. Increase exercise (30 minutes 5 days per week) - include muscle building as well as aerobic

5. Avoid trans fats (hydrogenated oils in baked goods, fried foods)

6. Avoid environmental endocrine disruptors (like PCB's, phthalates, BPA, PFOAs, etc.) - learn more at healthychild.org

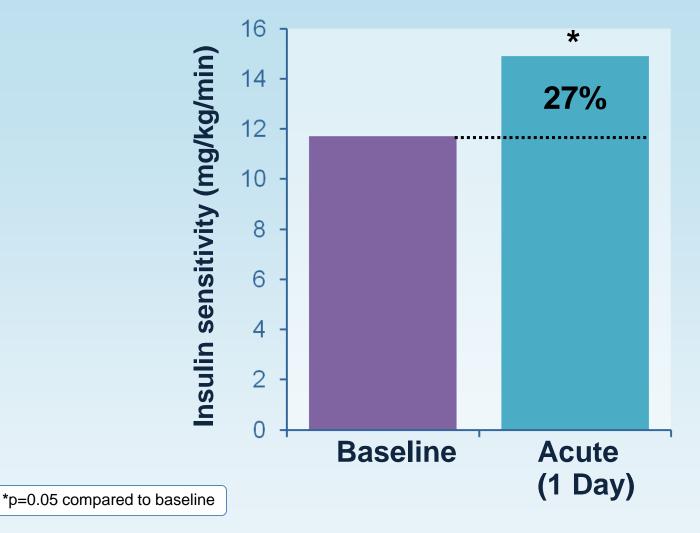
Increasing nuts in the diet may be helpful, and eating cinnamon, about  $\frac{1}{2}$  tsp per day, may also be helpful, as may the medication metformin.

## Exercise

• Q: What type do you recommend?

• A: Aerobic and Resistance

#### Effect of Acute Exercise on Insulin Sensitivity in Men and Women





Adapted from Perseghin G et al. N Engl J Med 1996;335:1357-62

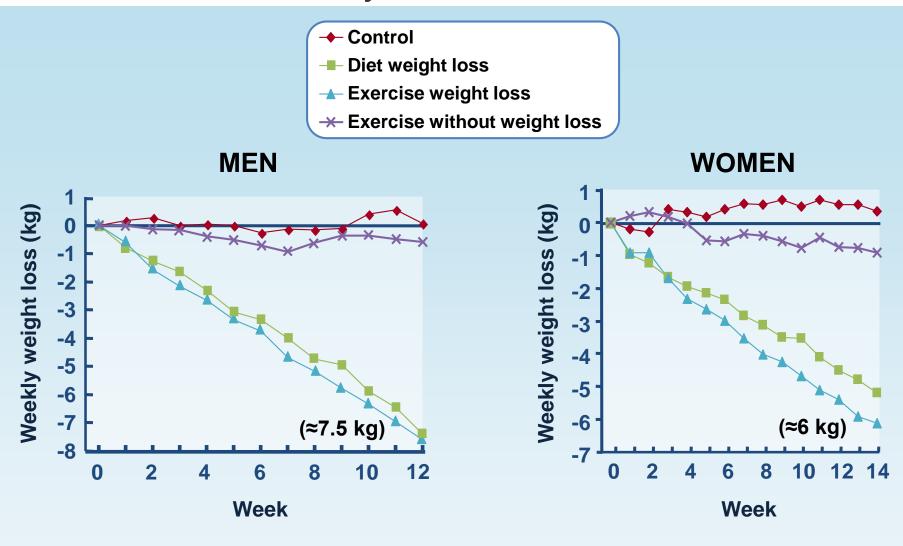
Effects of Diet or Exercise With or Without Weight Loss on Abdominal Obesity and Insulin Resistance



□ Abdominally obese men and women (age ≈45 years): 14-16 weeks
 □ Intervention ≈50 minutes of daily walking on treadmill under supervision
 □ All participants: balanced diet, no caloric restriction



Effects of Diet or Exercise with or Without Weight Loss on Abdominal Obesity and Insulin Resistance



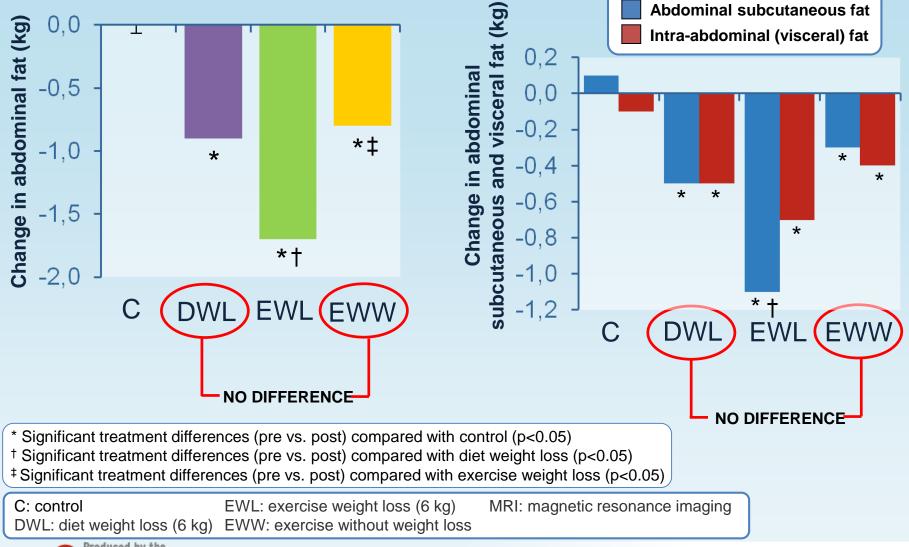


Source: www.myhealthywaist.org

Adapted from Ross R et al. Ann Intern Med 2000;133:92-103 and Ross R et al. Obes Res 2004;12:789-98



Influence of Equivalent Diet- or Exercise-Induced Weight Loss on Abdominal Fat (MRI) in Obese Women



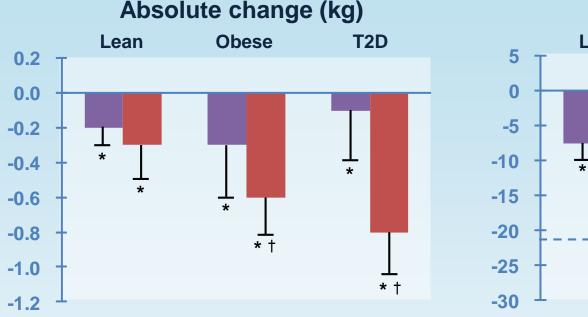


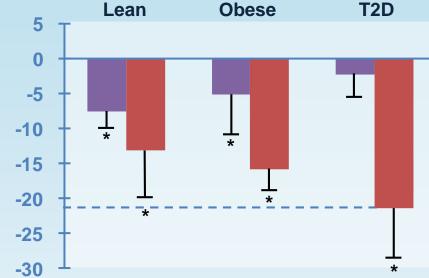
Adapted from Ross R et al. Obes Res 2004;12:789-98

#### **Exercise Without Weight Loss is an Effective Strategy for Obesity Reduction in Men With and Without Type 2 Diabetes (T2D)**

Abdominal subcutaneous adipose tissue Intra-abdominal (visceral) adipose tissue

**Relative change (%)** 





Significant treatment differences (pre vs. post) within group, p<0.01

Significantly greater reduction in intra-abdominal fat by comparison to the lean group, p<0.01

#### Balanced diet, no caloric restriction, no weight loss



Adapted from Lee S et al. J Appl Physiol 2005;99:1220-5

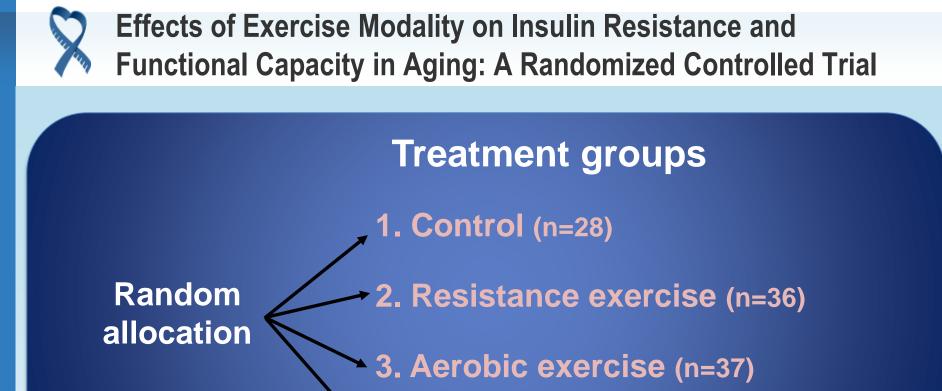
Exercise With or Without Weight Loss on Skeletal Muscle Mass in Obese Men and Women



\* Significant treatment differences (pre vs. post) compared with control (p<0.05) † Significant treatment differences (pre vs. post) compared with diet weight loss (p<0.05) C: control

DWL: diet weight loss (6 kg) EWL: exercise weight loss (6 kg) EWW: exercise without weight loss MRI: magnetic resonance imaging





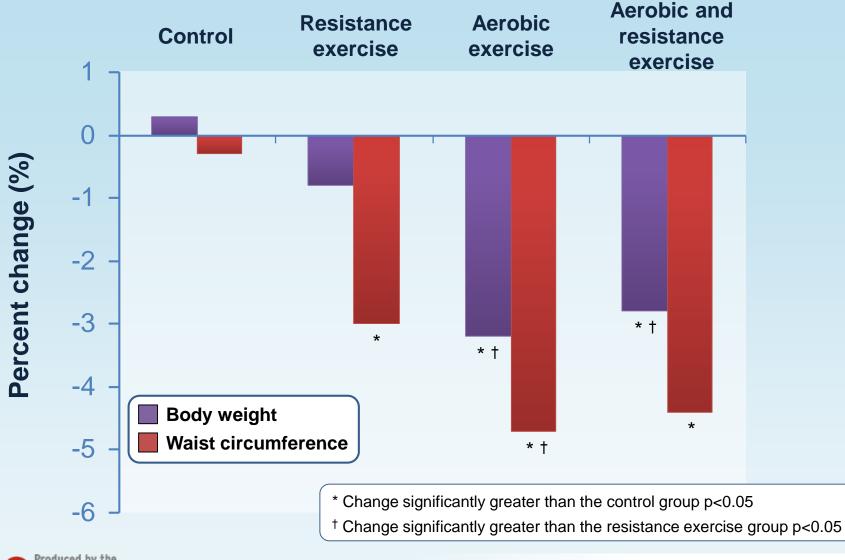
4. Resistance and aerobic (n=35)

Abdominally obese men and women (age ≈68 years): 6-month exercise intervention, without caloric restriction.



Adapted from Davidson LE et al. Arch Intern Med 2009;169:122-31

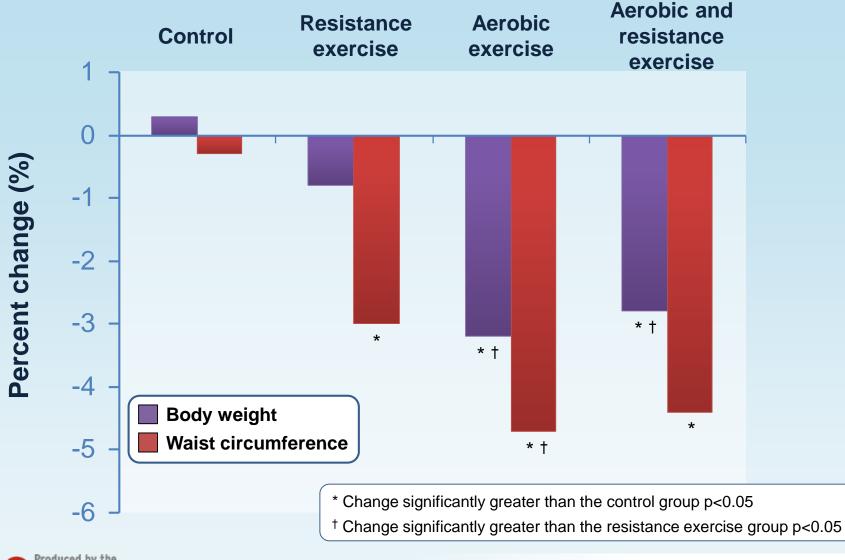
## Effects of Exercise Modality on Body Weight and Waist Circumference in Older Men and Women





Adapted from Davidson LE et al. Arch Intern Med 2009;169:122-31

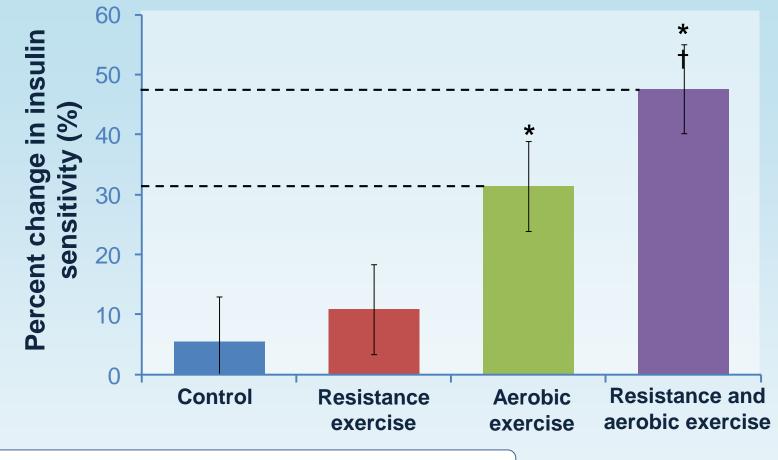
## Effects of Exercise Modality on Body Weight and Waist Circumference in Older Men and Women





Adapted from Davidson LE et al. Arch Intern Med 2009;169:122-31

## Effects of Exercise Modality on Insulin Sensitivity in Older Men and Women



\* Change significantly greater than the control group p<0.05

<sup>†</sup> Change significantly greater than the resistance exercise group p<0.05



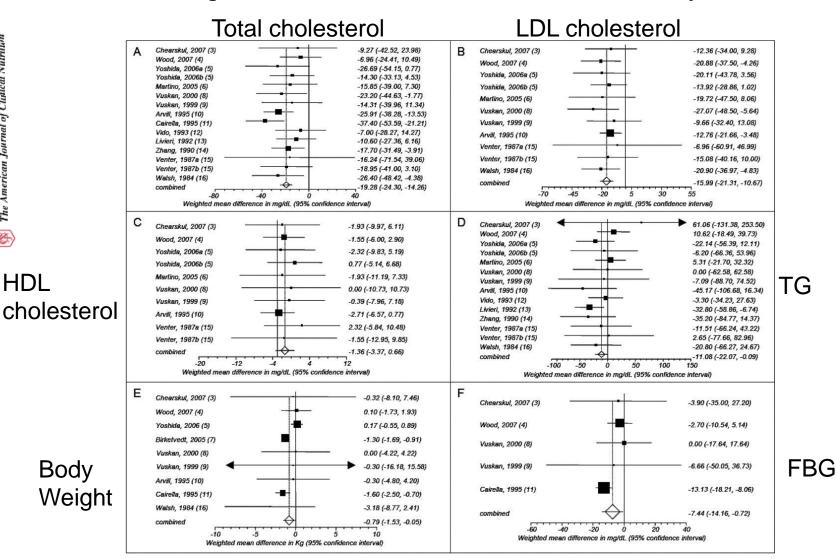
Adapted from Davidson LE et al. Arch Intern Med 2009;169:122-31

Source: www.myhealthywaist.org

### Some other issues

- Stress Reduction
  - Relaxation
  - Build Community thedanielplan, etc.
    - If you want to travel swiftly go alone, if you want to travel far, travel together. ---African Proverb
- Gut Flora
- Dietary Supplements

#### Effect of glucomannan on characteristics of the metabolic syndrome.



Sood N et al. Am J Clin Nutr 2008;88:1167-1175

HDI

#### ©2008 by American Society for Nutrition

## And a word on Diabetes Treatment

Embedded polls only work in PowerPoint for Windows

### This object is the poll's placeholder

# To view the poll live, enter slideshow mode by pressing F5

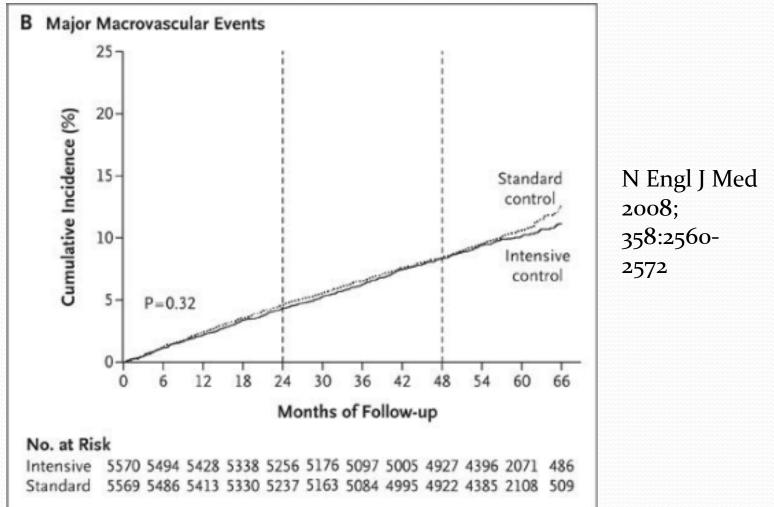
Poll: In treating Diabetes:

### The paradox. . .

- In prospective epidemiologic studies, the incidence of many of these outcomes is directly associated with the degree of hyperglycemia
- After adjustment for other risk factors, an increase of 1% in hgbA1C is associated with an increase of
  - 18% in the risk of cardiovascular events
  - 12 to 14% in the risk of death
  - 37% in the risk of retinopathy or renal failure

N Engl J Med 2008; 358:2545-2559

### ADVANCE



### ACCORD

#### B Death from Any Cause No. of No. of Hazard Ratio Subgroup **Patients** P Value Events. 10,251 Total. 450 Previous cardiovascular event 0.53 6,643 No 220 Yes. 3,608 240 Sex 0.92 Female 3.952 132 6,299 328 Male. Age at baseline 0.19 6,779 212 ×65 yr. ≥65 yr 3,472 248 0.15 Glycated hemoglobin at baseline \*8.0% 4,868 204 >8.096 5,360 256 0.93 Race. Nonwhite 3,647 131 White 6,604 329 1.2 1.6 0.8 Intensive Standard Therapy Therapy **Better Better**

N Engl J Med 2008; 358:2545-2559

# Hyperinsulinemia is toxic, even with normal glucose

• "The real problem is that muscle and fat are resistant to the insulin signal, BUT other tissues, bathed in high insulin, are still exquisitely sensitive."

- Drives appetite and further weight gain
- Atherogenic
  - Inhibition of Fatty Acid Oxidation
  - Growth factor properties, stimulating cell hypertrophy
- Carcinogenic

### Epidemiology:

### **Diabetes Treatment and Cancer Incidence**

	Diagnosis of cancer	Adjusted for age, sex, HbA <sub>1c</sub> , smoking status, and BMI				
	N (%)	OR	95% CI	Р		
No DM2	185 (3.0 %)	1.00				
DM2	66 (5.1 %)	1.64	1.12 - 2.41	.01		
DM2: monotx with insulin	6 (2.8 %)	1.19	0.46 - 3.08	.71		
DM2: monotx w/ metformin	6 (3.1 %)	0.92	0.39 - 2.20	.85		
DM2: oral combo incl metformin	9 (3.9 %)	1.53	0.71 - 3.31	.28		
DM2: oral combo excl metformin	3 (10.7 %)	4.04	1.07 - 15.26	.04		

Metabolism (2010), doi:10.1016/j.metabol.2010.09.012

From: Cardiovascular Outcomes in Trials of Oral Diabetes Medications: A Systematic Review

Arch Intern Med. 2008;168(19):2070-2080. doi:10.1001/archinte.168.19.2070

Meta-analysis suggested that, compared with other oral diabetes agents and placebo, metformin was moderately protective and rosiglitazone possibly harmful

#### Or even metformin may not be helpful....

4		Metform	nin	Contr	ol		Risk Ratio		Risk Ratio
	y or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
DeFre	onzo 1	0	143	0	146		Not estimable	1995	
DeFre	onzo 2	0	213	0	209		Not estimable	1995	
UKPD	DS 34a	50	342	89	411	25.7%	0.68 [0.49, 0.93]	1998	
UKPD	DS 34b	47	268	31	269	20.4%	1.52 [1.00, 2.32]	1998	
Horto	'n	1	178	0	172	0.7%	2.90 [0.12, 70.69]	2000	
Chias	sson	0	83	0	83		Not estimable	2001	
Blond	ie	2	322	1	164	1.3%	1.02 [0.09, 11.15]	2002	
Rach	mani	62	195	64	198	27.2%	0.98 [0.74, 1.31]	2002	
Garbo	er	2	171	0	151	0.8%	4.42 [0.21, 91.32]	2003	
COS	MIC	79	7227	20	1505	17.6%	0.82 [0.51, 1.34]	2005	
HOM	E	9	196	6	194	6.3%	1.48 [0.54, 4.09]	2009	
Total	I (95% CI)		9338		3502	100.0%	0.99 [0.75, 1.31]		
	events	252		211	0002	100.070	0.00 [0.10, 1.01]		T
Heter	rogeneity: Tau <sup>2</sup> = (	0.05; Chi <sup>2</sup>	= 11.93	2, df = 7 (	P = 0.1	0); l <sup>2</sup> = 419	6		
Test f	for overall effect: 2	z = 0.06 (F	P = 0.9	5)					0.1 0.2 0.5 1 2 5 1 Favours metformin Favours control

в

	Metfor	min	Contr	lo		Risk Ratio		Risk Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% Cl	Year	M-H, Random, 95% Cl
DeFronzo 2	0	213	0	209		Not estimable	1995	
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UKPDS 34a	25	342	51	411	24.0%	0.59 [0.37, 0.93]	1998	
UKPDS 34b	30	268	13	269	19.6%	2.32 [1.24, 4.34]	1998	
Horton	1	178	0	172	1.9%	2.90 [0.12, 70.69]	2000	
Chiasson	0	83	83	0		Not estimable	2001	
Rachmani	50	195	52	198	27.1%	0.98 [0.70, 1.36]	2002	· •
Blonde	2	322	1	164	3.2%	1.02 [0.09, 11.15]	2002	
COSMIC	51	7227	14	1505	20.6%	0.76 [0.42, 1.37]	2005	
HOME	4	196	1	194	3.7%	3.96 [0.45, 35.10]	2009	
Total (95% CI)		9167		3268	100.0%	1.05 [0.67, 1.64]		+
Total events	163		215					
Heterogeneity: Tau <sup>2</sup> = 0.17; Chi <sup>2</sup> = 14.66, df = 6 (P = 0.02); I <sup>2</sup> = 59%								
Test for overall effect:	Z = 0.20 (	P = 0.8	4)					0.1 0.2 0.5 1 2 5 10 Favours metformin Favours control

But note they included metformin + sulfonylurea in their analysis

Boussageon R, Supper I, Bejan-Angoulvant T, Kellou N, et al. (2012) Reappraisal of Metformin Efficacy in the Treatment of Type 2 Diabetes: A Meta-Analysis of Randomised Controlled Trials. PLoS Med 9(4): e1001204. doi:10.1371/journal.pmed.1001204 http://www.plosmedicine.org/article/info:doi/10.1371/journal.pmed.1001204

#### PLOS MEDICINE

RIZARROCOMIC REOGSPOT.COM Take one a day with tomato and cucumber. FARMACY

### **Bottom Line in Treating Diabetes**

- Shorthand: .dmplan
- Individualized target:
  - Low risk/high benefit patients: <6.5%.
  - Intermediate risk/intermediate benefit patients: < or = 7%.
  - High Risk/low benefit patients(elderly, high risk for developing hypoglycemia or being injured by low blood sugar): 7.5-8%.
- Identify and Treat Comorbidities
  - HTN
  - HPL
  - Depression
  - Tobacco
  - (+/- periodontal disease, etc.)

### Medication changes/additions:

- Step 1: Lifestyle +/- metformin
- Step 2: Lifestyle + metformin +sulfonylurea or Lifestyle + metformin + basal insulin
- Step 3: Lifestyle + metformin + Intensive insulin
- Tier 2 (less proven therapies): lifestyle + metformin + pioglitazone or GLP-1 agonist

### Additional medications:

- ACEI/ARB or reason patient cannot take one
- Aspirin for documented CAD, additional risk factors for CAD, or men >50 or women > 55
- Statin if overt cardiovascular disease or if > 40 yo and have one or more other CVD risk factor
  - note one recommendation that all should be on statins unless T2DM <32 yo men/38 yo women with disease < 10 years and no apparent CVD risks factors Diabetes Care November 2009 vol. 32 no. suppl 2 S384-S391

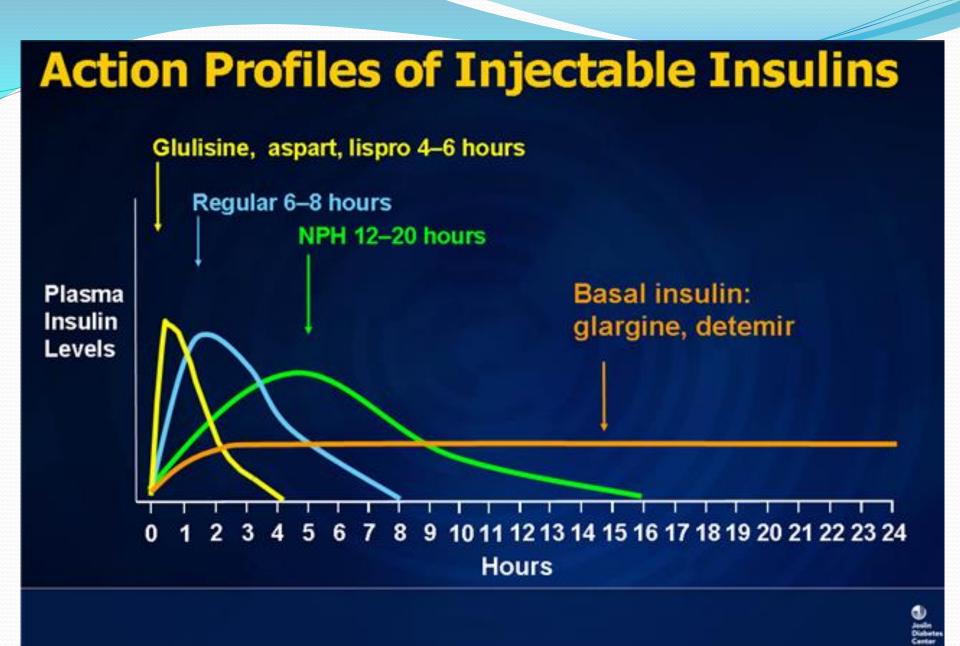
### Patient education/empowerment

- See list in .dmplan
  - Emphasis on lifestyle
  - Hypoglycemia
  - Finding support
- Shorthand: .dmpted
  - Set a goal!!

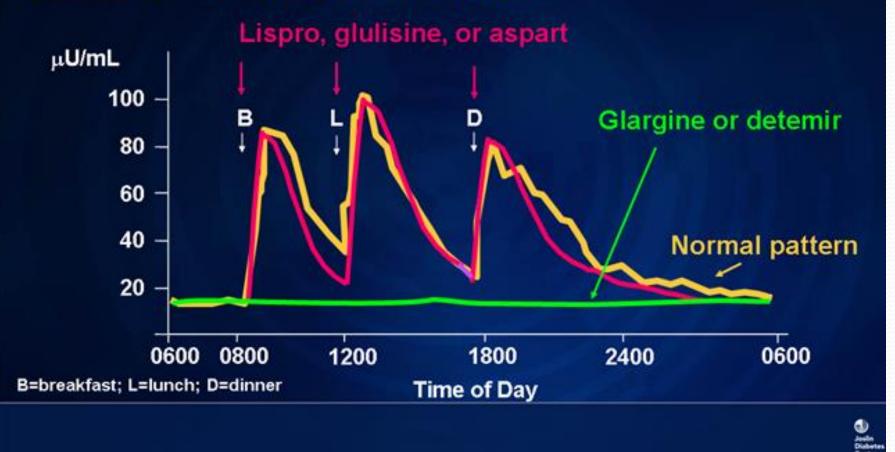
### **Integrative Additions**

- Glucomannan 1-8 grams before meals
- Fish oil 2000 mg EPA+DHA per day
- ALA (alpha lipoic acid) 100 mg BID
- Cinnamon 500mg BID
- I am less convinced:
  - [Vanadium 0.5 mg BID]
  - [Chromium picolinate 600 mg BID]
  - Bitter melon
  - Etc.

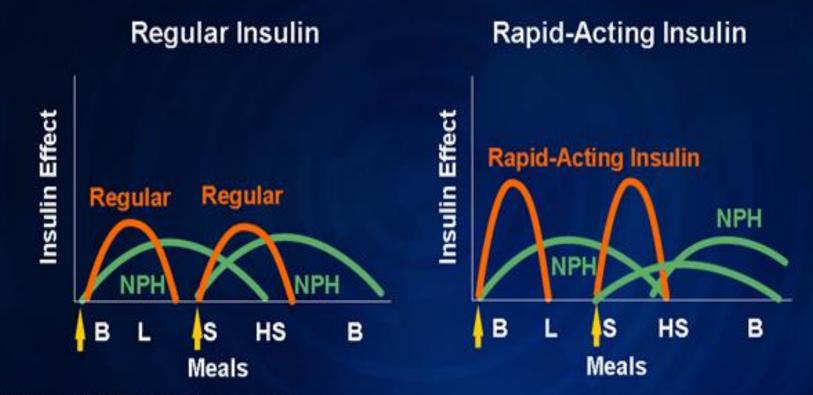
Insulin Varieties



### **Basal-Bolus Insulin Treatment** with Insulin Analogues

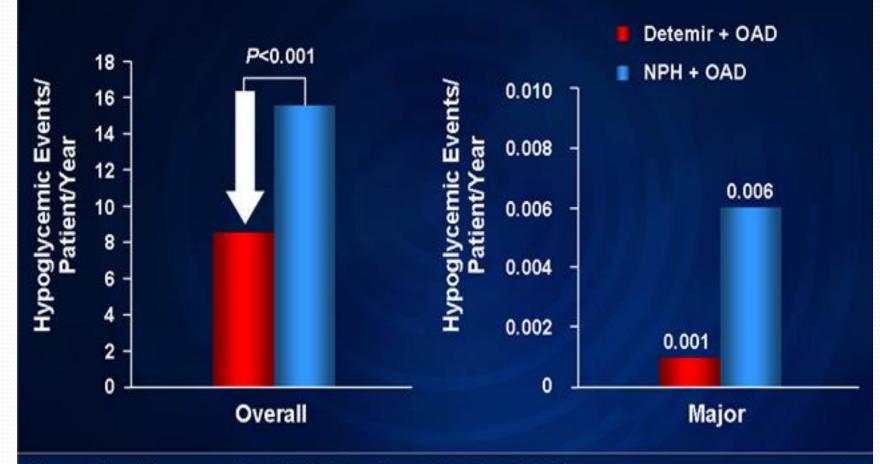


### Twice Daily Split-Mixed Regimens: Adjustments in Overnight Coverage



NPH moved to hs for better a.m. peak NPH added to supper for better early night coverage

### **Hypoglycemia Rates with Detemir vs NPH**



Adapted from Hermansen K et al. Diabetes Care. 2006;29:1269-1274.



# Cost

\_\_\_\_

	Cost for 10 mL
NPH	\$73.99
Humulin R	\$73.99
Novolin 70/30 vial	\$75.99
Levemir 10 mL	\$136 (\$378 for 3)
Levemir flexpen	\$161.99
Novolog 70/30 flexpen	\$172.65
Humulin 70/30 pen	\$150.66
Lantus	\$124.99
Novolog	\$140.70

On drugstore.com 1/2012

### Starting insulin in Type 2 DM

- Start with basal at hs
  - 0.1 units/kg, or 8-10 units

If FBG >	Increase insulin by every 3-4 days
120	2 units
140	3 units
160	4 units

- <sup>12</sup>Omega 3 fatty acids
- 🛛 Anti-oxidants
- **Phytonutrients**
- ISupplements
- <sup>12</sup>High dose EPA+DHA
- 🛛 Insulin sensitizers Insulin sensitizers: Glucomannan 1-2 gm 5-10 minutes before
- Meals, Chromium 600 mg BID
- 🛛 ALA 100 mg BID
- Cinnamon 500mg BID
- • Vanadium 0.5 mg BID
- 2 Hypertriglyceridemia
- 🛛 Obesity/ Weight gain
- IBiotransformation/Elimination support
- IMovement Medicine
- IStress Management
- IReduce Toxic Burden