Obesity, Youth and Diabetes (DiaObesity)

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11-8/12 y/o Female Patient

T2

- Chief Complaint - urinates 2-3 times at night times 2 months
- Weight 78 kg, BMI > 95th %ile for age/gender
  - Reported 30 lb weight gain last year, recent loss
- BP – 128/83
- Menses age 10 yrs – irregular
- Pre-natal - excessive maternal weight gain, ? diabetes,
- FH –
  - Mother from Arizona, AI/HA, + for obesity
  - Father is Non-Hispanic White, hypertension

Outline of Presentation

1. Presentation, Diagnostic Criteria, Screening
2. Rates, Causes – Genes/Environment
3. Treatment
4. Co-morbidities and complications
5. Prevention

1. Presentation, Diagnostic Criteria, Screening

- Presentation
  - T2 indolent, mild hyperglycemia, rare acidosis, no DKA
    - AA high rate of mild DKA, higher glucose/A1C, symptomatic at presentation
- Diagnostic Criteria
  - Symptoms of diabetes plus casual glucose ≥ 200 mg/dL
  - Fasting plasma glucose ≥ 126 mg/dL
  - 2-hour post-load glucose ≥ 200 mg/dL during OGTT
- ?A1C ≥6.5%
  - Used in adults but not established in children

1. Presentation, Diagnostic Criteria, Screening

- **Evidence of insulin resistance, hypertension, dyslipidemia, NASH**
- **Presentation during or after puberty**
- **T2 in first-degree relative**
- **Acanthosis nigricans, sleep apnea, PCOS, candidiasis**

J Clin Endocrinol Metab, December 2010, 95(12):5163-5170

1. Screening for T2

Results of the HEALTHY Study and Pilot – Diabetes Not Found

Measurement		6th grade N = 6367	8th grade N = 1740
BMI (kg/m^2)	Mean (SD)	22.4 (5.7)	24.3 (5.9)
BMI percentile (adjusted for age and gender)	< 85	50.5%	51.0%
	85-94	19.8%	19.8%
	≥ 95	29.7%	29.2%
Fasting glucose (mg/dL)	Mean (SD)	93.4 (6.7)	98.2 (8.5)
	< 100	84.0%	59.5%
	100-109	14.7%	34.3%
	110-125	1.2%	5.8%
	≥ 126	0.1%*	0.4%**
*n=6 of which only 1 confirmed on follow-up testing; **n=7*			
Fasting insulin (μU/mL) ≥ 30		6.2%	36.2%

HEALTHY

Diabetes Care 29;212;2006; Diabetes Care 32:953;2009

1. Screening for T2

ADA\AAP Consensus Statement 2000

- **Criteria***: Overweight **(BMI> 85th %ile for age and sex, wt for ht >85th %ile, or wt > 120% of ideal for ht)**

  PLUS: any two of the following risk factors:
  - Family history of DM 2 in 1st or 2nd degree relative
  - Race/Ethnicity
  - Signs of insulin resistance

- **Age of Initiation**: age 10 or at onset of puberty
- **Frequency**: every two years in the context of health visit
- **Test**: Fasting plasma glucose preferred

* **Clinical judgement should be used**

Diabetes Care 2000;23:381

1. Associated with Overweight and Obesity

- **Dyslipidemia**
  - **Low HDL**
  - **Any lipid abnormality - 12%-17%**
- **Elevated BP**
  - **7%-16% with BP >95th percentile BP**
  - **3.26 RR for HTN**
- **Metabolic Syndrome**
  - **Overall rate in US 12-19 year old – 4.2%**
  - **BMI > 40, 50% have MS**
- **Acanthosis nigricans**
  - **African American youth - 51%**
  - **Caucasians - 8%**
- **Earlier onset of pubarche and thelarche**
  - **Not earlier gonadarche**
- **Hyperandrogenemia and polycystic ovary syndrome**

J Clin Endocrinol Metab 93 (12):4576-4599;2008

1. Associated with Overweight and Obesity

- Glomerulosclerosis
  - 10-fold increase in adults, rate in children not known
- Obstructive sleep apnea
  - Six-fold increase
  - OSA independently related to HTN, CVD, behavioral disorders, poor school performance, poor quality of life
- Non-alcoholic fatty liver disease (NAFLD)
  - 10-25 % elevated transaminases
  - Abdominal sonography detects fatty liver in 52%
  - Hispanic children - higher incidence
  - Rare - increasing fibrosis and eventual cirrhosis
- Gallstones
  - 2%
- Orthopedic
  - Slipped capital femoral epiphysis, genu valga, tibia vara (Blount disease), scoliosis, and osteoarthritis
- Pseudotumor cerebri
  - 15-fold increase

J Clin Endocrinol Metab 93 (12):4576-4599;2008.

2. Causes T2 - THE HEALTHY MIDDLE SCHOOL STUDY

6th grade students – predominately minority students

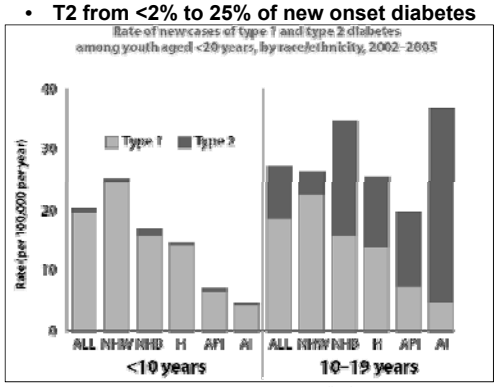
Distribution of Glycemic Risk Factors by BMI Percentile

	< 85 (N=3221)	85 - 94 (N=1255)	≥ 95 (N=1882)
Fasting glucose (mg/dL)†	**92.8 (6.7)**	**93.3 (6.8)**	**94.5 (6.6)**
Fasting glucose ≥ 100	**13.5%**	**15.5%**	**20.8%**
		p < .0001§	
Fasting insulin (μU/mL)†	**8.4 (5.2)**	**12.8 (7.5)**	**22.1 (15.8)**
Fasting insulin ≥ 30	**0.8%**	**3.0%**	**19.6%**

•Diabetes Care 29;212;2006 •Diabetes Care 32:953;2009 ***p < .0001§***

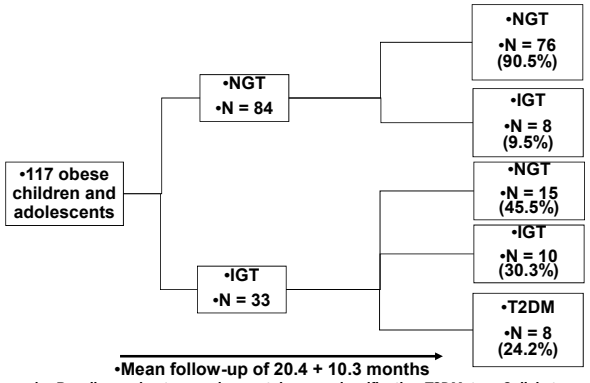
2. Causes – Genes and the Environment

- 3-5% increase in T1 consistently
- T2 from <2% to 25% of new onset diabetes



SEARCH for Diabetes in Youth Study Group *Pediatrics* 2006; 118; 1510 – 1518 DOI: 10.1542/peds.2006-0690

2. Causes – T2



•Figure 1 – *Baseline and outcome glucose tolerance classification T2DM, type 2 diabetes.*

•Weiss, et al, Diabetes Care, 28;902:2005

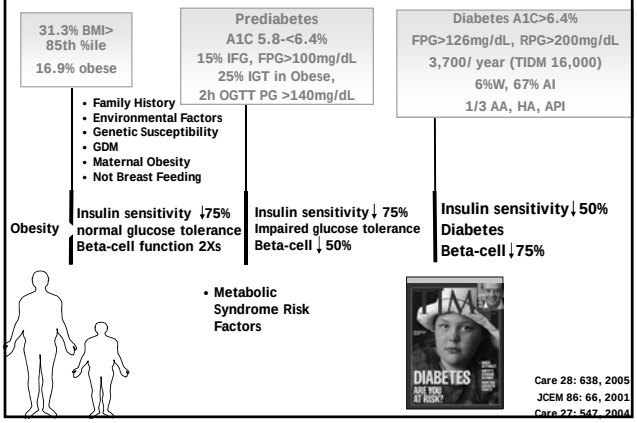
2. Causes T2

Table 3—*Comparison of subjects with IGT who developed type 2 diabetes and who reverted to NGT*

•	IGT to NGT		IGT to T2D
•BMI	33	versus	44
•BMI z-score	2.27	versus	2.76
•Weight Δ kg	6.1	versus	27
•BMI Δ	1.06	versus	6.8

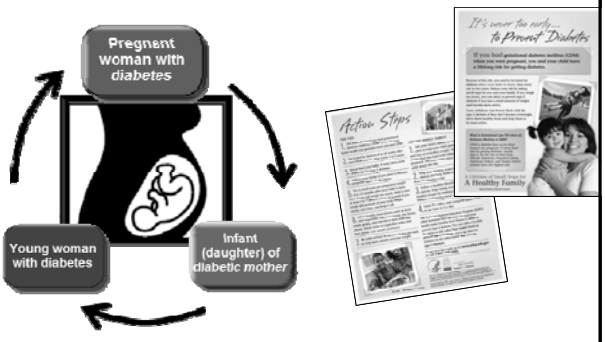
•Weiss, et al, Diabetes Care, 28;902:2005

2. Causes T2 - Progression from pre-diabetes to diabetes



Care 28: 638, 2005
JCEM 86: 66, 2001
Care 27: 547, 2004

2. Causes T2 - Gestational Diabetes As A Driver of T2



Diabetes in pregnancy can lead to a cycle of diabetes affecting future generations.

Diabetologia. 1998;41:904-10)

11 8/12 y/o Female Patient

- **Obtain the following work up:**
  - **Random plasma glucose 247 mg/dL, Repeat A1C 8.5%**
  - **CO2 20 meq/L, venous pH 7.38, LDL 178 mg/dL, Triglycerides 215 mg/dL**
- **ANTIBODIES ALL NEGATIVE**
- **Treatment - In or outpatient?**
  - **Do you start insulin?**
  - **Metformin alone is first line therapy when glucose level is < 250 mg/dL and patient is non-ketotic**
  - **All patients and families receive diabetes and lifestyle education**

3. Treatment - Diabetes is Hard to Manage

Early and persistent glucose control is important

Age	Pre-Meal BG	HS/Night BG	A1c
Toddler (0-5 yrs)	100-180	110-200	≥7.5 & ≤8.5%
School-age (6-11 yrs)	90-180	100-180	<8%
Adolescent (12-19 yrs)	90-130	90-150	<7.5%
Type 2	80-130	90-150	<7.0%

Diabetes Care **28:186-212, 2005**

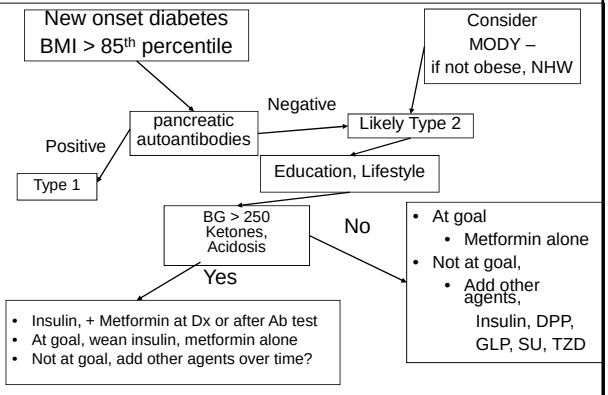
Diabetes Care **28:186-212, 2005**

3. Treatment

Early and persistent glucose control is important

- **Glucose monitoring**
  - **Self-monitoring Glucose, Understanding Glucose Targets, A1C Quarterly**
- **Medications**
  - **Glucose Lowering Agents**
    - **Metformin, Insulin therapy, ? Other agents**
    - **Others Not Approved**
- **Medical Nutrition Therapy**
  - **Weight Reduction, Lifestyle Counseling**
- **Psychosocial Support**
- **Assess, Treat Co-morbidities, Complications**
  - **BP, Cholesterol, Disordered Eating, PCOS, NASH, Microalbuminuria, Eye Exams**
- **Visits to Health Care Team**
  - **Routine Pediatric Care, Flu Shots, Hep B Immunization, Transition Planning**
  - **Sick Day Management**

3. Treatment - Determining diabetes type in youth with BMI > 85th percentile and Treatment



ISPAD Guidelines, 2009,J Clin Endocrinol Metab, December 2010; 95(12):5163-5170

3. Treatment T2

TODAY

Funded by National Institute of Diabetes and Digestive and Kidney Diseases National Institutes of Health

- **Randomized clinical trial with a pre-randomization run-in period**
  - **704 patients at 15 clinical centers**
  - **3 treatment regimens**
    - **Metformin + Placebo**
    - **Metformin + Rosiglitazone**
    - **Metformin + Intensive Lifestyle Program**
    - **At treatment failure: Standardized approach to insulin initiation**
- **Primary outcome: time to failed glycemic control**
- **Inclusion criteria**
  - **Age 10 to 17 years**
  - **Duration of diabetes < 2 years**
  - **BMI ≥ 85th percentile**

J Clin Endocrinol Metab, January 2011, 96(1):159-167

3. Treatment T2 - The TODAY Trial

	Mean ± SD or %
Age (years)	14.3 ± 2.0
Race/Ethnicity	
White	19.6%
African American	37.4%
Hispanic	32.2%
Native American	5.5%
Other/Unknown	5.3%
BMI (kg/m²)	36.2 ± 7.9 25 - 71
BMI Z-score	+2.3 ± 0.5

Medications at Presentation

- No medication 11%
- Insulin only 12%
- Metformin only 49%
- Metformin + Insulin 25%
- Other medication 4%

- 26% hypertension
- 56% dyslipidemia
- 50% depression

J Clin Endocrinol Metab, January 2011, 96(1):159-167

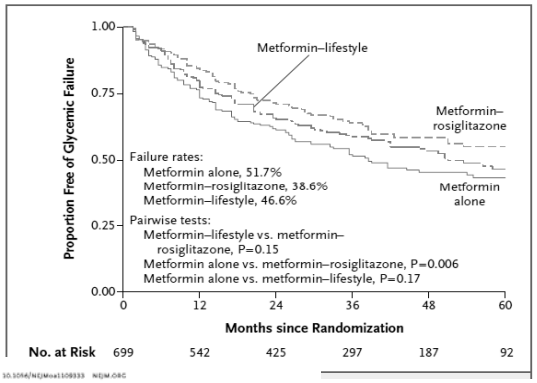
3. Treatment T2

Funded by National Institute of Diabetes and Digestive and Kidney Diseases National Institutes of Health

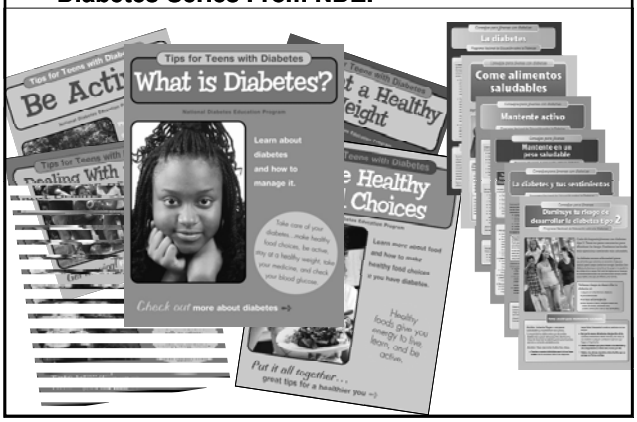
- At the time of treatment failure, patients began basal insulin
- Half of the subjects failed and needed insulin treatment
- Of those on insulin, most could not be treated with basal alone
  - They progressed to MDI or insulin pumps
  - In my center, half of those on insulin used insulin pump therapy

J Clin Endocrinol Metab, January 2011, 96(1):159-167

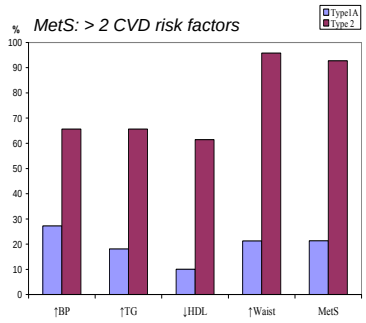
3. Treatment T2 - The TODAY Trial The Study Results



3. Treatment – Lifestyle Tips for Teens with Diabetes Series From NDEP



4. Co-morbidities and complications
Cardiovascular Risk Factors – SEARCH Trial



68% AI, 37% Asian, 32% AA, 35% Hispanics, 16% Whites (p<0.0001)

At least 2 risk factors
- **92% of type 2**
- **14% of type 1**
- **(p<0.0001)**

Rodriguez et al, Diabetes Care, 2006
Diabetes Care 29:1891,2006

4. Complications – T2
Type 2 Diabetes is a Severe Disease

Kaufman, Type 2 Youth

- Hyperglycemic Hyperosmolar Non-Ketotic Syndrome – at onset –very high glucose levels
  - 3.7% (7/190) in Philadelphia
    - Mortality 14.3%
  - Currently 28 reported other cases
    - Mortality 43%
- Pima Indians - diagnosed < 20 years of age
  - 22% had microalbuminuria at diagnosis
  - Increased to 60% at 20-29 years of age
- Indigenous Canadians - age 23 yrs, 9 yrs duration
  - HbA1c 10.9%
    - 67% poor glycemic control
  - 45% hypertension requiring treatment
  - 35% microalbuminuria (6% required dialysis)
  - 38% pregnancy loss
  - 9% mortality

Fournier, et al: Pediatr.Diabetes 2005;6(3):129-35
Dean., Diabetes 2002;51(Suppl 2):A24.

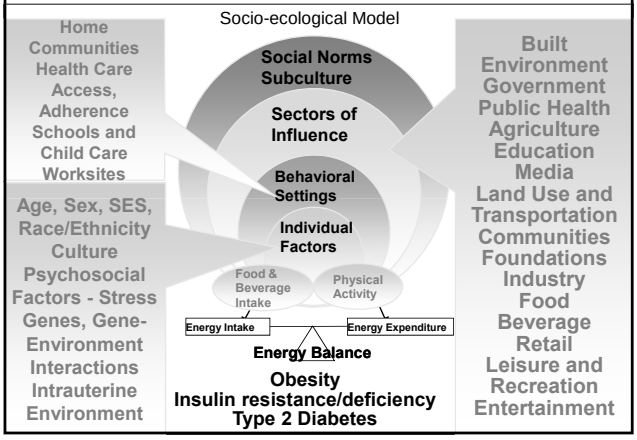
4. Co-morbidities and complications - Australia

Diabetes Care 29:1300,06

	Type 1 diabetes	Type 2 diabetes	*P* value
n	1,433	68	
Age at last assessment (years)	15.7 (13.9–17.0)	15.3 (13.6–16.4)	0.23
Age at diagnosis (years)	8.1 (4.8–10.8)	13.2 (11.6–15.0)	<0.0001
Sex (male/female)	674/759	34/34	0.63
Duration (years)	6.8 (4.7–9.6)	1.3 (0.6–3.1)	<0.0001
A1C (%)	8.5 (7.8–9.5)	7.3 (6.0–8.3)	<0.0001
A1C <7.5%	230/1,393 (17)	42/66 (64)	<0.0001
Insulin/weight	1.15 (0.86–1.39)	0.89 (0.51–1.31) (*n* = 9)	0.063
BMI SD score	0.80 (0.25–1.27)	1.85 (1.28–2.40)	<0.0001
Social disadvantage risk score	0.23 (−0.17–0.80)	0.14 (−0.47–0.56	0.058
From urban area	95/1,419 (6.7)	60/63 (95)	0.26
Microalbuminuria	81/1,325 (6)	10/36 (28)	<0.0001
Hypertension	223/1,393 (16)	21/58 (36)	<0.0001
Retinopathy	254/1,264 (20)	1/25 (4)	0.043
Peripheral nerve abnormality	375/1,376 (27)	5/24 (21)	0.48
Pupillary abnormality	568/928 (61)	13/23 (57)	0.65
Overweight	452/1,411 (32)	16/64 (25)	0.24
Obese	100/1,411 (7)	36/64 (56)	<0.0001

Data are median (interquartile range) or *n* (%) and are from last complications assessment

5. Prevention



5. Prevention
The HEALTHY Study

HEALTHY

School unit of randomization

Primary outcome: Combined prevalence of overweight plus obesity

42 schools

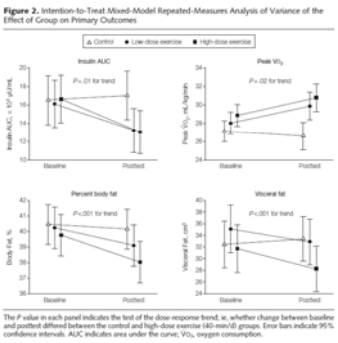
≥ 50% minority &/or ≥ 50% with free/reduced lunch

Comprehensive health screening, results sent to parents

- Intervention Schools
  - Environmental changes Food service, PE
  - Behavior change - curriculum based
  - Communications and promotional campaign

Exercise Dose and Diabetes Risk in Overweight and Obese Children
Davis et al JAMA 2012

- 222 subjects
  - 2003-07
- 15 public schools in Georgia
- Random assignment
  - Low-dose (20 min/d, n= 71)
  - High-dose (40 min/d, n=73)
  - Control n=78



JAMA. 2012;308(11):1103-1112

5. Prevention
The HEALTHY Trial RESULTS

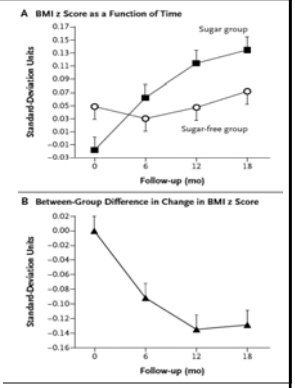
HEALTHY

- Reduction in percentage of overweight/obesity 4% in both groups
- Prevalence of obesity declined more in intervention schools (p=0.05)
- Significant reduction in intervention schools (p=0.04)
  - BMI z-score
  - Prevalence of large waist circumference
  - Fasting insulin fell
- In the overweight/obese subgroup (n=2292), intervention schools had significantly greater decreases in prevalence of:
  - Obesity (p=0.04)
  - Large waist circumference (p=0.03)
  - Insulin (p=0.04)

NEJM;363;443-53;2010.

A Trial of Sugar-free or Sugar-sweetened Beverages and Body Weight in Children
de Ruyter et al

- 18 month trial
- 641 normal-weight children
  - 4y 10m – 11y 11m
- Random assignment to 250 ml sugar-free or sugar-containing at school
- 18 month, 26% stopped taking
- BMI z-score increased by 0.06 SD units in sugar-free group and 0.12 SD in sugar-containing group (p=0.06)

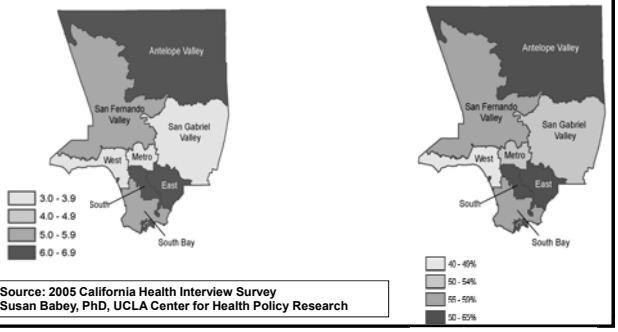


N Engl J Med 2012;367:1397-406.
DOI: 10.1056/NEJMoa1203034

The Maps of LA County - Highest rates of Fast Food Restaurants and Convenience Stores in Areas with Greatest Obesity, 2005

•Retail Food Environment Index (RFEI)
•Red 6X> than Beige

•Obesity Rates



Source: 2005 California Health Interview Survey
Susan Babey, PhD, UCLA Center for Health Policy Research

California
11th Lowest % of Obese Adults
28th Highest % of Obese and Overweight Children

- Provide healthy foods and beverages in schools –
  - Banned sodas
- Increase healthy foods in all communities –
  - Banned transfats, menu labeling, no fast food restaurants
  - Physical activity at school –
  - Regs amount minutes, class size
- Improve access to safe and healthy places to live, work, learn, and play
  - Zoning changes, public transit funded, walking communities
- Encourage employers to provide workplace wellness programs
  - Implemented for state/county employees
  - Revamp food assistance programs
  - Healthy hospital initiative

Environmental Strategies

- Candy at the Cash Register – A Risk for Obesity and Chronic Disease
  Cohen and Babey, Rand, NEJM
- Goods placed in prominent end-of-aisle locations account for 30% of supermarket sales
- Sales of those items increases 5-fold

- Improve the hospital environment
  - Vending, gift shops, patient food, employee foods, cafeterias

5. Prevention
RWJ F as in Fat

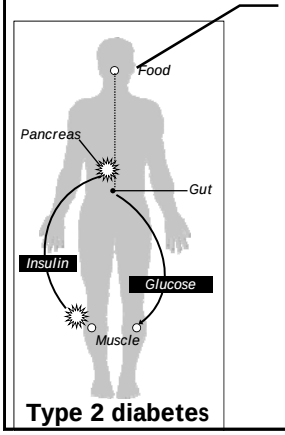
1. All foods and beverages served in schools meet Dietary Guidelines for Americans.
2. Increasing access to high-quality, affordable foods through new or improved grocery stores & healthier corner stores and bodegas.
3. Increasing the time, intensity, & duration of physical activity during the school day.
4. Increasing physical activity by improving the built environment in communities.
5. Using pricing strategies – both incentives and disincentives – to promote the purchase of healthier foods.
6. Reducing youths' exposure to the marketing of unhealthy foods through regulation, policy, and effective industry self-regulation.

Population Approaches to Improve Diet, Physical Activity and Smoking Habits: A Scientific Statement from the American Heart Association

Mozaffarian, et al; Circulation on line August 20, 2012

Local environment	Improved accessibility of recreation and exercise spaces and facilities (eg, building of parks and playgrounds, increasing operating hours, use of school facilities during nonschool hours) (IIa B)†
	Improved land-use design (eg, integration and interrelationships of residential, school, work, retail, and public spaces) (IIa B)†
	Improved sidewalk and street design to increase active commuting (walking or bicycling) to school by children (IIa B)†
	Improved traffic safety (IIa B)†
	Improved neighborhood aesthetics (to increase activity in adults) (IIa B)†
	Improved walkability, a composite indicator that incorporates aspects of land-use mix, street connectivity, pedestrian infrastructure, aesthetics, traffic safety, and/or crime safety (IIa B)†
Media and education	Sustained, focused media and educational campaigns, using multiple modes, for increasing consumption of specific healthful foods or reducing consumption of specific less healthful foods or beverages, either alone (IIa B) or as part of multicomponent strategies (I B)†‡§
	On-site supermarket and grocery store educational programs to support the purchase of healthier foods (IIa B)†
Labeling and information	Mandated nutrition facts panels or front-of-pack labels/icons as a means to influence industry behavior and product formulations (IIa B)†
Economic incentives	Subsidy strategies to lower prices of more healthful foods and beverages (I A)†
	Tax strategies to increase prices of less healthful foods and beverages (IIa B)†
	Changes in both agricultural subsidies and other related policies to create an infrastructure that facilitates production, transportation, and marketing of healthier foods, sustained over several decades (IIa B)†
Schools	Multicomponent interventions focused on improving both diet and physical activity, including specialized educational curricula, trained teachers, supportive school policies, a formal PE program, healthy food and beverage options, and a parental/family component (I A)†
	School garden programs, including nutrition and gardening education and hands-on gardening experiences (IIa A)†
	Fresh fruit and vegetable programs that provide free fruits and vegetables to students during the school day (IIa A)†

Conclusion



Type 2 diabetes

- **Genetic predisposition & environmental trigger of obesity, insulin resistance and deficiency**
- **Common in 1st, 2nd relatives**
- **Screening criteria but rare to find asymptomatic**
- **Presentation slow, mild but not always, and maybe less than thought**
- **Treatment needs to be more aggressive than monotherapy to maintain glycemic control**
  - **Likely require basal/bolus insulin therapy**
- **Complications common, early, co-morbidities related to insulin resistance**
- **Prevention addresses the environment to support healthy lifestyle adoption**