

Reducing the Diabetes Burden in American Indians and Alaska Natives

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Nothing to Disclose

Objectives

- Recognize contributions of research in AI/AN populations to the understanding of type 2 diabetes
- Review current trends in diabetes prevalence and complications
- Assess interventions in AI/AN patients with diabetes and prediabetes

National Diabetes Statistics Report

2020

Estimates of Diabetes and Its Burden in the United States

Prevalence of Diabetes (Diagnosed and Undiagnosed)

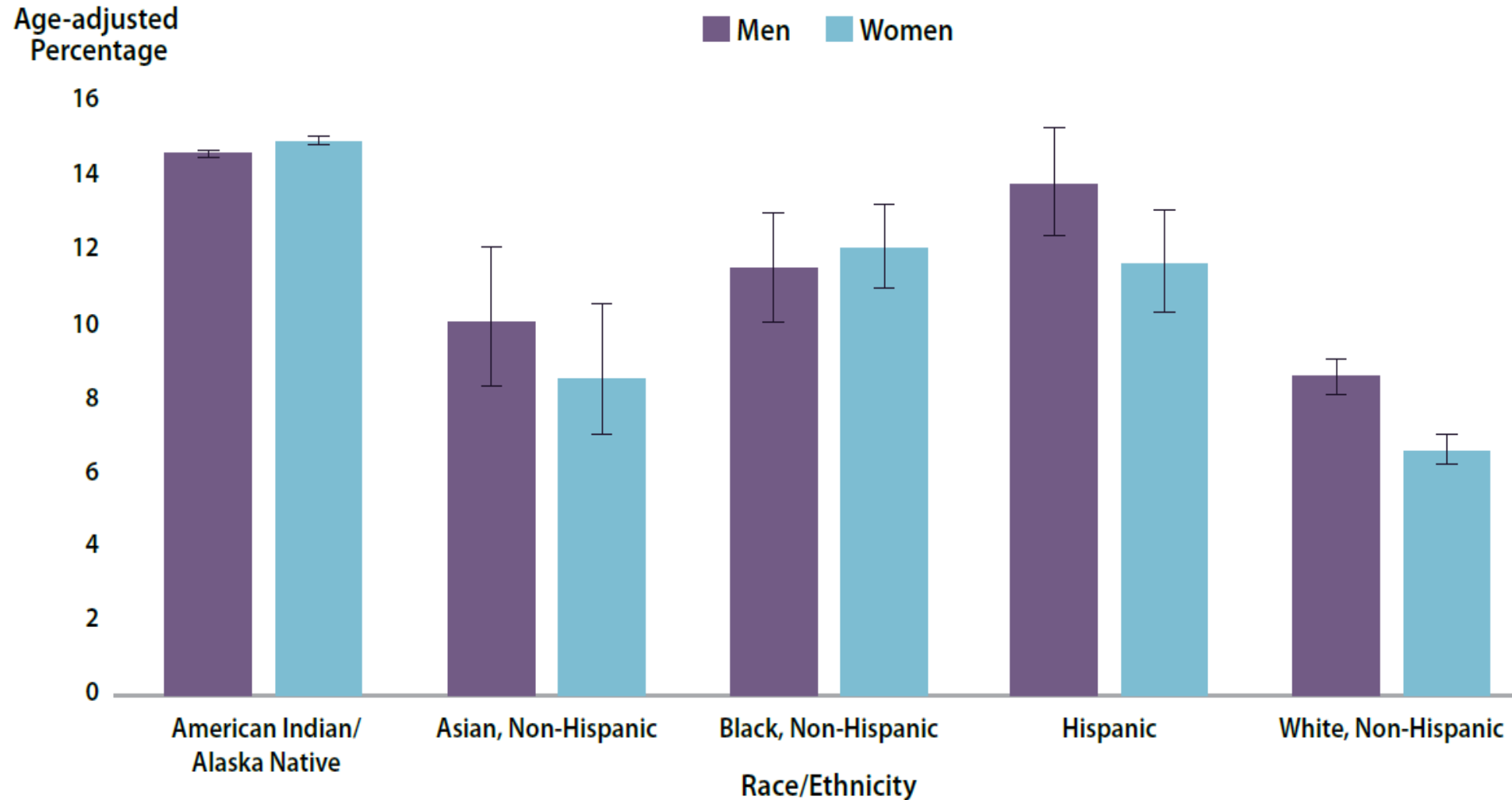
- **34.2 million people or 10.5% of US population**
- **34.1 million adults > 18 yrs or 13.0% of US adult population**
- **7.3 million adults undiagnosed, 21.4% of adults with diabetes**
- **26.8% of adults age 65 years and older have diabetes**

Centers for Disease Control and Prevention. National Diabetes Statistics Report, 2020. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Dept of Health and Human Services; 2020.

<https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf>

Diagnosed Diabetes Prevalence from the National Diabetes Statistics Reports, 2020

Figure 2. Age-adjusted estimated prevalence of diagnosed diabetes by race/ethnicity group and sex for adults aged 18 years or older, United States, 2017–2018

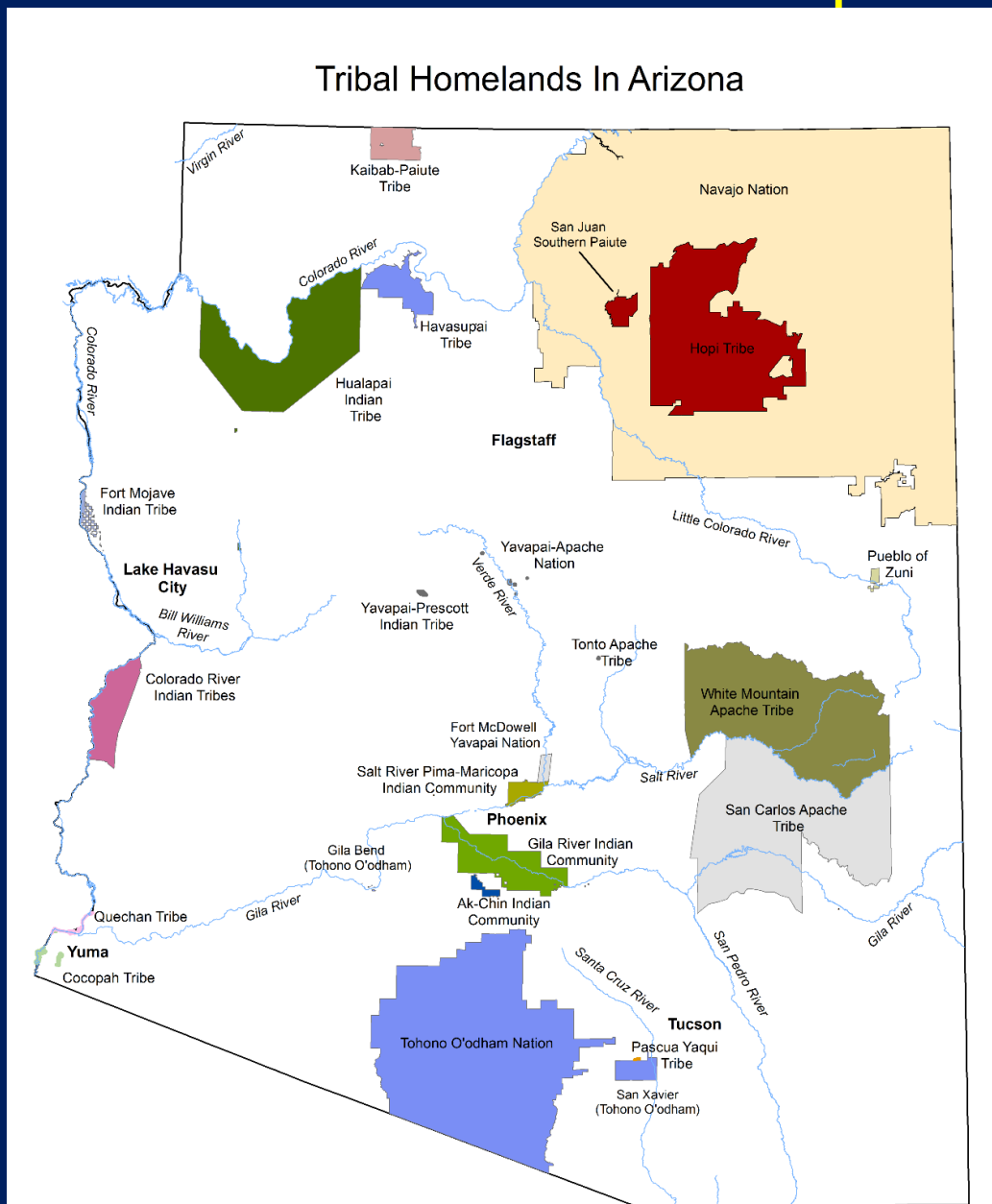


Note: Error bars represent upper and lower bounds of the 95% confidence interval.

Data sources: 2017–2018 National Health Interview Survey; 2017 Indian Health Service National Data Warehouse (for American Indian/Alaska Native group only).

Arizona Landscape

Ak Chin Indian Community
Chemehuevi Tribe
Cocopah Tribe
Colorado River Indian Tribes
Fort McDowell Yavapai Nation
Fort Mojave Indian Tribe
Gila River Indian Community
Havasupai Tribe
Hopi Tribe
Hualapai Tribe
Kaibab Paiute Tribe
Pasqua Yaqui Tribe



Pueblo of Zuni
Quechan Tribe
Salt River Pima-Maricopa Indian Community
San Carlos Apache Tribe
San Juan Southern Paiute Tribe
Tonto Apache Tribe
White Mountain Apache Tribe
Yavapai-Apache Nation
Yavapai-Prescott Indian Tribe
Tohono O'odham Nation
Navajo Nation

AI/AN in Arizona – CDC Survey

- 2017 Behavioral Risk Factor Surveillance System (BRFSS) data analysis; a landline and cellular telephone survey conducted by State Departments of Health, funded by the CDC (~15,000 respondents)
- Over sampling of AI/AN residents (self-reported categorization of race); 766 individuals (5.1% of surveyed; US percentage 2.3%)
- Compared to Whites; AI/AN respondents were
 - Younger (56.6% vs 41.9% < 45 yo; 11.7% vs 26.5% > 65 yo)
 - Less years of education (45.2% vs 63.9% with college/technical or higher)
 - Less annual income (49.2% vs 28.6% with < \$35,000/yr)
 - Less employment (45.8% vs 58.5%)
 - More access to health care coverage (74.1% vs 71.7%); attributed to IHS.

AI/AN in Arizona – CDC Survey: Summary

- 2017 Behavioral Risk Factor Surveillance System (BRFSS) data analysis; identified overweight/obesity-related metabolic consequences continues among AI/AN people in AZ.
 - Diabetes: 21.4% vs 8.0% (whites)
 - Overweight/obesity: 76.7% vs 63.7% (whites)
 - More HTN, hypercholesterolemia
 - Less physical activity
- What's needed are culturally-tailored approaches.
 - Understanding the health disparities and Tribal/traditional/cultural health practices
 - Integrating services with stakeholders; Tribal communities and Tribal/Federal/Urban facilities
 - Adequate and appropriate funding

Diagnostic Criteria for Diabetes Mellitus- 1997

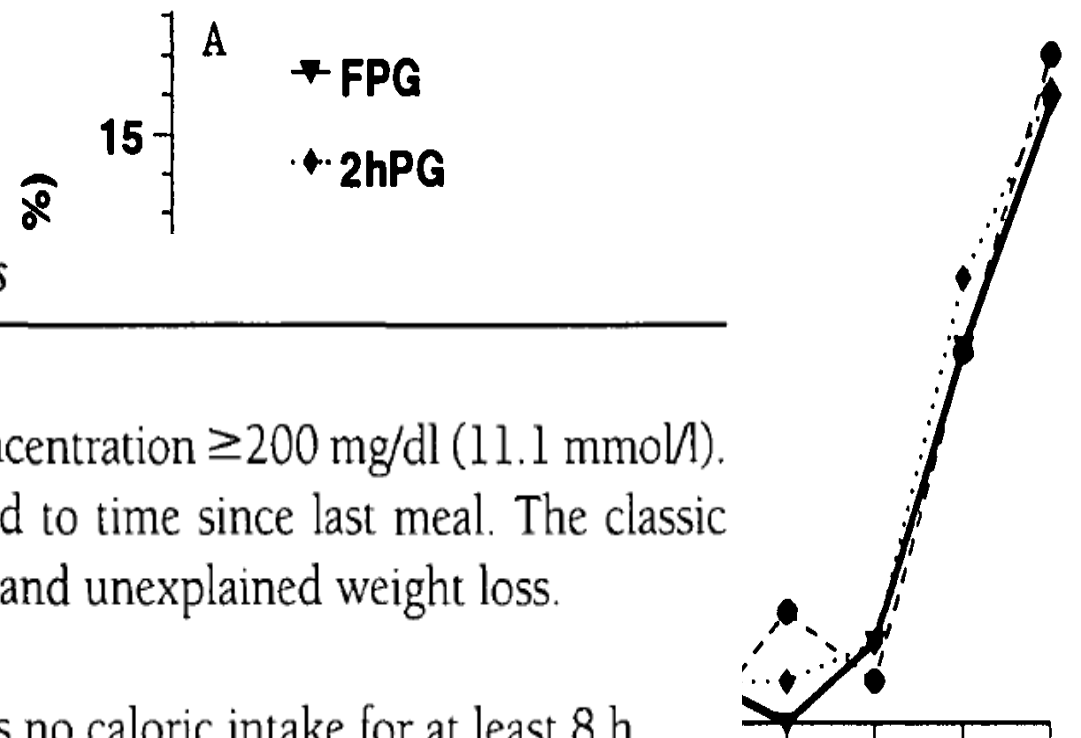


Table 5—FPG cutpoint Table 3—Criteria for the diagnosis of diabetes mellitus

Study and reference

Pima Indians (129)

Pima Indians (129)

Several Pacific populatio

NHANES III§

*The results for the receiver from the Pacific population not been published. †Equi for retinopathy from analy: III subjects ages 40–74 year ing to sampling plan (K. Fl

1. Symptoms of diabetes plus casual plasma glucose concentration ≥ 200 mg/dl (11.1 mmol/l). Casual is defined as any time of day without regard to time since last meal. The classic symptoms of diabetes include polyuria, polydipsia, and unexplained weight loss.

or

2. FPG ≥ 126 mg/dl (7.0 mmol/l). Fasting is defined as no caloric intake for at least 8 h.

or

3. 2hPG ≥ 200 mg/dl during an OGTT. The test should be performed as described by WHO (2), using a glucose load containing the equivalent of 75-g anhydrous glucose dissolved in water.

109- 116- 136- 226-
156- 185- 244- 364-
5.7- 6.0- 6.7- 9.5-
concentrations

McCance DR as diagnostic

In the absence of unequivocal hyperglycemia with acute metabolic decompensation, these criteria should be confirmed by repeat testing on a different day. The third measure (OGTT) is not recommended for routine clinical use.

Disorders of Glycemia: 1997 Guidelines

Types \ Stages	Normoglycemia	Hyperglycemia			
	Normal glucose regulation	Impaired Glucose Tolerance or Impaired Fasting Glucose	Diabetes Mellitus		
			Not insulin requiring	Insulin requiring for control	Insulin requiring for survival
Type 1*	←—————→				
Type 2	←————→				
Other Specific Types**	←————→				
Gestational Diabetes **	←————→				

Figure 1—Disorders of glycemia: etiologic types and stages. *Even after presenting in ketoacidosis, these patients can briefly return to normoglycemia without requiring continuous therapy (i.e., “honeymoon” remission). **In rare instances, patients in these categories (e.g., Vacor toxicity, type 1 diabetes presenting in pregnancy) may require insulin for survival.

Progression to Diabetes

TABLE 2

Summary of studies and cumulative number of NIDDM events in participants with IGT at baseline

Study	Number of participants with IGT	Number of visits	Years to first post-IGT visit	IGT to NIDDM progression	Total person-years	Incidence rate (per 1,000 person-years)	95% CI
Baltimore Longitudinal Study of Aging (BLSA)	675	4.2 ± 2.2 (2 to 8)	3.8 ± 2.9 (1.2 to 9.4)	191 (28)	5,337	35.8 ± 2.6	30.7–40.8
Rancho Bernardo Study (RBS)	186	2	8.2 ± 0.8 (7 to 9)	49 (26)	1,227	40.0 ± 5.7	28.8–51.2
San Antonio Heart Study (SAHS)	353	2	8.2 ± 0.6 (8 to 9)	107 (30)	2,463	43.4 ± 4.2	35.2–51.6
Nauru Study	305	2.6 ± 0.7 (2 to 4)	6.2 ± 2.2 (5.0 to 12.0)	142 (47)	2,262	62.8 ± 5.3	52.5–73.1
San Luis Valley Diabetes Study (SLVDS)	177	3.1 ± 0.9 (2 to 4)	1.9 ± 0.8 (1.0 to 3.2)	41 (23)	562	72.9 ± 11.4	50.6–95.2
Pima Indian Study	693	5.2 ± 3.0 (2 to 11)	3.9 ± 3.6 (1.8 to 11.4)	430 (62)	4,924	87.3 ± 4.2	79.0–95.6

Data are *n* (%), means ± SD (5th to 95th percentiles), or, for incidence rate, means ± SE. Person-years assume an average NIDDM progression time of half an interval since the last visit; incidence rates may not be exact because of rounding.

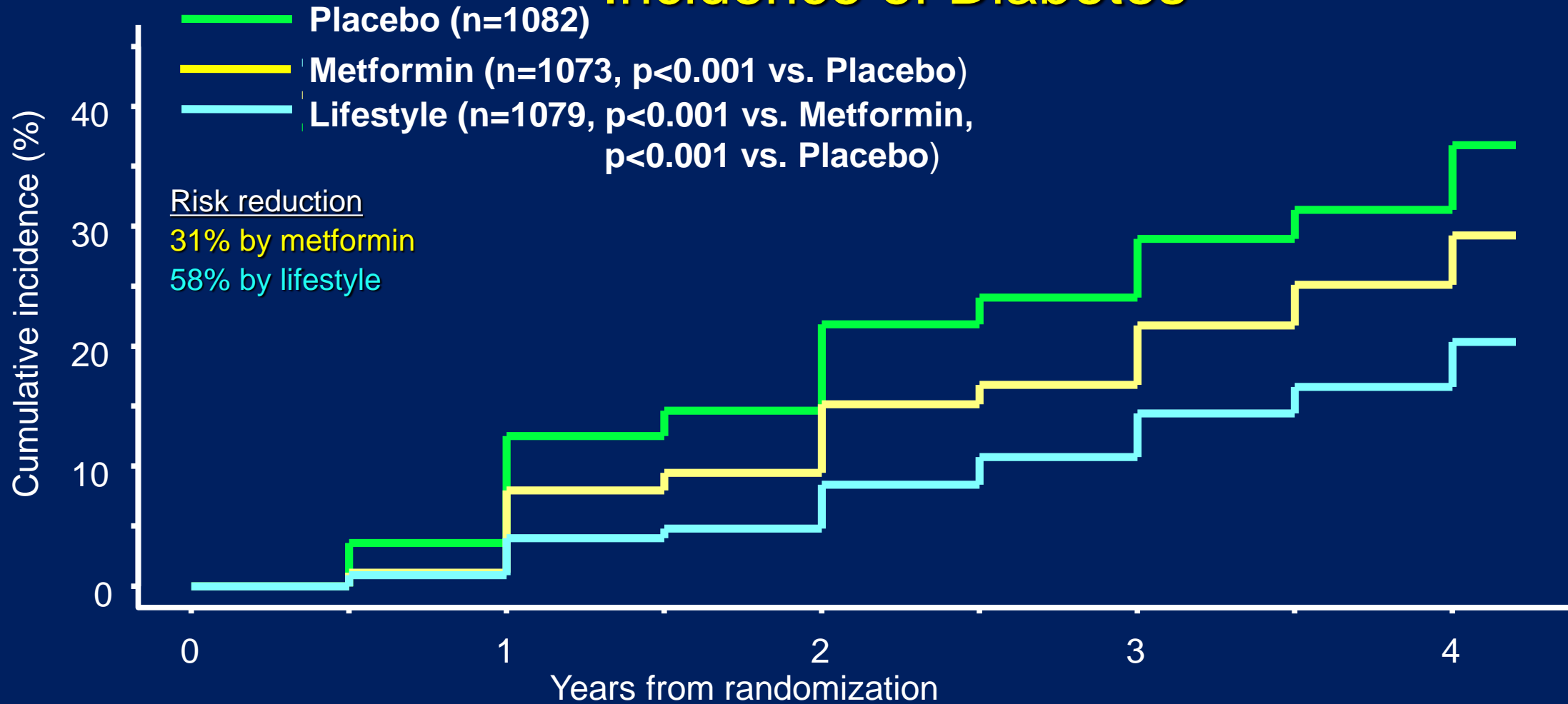
Progression to Diabetes

TABLE 4
Study-specific IGT-to-NIDDM progression rates by fasting and 2-h postchallenge glucose levels

Study	Fasting glucose (mmol/l)	2-h postchallenge glucose (mmol/l)	<i>n/N</i> (progression rate)	Total patient-years	Incidence rate (per 1,000 person-years)
Pima Indian Study*	<7.8	7.8–11.0	132/245 (54.6)	1,426.3	92.5
		8.9–11.0	68/109 (62.4)	557.7	121.9
		9.7–11.0	43/64 (67.2)	275.4	156.1
	5.6–7.7	7.8–11.0	91/154 (59.1)	867.3	104.9
		8.9–11.0	50/81 (61.7)	402.7	124.2
		9.7–11.0	33/53 (62.3)	236.5	139.5
	6.1–7.7	7.8–11.0	47/68 (69.1)	330.0	142.4
		8.9–11.0	27/42 (64.3)	192.7	140.1
		9.7–11.0	19/30 (63.3)	124.5	152.6
All studies combined*	<7.8	7.8–11.0	664/1941 (34.2)	13,276	50.0
		8.9–11.0	400/907 (44.1)	5,658.7	70.7
		9.7–11.0	220/450 (48.9)	3,186.1	69.0
	5.6–7.7	7.8–11.0	411/966 (42.5)	6,192.8	66.4
		8.9–11.0	264/520 (50.8)	3,034.2	87.0
		9.7–11.0	160/280 (57.1)	1,393.0	114.9
	6.1–7.7	7.8–11.0	198/36 (55.0)	1,873.0	105.7
		8.9–11.0	129/203 (63.5)	951.9	135.5
		9.7–11.0	85/125 (68.0)	497.6	170.8

*Fasting plasma glucose levels were measured in the Pima Study only in recent years; this table includes only the Pima sample ($n = 245$) with available fasting plasma glucose measurements.

Diabetes Prevention Program (DPP) Incidence of Diabetes



The epidemiological studies from the Gila River Indian Community has contributed to the understanding of type 2 diabetes and provided the basis for national intervention efforts.

Lowering the Risk of Diabetes Complications

Foremost: Hyperglycemia management, A1C < 7 (individualize)

Addressing other co-morbid conditions

- **Blood pressure < 140/90**
- **Statin therapy for high risk; targeting LDL Cholesterol**
- **RAS Inhibitor**
- **Anti-platelet treatment**
- **Smoking cessation**
- **Lifestyle Changes for weight loss**
- **Recommended screenings and early treatment**

Complications and Co-morbidities of Diabetes

- **Macrovascular Complications**

Heart disease, peripheral arterial, CHF, and stroke

- **Microvascular Complications**

Retinopathy: Blindness, eye problems

Nephropathy: CKD and ESRD

Neuropathy

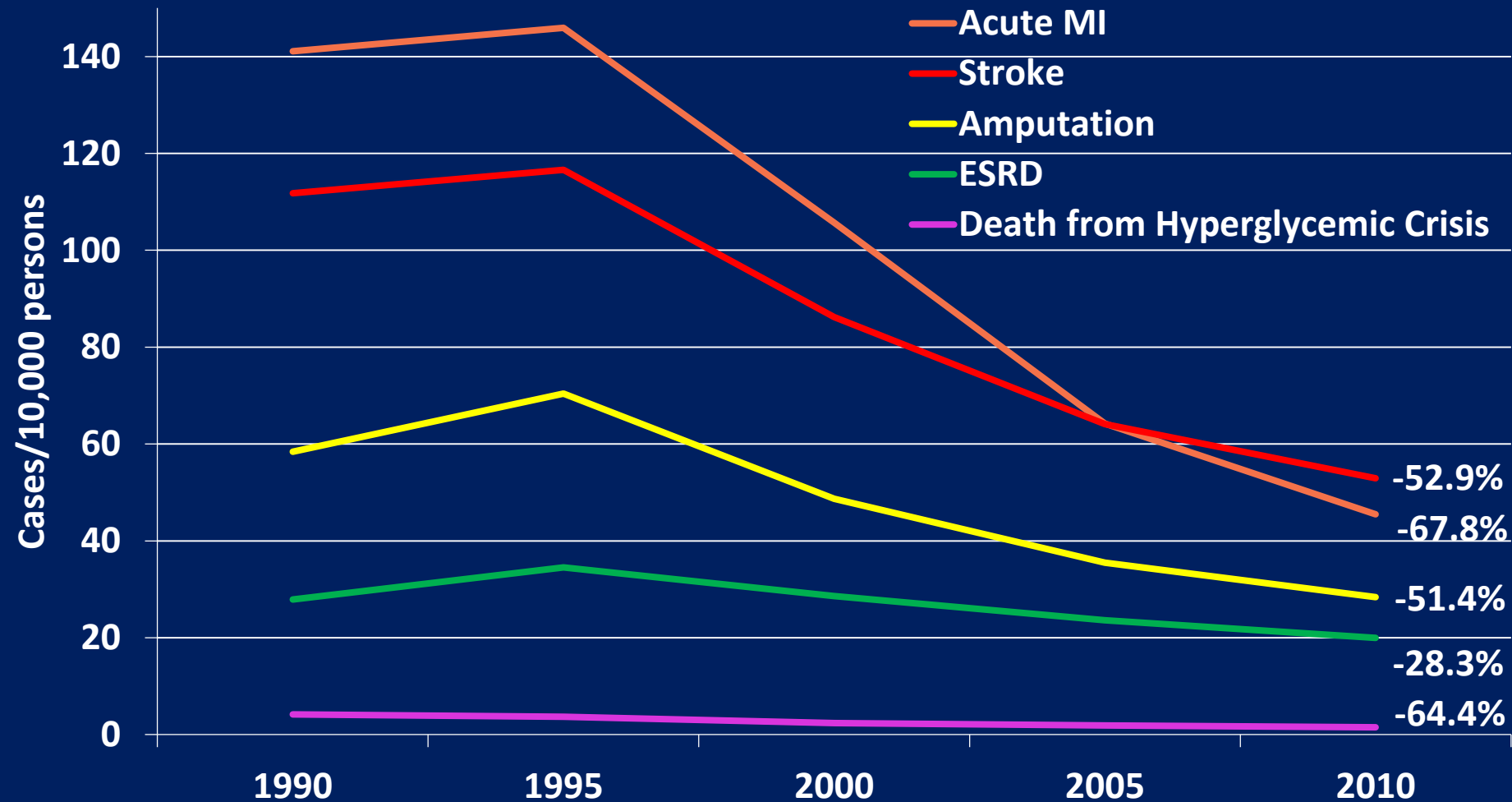
- **Foot Disease**

Ulcers and Amputations

- **Co-morbid conditions**

Hypertension; Hyperlipidemia; Obesity; NASH; Sleep Apnea

Trends in age-standardized rates of diabetes-related complications among U.S. adults with diabetes, 1990-2010



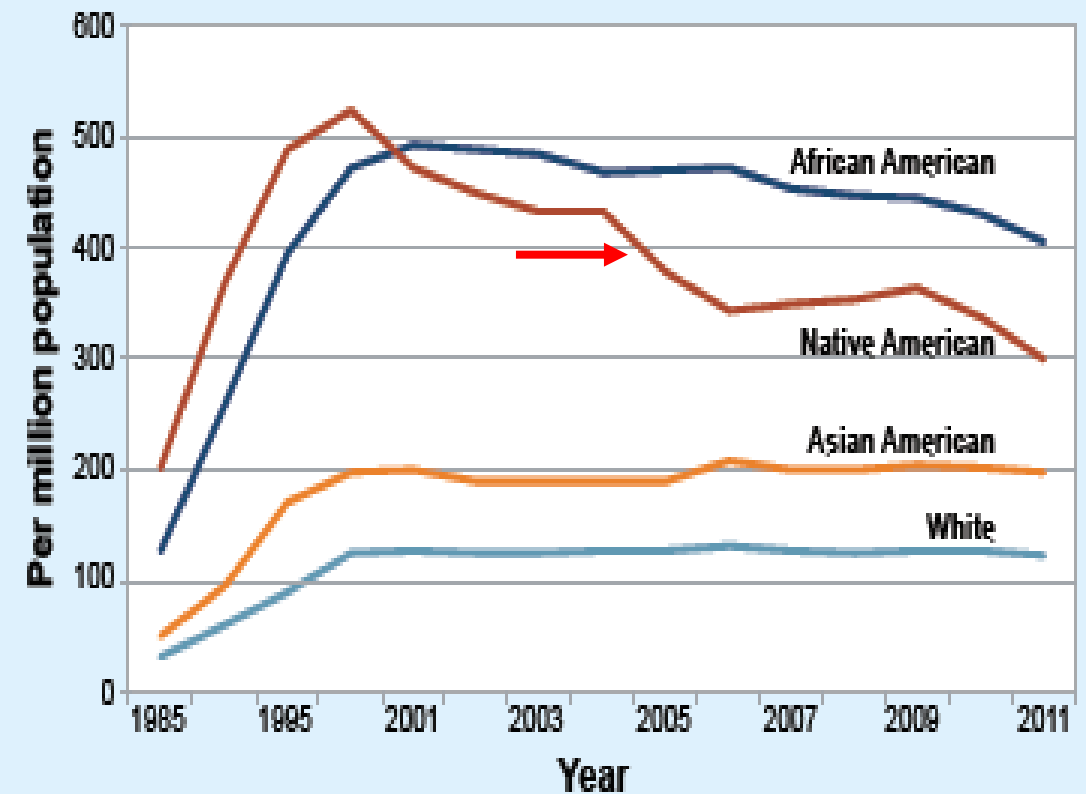
Changes in Diabetes-Related Complications in the United States, 1990-2010

- Findings reflect a combination of advances in acute clinical care, improvements in the performance of health care system, and health promotion efforts directed at patients with diabetes.
- Conclusion: Rate of diabetes-related complications declined substantially in the past 2 decades, but large burden of diabetes persists because of increase in the prevalence of disease

A Decade of Dramatic Reduction in Rates of ESRD

- End Stage Renal Disease (ESRD) in AI/AN persons with diabetes has been reduced by over 40%.
- This reduction is greater than that achieved in any other racial group.
- The average medical costs of one year of care of a patient on dialysis in 2011 dollars was \$88,000.
- Estimated savings to Medicare of \$430 to \$520 million over a 10 year period (2006-2015; ASPE Issue Brief, aspe.hhs.gov).

Figure 8. Incidence Rates of ESRD due to Diabetes, by Race



Source: United States Renal Data System 2013

Reduction of Diabetes ESRD in AI/AN: Addressing Multiple Factors

- Blood Pressure Control
 - Average BP: 132/76 mmHg in 2016
- Blood Sugar Control
 - Mean A1c level decreased by 10% between 1996-2016
- Use of Renin Angiotensin System Inhibitors
 - 76% of patients prescribed medications in 2014
 - 36% higher than in NHANES cohort (2009-2014)
- Increase Screening for diabetes nephropathy
 - 62% of patients over the age of 65 yrs had UACR test in 2015
 - Compared with 40% among Medicare patients with diabetes in 2013

Improvement in DM Retinopathy among AI/AN

- IHS Joslin Vision Network Teleophthalmology Program (JVN)
 - Established in 2000 to increase retinal examination rates
 - Nonmydriatic fundus photography digital imaging system at IHS and Tribal facilities (mobile units also)
 - Central reading center at Phoenix Indian Medical Center
 - In 2019, 99 active sites across 23 States and nearly 30,000 patients examined; cumulative estimate- JVN serves 25% of the IHS user population
- Outcomes
 - 2011-2016 retrospective analysis of approximately 54,000 patient images, revealed DR and ME rate of 17.7% with sight threatening retinopathy of 4.2%.
 - These prevalence rates are slightly lower than national average.
 - The rate of DR in AI/AN appears to have decreased by nearly 50% as compared to historical data from the 1980-1990 epidemiological studies.

Bursell S-E, et al. Prevalence of diabetic retinopathy and diabetic macular edema in a primary care-based teleophthalmology program for AI and AN. PLoS One. <https://doi.org/10.1371/journal.pone.0198551>

Fonda SJ et al. The Indian Health Service Primary Care-Based Teleophthalmology Program for Diabetic Eye Disease Surveillance and Management. Telemed J E Health. 2020. doi:10.1089/tmj2019.0281.

Strong Heart Study (SHS)

- Longitudinal Study of CVD among American Indians initiated in 1988
 - 4549 participants, aged 45-74 year, ~60% female at baseline
 - Follow up examinations; SHS 1992-95 and 1996-2000
 - 13 communities in Arizona (Ak-Chin Tohono O'odham-Pima/Papago, Gila River Pima-Maricopa, and Salt River Pima-Maricopa Tribes); Oklahoma (Apache, Caddo, Comanche, Delaware, Fort Sill Apache, Kiowa, Wichita Tribes); and North and South Dakota (Cheyenne River Sioux, Oglala Sioux, Spirit Lake Sioux)
- Primary Outcomes: CVD (MI, Stroke, CHD, Congestive Heart Failure) Incidence and prevalence and mortality; PCI
- Secondary Outcomes: CVD risk factors
- Comparative population studies: Atherosclerosis Risk in Communities (ARIC- 25% blacks and 75%whites); Cardiovascular Health Study (CHS- primarily white)

Strong Heart Study (SHS)

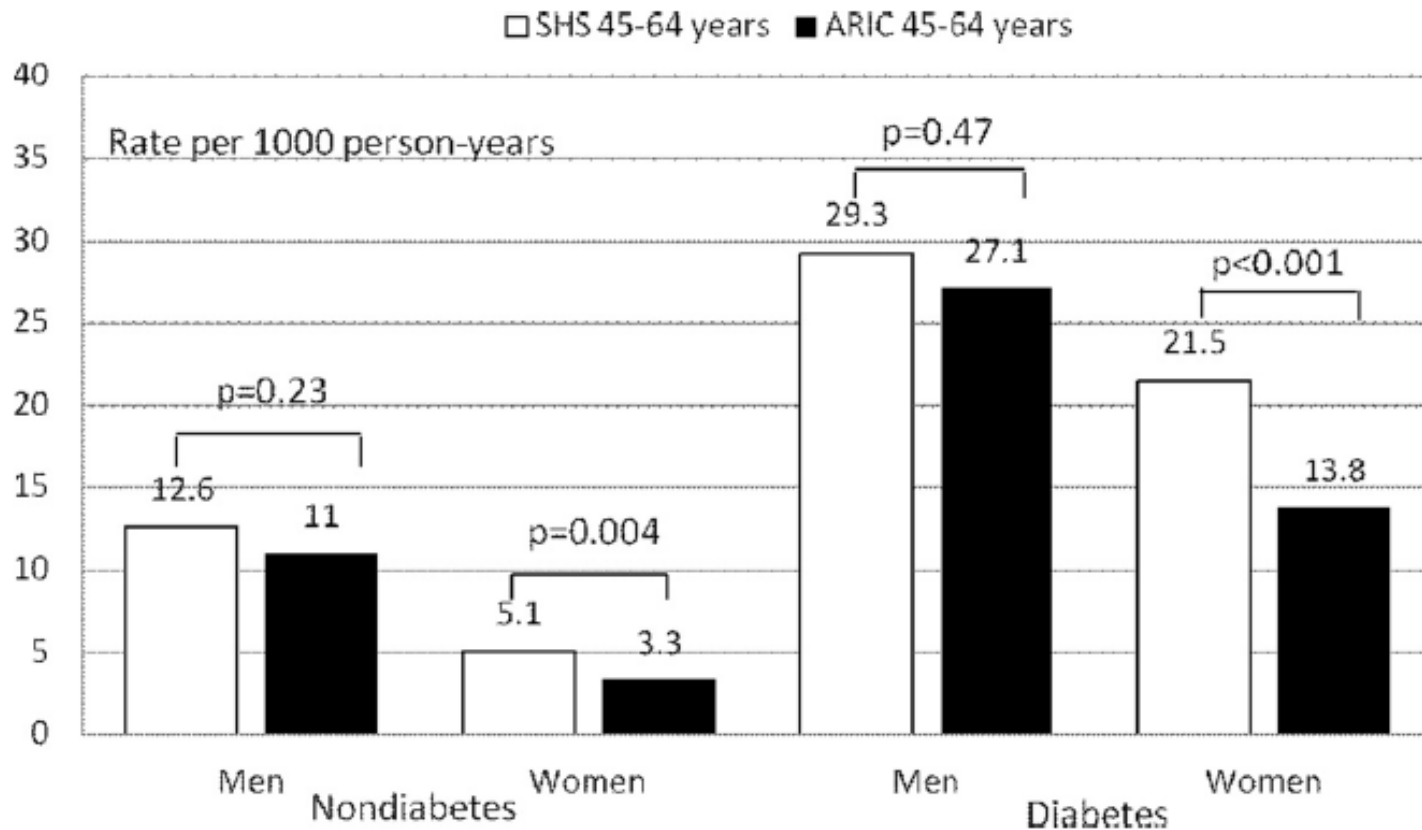


FIG. 1. Crude incidence rates (per 1000 person-years) of CHD (fatal and nonfatal) in diabetic and nondiabetic American Indians, ages 45–64 yr, in the SHS compared with those in the same age group from the ARIC Study (22). Average follow-up was 11 yr.

Risk Factor	Women		Men	
	Hazard Rate Ratio	95% CI	Hazard Rate Ratio	95% CI
Hypertension (Y/N)	2.48	1.75–3.52	1.67	1.37–2.64
Current smoking (Y/N)	1.18	0.81–1.73	1.20	0.88–1.63
LDL cholesterol	1.43	0.94–2.17	2.13	1.45–3.13
HDL cholesterol	0.52	0.32–0.84	0.55	0.36–0.84
Triglycerides	1.58	1.33–1.88	1.08	0.97–1.22
Diabetes (DM vs IGT + NGT)	3.50	2.34–5.23	2.16	1.58–2.95
Insulin	1.13	0.94–1.36	1.24	1.06–1.45
Albuminuria				
Micro vs normal	2.38	1.55–3.67	1.65	1.12–2.43
Macro vs normal	5.36	3.48–8.27	3.81	2.54–5.71
Percent body fat	0.46	0.32–0.72	0.64	0.57–1.25
Waist	0.94	0.61–1.46	0.97	0.66–1.43
Fibrinogen	2.38	1.64–3.46	1.84	1.35–2.50
Full-blooded Indian (Y/N)	1.06	0.70–1.59	0.94	0.66–1.32

Mean of the lowest quartile group vs mean of the upper quartile group: 156 vs 74 mg/dL in women, 158 vs 74 mg/dL in men for LDL cholesterol; 66 vs 34 mg/dL in women, 61 vs 30 mg/dL in men for HDL cholesterol; 278 vs 66 mg/dL in women, 306 vs 61 mg/dL in men for triglycerides; 42.29 vs 7.31 μ U/mL in women, 39.90 vs 5.24 μ U/mL in men for insulin; 50% vs 32% in women, 37% vs 21% in men for percent body fat; 127 vs 88 cm in women, 120 vs 88 cm in men for waist; and 416 vs 222 mg/dL in women, 387 vs 205 mg/dL in men for fibrinogen. DM indicates diabetes; IGT, impaired glucose tolerance; and NGT, normal glucose tolerance.

Table 4. Age- and Center-Adjusted Hazard Rate Ratios for Fatal and Nonfatal CVD by Major CVD Risk Factors: Strong Heart Study

Howard BV et al. Rising Tide of Cardiovascular Disease in American Indians: The Strong Heart Study. *Circulation* 1999;99(18):2389-95.

Xu J et al. Differences in Risk Factors for Coronary Heart Disease among Diabetic and Nondiabetic Individuals from a Population with High Rates of Diabetes: The Strong Heart Study. *J Clin Endocrinol Metab* 2012;97:3766-74.

Strong Heart Study (SHS) and Strong Heart Family Study (SHFS)

- The SHS (Strong Heart Study) is the only population-based cohort study that allows longitudinal analysis of age-specific cardiovascular disease outcomes in American Indians.
- Over a 25-year period, cardiovascular disease incidence decreased among American Indian women and men from 3 geographic regions who were aged 30 to 85 during follow-up.
- Over the same period, cardiovascular disease mortality decreased in men but not in women.

- Cardiovascular disease appears to be declining in the American Indian communities represented in the SHS, but women may have experienced less improvement in cardiovascular disease mortality than men.
- The SHS protocols included medical referral for management of cardiovascular disease risk factors, and so improvement observed in cohort participants may not reflect the experience of other American Indian people across the United States.

National Diabetes Statistics Reports: 2014,2017,2020

Prevalence of Prediabetes Among Adults

- An estimated 88 million adults aged 18 years or older had prediabetes in 2018 (Table 3).
- Among US adults aged 18 years or older, crude estimates for 2013–2016 were:
 - » 34.5% of all US adults had prediabetes, based on their fasting glucose or A1C level (Table 3).
 - » 10.5% of adults had prediabetes based on both elevated fasting plasma glucose and A1C levels ([Appendix Table 5](#)).
 - » 15.3% of adults with prediabetes reported being told by a health professional that they had this condition (Table 3).

Prevalence of Prediabetes

- An estimated 33.9% of U.S. adults aged 18 years or older (84.1 million people) had prediabetes in 2015, based on their fasting glucose or A1C level. Nearly half (48.3%) of adults aged 65 years or older had prediabetes (Table 3) ([Methods](#)).
- Among adults with prediabetes, 11.6% reported being told by a health professional that they had this condition (Table 3).
- Age-adjusted data for 2011–2014 indicated that more men (36.6%) than women (29.3%) had prediabetes. Prevalence of prediabetes was similar among racial and ethnic groups (see [Table 3a](#) in the Appendix for more details).

Prediabetes among people aged 20 years or older, United States, 2012

- In 2009–2012, based on fasting glucose or A1C levels, 37% of U.S. adults aged 20 years or older had prediabetes (51% of those aged 65 years or older). Applying this percentage to the entire U.S. population in 2012 yields an estimated 86 million Americans aged 20 years or older with prediabetes.
- On the basis of fasting glucose or A1C levels, and after adjusting for population age differences, the percentage of U.S. adults aged 20 years or older with prediabetes in 2009–2012 was similar for non-Hispanic whites (35%), non-Hispanic blacks (39%), and Hispanics (38%).

New directions in incidence and prevalence of diagnosed diabetes in the USA

Stephen R Benoit,¹ Israel Hora, Ann L Albright, Edward W Gregg²

BMJ Open Diab Res Care 2019;**7**:e000657. doi:10.1136/bmjdr-2019-000657

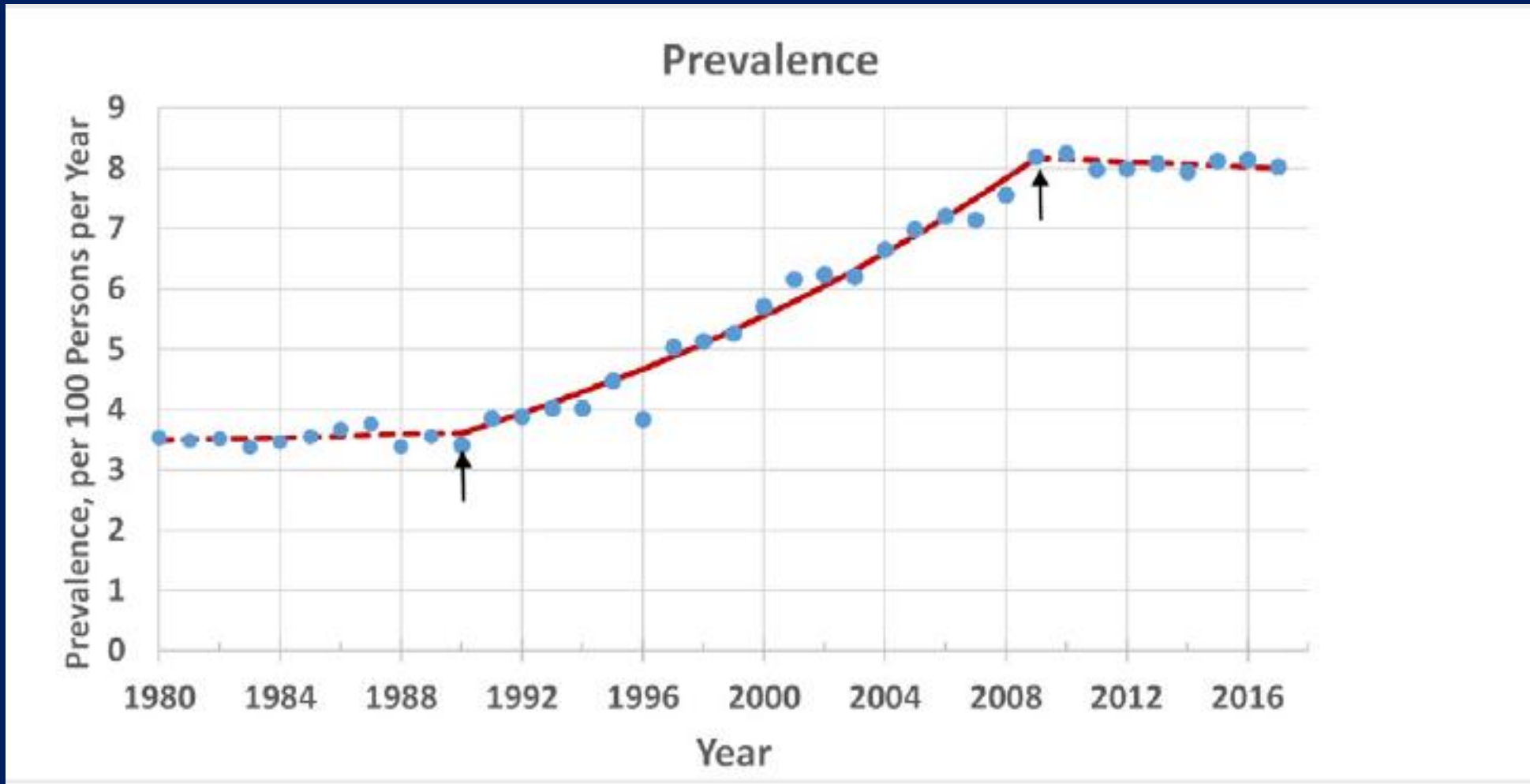


Figure 1 Trends in age-adjusted diagnosed diabetes prevalence and incidence among adults aged 18–79 years, 1980–2017. Data are from the Centers for Disease Control and Prevention’s (CDC) National Health Interview Survey.

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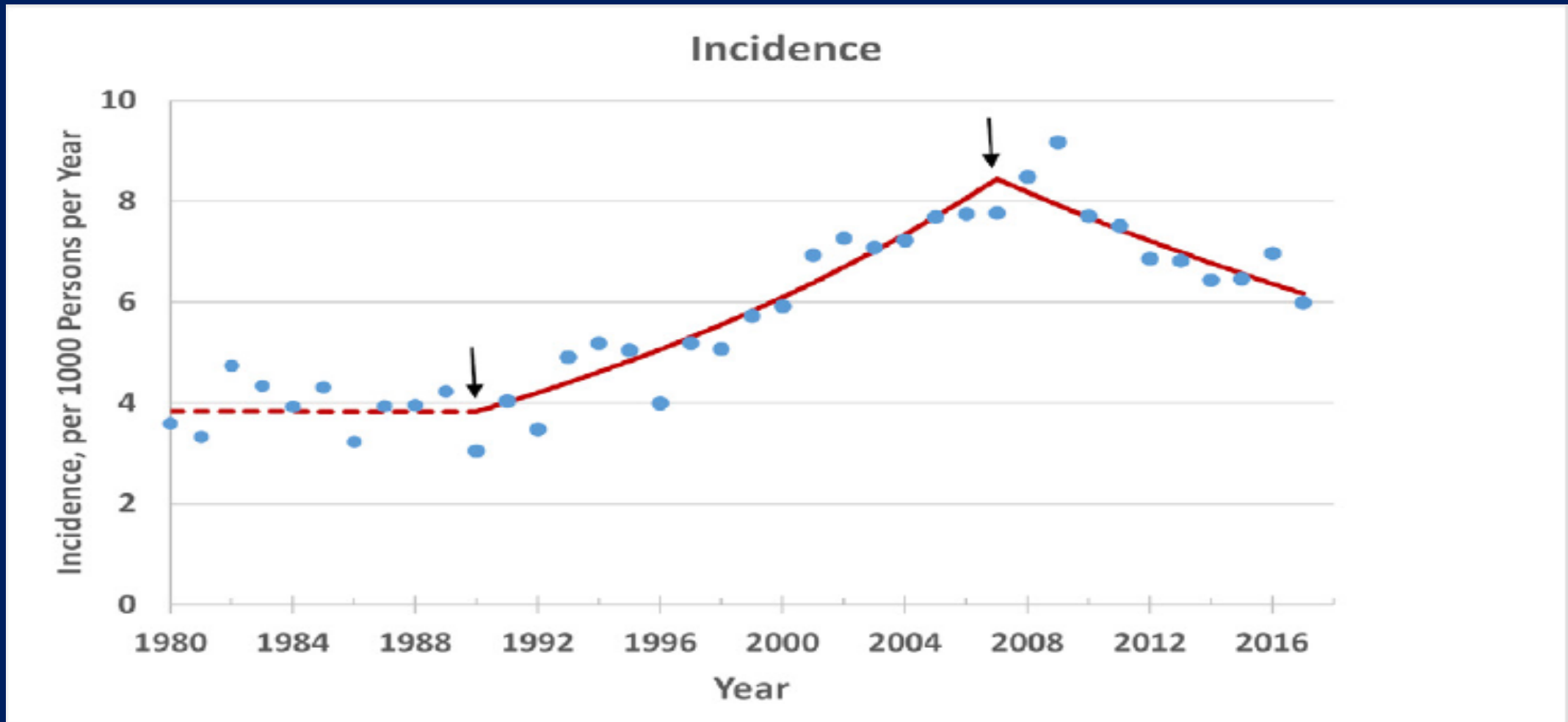
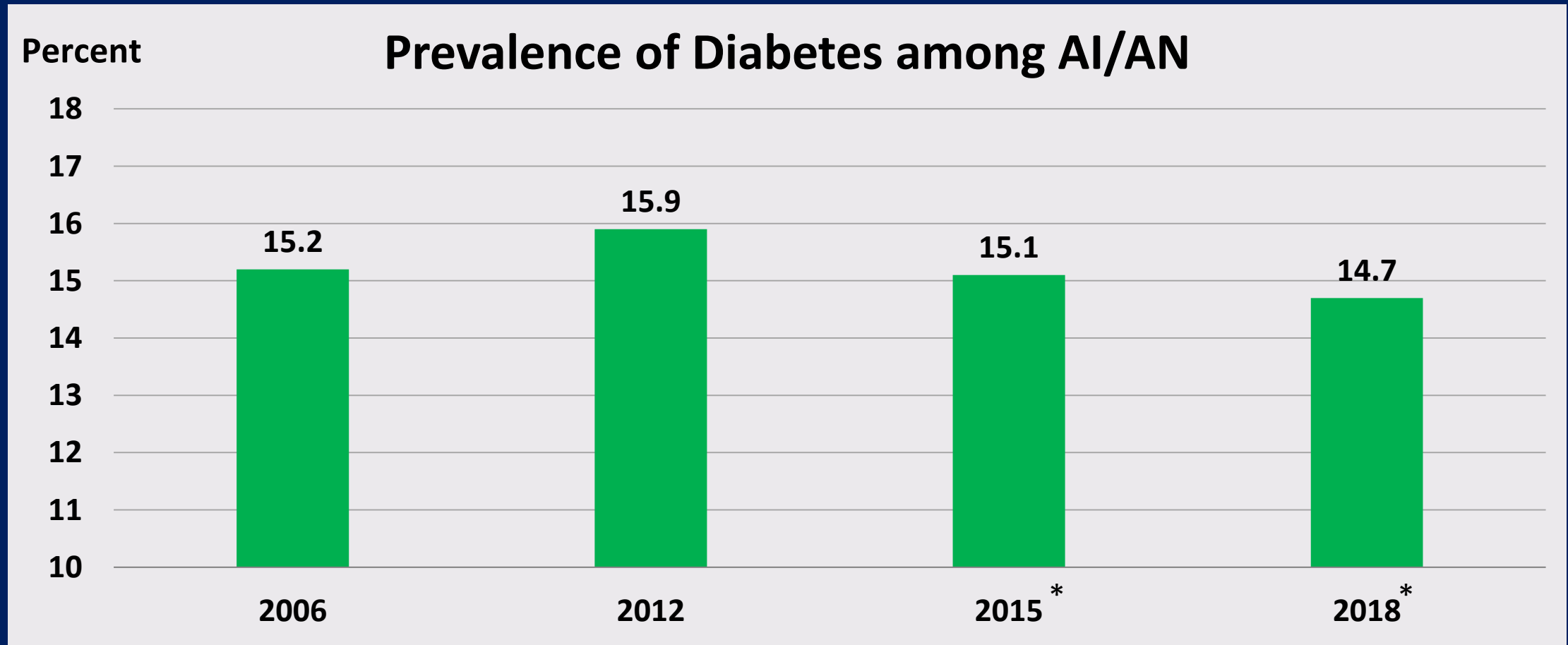


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Diagnosed Diabetes Prevalence Trends from National Diabetes Statistics Reports (2008, 2014, 2017, 2020)

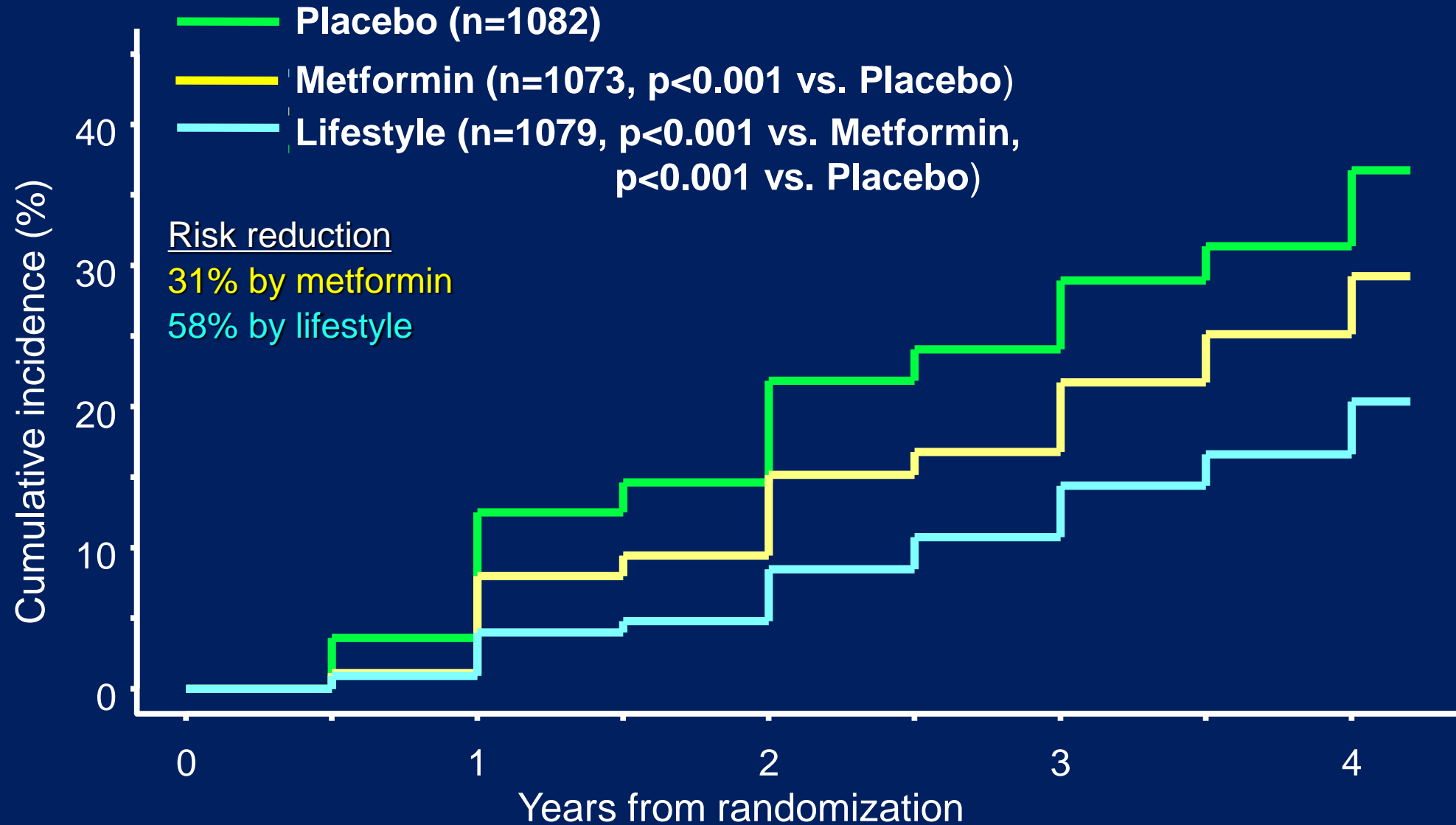


* Adults 18 years and older; previous years were 20 years and older

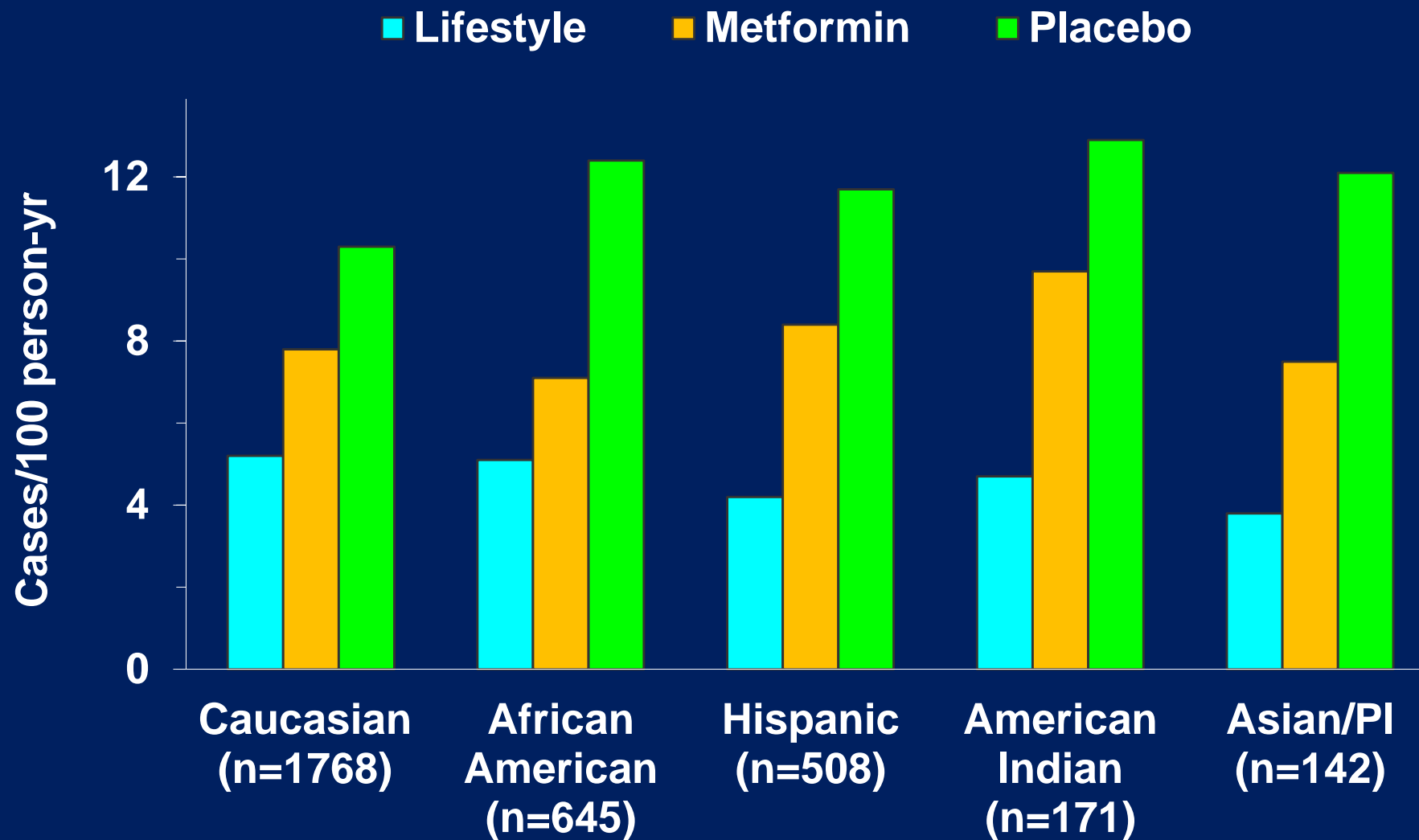
Diabetes Prevention Program and Diabetes Prevention Program Outcomes Study

- NIH-Study to determine if diabetes can be prevented and/or delayed in subjects at high risk for diabetes (participants with IGT and from high risk populations)
- Interventions:
 - Intensive Lifestyle (weight loss >7% and exercise >150 min/week from baseline; N=1079)
 - Metformin 850 mg BID (N=1073) and Placebo (N=1082)
- Baseline Characteristics (3234 cohort):
 - Mean BMI: 35 women, 32 for men; except Asian/Pacific Islanders, 2/3 with family history of DM, 45% from minority populations
 - 1/3 with hypercholesterolemia except American Indians; 30% with HTN;
 - Glycemia: FBG – 106; 2 Hr PP – 165; HbA1c - 5.9% (nearly 30% of cohort with HbA1c > 6.1%)

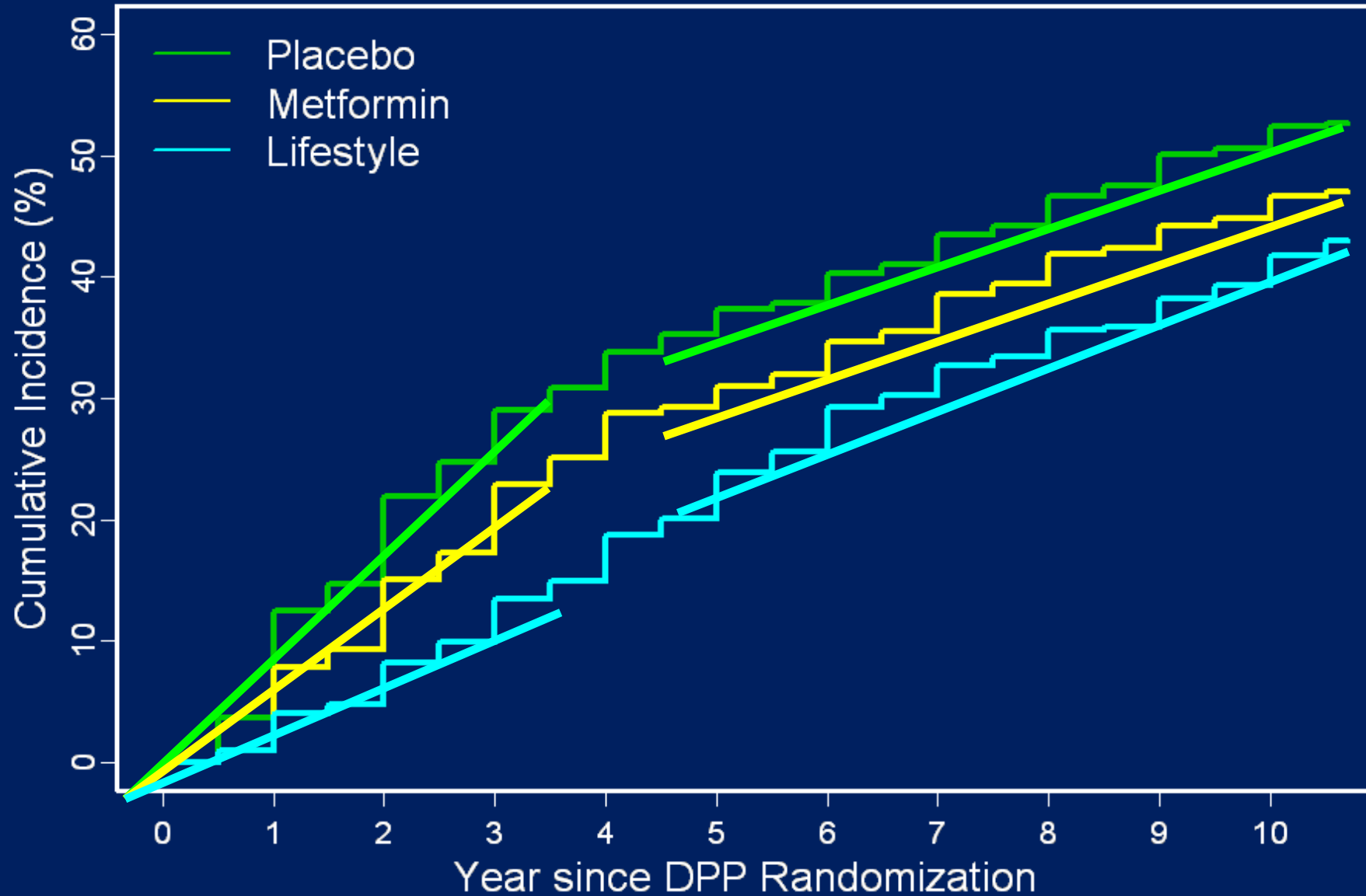
DPP Incidence of Diabetes



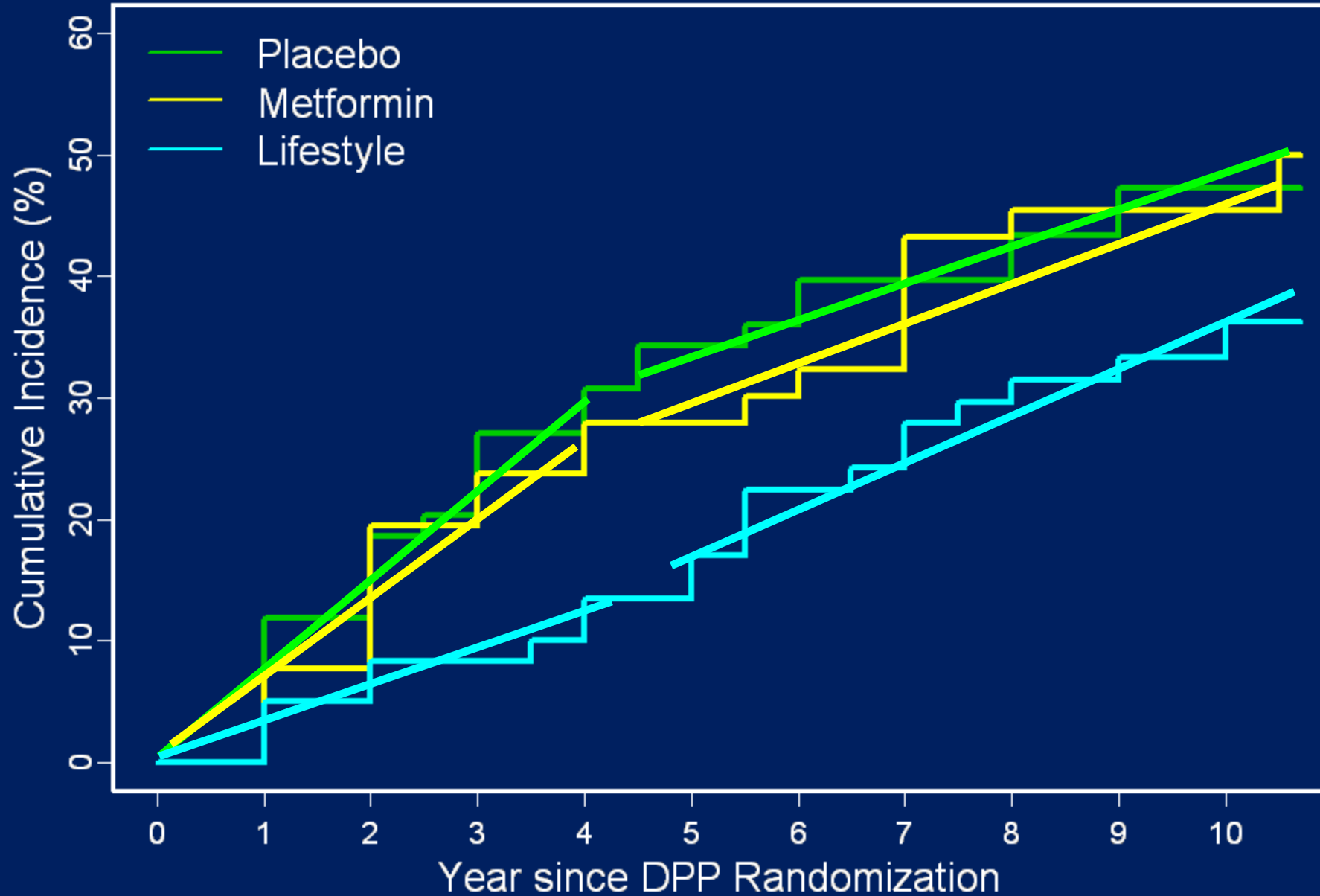
Diabetes Incidence Rates by Ethnicity



Incidence of Diabetes – Overall



AI Incidence of Diabetes – Overall



Subgroups that benefited from DPP Interventions: 15 Year Follow Up

- Intensive Lifestyle Intervention
 - Everyone (all ethnicities; sizes; ages)
 - Greater class attendance (higher participation rate)
 - More weight loss (1kg = 16% RRR)
 - More weight loss maintenance
- Metformin
 - Younger subjects (<60 yrs old)
 - Greater BMI (>35)
 - History of GDM
 - Higher Fasting Plasma Glucose and A1c levels

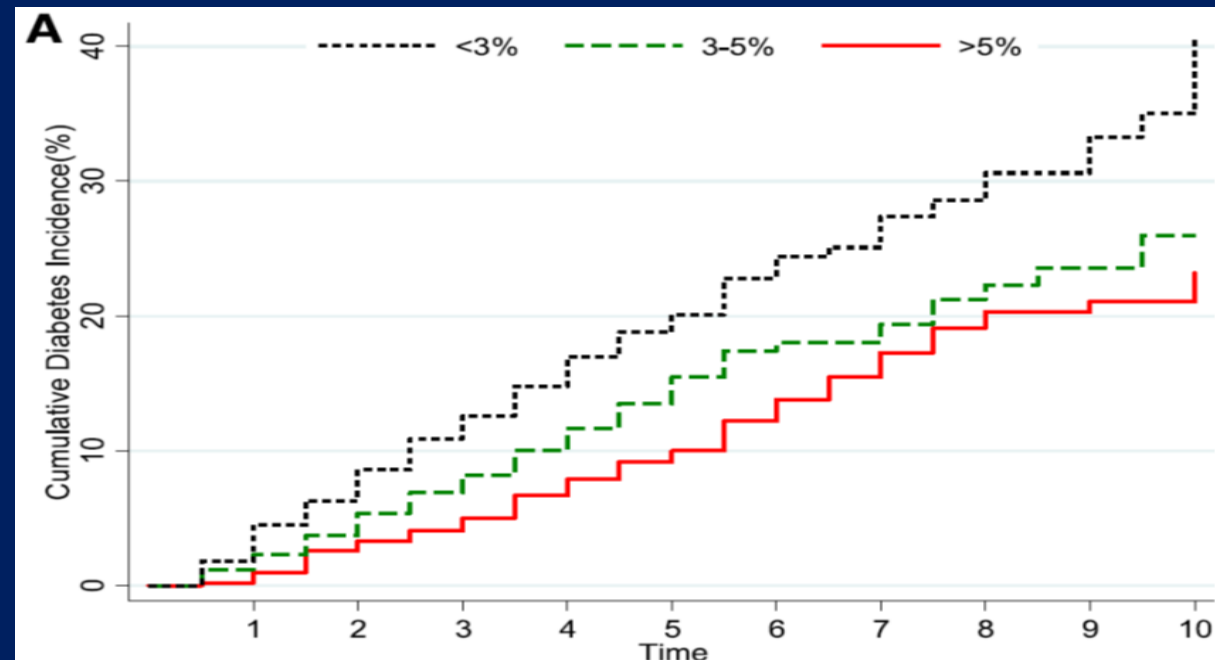
DPP Research Group. Identification of Subgroups That Benefited Most in the Diabetes Prevention Program and Diabetes Prevention Program Outcomes Study. *Diabetes Care* 2019;42:601-608.

DPP Research Group. Long-term Effects of Lifestyle Intervention or Metformin on Diabetes Development and Microvascular Complications: the DPP Outcomes Study. *Lancet Diabetes Endocrinol* 2015;3(11):866-875.

The Special Diabetes Program for Indians Diabetes: Diabetes Prevention Demonstration Project

- Enrolled approximately 8,650 individuals with prediabetes across 36 sites funded by the Special Diabetes Program for Indians.
- Instituted community-tailored Native Lifestyle Balance Curriculum (modified DPP Lifestyle curriculum - 16 sessions over 6 months; monthly maintenance thereafter; classes and individuals sessions).
- No medication treatment; no placebo group
- Outcomes measured every 6-months
 - Diabetes development (FPG, A1c, confirmation OGTT if needed)
 - Weight loss and exercise monitoring
 - Blood Pressure and Lipid profiles
 - Other medication starts or discontinue
- Initial results of SDPI-DP showed 6.8%/year diabetes incidence rate for the entire cohort; historical comparison to DPP Intensive Lifestyle group rate of 4.8%/year and placebo rate of 11%/year.

Long-term Outcomes of Lifestyle Intervention to Prevent Diabetes in American Indian and Alaska Native Communities: The Special Diabetes Program for Indians Diabetes Prevention Program



- Summary:
 - Lifestyle Intervention Curriculum can be implemented in native communities.
 - Less diabetes incidence with more weight loss and remission to Normal Glucose Regulation
 - More weight loss associated with higher participation rate
- Challenges: High attrition rate after initial 16 sessions of the curriculum

Objectives

- Recognize contributions of research in AI/AN populations to the understanding of type 2 diabetes
- Review current trends in diabetes prevalence and complications
- Assess interventions in AI/AN patients with diabetes and prediabetes

Thank you for your attention

Questions or Comments?