

# Enrollment of Women and Racial Minorities in Clinical Trials for Diabetes Medications

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# Disclaimer

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Views expressed in this presentation are those of the speaker and not, necessarily, of the Food and Drug Administration

# Background

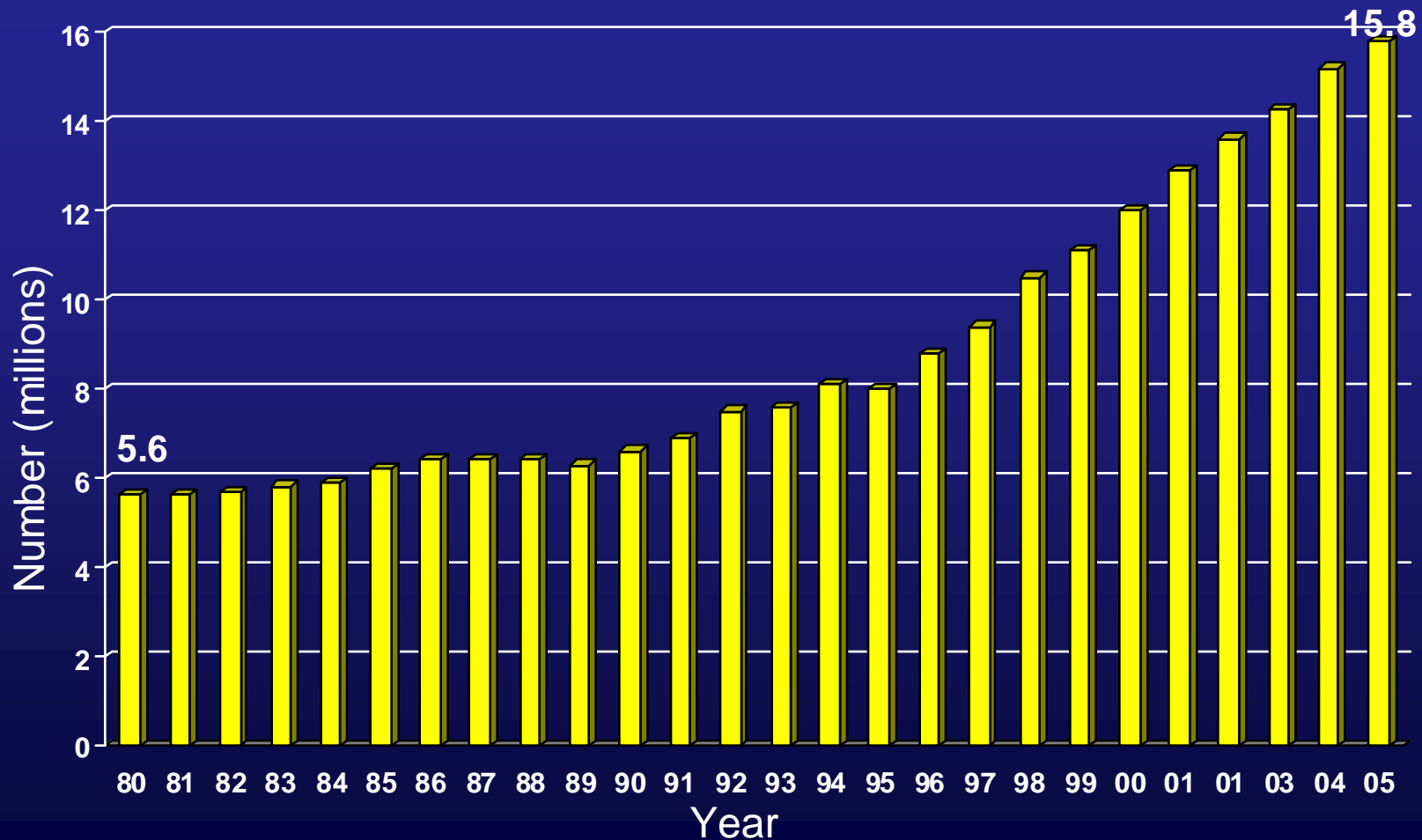
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- 15.8 million in US diagnosed with diabetics
- 8 million women
- Sex
  - 6.7% males
  - 7.7% female
- Race
  - 13.1% African-Americans
  - 10.1% Hispanics
  - 5.5% Caucasians

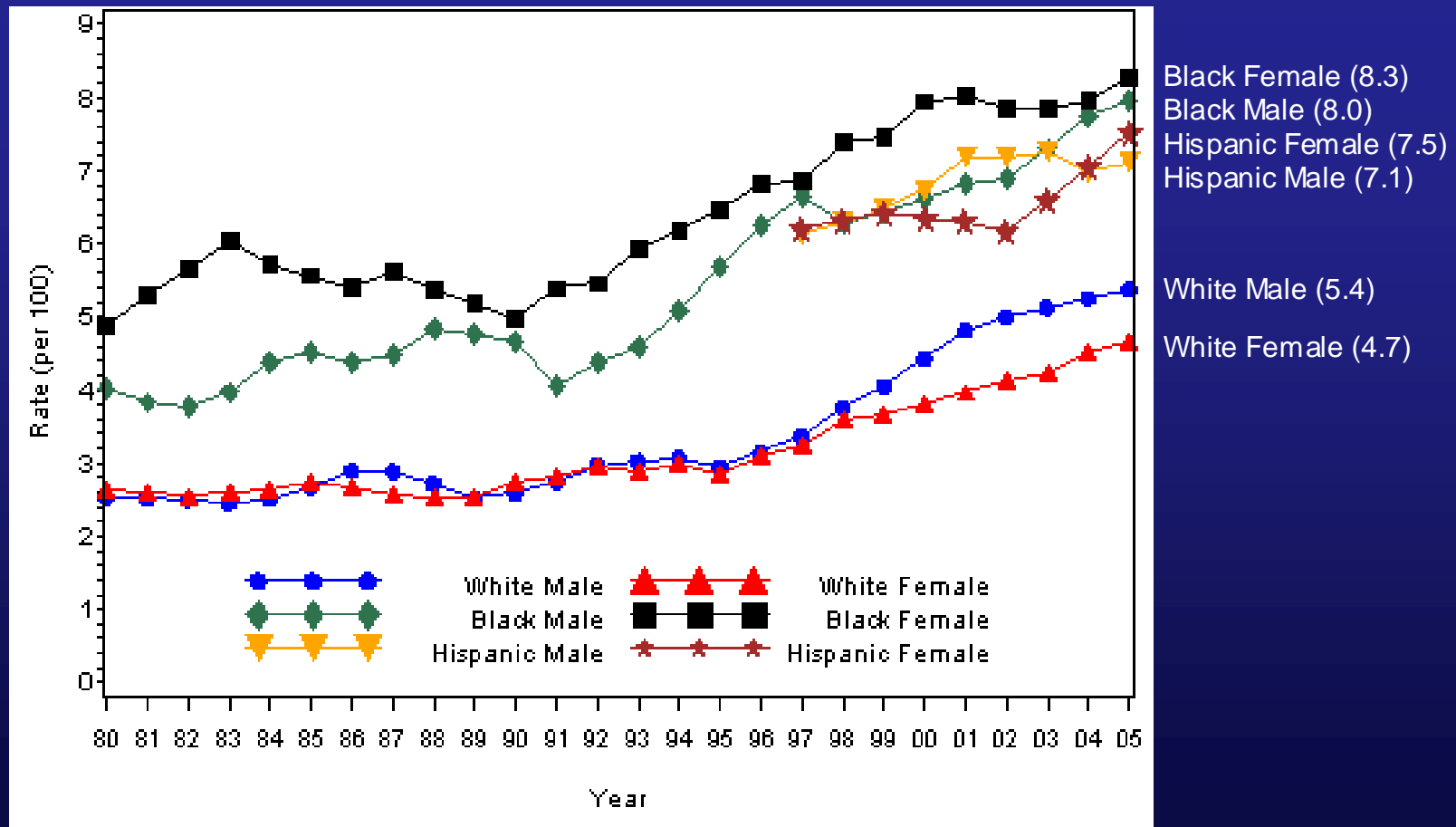
Source: Centers for Disease Control and Prevention (CDC), National Center for Health Statistics, National Health Interview Survey. 2005 Data.

# Number (in Millions) of Persons with Diagnosed Diabetes, United States, 1980–2005



Source: CDC Diabetes Program (<http://www.cdc.gov/diabetes/statistics/prev/national/figpersons.htm>)

# Age-Adjusted Prevalence of Diagnosed Diabetes by Race/Ethnicity and Sex, United States, 1980–2005



Source: CDC Diabetes Program (<http://www.cdc.gov/diabetes/statistics/prev/national/figraceethsex.htm>)

# Background

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- Minorities have the highest incidence of diabetes related complications.
- African-Americans and Hispanic diabetics have higher rate of End-Stage Renal Disease compared to Caucasians.<sup>1</sup>
- The lower extremity amputation rate per 1,000 persons with diabetes was 5.0 among blacks and 3.2 among whites.<sup>2</sup>
- Stroke rate for blacks (8.9 per 1,000 diabetic population) was 37% higher than the rate for whites (6.5 per 1,000 diabetic population).<sup>2</sup>

<sup>1</sup> MMWR Weekly; November 4, 2005; 54(43);1097-1100.

<sup>2</sup> Centers for Disease Control and Prevention (CDC), National Center for Health Statistics, National Health Interview Survey. 2003, age-adjusted data.

# Background

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- Women with diabetes are at greater risk for heart disease and first fatal events, than men or women without diabetes.<sup>1</sup>
- Prevalence of mobility limitation per 100 adults with diabetes was higher among women (56) than among men (40).<sup>2</sup>
- Prevalence of visual impairment among women was 19.3%, compared with 16.2% among men.<sup>3</sup>

<sup>1</sup> Centers for Disease Control and Prevention (CDC), Diabetes Women's Health Across the Life Stages.

<sup>2</sup> CDC, National Center for Health Statistics, National Health Interview Survey. 2003, age-adjusted data.

<sup>3</sup> CDC, National Center for Health Statistics, National Health Interview Survey. 2005, age-adjusted data.

# Role of the FDA

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- FDA's Mission
  - The FDA is responsible for protecting the public health by assuring the safety, efficacy, and security of human and veterinary drugs, biological products, medical devices, our nation's food supply, cosmetics, and products that emit radiation.
- FDA requires that clinical trials include the population expected to use the drug.



# Current Regulations

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- 1998 Demographic Rule for Investigational New Drug Applications and New Drug Applications Regulation:  
*(<http://www.fda.gov/OHRMS/DOCKETS/98fr/021198.txt>)*  
*(21 CFR Parts 312 and 314, February 11, 1998)*
- 2000 Amendment to the Clinical Hold Regulations for Products Intended for Life-Threatening Diseases  
*(21 CFR 312, June 1, 2000)*

# History

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- ***1992 - GAO report, “Women’s Health: FDA Needs to Ensure More Study of Gender Differences in Prescription Drugs”***

*(<http://archive.gao.gov/d35t11/147861.pdf>)*

—FDA not adequately ensuring representation of women or the study of sex differences in clinical trials

# History

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- ***2001 - GAO Report, “Women Sufficiently Represented in New Drug Testing, but FDA Oversight Needs Improvement”***

*(<http://www.gao.gov/new.items/d01754.pdf>)*

- Participation is similar to that of men: Except earliest phases of clinical trials & some therapeutic areas
- Reviewers should consistently discuss sex differences in reviews

# Prescription Drugs Withdrawn from the US Market 1997-2000

Drug	Type of Drug	Patient Population	Primary Health Risk
<b>Prescription Drugs with Evidence of Greater Health Risks In Women</b>			
Pondimin	Appetite suppressant	Women	Valvular heart disease
Redux	Appetite suppressant	Women	Valvular heart disease
Rezulin	Diabetic	Women	Liver failure
Lotronex	Gastrointestinal	Women	Ischemic colitis
Seldane <sup>a</sup>	Antihistamine	Women and Men	Torsades de Pointes
Posicor	Cardiovascular	Women and Men	Lowered heart rate in elderly women and adverse interactions with 26 other drugs
Hismanal	Antihistamine	Women and Men	Torsades de Pointes
Propulsid <sup>b</sup>	Gastrointestinal	Women and Men	Torsades de Pointes

Source: 2001 GAO Report, "Drug Safety: Most Drugs Withdrawn in Recent Years Had Greater Health Risks for Women" (<http://www.gao.gov/new.items/d01286r.pdf>)

# Fracture Risk: ADOPT study Avandia (rosiglitazone)

	Rosiglitazone n (%), rate	Metformin n (%), rate	Glyburide n (%), rate
Male	32 (3.9%) 1.16/100 PY	29 (3.4%) 0.98/100 PY	28 (3.4%) 1.07/100 PY
Female	60 (9.3%) 2.74/100 PY	30 (5.1%) 1.54/100 PY	21 (3.5%) 1.29/100 PY

Source: Kahn, et al *NEJM*. 2006; 355 (23):2427-43;  
GSK Dear HealthCare Professional Letter, February 2007

# Office of Women's Health

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- Founded in 1994

## OWH Mission

- Protect and advance the health of women through policy, science, and outreach
- Advocate for inclusion of women in clinical trials and analysis of sex/gender effects

# Purpose

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- The purpose of this study is to evaluate if women and minorities are enrolled in clinical trials for oral diabetes drugs in proportion to their prevalence of diabetes.

# Methods

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- Clinical data available in the Center for Drug Evaluation and Research (CDER) Electronic Document Room (EDR) for oral diabetes drugs were compiled.
  - Drugs approved between 1999 and 2006
  - 4 New Drug Applications (NDAs)
  - 69 studies



# Methods

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- In 59 studies race coded as:
  - Caucasian
  - African-American
  - Hispanic
  - Asian
  - Native American
  - Other
- In 10 studies race coded as:
  - Caucasian
  - African-American
  - Other
- Sex re-coded to the M/F format

# Results

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- Of the 27,405 participants enrolled
  - 38.9% female
  - 61.1% male
- Age 58.2+10.7 years (range 18-92)

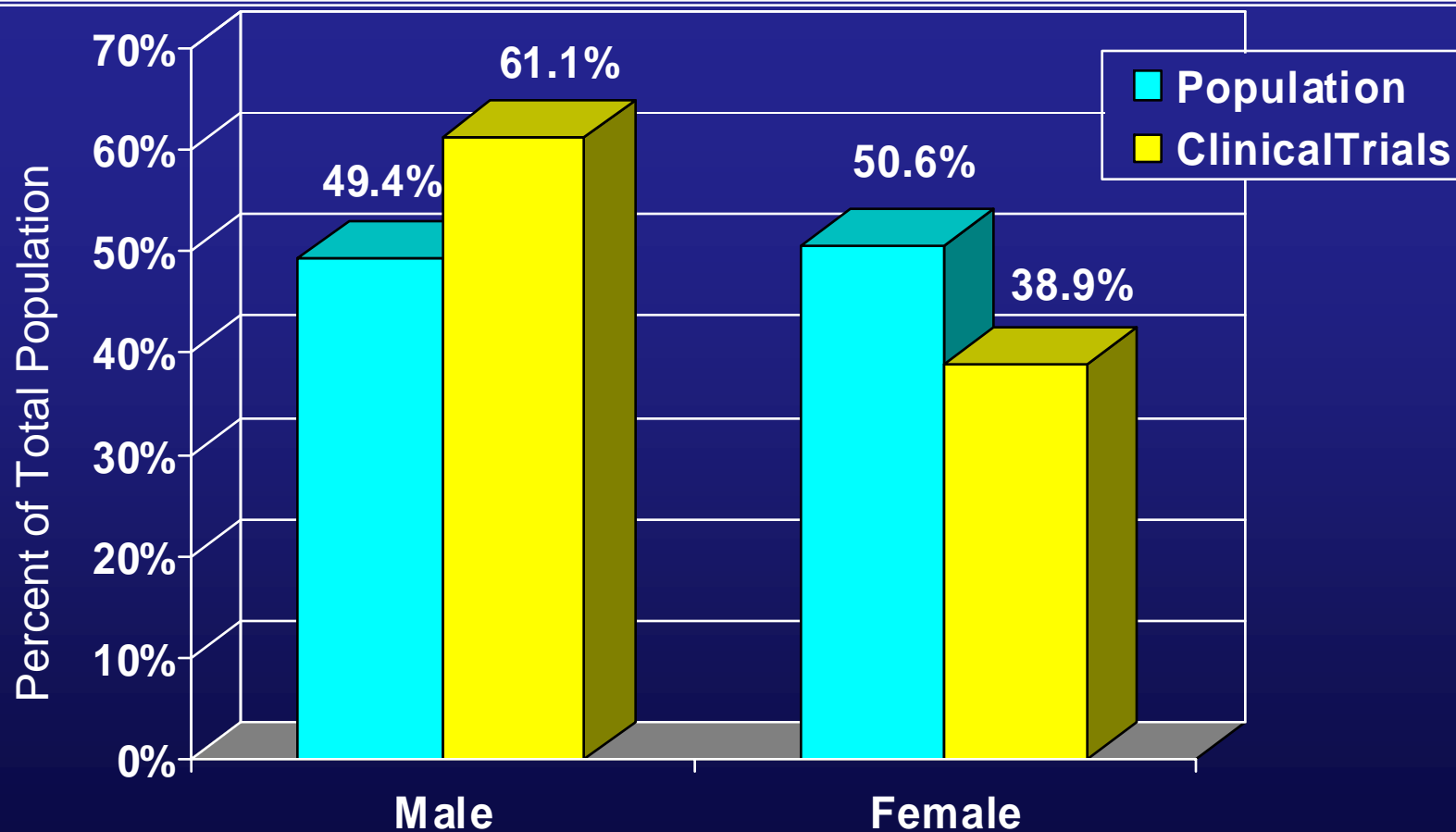
# Results

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- Race was provided on 27,371 participants
  - 78.2% Caucasian
  - 6.3% African-American
  - 15.5% Other
- For the trials with an expanded racial breakdown
  - 78.3% Caucasian
  - 5.9% African-American
  - 6.4% Hispanic
  - 6.4% Asian
  - 0.1% Native American

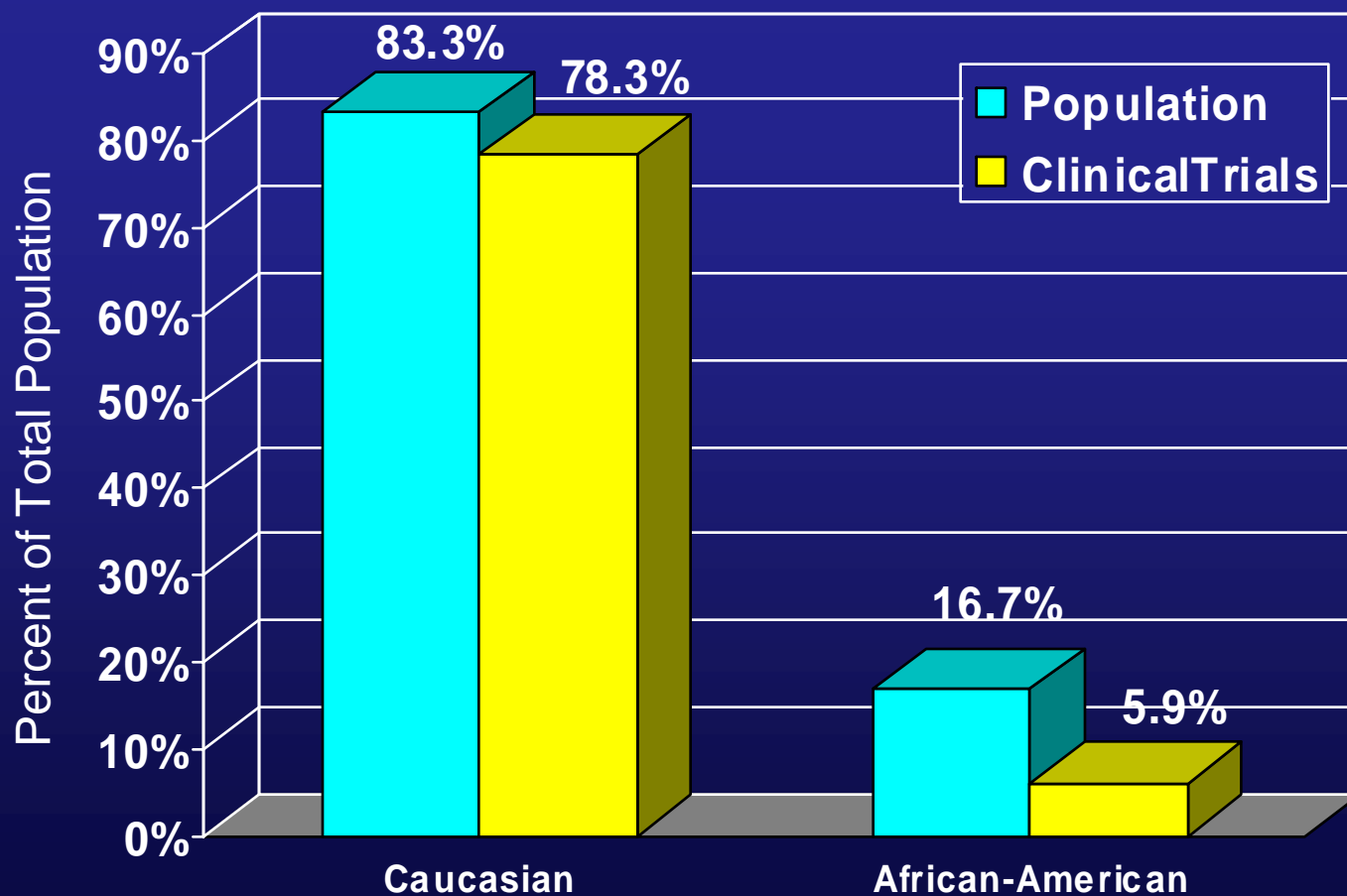
# Results



Source: CDC Diabetes Program; 2005 Data.

(<http://www.cdc.gov/diabetes/statistics/prev/national/menupersons.htm>)

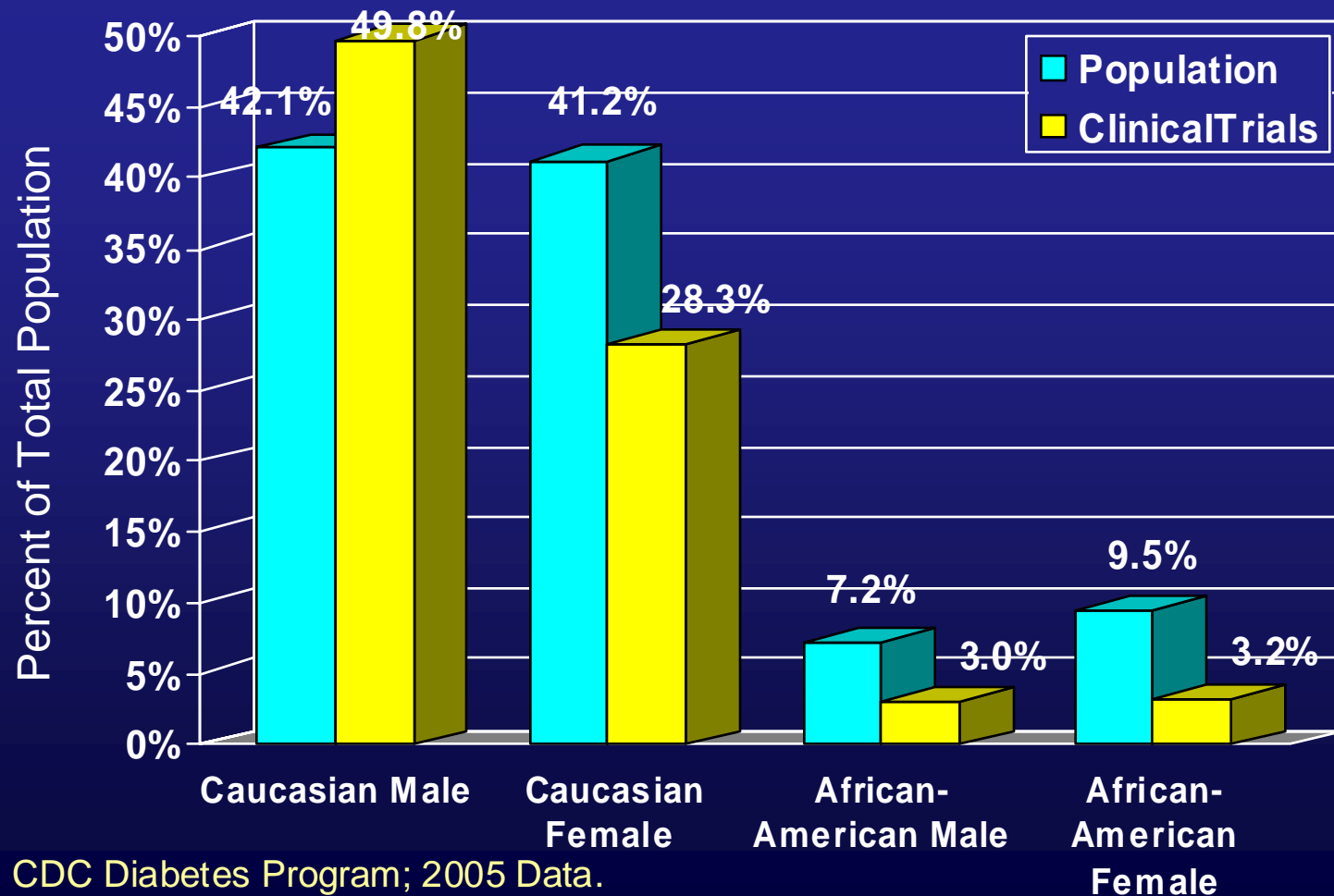
# Results



Source: CDC Diabetes Program; 2005 Data.

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# Results



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# Conclusions

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- Women and minorities are under represented in trials of oral diabetes drugs.
- There is need for continued monitoring of participation of these groups in clinical studies.
- With increased diabetic morbidity and mortality in women and minorities, it is important that drugs be tested for safety and efficacy in subgroups.

# OWH - Going Forward

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- Continued monitoring of inclusion
  - Strengthen FDA infrastructure, bioinformatics initiatives
  - FDA inclusion initiative
- Research on sex differences
  - Intramural funding (\$15.8 million)
  - Inter-agency partnerships
- Participate in working groups for new guidance and regulations