



Making Data Count

Measuring Diabetes and Obesity in the Indian Health System

December 18-20, 2007

IHS Division of Diabetes Treatment and Prevention

Epidemiology of Diabetes and Obesity

Jonathan Krakoff, MD

Session: B2

Diabetes and Obesity Epidemiology

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OUTLINE

- **Define Epidemiology**
- **Examples of Use of Epidemiology**
 - **Incidence and Prevalence**
 - **Confounding**
 - **Importance of Family Data**
 - **Cross-sectional study**
 - **Prospective studies**
- **Randomized Control Trial**

Epidemiology is Multidisciplinary

- **Clinical medicine, nutrition**
- **Infectious diseases**
- **Environmental health**
- **Biostatistics, mathematics, computing**
- **Clinical trials**
- **Genetics**
- **Health services research & policy**
- **Social sciences, psychology, economics**

Statistical Methods in Epidemiology: Purposes

- **Estimate prevalence or incidence rates**
- **Evaluate variables affecting these rates**
- **Estimate associations among variables**
- **Control confounding**
- **Effect modification and summary effects**

Some definitions

Variable= anything that is measured or counted

Continuous variables=those that can have any numbered value (age, weight, glucose)

Catagorical variables=those values that can only be one or the other (sex, diabetes status)

What are Epidemiology and Clinical Research?

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- Epidemiology is the study of distributions and dynamics of disease in human populations.
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- Epidemiology is the study of factors affecting the health and illness of populations, and serves as the foundation and logic of interventions made in the interest of public health and preventive medicine. It is considered a cornerstone methodology of public health research, and is highly regarded in evidence-based medicine for identifying risk factors for disease and determining optimal treatment approaches to clinical practice (Wikipedia, 2007)

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What are Epidemiology and Clinical Research?

- **Clinical research** is patient-oriented research. Research may be conducted in human volunteers or on samples from humans. . . .**Clinical trials** or interventional trials determine whether experimental preventions, treatments, or new ways of using known therapies are safe and effective under controlled conditions. **Observational or natural history studies** examine health issues and disease development in groups of people or populations. (NIDDK web site, 2007)

Measures of Disease Frequency

- Prevalence
- Incidence density (hazard)
- Cumulative incidence (risk, survival)

Prevalence =

cases / # who could be cases

e.g., 5%

Incidence =

new cases / person-time at risk

e.g., 12/1,000 person-years

Cumulative incidence (at time t) =

new cases in t yrs / # at risk at beginning

e.g., 8% in 5 years

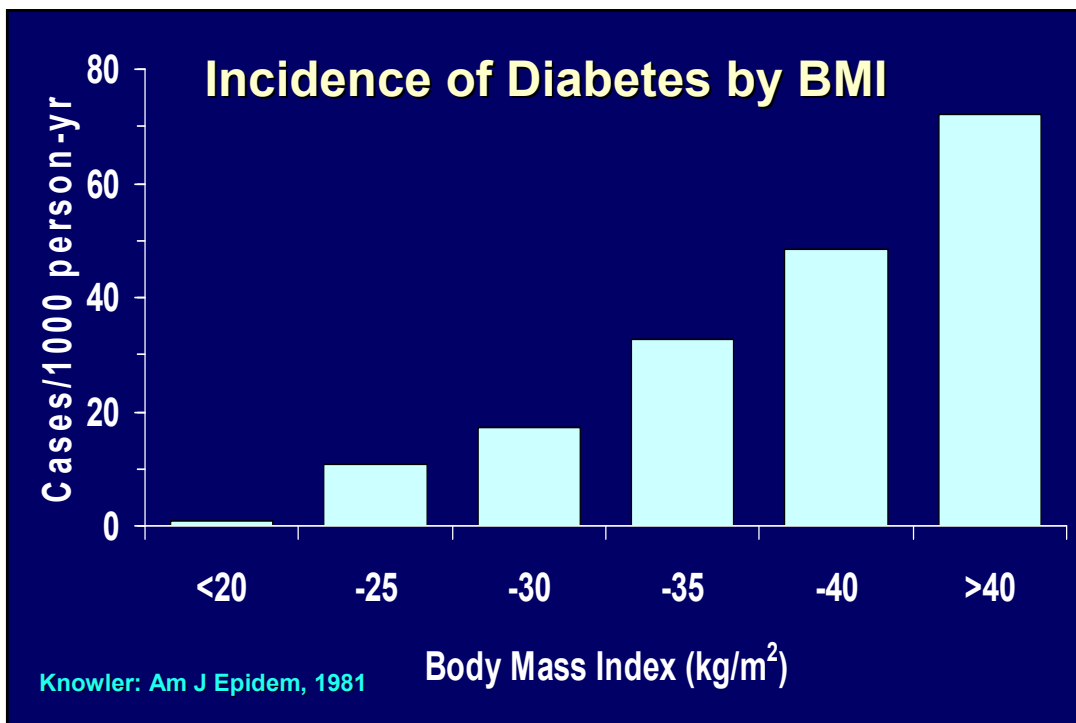
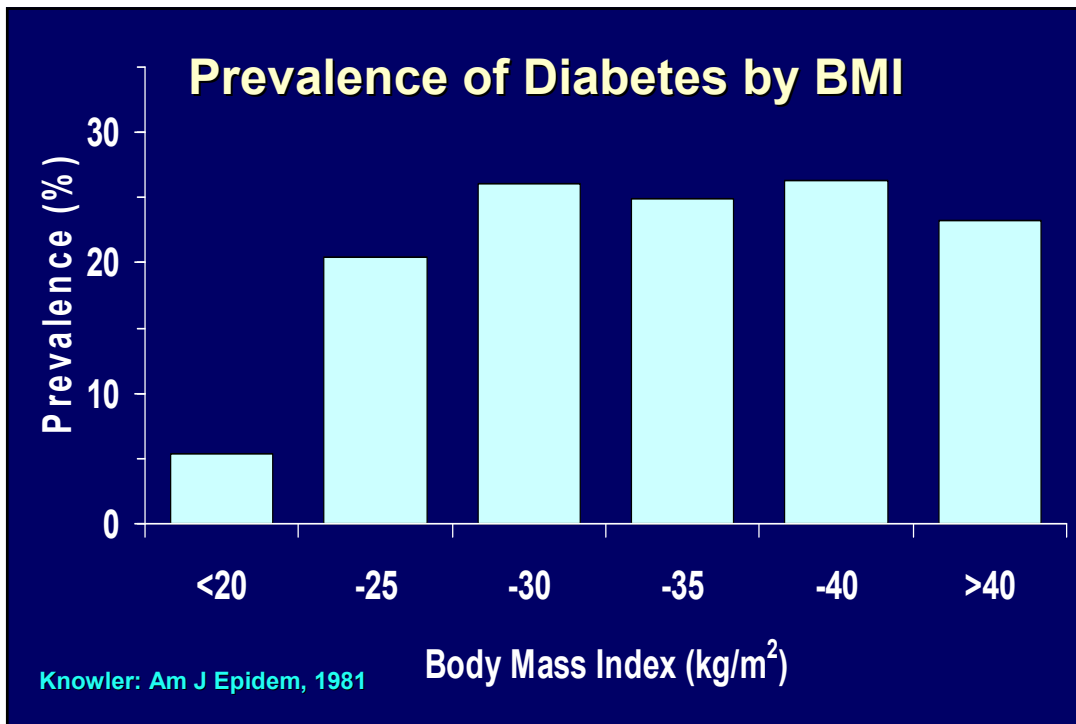
**Prevalence or Incidence Study:
When Does It Matter? (1)**

- Incidence study needed if causal directions not clear or if the “outcome” affects the “predictor”
 - BMI predicts diabetes, diabetes causes weight loss
 - Insulin secretion and sensitivity predict diabetes but change with diabetes
 - A behavior (e.g., diet) predicts disease but changes with disease

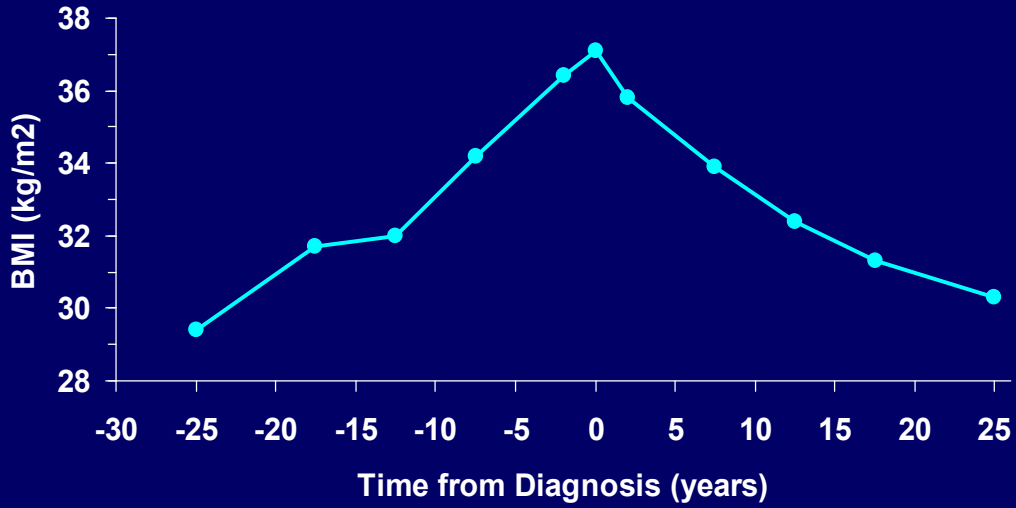
Prevalence or Incidence Study: When Does It Matter? (2)

- **Incidence study can be retrospective (historical data) if the historical data are accurate and not affected by outcome**
- **Prevalence study is sufficient if the “risk factor” is unchangeable (e.g., sex, ethnicity, genotype)**
- **Mixed situations require incidence studies (e.g., genotype and behavior)**

How prevalence and incidence can show us different pictures of what is happening



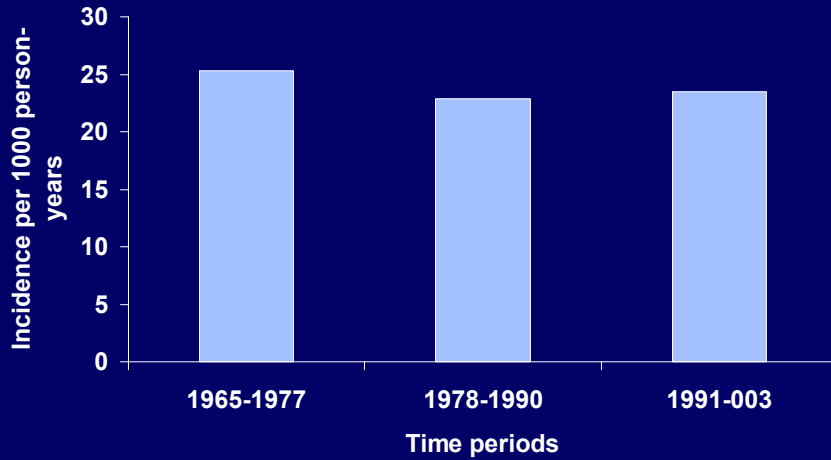
BMI Before and After Onset of Diabetes in Pima Indians



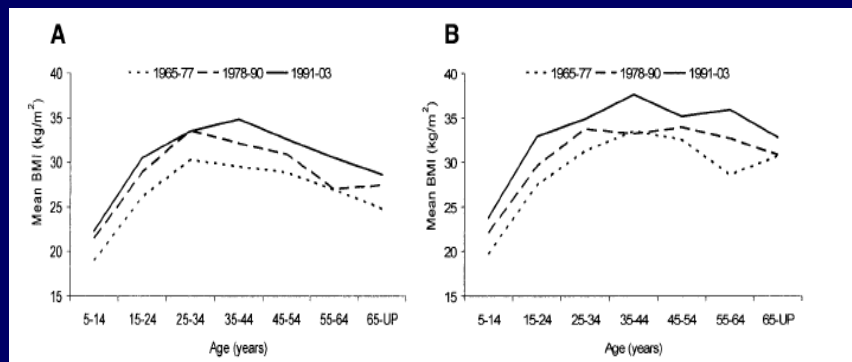
Looker: Diabetes Care, 2001

**Use of Incidence to Whether Diabetes
is increasing in a community**

Incidence of Type 2 Diabetes in Gila River Indian Community

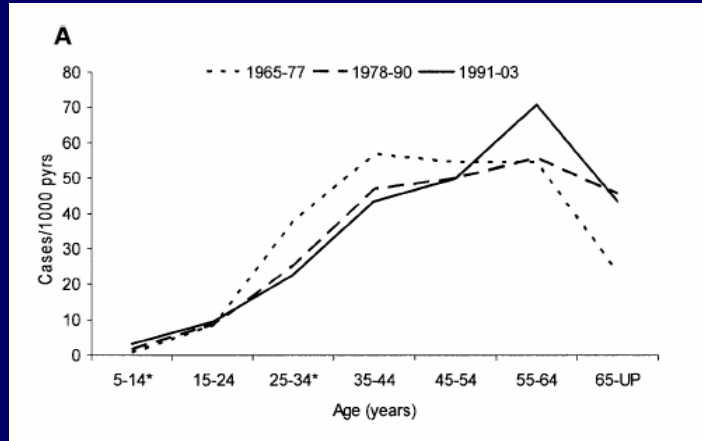


Increasing BMI despite no increase in diabetes incidence

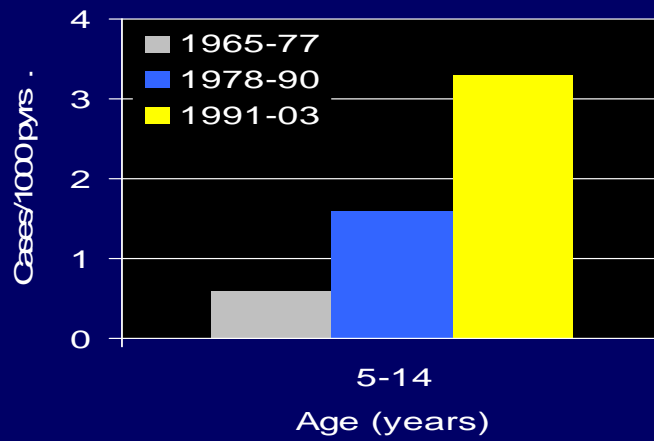


Pavkov ME Diabetes Care, 2007

Incidence of Diabetes by Age



Increasing Incidence of Type 2 Diabetes in Youth

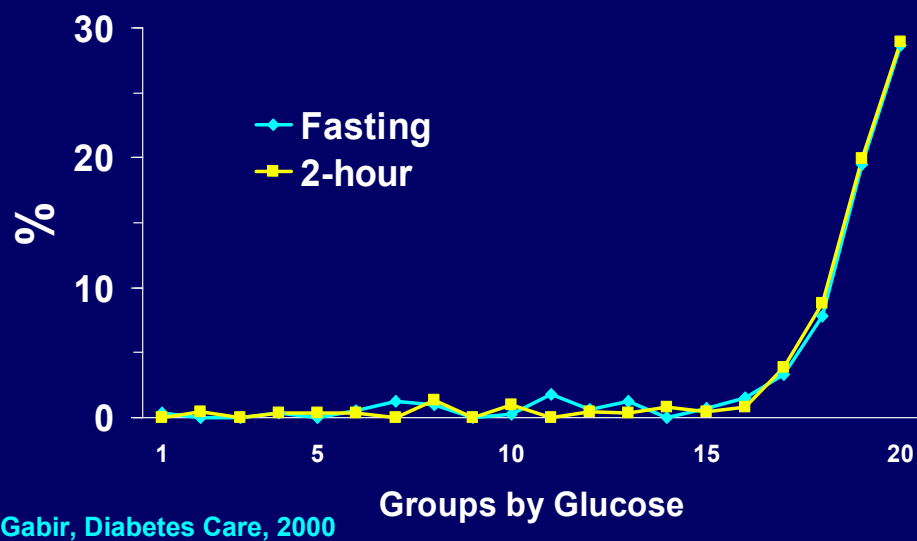


Pavkov ME et al, Diabetes Care 2007

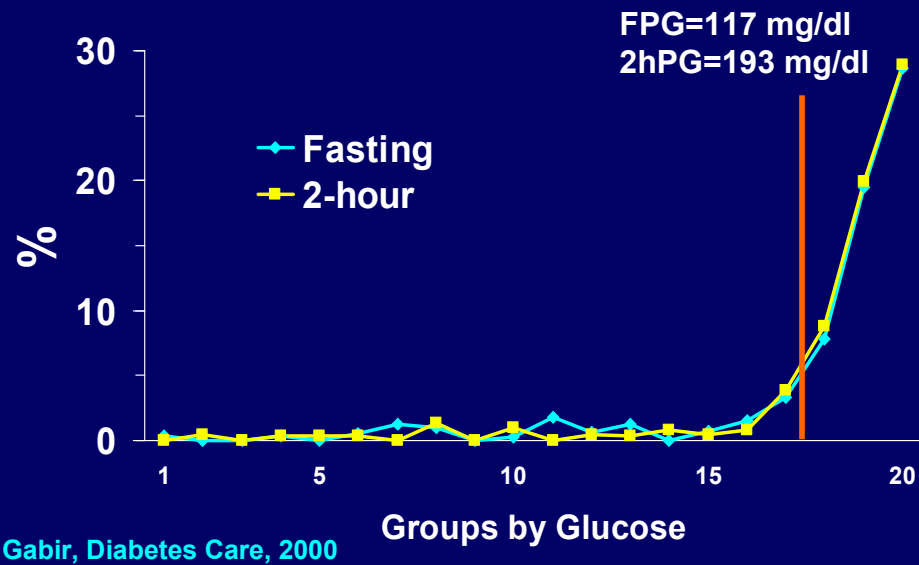
Use of Prevalence to understand how glucose is related to diabetes specific outcome

How this can inform us about how to diagnose diabetes

Retinopathy in 5,023 Pima Indians by 5-Percentile Groups of Plasma Glucose



Retinopathy in 5,023 Pima Indians by 5-Percentile Groups of Plasma Glucose



Diagnosis of Diabetes

Fasting glucose ≥ 126 mg/dl

Two hour glucose ≥ 200 mg/dl

BMI Predicts Type 2 Diabetes

- **Due to confounding?**
 - A metabolic factor associated with BMI and diabetes
 - A genotype predisposing to both
- **Is it subject to intervention?**
- **Neither question can be fully answered by observational studies**

Confounding

An association between a risk factor & disease due to a third factor

Arthritis	Person -years	Deaths	Deaths/ 1,000 per-yr
No	15,000	50	3.3
Yes	5,500	31	5.6

Confounding

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	Yes	500	1	2.0
Old	No	5,000	30	6.0
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Measured confounders - account for in analysis
Unmeasured confounders - trouble

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Confounder

- In evaluation of **X** predicting **Y**,
 - if **W** is associated with **X** and **Y**, then
 - **W** may confound the relationship of **X** and **Y**
- Common examples of confounders
 - Age
 - Sex
 - Time
- **W** is not considered a confounder if it is in the causal pathway, e.g., **X** causes **W** causes **Y**
- In this case, “**adjusting for W**” is over-adjustment

Confounder

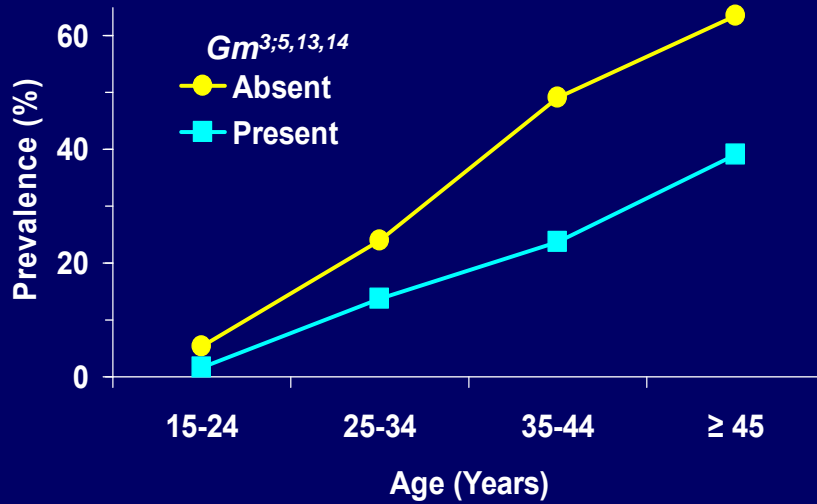
- **W** is not considered a confounder if it is in the causal pathway, e.g., **X** causes **W** causes **Y**
- In this case, “**adjusting for W**” is over-adjustment
- How do you know if **W** is in the causal pathway?
 - Often from knowledge outside the study
 - Age, sex, demographic variables are rarely confounders because we rarely consider **X** variables that cause them
 - Adjustment for age, sex, demographic variables should almost always be done

Controlling Confounding: The Major Issue in Many Studies

- **Measured variables: statistical control**
 - Stratification
 - Modeling
 - Matching
 - Control depends on distributions of confounder variables with respect to the main variables
- **Unmeasured confounding variables**
 - Not measurable
 - Not thought of
 - Cannot apply statistical methods

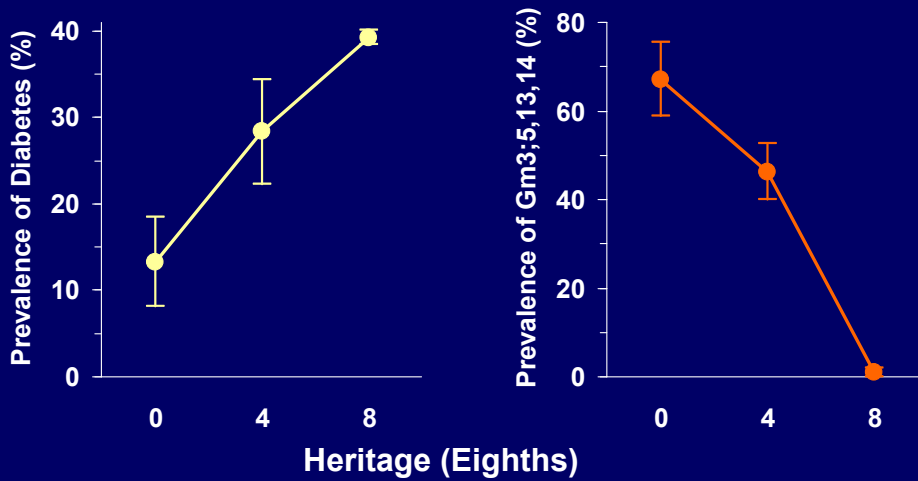
Another example of confounding

Diabetes Prevalence by $Gm^{3;5,13,14}$



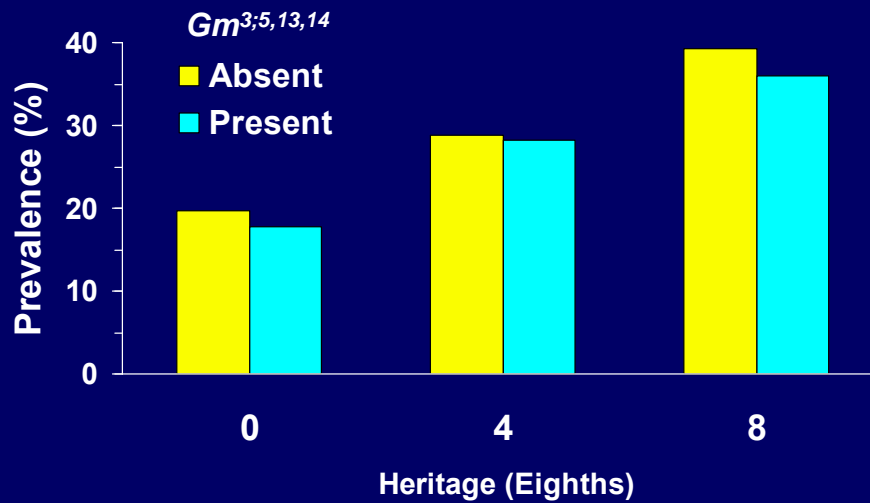
Knowler, Williams, Pettitt, Steinberg: Am J Human Genet, 1988

Age-adjusted Prevalence (\pm SE) of Diabetes and of $Gm^{3;5,13,14}$ by Heritage



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Age-adjusted Prevalence of Diabetes by $Gm^{3;5,13,14}$ and Heritage

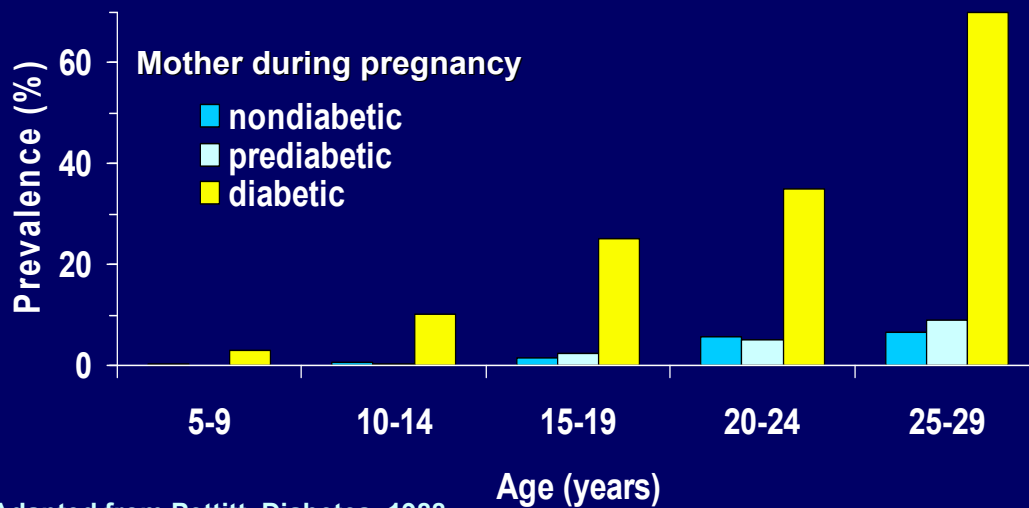


Knowler, Williams, Pettitt, Steinberg: Am J Human Genet, 1988

Importance of Family data in epidemiology

How this can shed light on a clinical problem

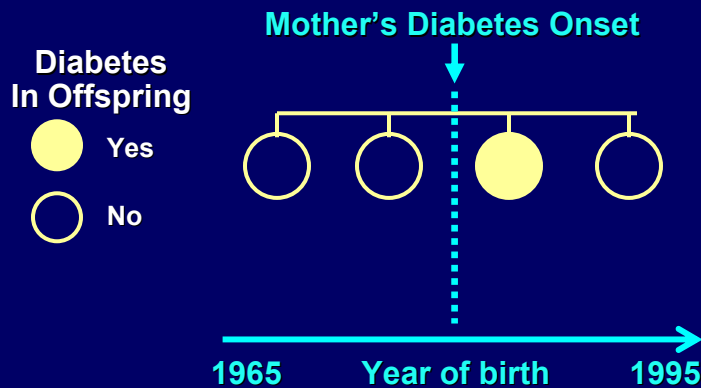
Diabetes in Offspring By Maternal Diabetes in Pregnancy



Why are Obesity & Diabetes More Common in Offspring of Diabetic than Prediabetic Mothers?

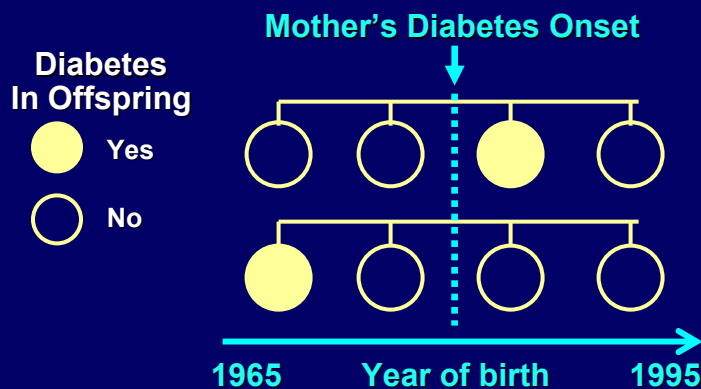
1. Women who develop diabetes before pregnancy have a greater genetic load and hence are more likely to transmit diabetes susceptibility genes.
 2. The diabetic intrauterine environment programs offspring to develop obesity and diabetes.
- Siblings discordant for maternal diabetes have the same probability of inheriting susceptibility genes.

19 Sibships (58 Sibs) Discordant for Maternal Diabetes in Pregnancy



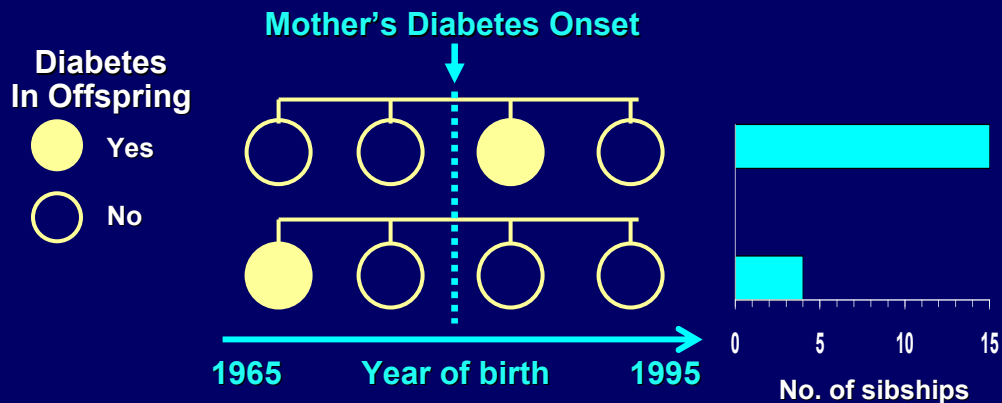
Dabelea: Diabetes, 2000

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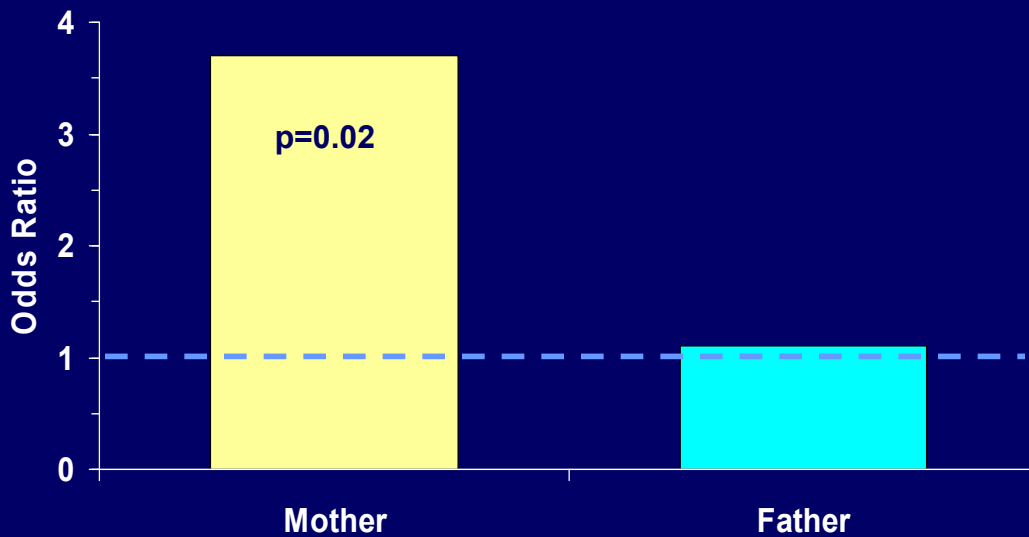
Dabelea: Diabetes, 2000

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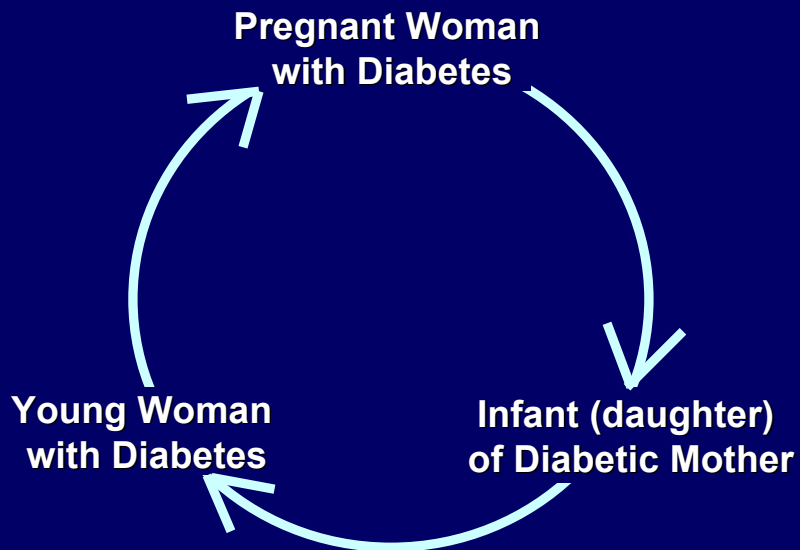
Dabelea: Diabetes, 2000

Discordance for Mother's or Father's Diabetes: Odds Ratio for Diabetes in Sibs Born After Parent's Onset



Dabelea: Diabetes, 2000

Diabetes in Pregnancy and Offspring: The Vicious Cycle



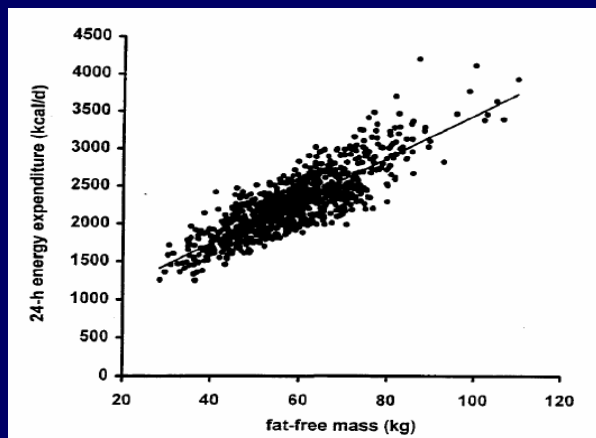
Cross-sectional Studies
Longitudinal Studies

Cross-Sectional Study

- Evaluate how one measured variable is related to (associated with) another variable
- This may be evaluated before and after controlling for confounders

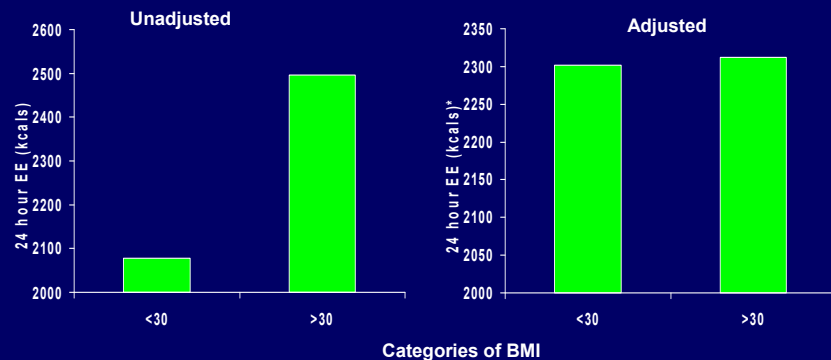
Energy Expenditure and Fat Free Mass

FFM strongest determinant, explains 72% of variance



Weyer C et al IJO, 1999

Associations can inform us about possible confounders



*adjusted for age, sex, fat free mass, fat mass

Prospective and Longitudinal Studies

- Evaluate how one measured variable predicts either:
 - A disease outcome (such as development of diabetes or kidney disease)
 - Change in another variable (change in weight or change in insulin concentrations)

Case-Control Studies (Case-referent)

From outcome to exposure

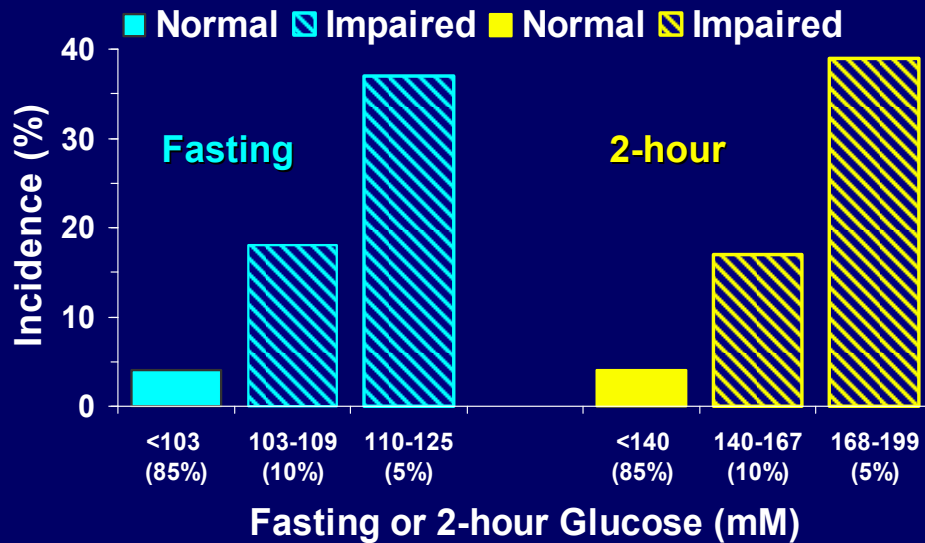
- **Cases of illness in defined time/space**
- **Controls (referents) in same time/space**
- **Assessment of exposure**
- **Incidence rate ratios**
- **Advantages**
 - Efficient for rare disease or when assessments expensive
 - Avoid loss to follow-up if all cases ascertained
- **Disadvantages**
 - Assessment of exposure
 - No direct estimate of incidence rates

Cohort Studies (non-interventional)

From exposure to outcome

- **Population defined and followed**
 - Static (participants are fixed)
 - Dynamic (participants can enter or leave)
- **Exposure or risk factors measured**
 - At baseline
 - Updated periodically (time dependent variables)
- **Outcomes assessed**
 - Periodic measurement
 - Surveillance of events (e.g., deaths, hospitalizations)
- **Estimate incidence rates and effects of exposures**

Diabetes Incidence in Pima Indians by Fasting or 2hr Glucose



Gabir, Diabetes Care, 2000

Randomized Clinical Trial

A cohort study in which the main exposure of interest is varied experimentally to reduce confounding.

Randomized Clinical Trial

A **cohort** study in which the main exposure of interest is varied experimentally to reduce **confounding**.

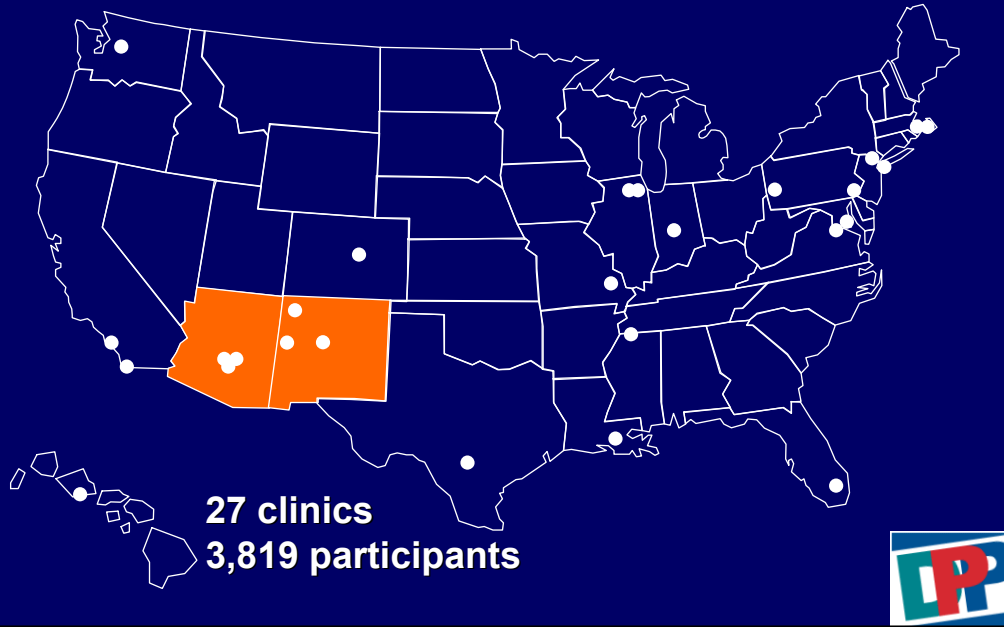
Perhaps the only way to control for **unmeasured confounders**, i.e. have exposed and unexposed groups differing only by the exposure.

Diabetes Prevention Program (DPP)

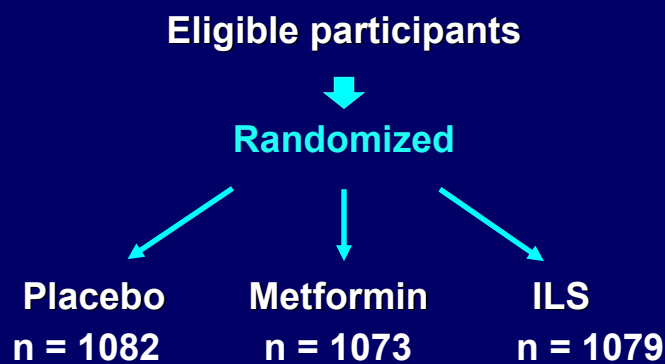
- Randomized clinical trial to prevent or delay type 2 diabetes by treating modifiable risk factors: **obesity, physical inactivity, elevated fasting or post-load glucose, insulin resistance, impaired insulin secretion**
- Identify persons at high risk (FPG, 2h-PG, BMI)
- Randomized to one of three interventions
 - Weight loss by diet & physical activity
 - Metformin
 - Placebo
- 1996 – 2001 with long-term follow-up



Diabetes Prevention Program Clinics



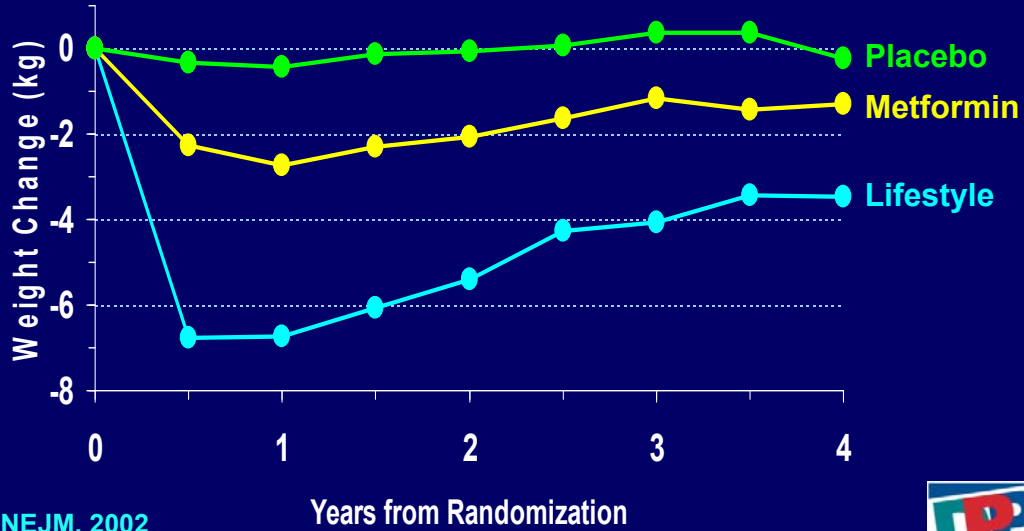
DPP Randomization to Treatment



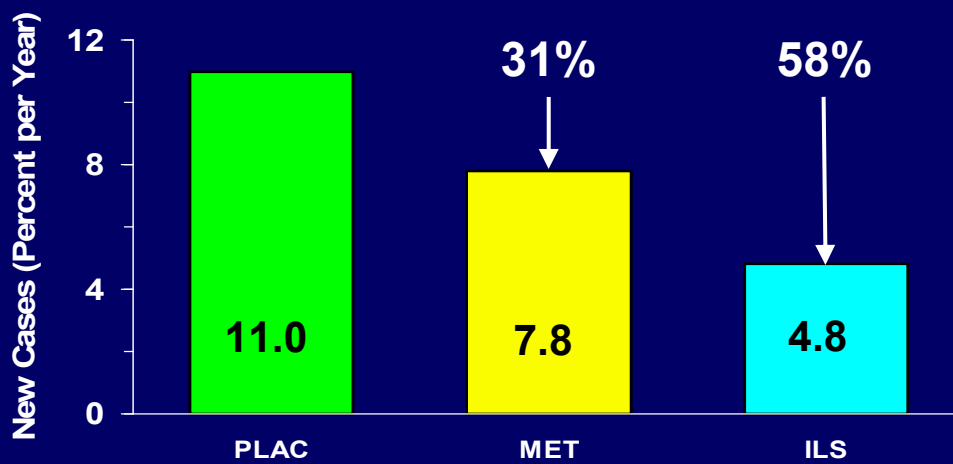
DPP: NEJM 346: 393-403, 2002

Total n = 3,234

Mean Weight Change in the DPP



Diabetes Incidence Rates in DPP



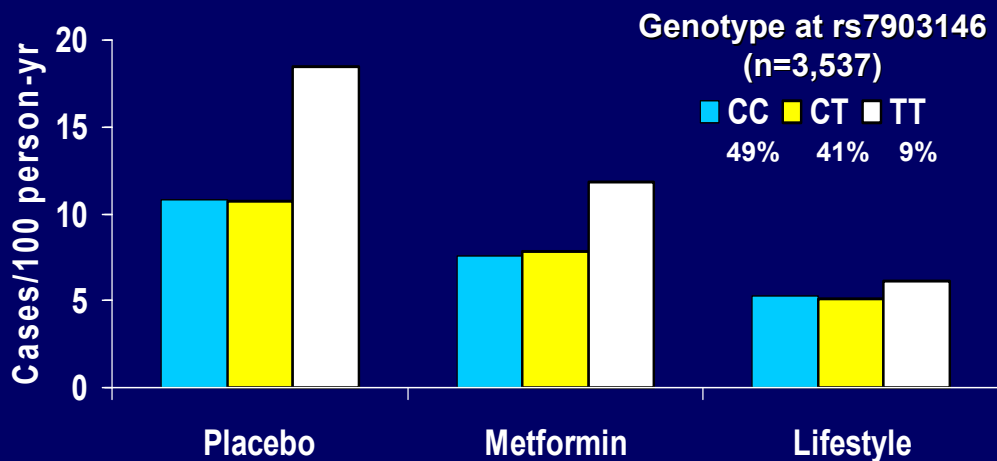
The DPP Research Group, *NEJM* 346:393-403, 2002

Genetics in the DPP, 2006-

Hypotheses

- Genes known or suspected to influence risk of type 2 diabetes predict diabetes in the DPP.
- Genotype by treatment interactions.
- Results will guide optimal selection of subjects and interventions.

TCF7L2 Genotype and Diabetes Incidence in the DPP



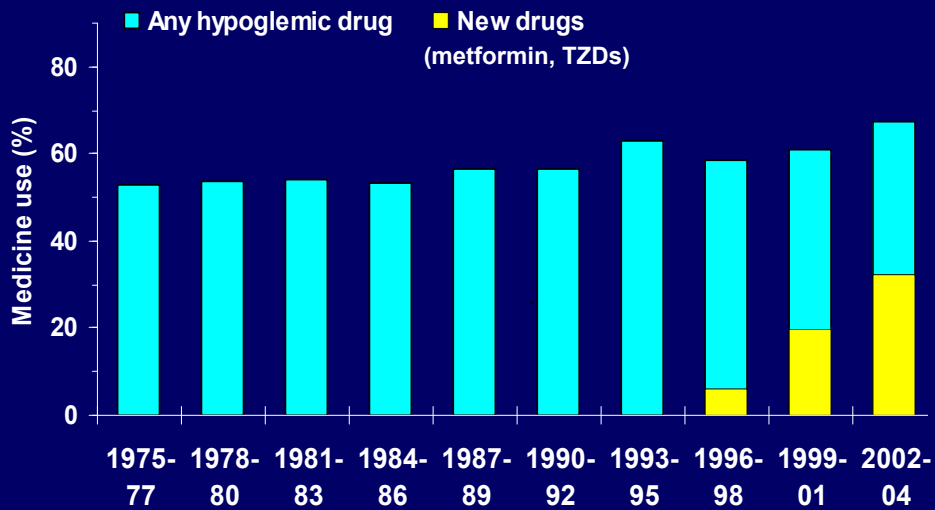
Florez et al. DPP Research Group: [NEJM](#), 2006

Limitations of Clinical Trials: Why We Still Need Observational Studies

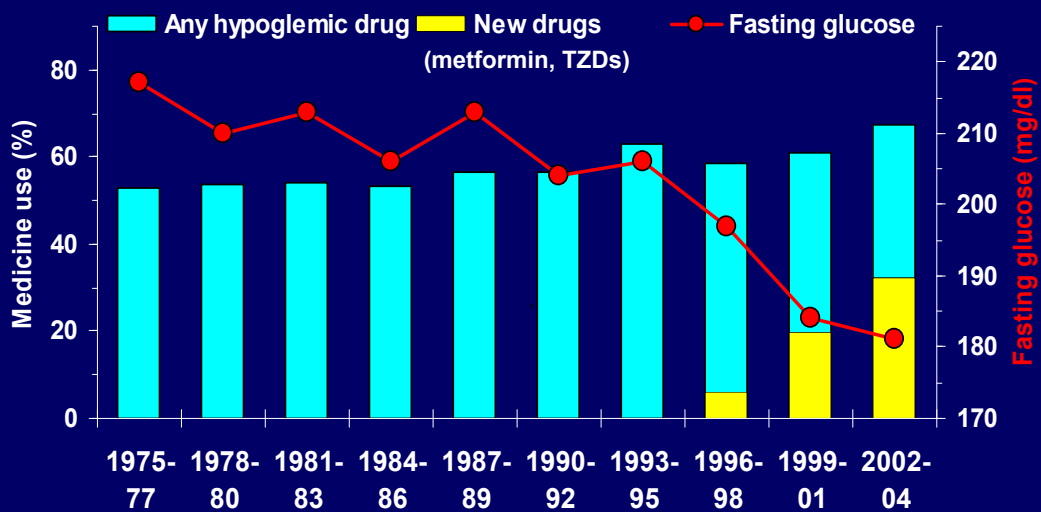
- **Can't do clinical trials for every question**
 - Too expensive: participants, researchers, \$
 - Not suitable for randomization
 - Not enough time
 - Too complex (multiple treatments & outcomes)
- **Results may not generalize**
 - Trial settings not representative
 - Trial participants not representative

**Epidemiology can also Inform
about Improvements in Diabetes
Care**

Diabetes Drug Treatment



Diabetes Drug Treatment and FPG



Other Indicators of Improved Care

- **Greater use of BP drugs**
- **Lower blood pressure**
- **Greater use of lipid drugs**
- **Improved lipids**
- **Reduced incidence of ESRD**

Epidemiology

- **Basis for research on obesity and diabetes**
- **Provides clues to causes**
- **Trials for testing whether reversible causes can affect disease**