Can We Slow Progression of Type 2 Diabetes?

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Can We Slow Progression of Type 2 Diabetes?

Simple Answer

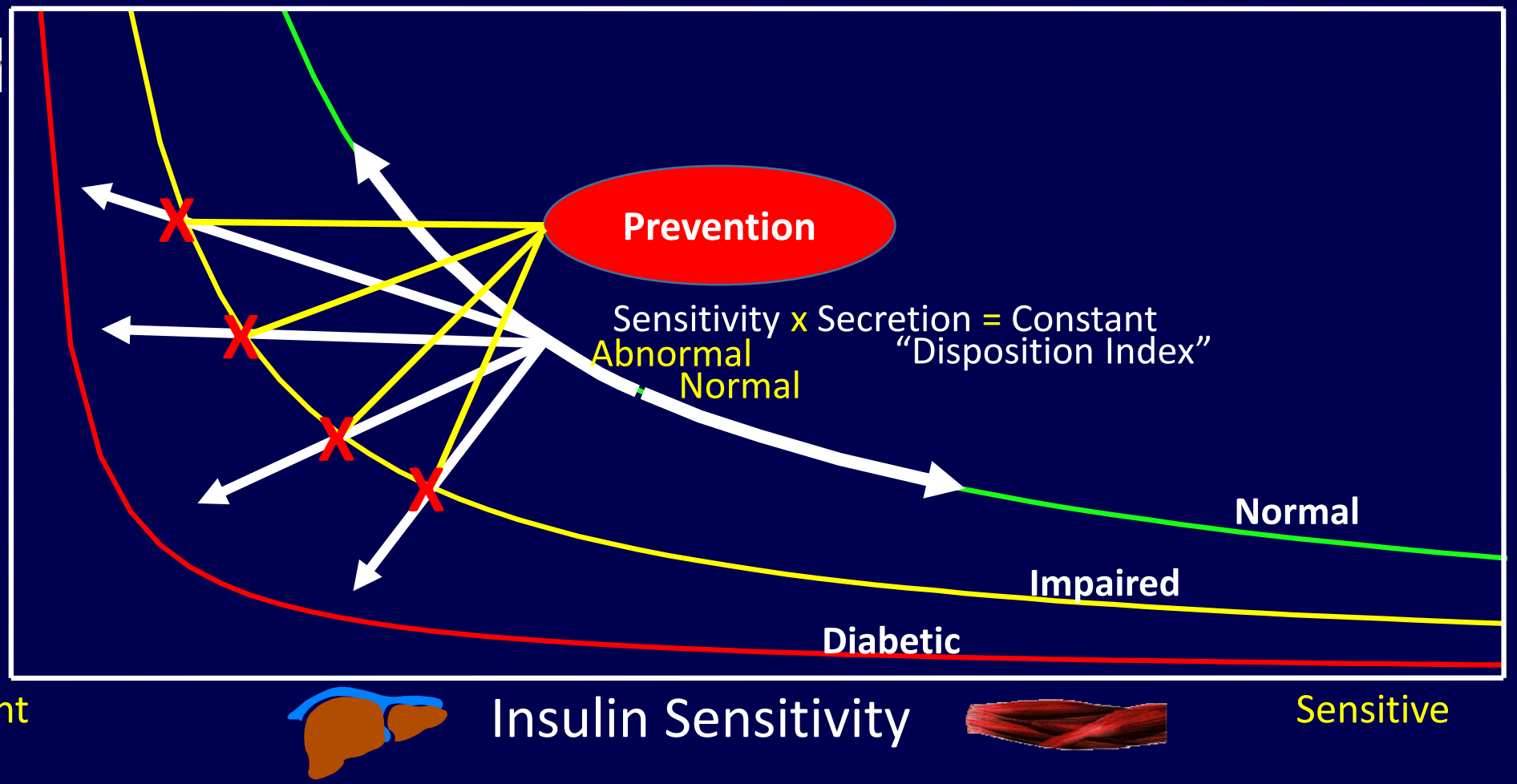
Yes, but it isn't easy!

Can We Slow Progression of Type 2 Diabetes?

Three Contexts

- Glucose Regulation
- Clinical Prevention Studies
- Mechanistic Studies

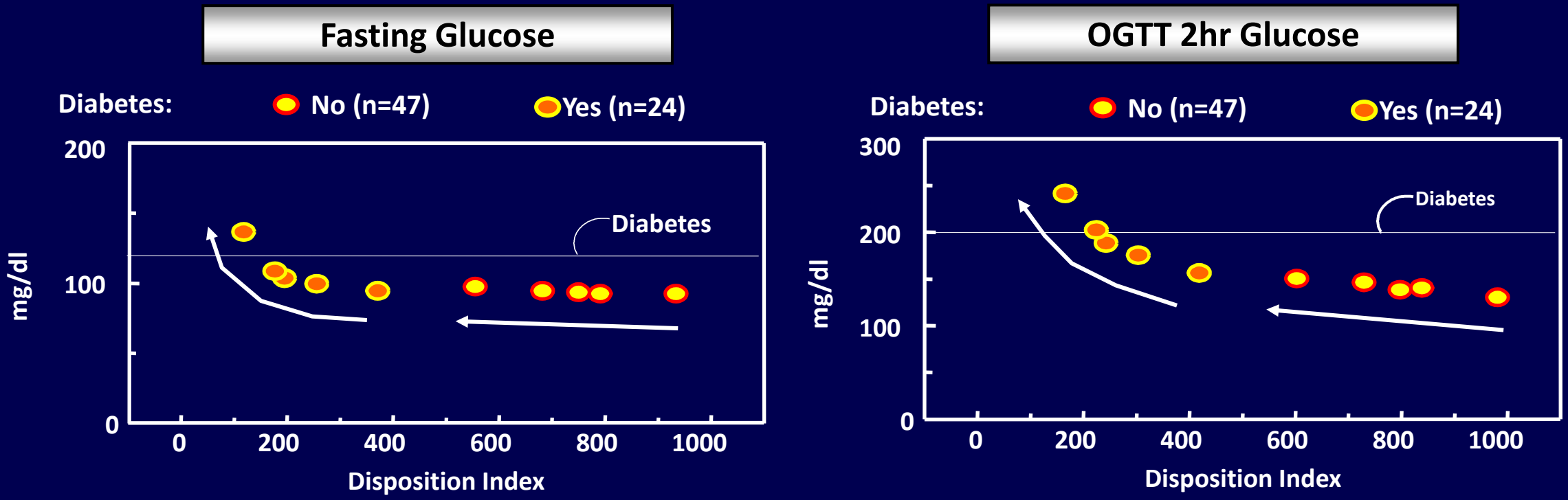
Regulation of Blood Glucose



Bergman et al. *J Clin Invest* 1981;68:1457-67.

Evolution of Hyperglycemia

Relation to β-cell Compensation

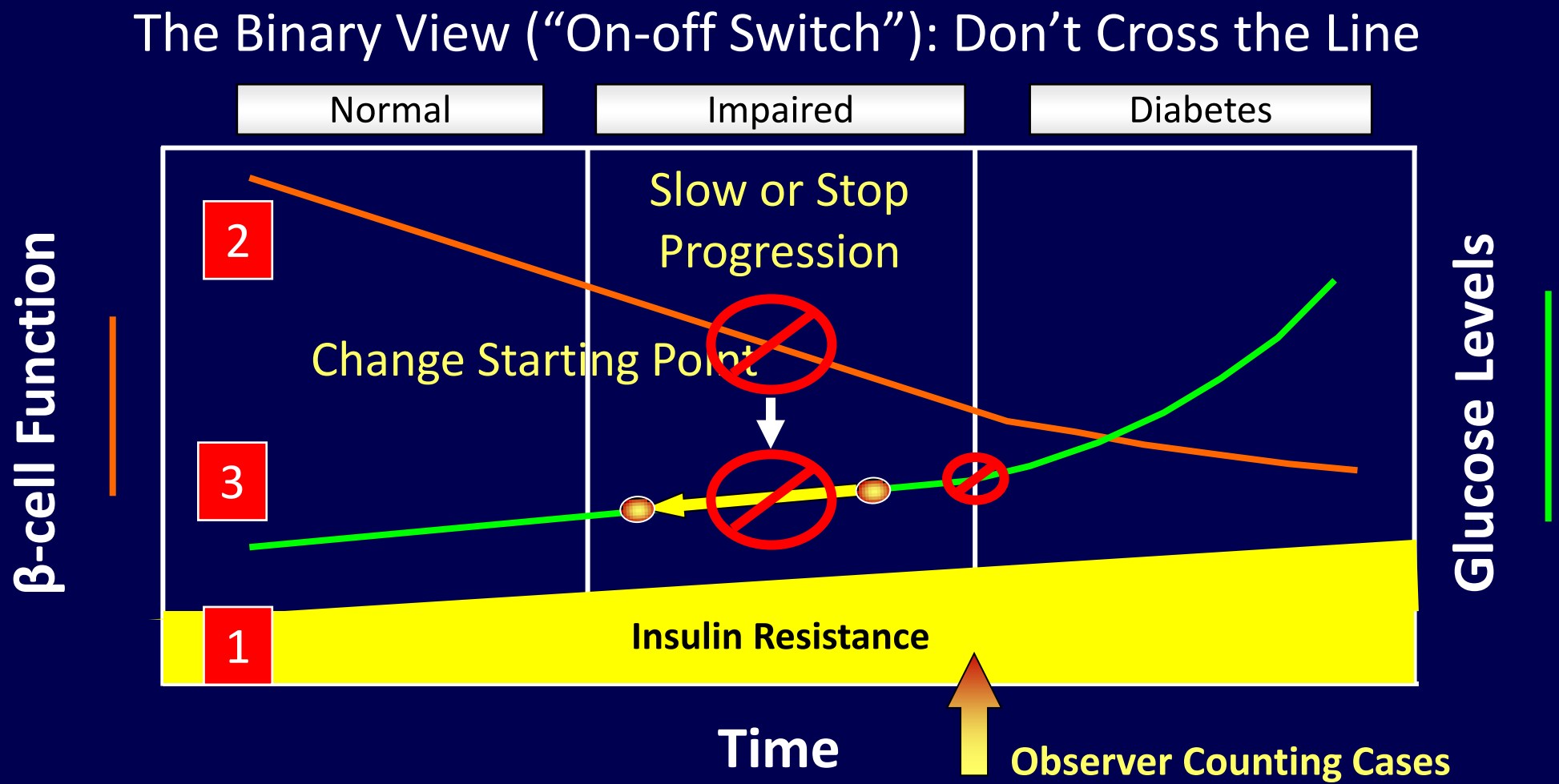


***Prior GDMs (n=71)*: OGTTs and IVGTTs at 15, 30, 45, 60, 75 months postpartum**

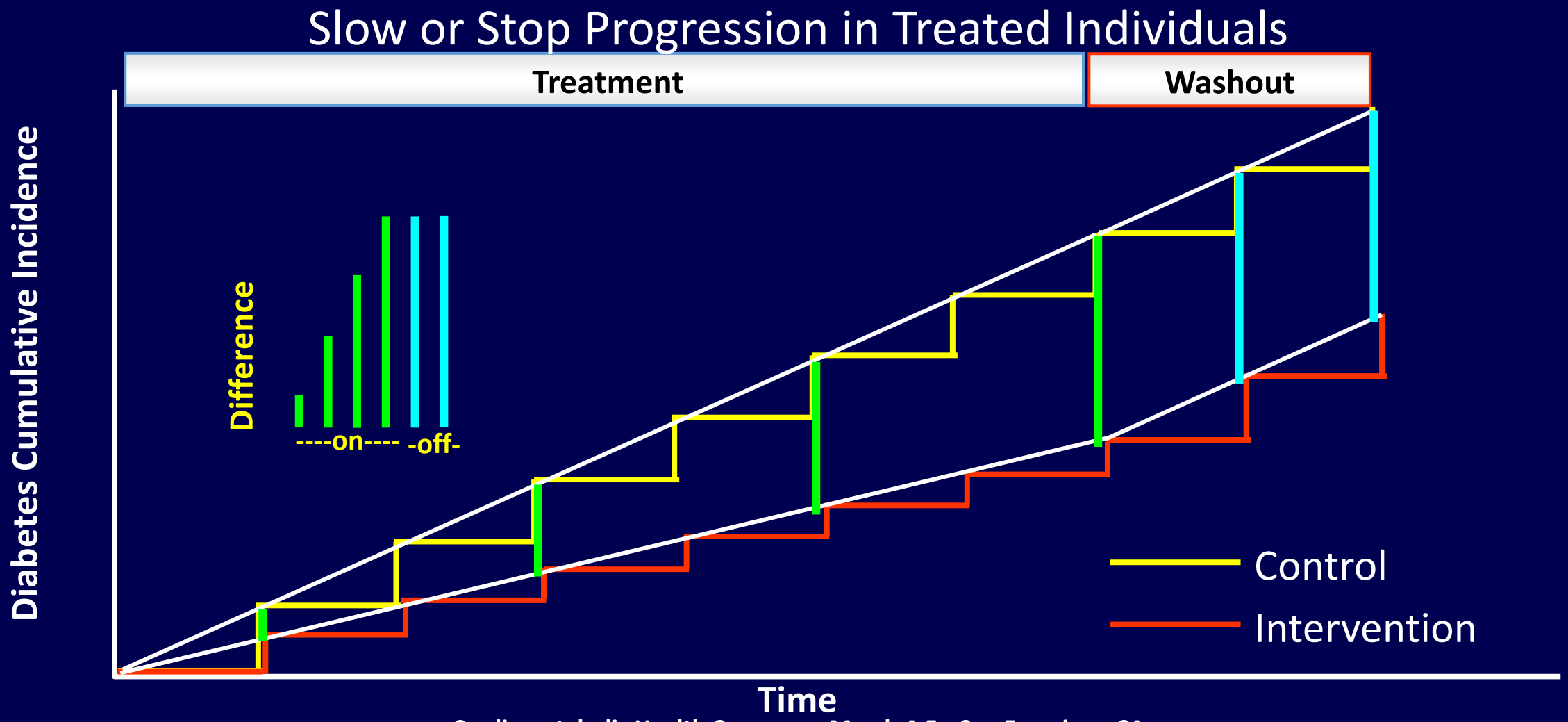
Xiang et al. 2006; *Diabetes* 55:1074-1079

5-11-05

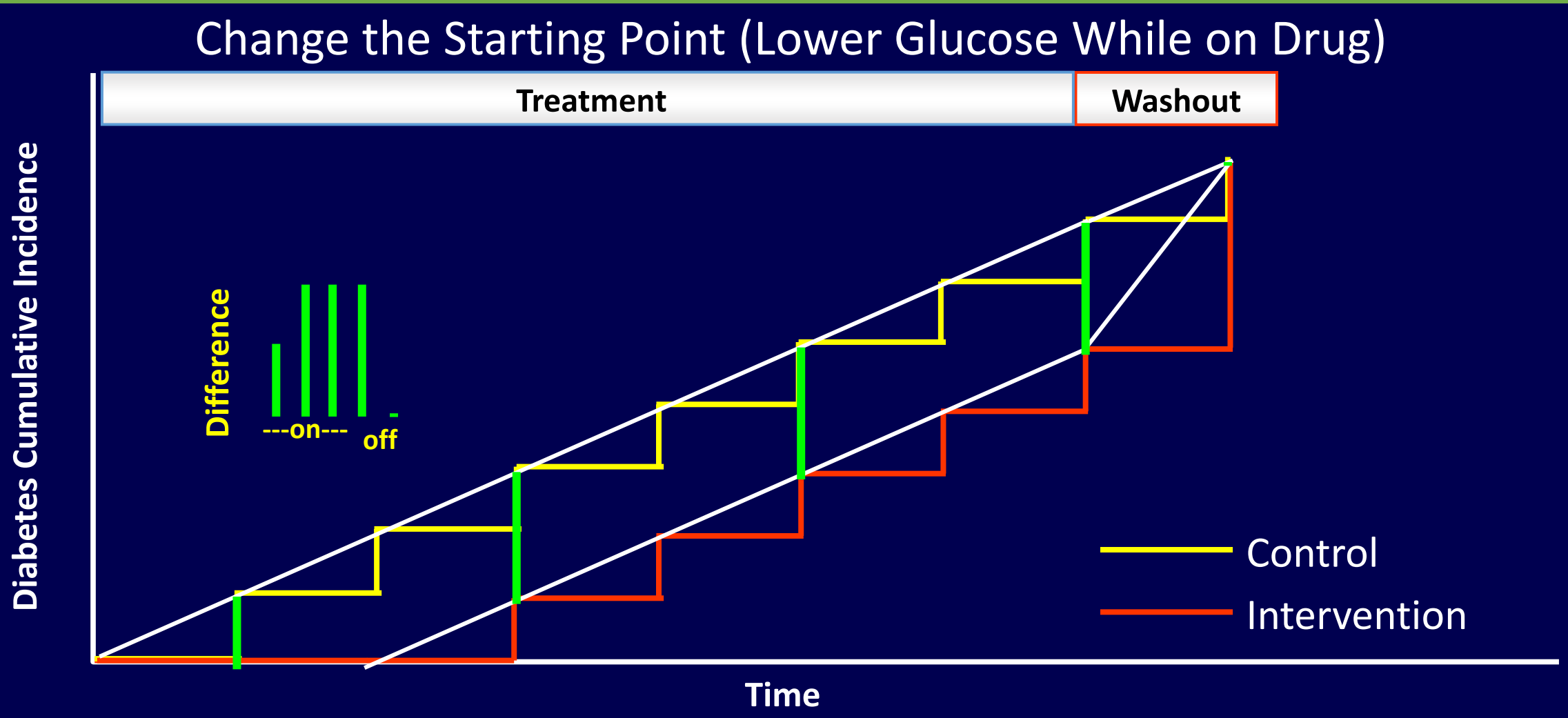
Diabetes "Prevention" in Clinical Trials



Real Disease Modification



Masking Disease Progression



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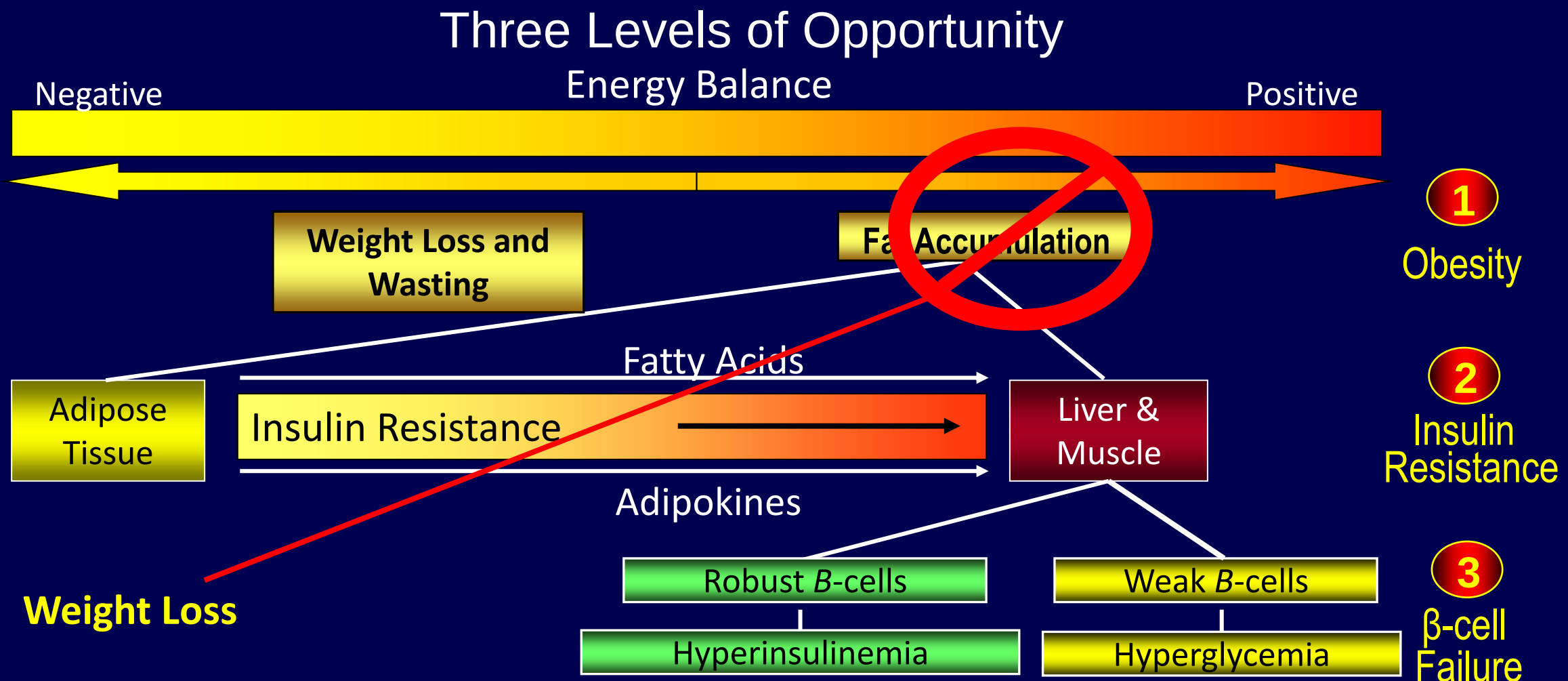
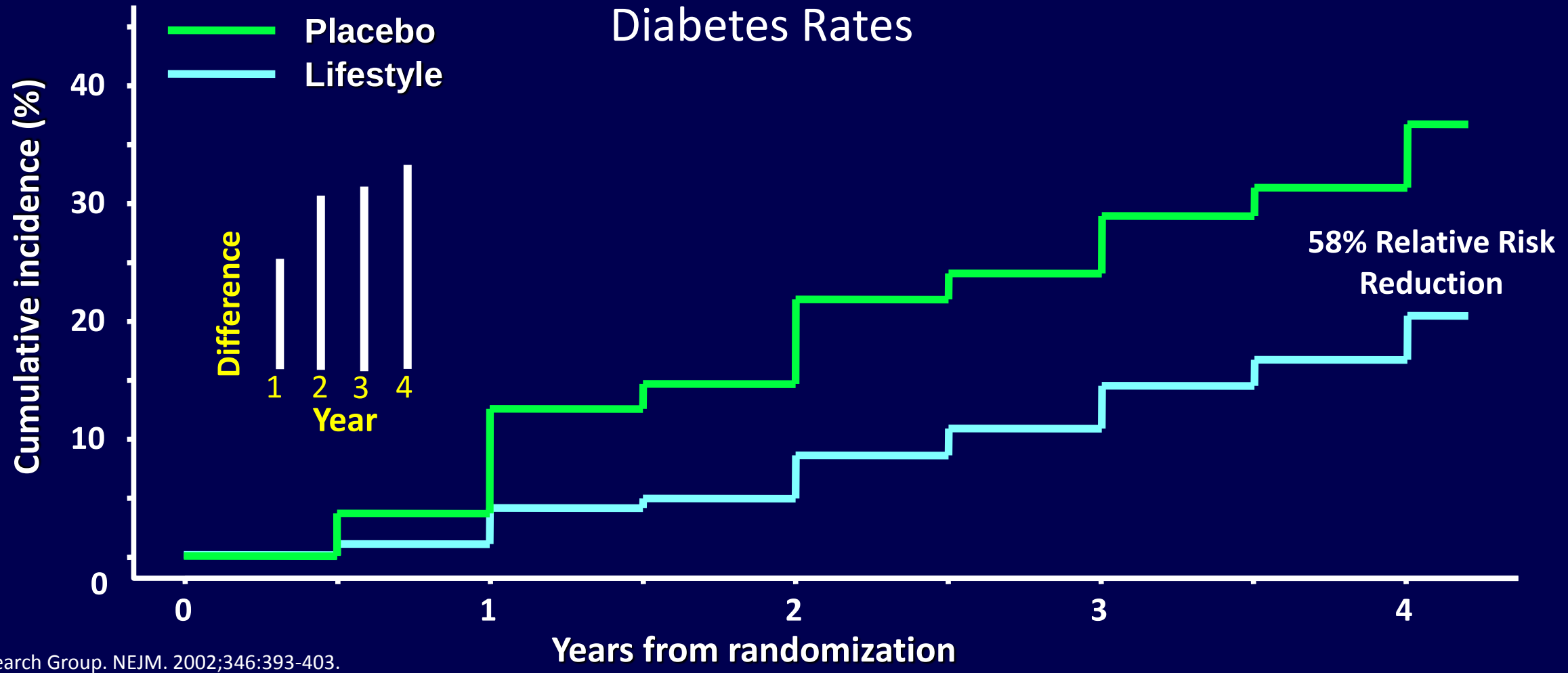
Results of T2DM Prevention Studies

Etiology of Diabetes Prevention

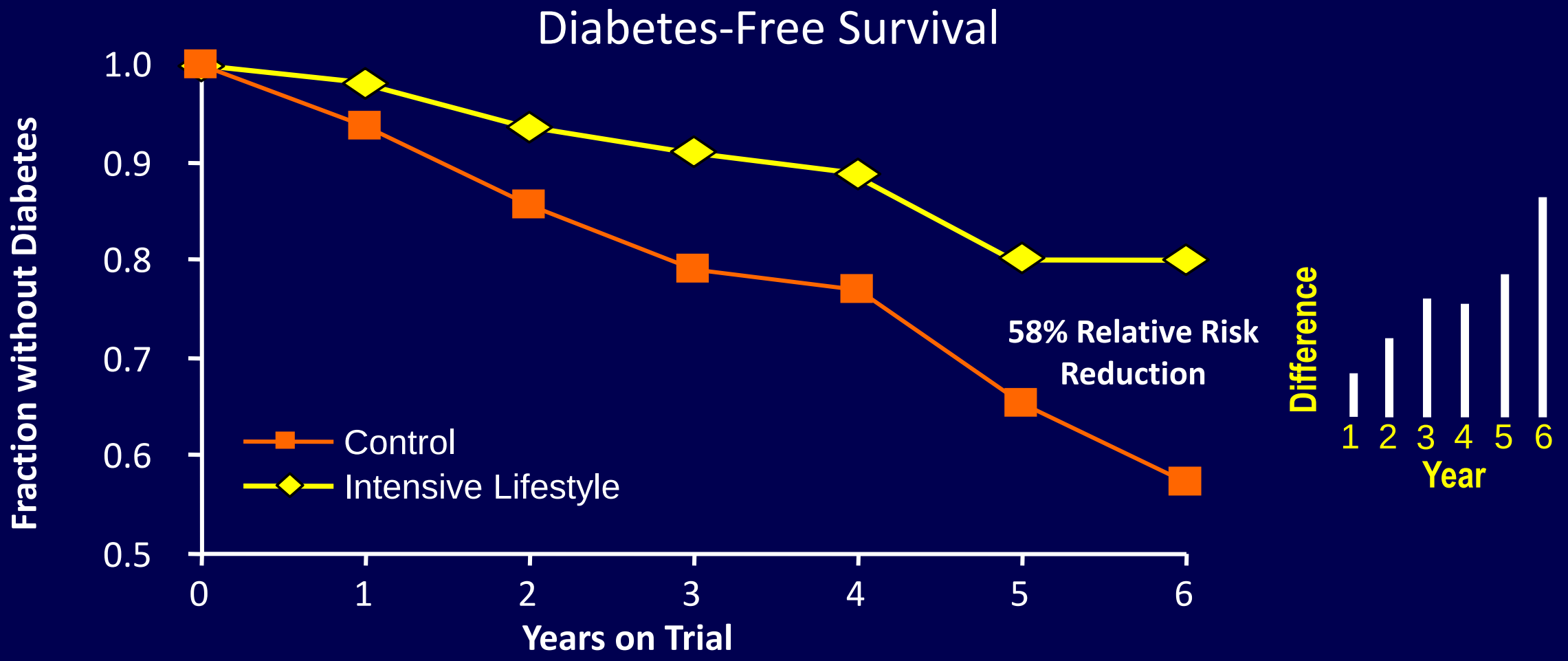


US Diabetes Prevention Program



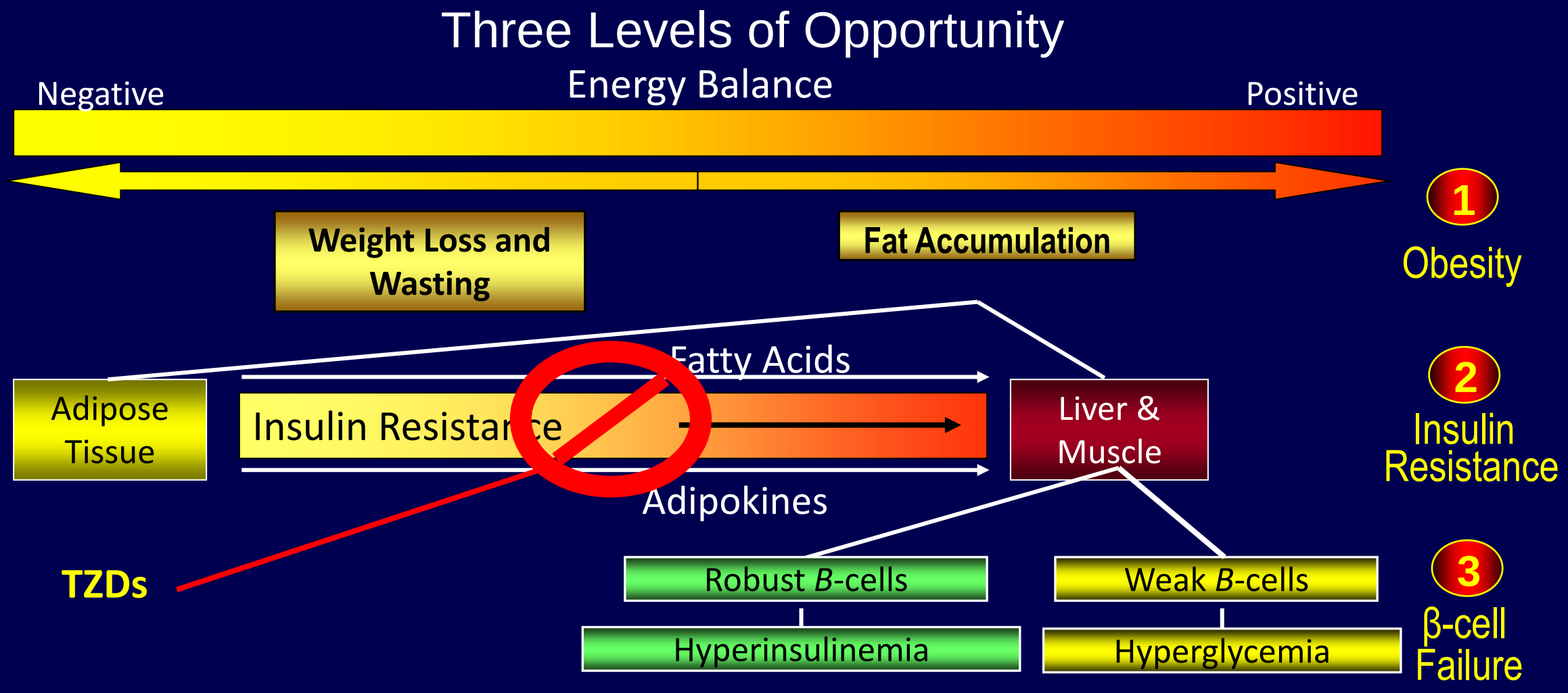
DPP Research Group. NEJM. 2002;346:393-403.

Finnish Diabetes Prevention Study

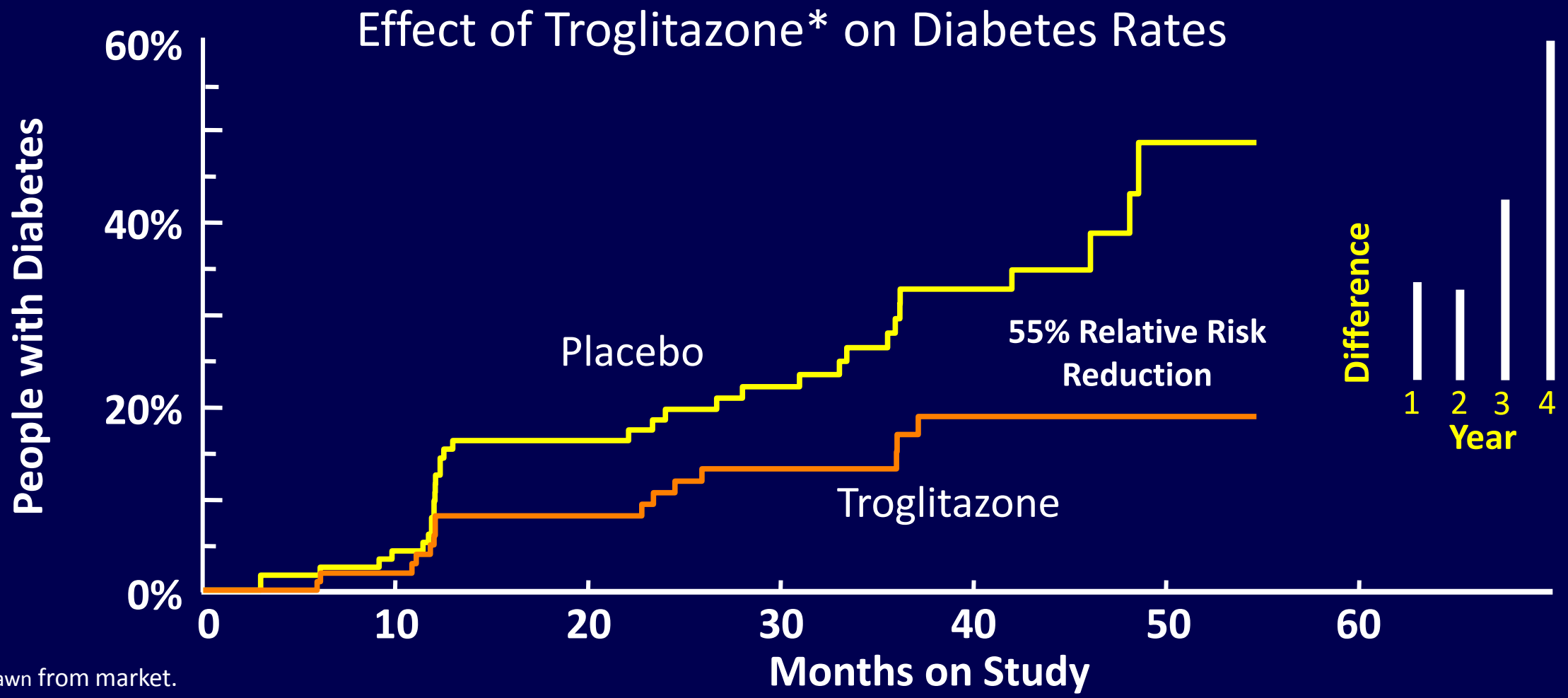


Tuomilehto et al. NEJM. 2001;344:1343-1350

Preventing Type 2 Diabetes



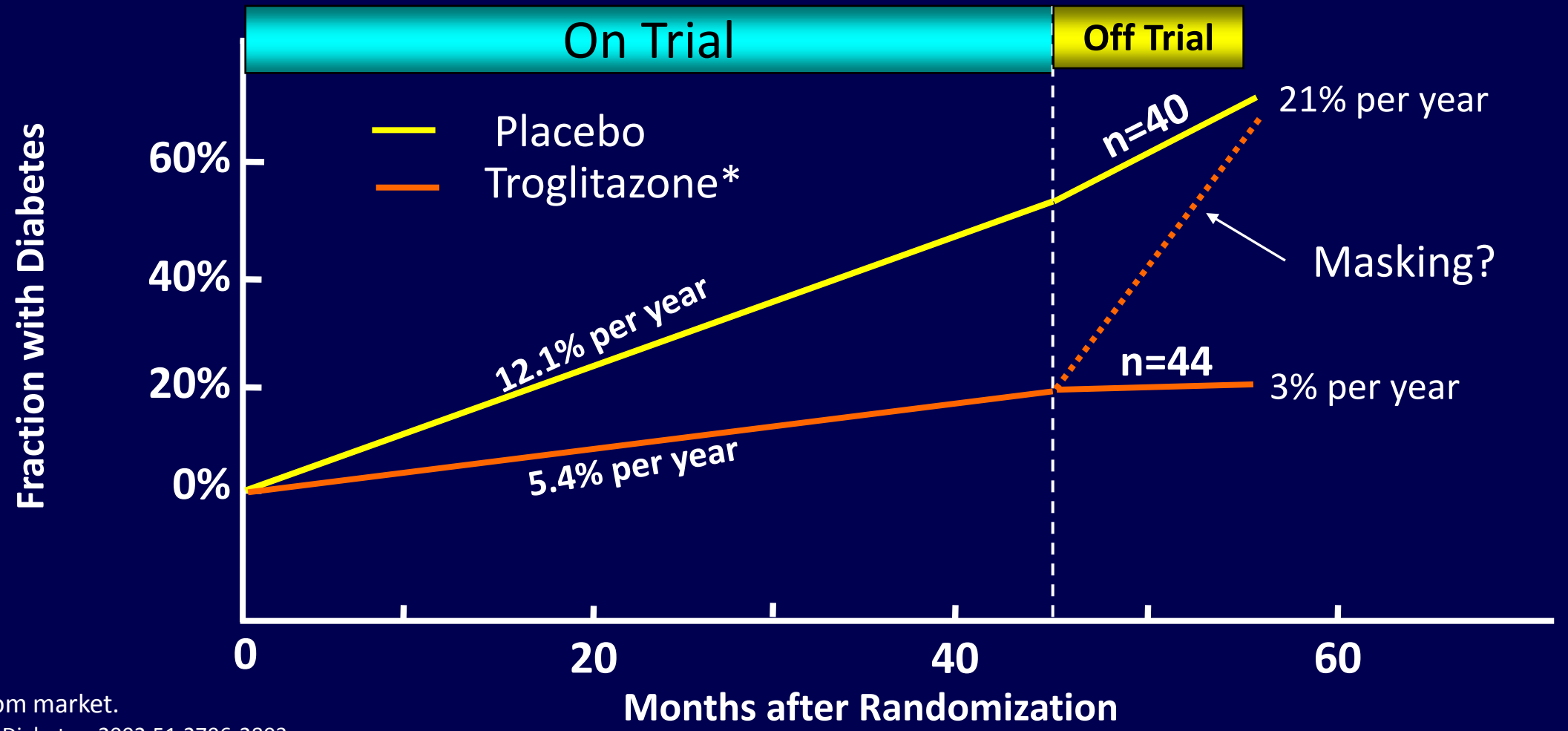
TRIPOD Study



*Withdrawn from market.

Buchanan et al. Diabetes. 2002;51:2796-2803.

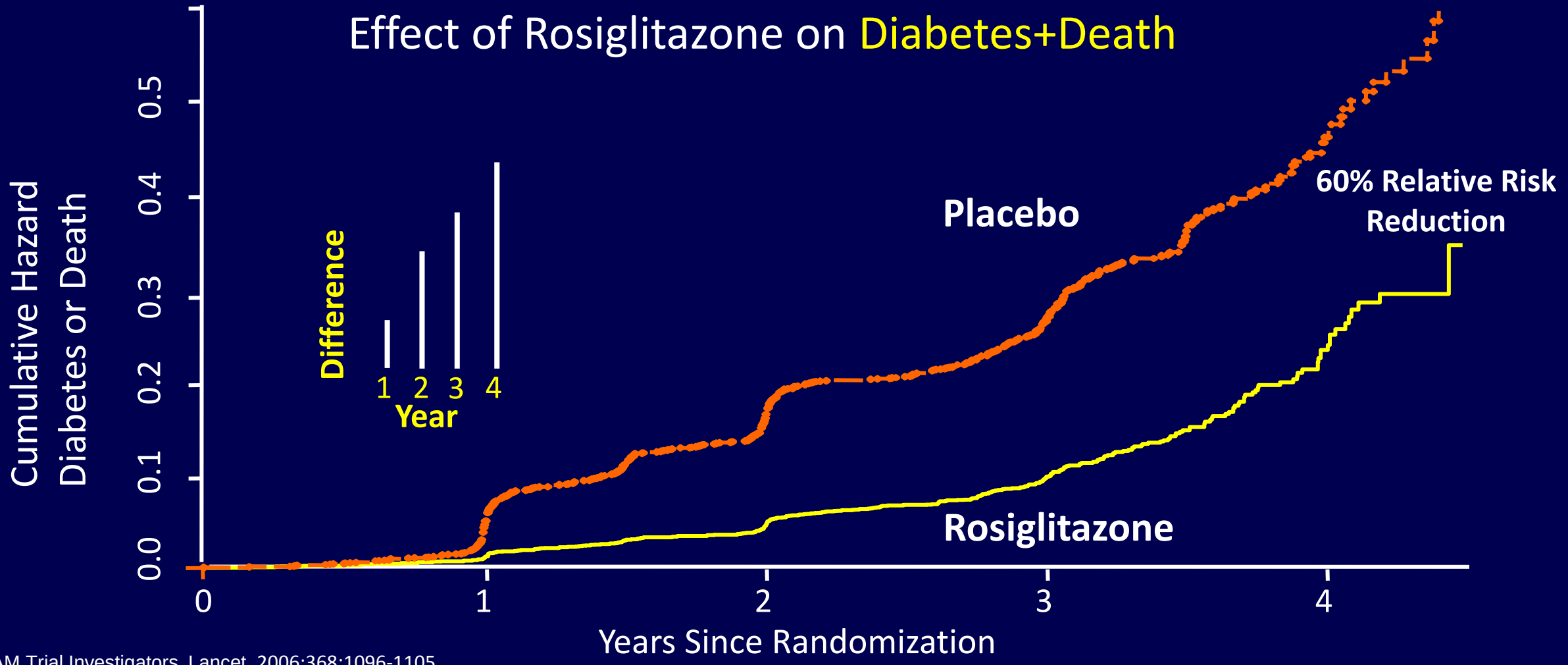
TRIPOD Study: Diabetes Rates During Washout



*Withdrawn from market.

Buchanan et al. Diabetes. 2002;51:2796-2803.

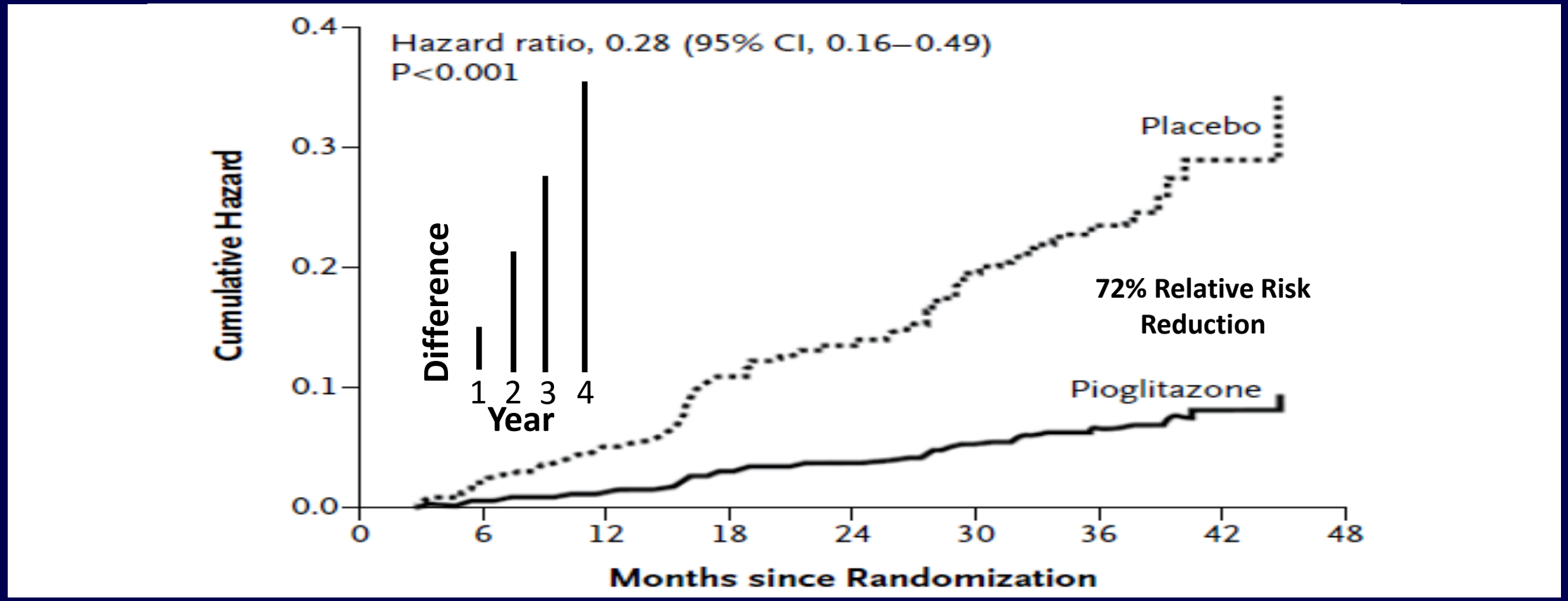
DREAM Study



DREAM Trial Investigators. Lancet. 2006;368:1096-1105.

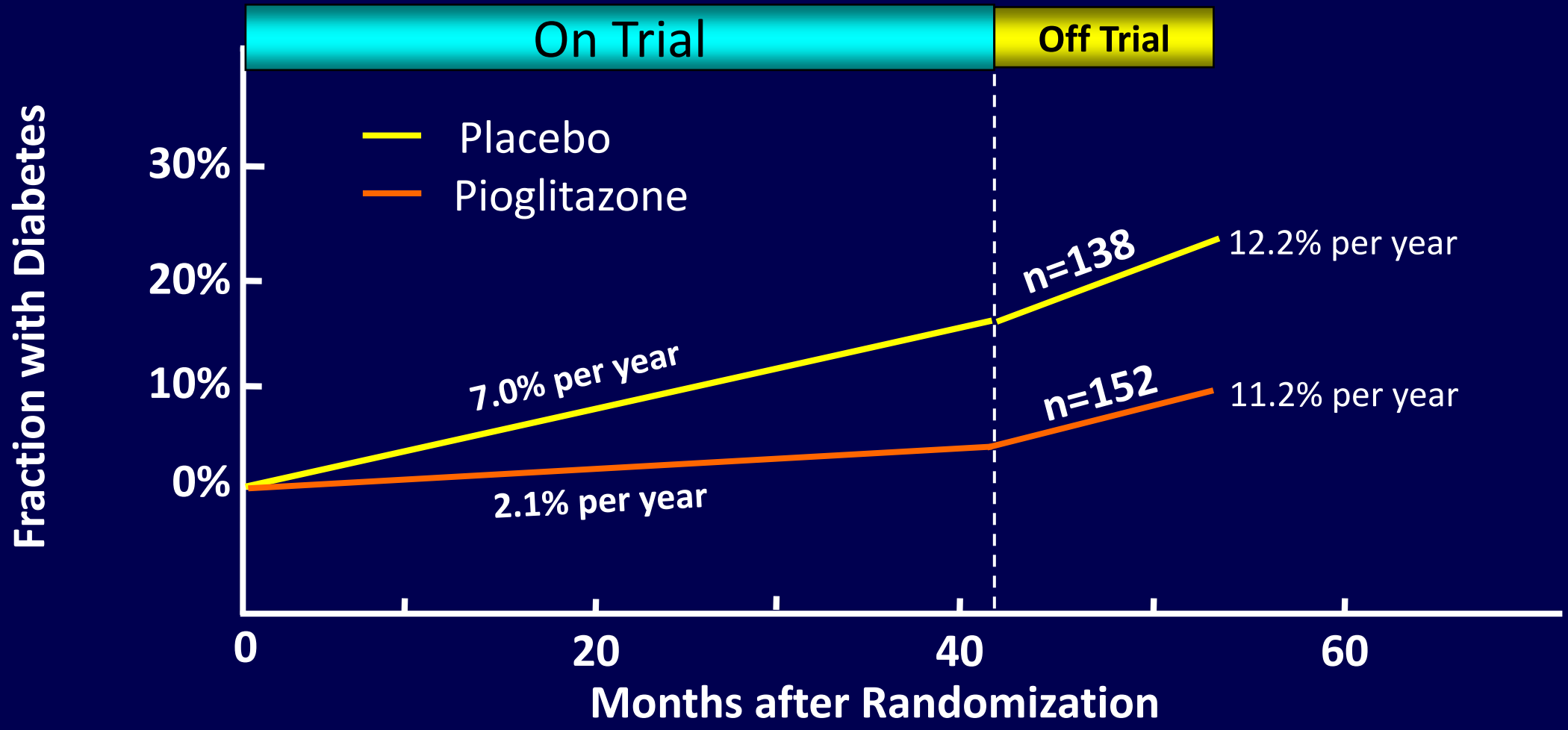
ACT NOW Study

Effect of Pioglitazone on Diabetes Rates



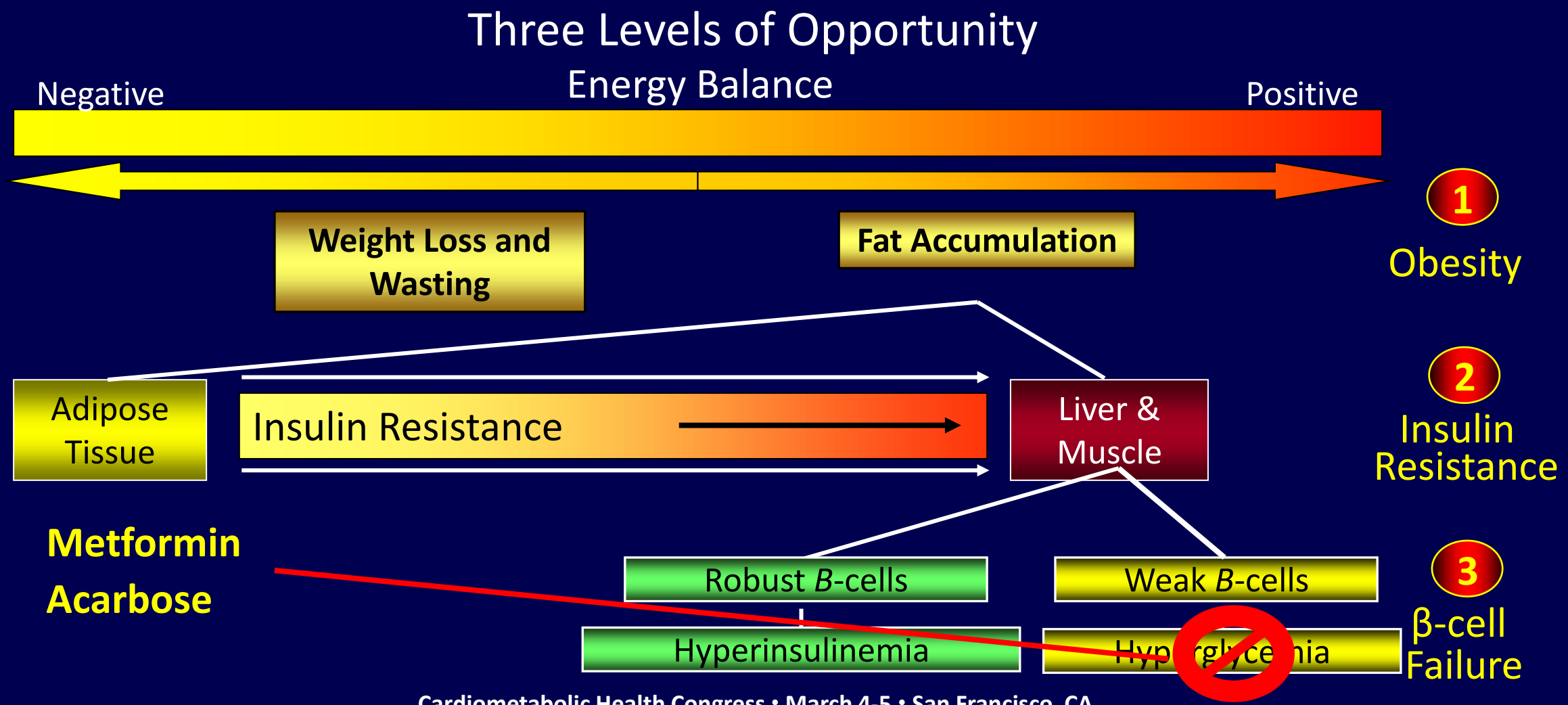
DeFronzo et al. NEJM. 2011;364:1104-1115

ACT NOW Study: Diabetes Rates During Washout

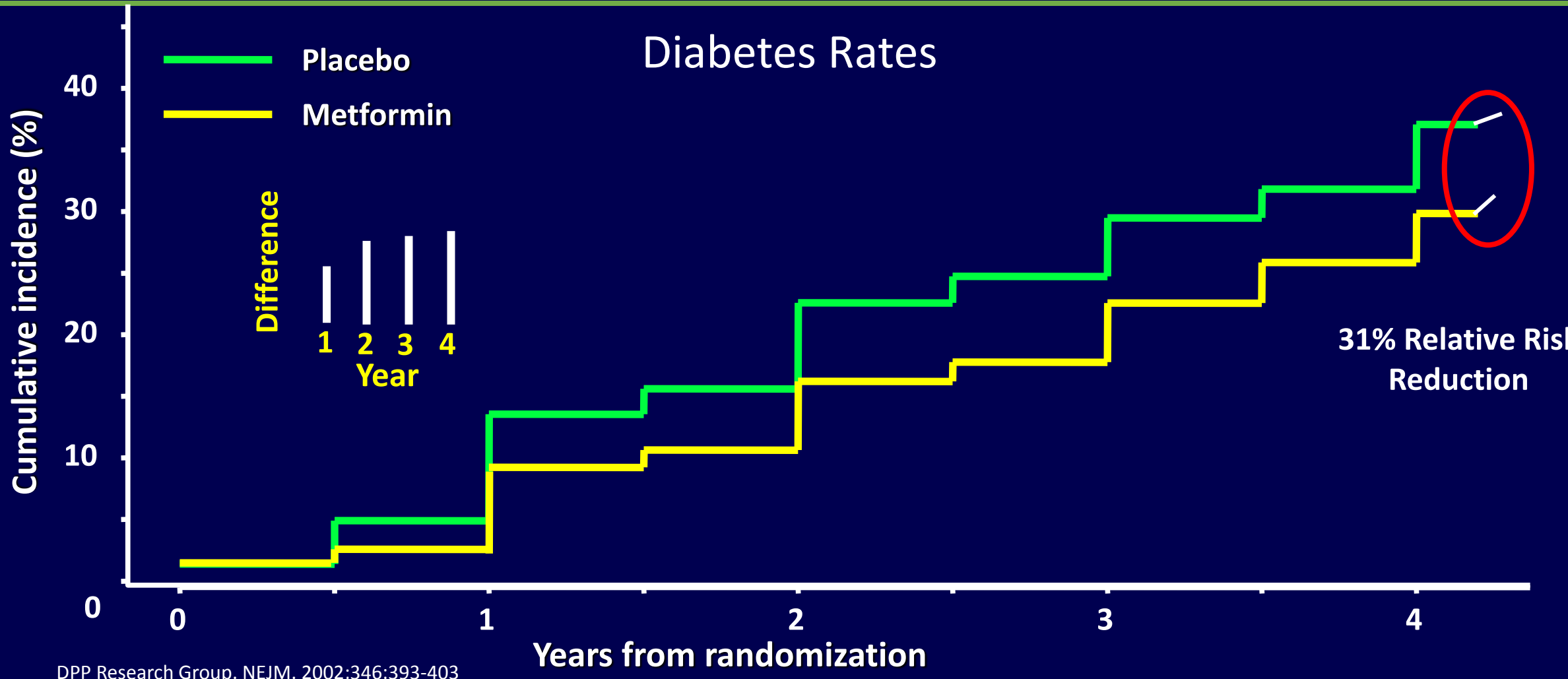


Tripathy et al. In revision

Etiology of Diabetes Prevention

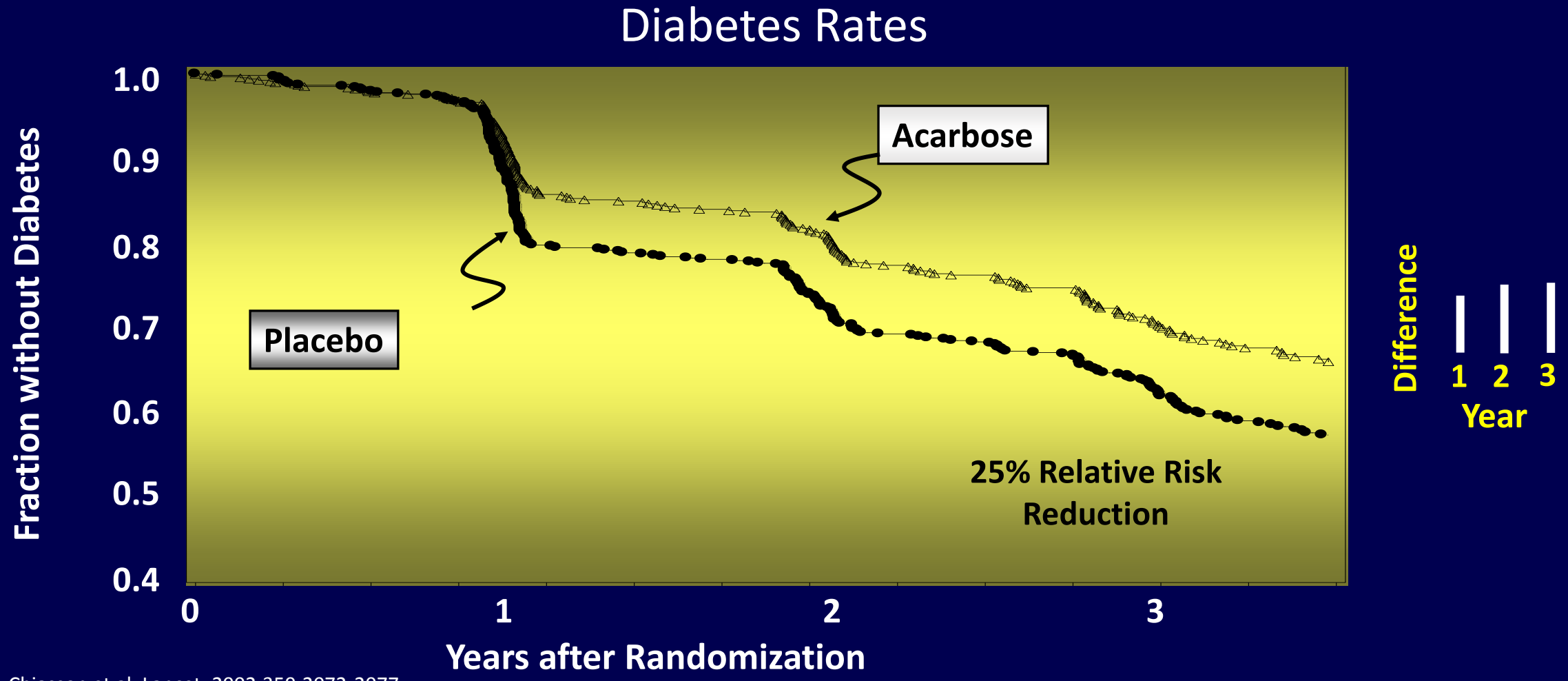


US Diabetes Prevention Program

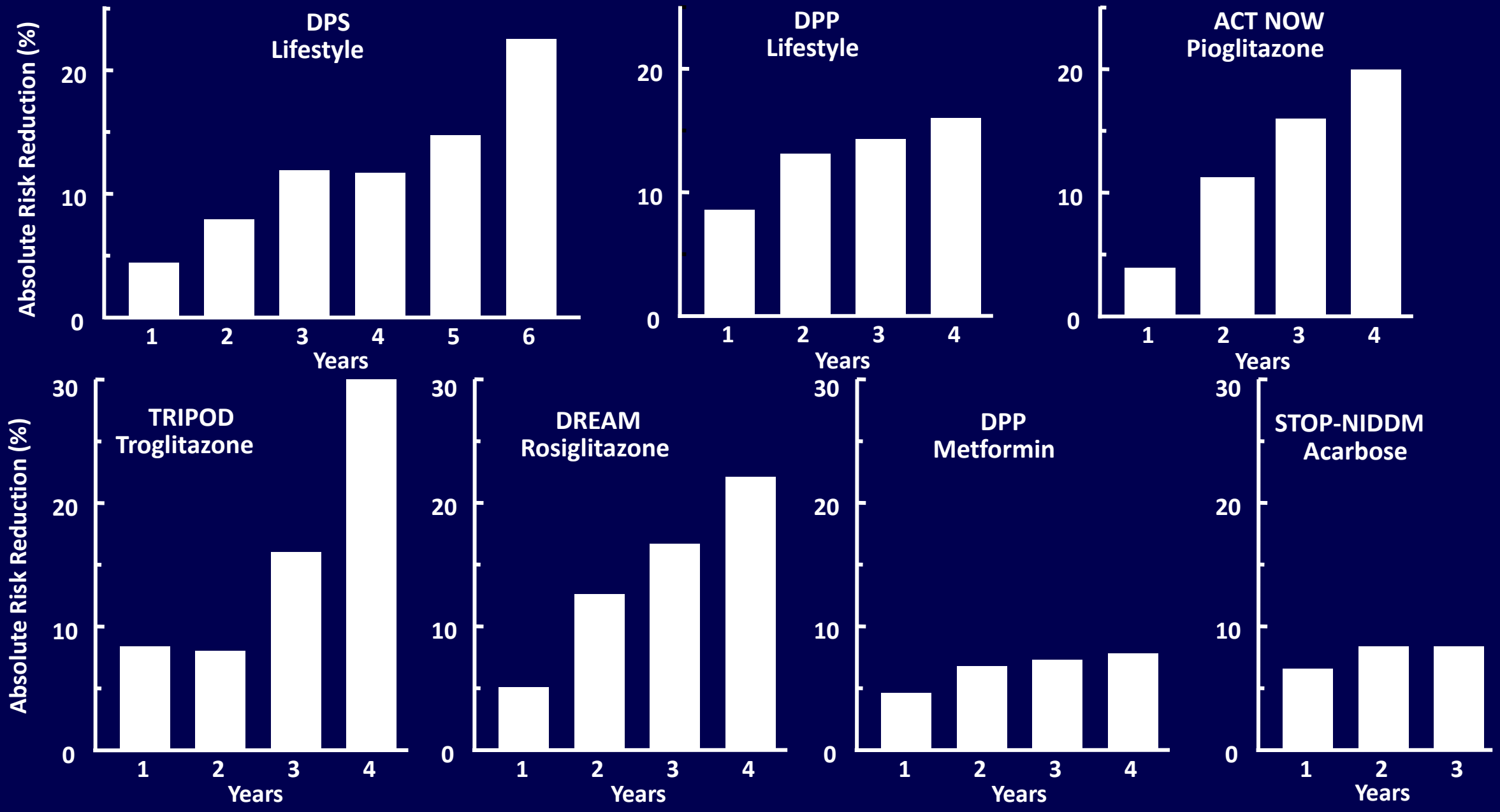


DPP Research Group. NEJM. 2002;346:393-403

The STOP-NIDDM Study



Chiasson et al. Lancet. 2002;359:2072-2077



Adapted from Buchanan, Diabetes 2007;56:1502-1507

Can We Slow Progression of Type 2 Diabetes?

Lesson from T2DM Prevention Studies

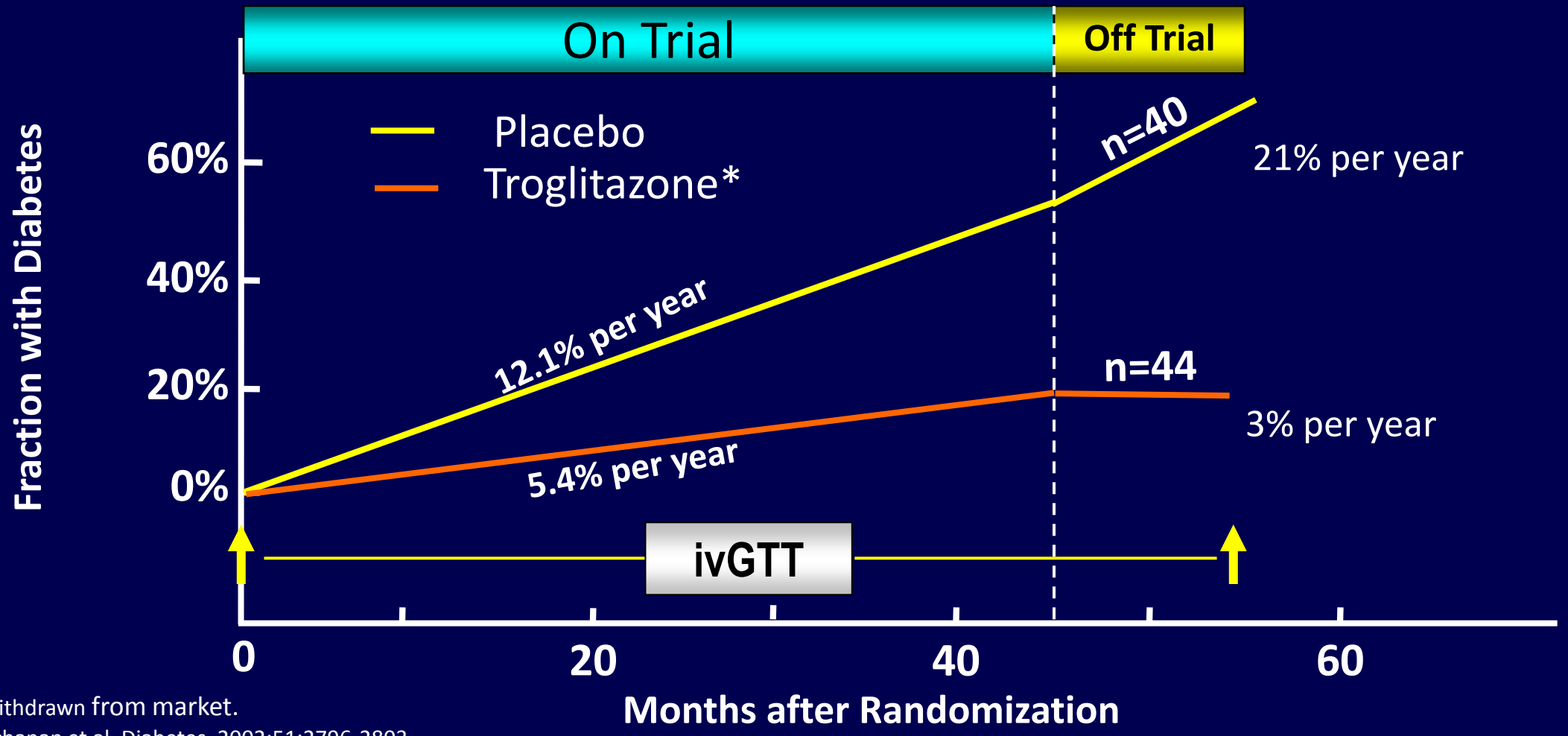
Interventions aimed at reducing body fat or its impact on insulin resistance provide the best evidence for slowing progression to T2DM.

Can We Slow Progression of Type 2 Diabetes?

Mechanistic Studies

- β-cell preservation
  - β-cell “rest”

TRIPOD Study: Was There β-cell Preservation?



*Withdrawn from market.

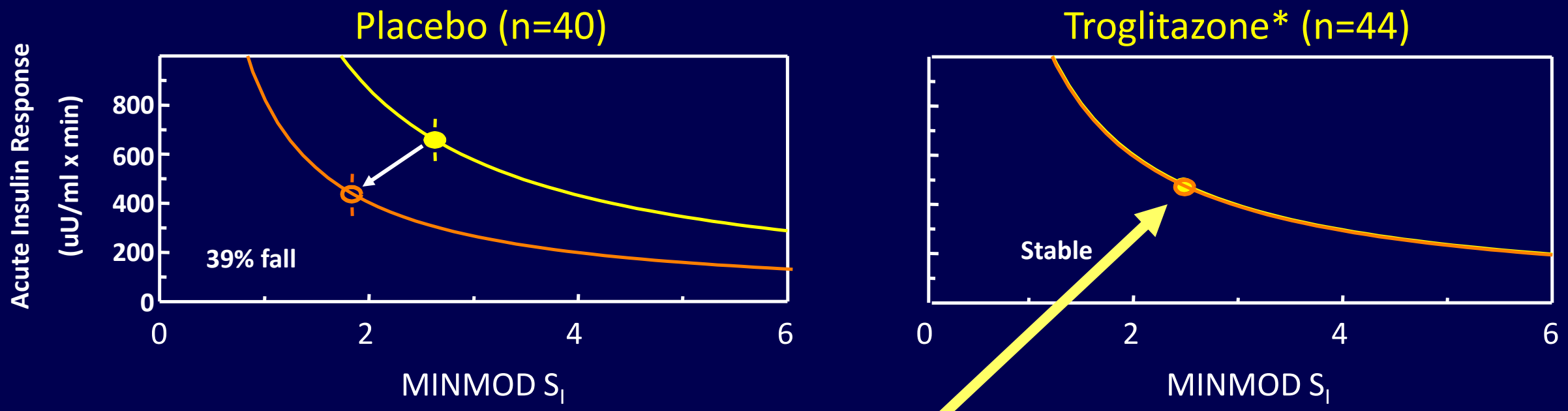
Buchanan et al. Diabetes. 2002;51:2796-2803.

TRIPOD: Preservation of *β*-cell Function

Women without diabetes during trial

Baseline

8 Months Post-trial

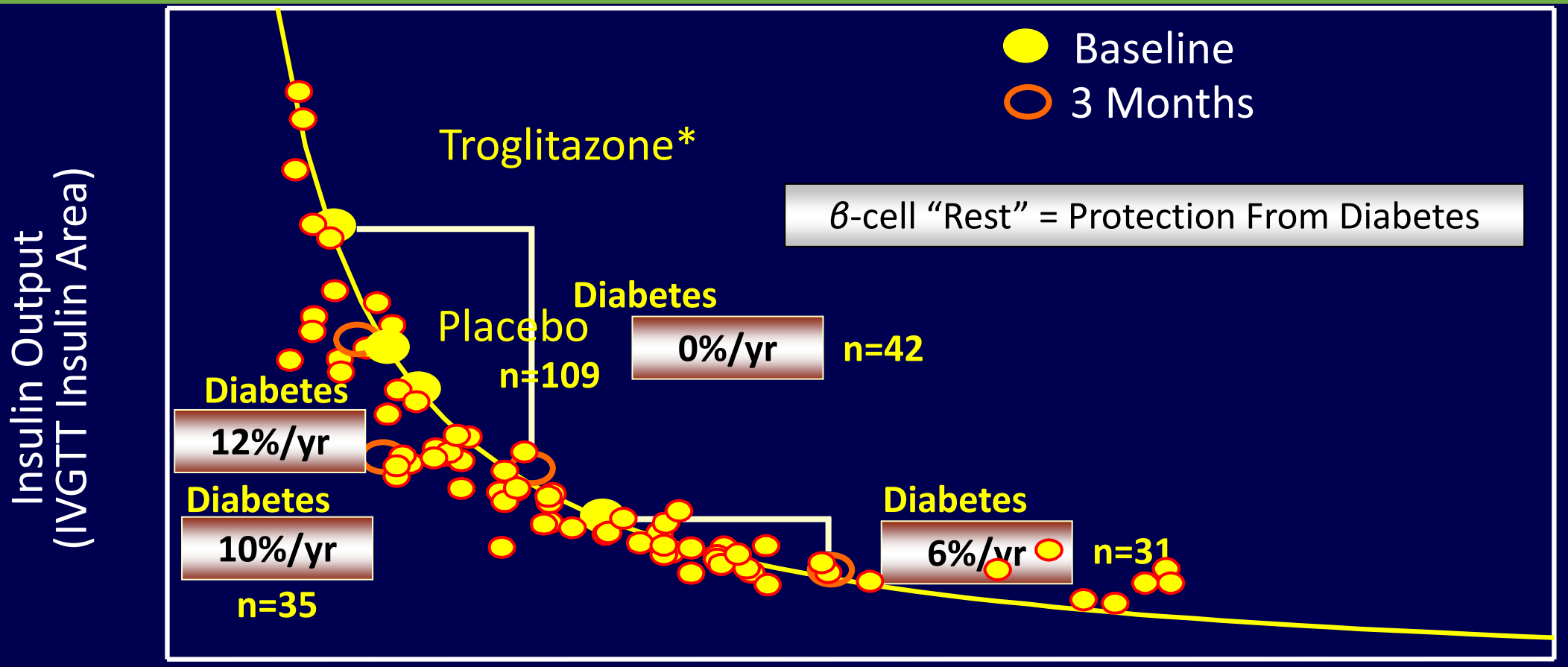


β-cell Preservation

*Withdrawn from market.

Buchanan et al. Diabetes. 2002;51:2796-2803.

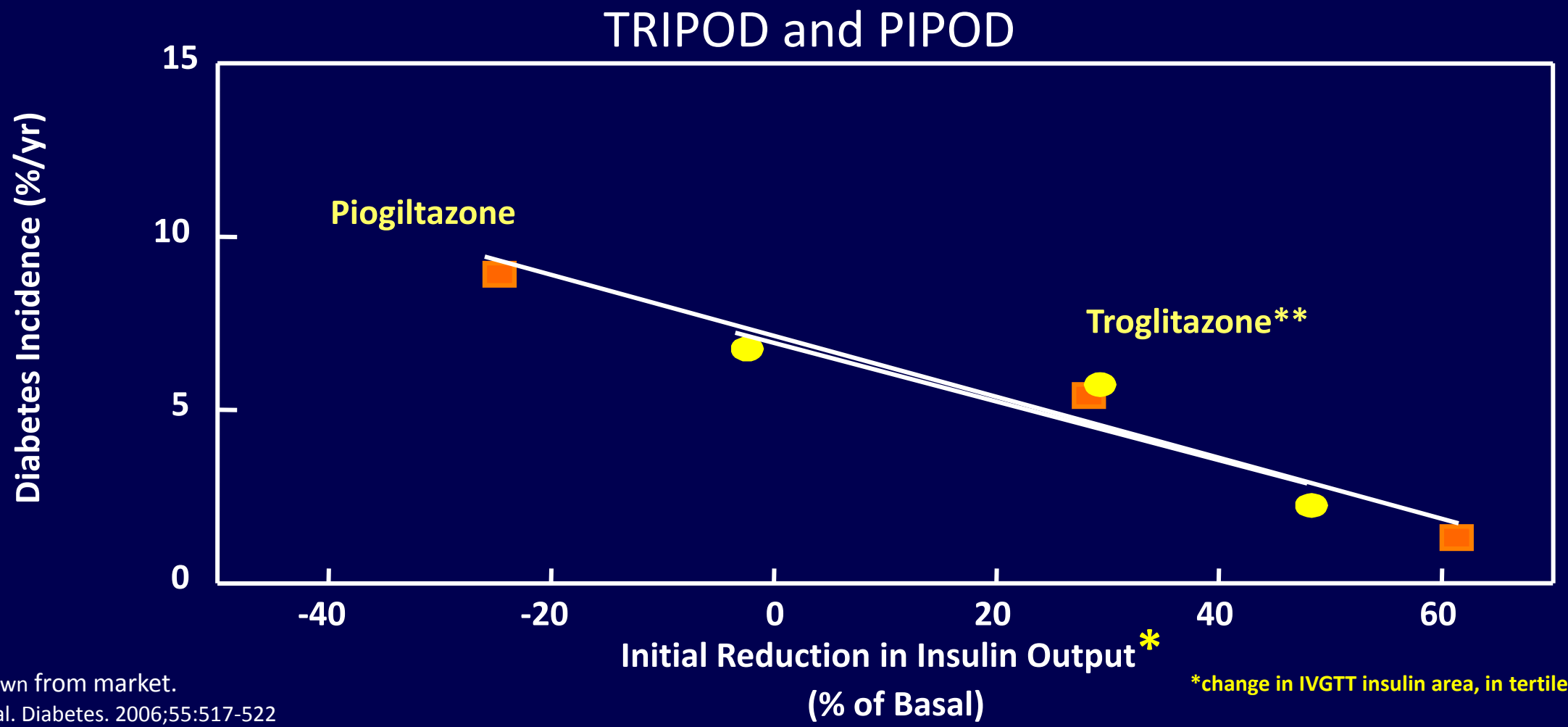
TRIPOD: β-cell "Rest" and Protection from Diabetes



*Withdrawn from market.

Buchanan et al. Diabetes. 2002;51:2796-2803.

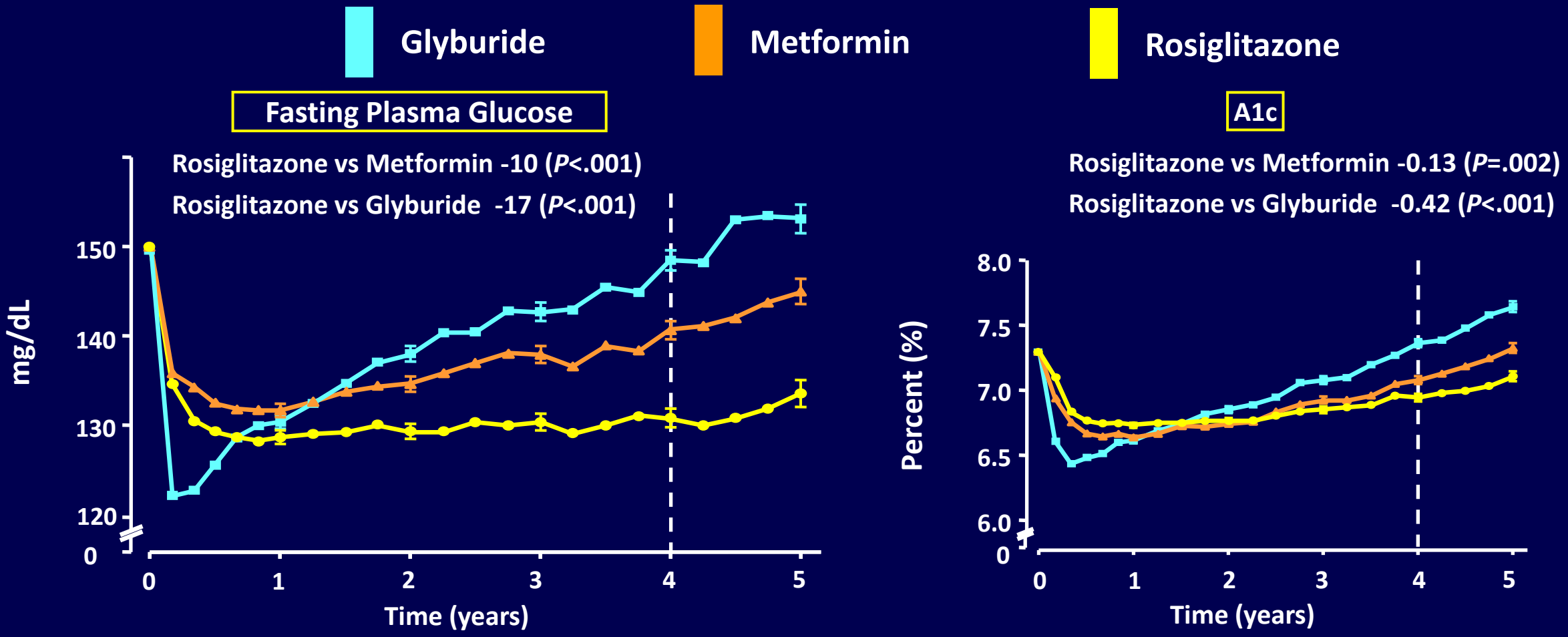
β-cell "Rest" and Diabetes Rates



*Withdrawn from market.

Xiang et al. Diabetes. 2006;55:517-522

ADOPT: Fasting Plasma Glucose and A1c Over Time



Kahn et al. NEJM. 2006;355:2427-2443

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Take Home Messages

- Progression to T2DM can be slowed, even stopped in some people.
- Interventions aimed at reducing body fat or its impact on insulin resistance provide the best evidence for slowing progression.
- β-cell "rest" appears to be an important mechanism for protection.
- Lifestyle and medical interventions tested to date fail to slow or stop progression in many patients.

We need more effective/aggressive approaches to mitigating obesity and/or its metabolic effects to stop the epidemic of T2DM.

Thank You


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