

Do high SHBG levels prevent Type II Diabetes?

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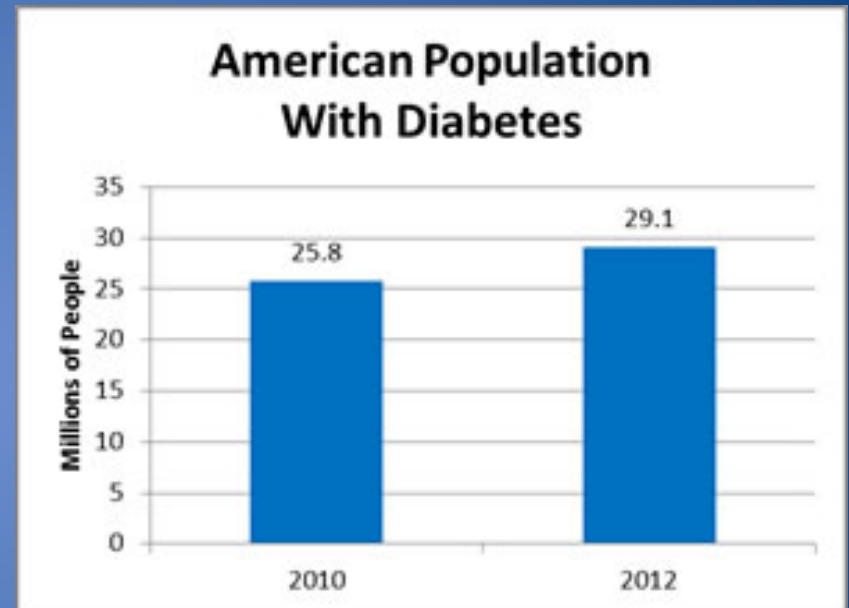
CAPS200

Outline

- Introduction
- Question/hypothesis
- Specific aims
- Research plan
- Expected results
- Significance
- References

Diabetes Mellitus

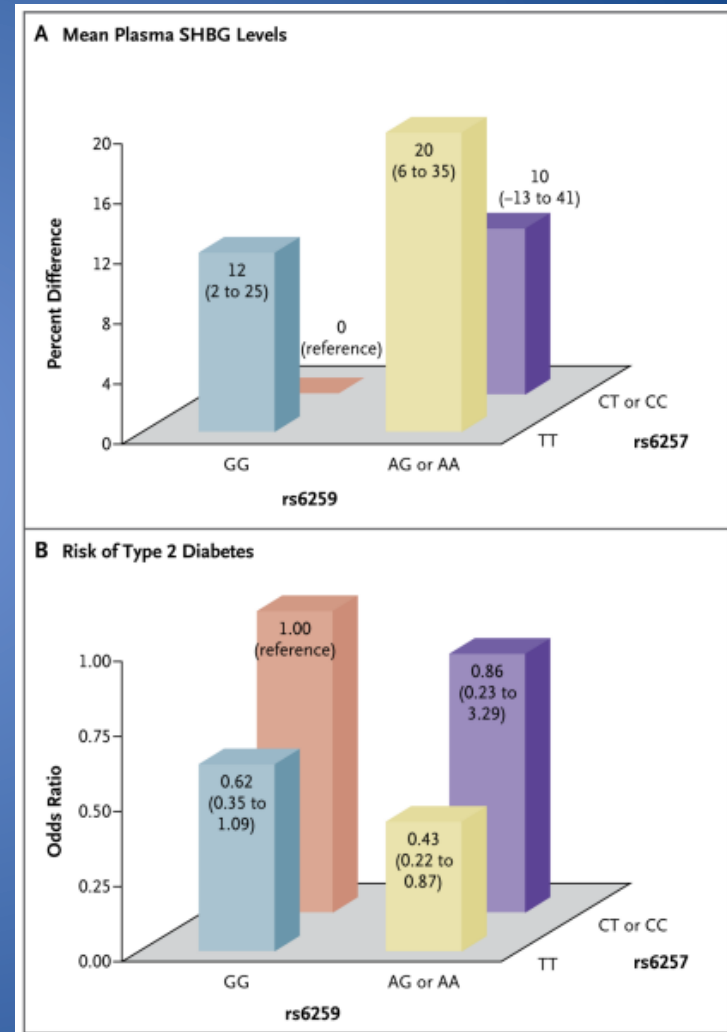
- 9.3% of Americans ¹
- Type II Diabetes (DM2)
 - Non-insulin dependent diabetes
 - High blood sugar
- Pathogenesis unknown



1: <http://www.diabetes.org/diabetes-basics/statistics/>

SHBG & Risk of DM2

- Ding et al. 2009 ²
- Epidemiological link
- Is this a causal relationship?



2: 2009, N Engl J Med. 12 1152–1163.

Question and Hypothesis

- Question:
Does high serum SHBG prevent development of DM2?
- Hypothesis:
High serum SHBG suppresses development of DM2

Specific Aims

1. Inducing DM2 in mouse model
2. Testing the effect of SHBG expression on DM2 in mouse model

Research Plan

Aim 1- Induction of DM2



C57BL-wt

High-fat diet



Glucose Increase 1 wk
(Type II DM) ³

Aim 2- Testing effect of
serum SHBG on DM2



C57BL-SHBG ⁴

High-fat diet



Glucose Increase 1 wk
(Type II DM)



3: 2004, Diabetes 3, 215-219.

4: 1998, Molecular Endocrinology 1, 123-136.

Measurements and Statistical Analysis

- SHBG Expression Verification
 - Saturation assay using ^3H -DHT
- Type 2 Diabetes Development
 - Serum glucose: glucose oxidase method (spectrophotometric)
- Statistical Analysis
 - Student's t-test
 - Kaplan-Meier

Expected Results

1. In 1 week, SHBG transgenic mouse will have a lower average serum glucose level than the wild type mouse
2. Kaplan-Meier, SHBG transgenic mouse, if they develop diabetes, will develop it at a much later date

Significance

- First indication of low SHBG causes DM2
- Increasing SHBG for DM2 prevention?
 - Injection of SHBG
 - Drugs increasing SHBG (eg. Tamoxifen)
- SHBG mouse as a model for SHBG-based therapy development

References

1. Centers for Disease Control and Prevention. National Diabetes Statistics Report: Estimates of Diabetes and Its Burden in the United States, 2014. Atlanta, GA: U.S. Department of Health and Human Services; 2014.
2. Ding, E.L. et al. 2009. Sex Hormone-binding Globulin and Risk of Type 2 Diabetes in Women and Men. *New England Journal of Medicine* 12, 1152-1163.
3. Winzell, M.S. and Ahren, B. 2004. The High-Fat Diet-Fed Mouse: A Model for Studying Mechanisms and Treatment of Impaired Glucose Tolerance and Type 2 Diabetes. *Diabetes* 3, 215-219.
4. Janne et al. 1998. Human Sex Hormone-Binding Globulin Gene Expression in Transgenic Mice. *Molecular Endocrinology* 1, 123-136.

Questions?