
Intervention Trials:

**Can glycemic control or weight loss
improve or prevent
lower urinary tract dysfunction?**

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Glycemic Control

- Intensive control delays onset and progression of microvascular complications in type 1 & type 2.
- If microvascular complications are an important etiology of LUT dysfunction:

Intensive glycemic control may prevent or improve severity of LUT dysfunction

Obesity, Weight Loss, & UI

- **Obesity: 50% of U.S. women; 300,000 deaths/year**
- **Obese women: 60% ↑ risk for UI (Brown 1996, Mommsen 1994, Mokdad 2001)**
- **Weight Loss ↓ UI (Bump 1992, Deitel 1998, Subak 2002)**
- **Can weight loss among women with IGT or diabetes improve UI?**

Intervention Trials

- **Early disease:**

- **Diabetes Prevention Program (DPP)**

- n = 3,234 with impaired glucose tolerance

- **Type 2 :**

- **Action for Health in Diabetes (Look AHEAD)**

- n = 5,000 obese with type 2 diabetes

- **Type 1:**

- **Epidemiology of Diabetes Interventions & Complications (EDIC)**

- n = 1375 with type 1 diabetes

Early disease: Diabetes Prevention Program

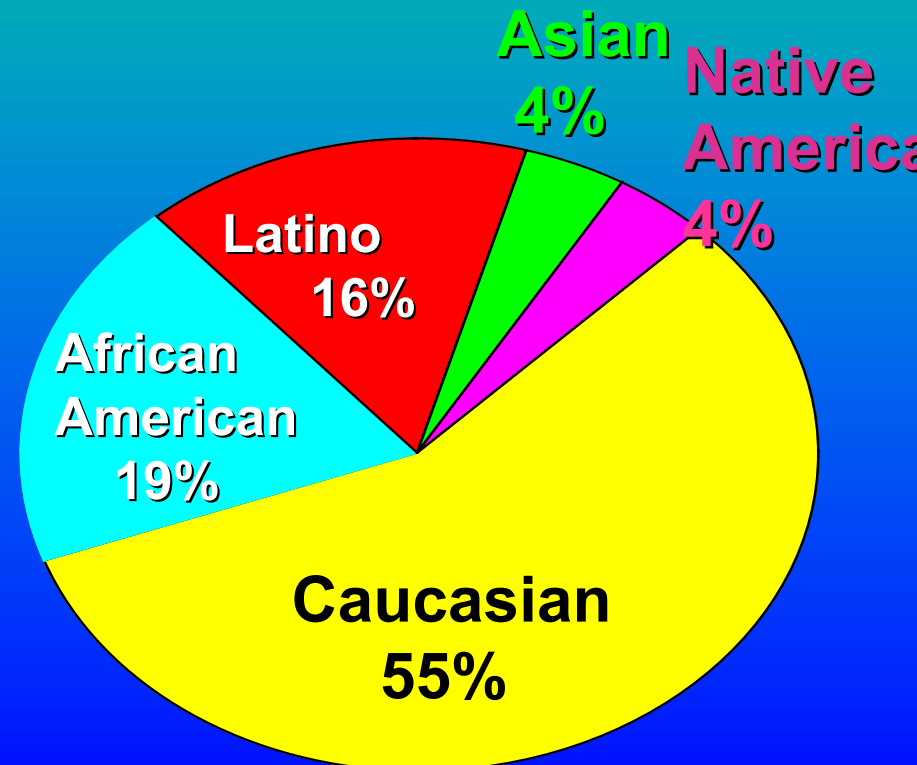
Impaired Glucose Tolerance (IGT) n=3,234

67% women

Mean age = 51 years

Mean BMI = 34 kg/m²

Ethnicity:



**Diabetes
Prevention
Program**

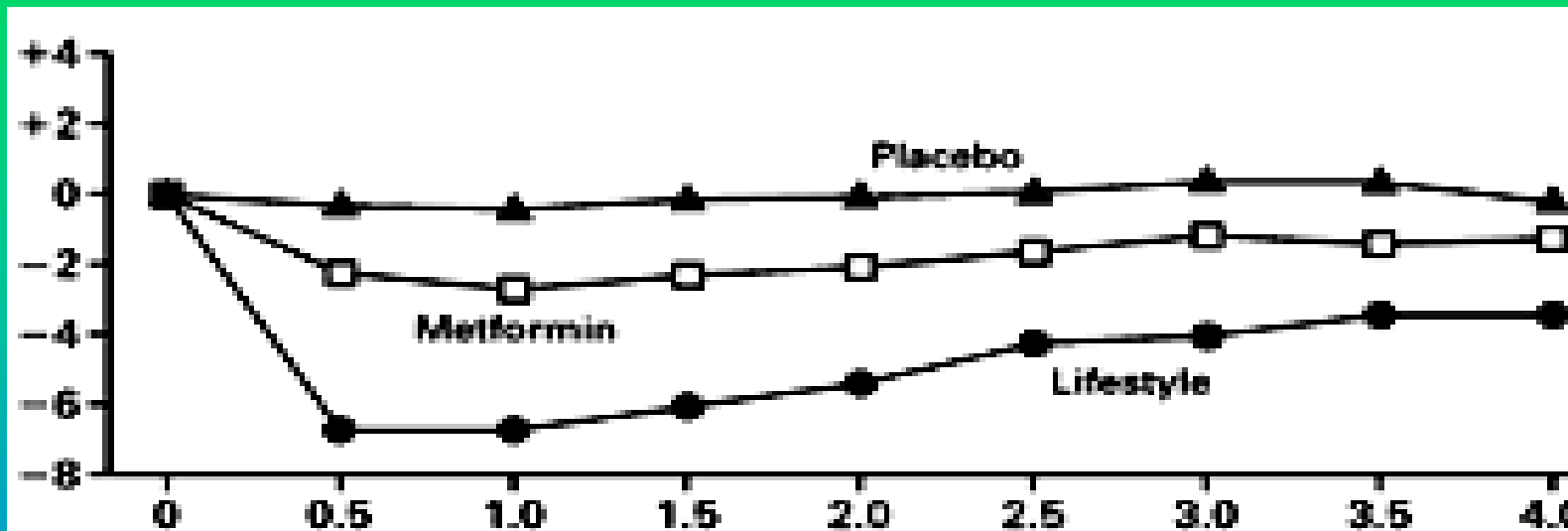
**Lifestyle
Intervention
N = 1079**

**Metformin
Therapy
N = 1073**

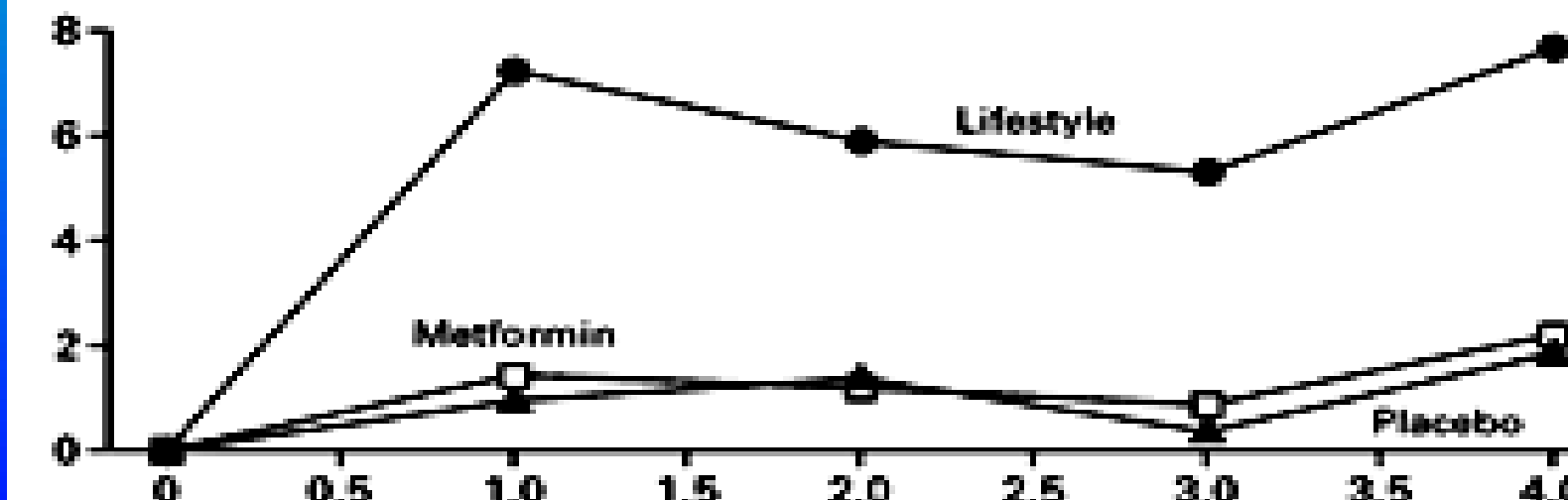
**Placebo
N = 1082**

What they achieved...

Change
Weight
(kg)

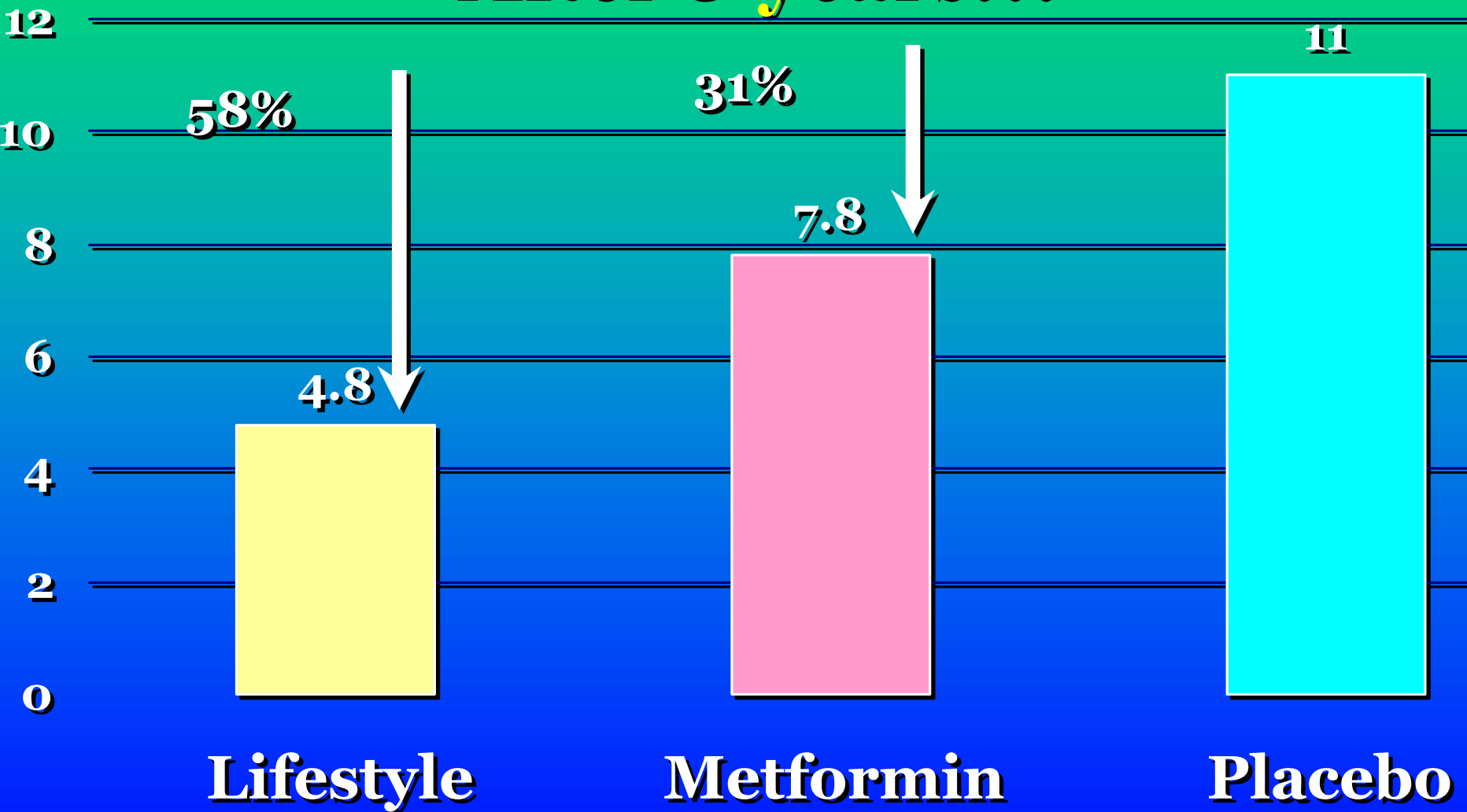


Change
Phys Act
MET-hr/wk



Years

After 3 years...



DPP Incontinence Study

Do interventions that:

↓ diabetes, ↓ weight, and ↑ exercise also ↓ UI?

- End-of-study visit
- Validated self-report UI questionnaire
- Prevalence and frequency of UI, overall and by type

Results

- Treatment groups were comparable at baseline
- N = 1987 women at end of study visit
- Mean age 50 yo (± 10)
- Overall: \geq Weekly UI: 43.9%
Daily UI: 14.1%
- \geq Weekly UI type:
Stress UI 27.7%
Urge UI 21.9%

Treatment Effects

End of Study Visit: Prevalence of \geq weekly UI

	Lifestyle	Metformin	Placebo	P
Total UI	38.7%	47.9%	45.8%	0.002
Stress UI	31.3%	39.4%	36.7%	0.008
Urge UI	23.9%	28.5%	25.8%	0.17

Summary

- Stress UI was substantially lower among women with IGT assigned to a lifestyle intervention of weight loss and exercise
- *Potential to motivate women to choose lifestyle modification to prevent diabetes*
- Mediation of treatment effect: weight loss, diabetes
- **DPP- Outcomes Study**: examination of longer-term effects for prevention and decreased severity.

Action for Health in Diabetes (Look AHEAD)

- **Clear association: obesity and type 2 diabetes**
- **RCT: Weight loss and activity vs Control**
 - Goal: > 7% weight loss; > 175 min/wk activity**
 - 4 yr intervention, 11.5 yr f/u in 5000 obese pts**
 - 45-75 yo; 50% women**
- **Primary outcome: Incidence of CV events**
- **UI measures: baseline, annually, end of study**

Look AHEAD Incontinence Study

Among obese men and women with type 2 diabetes

Do interventions that:

↓ diabetes, ↓ weight, and ↑ exercise also ↓ UI?

- Is the benefit of weight loss on UI mediated by improvement in diabetes? Or is it too late?
- Recruitment began July 2002
- Baseline data April 2004

Type 1 Diabetes

- **The Diabetes Control & Complications Trial (DCCT)**
1983-1993 RCT: Intensive vs Conventional Treatment
 - Primary outcome: ↓ Complications
- **Epidemiology of Diabetes Interventions & Complications (EDIC)** 1993 to present

Current EDIC cohort:

Mean age 40 (25-51 yo)

Type 1 diabetes mean duration: 20 yrs

Annual exams; Retention > 95%

Uro -EDIC

NIDDK Divisions of Urology & DEM:

- Are there long-term benefits of intensive glycemic control on:
 - LUTS, UI, ED, sexual dysfunction, UTI's?
- Prevalence of and diabetes severity risk factors for LUT dysfunction
- LUT measures: AUA Symptom Score, validated UI (type, frequency, severity, QOL)
- Data analysis 2004

Additional Observational Studies

- **NHANES 2001-2003**
- **Reproductive Risk factors for urinary Incontinence Study at Kaiser (RRISK 1 & 2)**

RRISK 1: 2110 ethnically diverse women 40-69 yo old
Black 14%; Asian/PI 20%; Hispanic 20%

RRISK 2: Prospective cohort 5 yr f/u

Diabetes RRISK 2: 400 with type 2 diabetes

400 age and race matched controls

Linkage: Kaiser Diabetes Registry: 176,000 current members

Extensive diabetes measures

RRISK 1 & 2

- Extensive LUT measures: Self-report, in-person:
AUA Symptom Score, 7-day voiding diaries, severity, bother, QOL, *lifetime UI history*
- **Chart Abstraction:** L & D records; Surgeries
- Menopausal status, lifetime hormone use; sexual function, medical conditions, anal incontinence, pelvic organ prolapse
- **RRISK 2 Diabetes:**
PVR, uroflow, urodynamics
Autonomic & Peripheral Neuropathy: Eva Feldman, MD PhD
UTI's & Biologic Specimens: Ann Stapleton, MD
- **Collaborators wanted!** www.ucsf.edu/scor

Diabetes Clinical Research Program

Observational Studies

- Nurses Health Study
- EPINCONT Study
- NHANES 2001-2003
- RRISK 1 & 2

Intervention Trials

- Diabetes Prevention Program (DPP);
DPP Outcomes Study (DPP OS)
- Action for Health in Diabetes (Look AHEAD)
- Epidemiology of Diabetes Interventions & Control (EDIC)

- About
- People
- Research
- Training
- Fellowship



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