The Diabetes Prevention Program

A Randomized Clinical Trial to Prevent Type 2 Diabetes in Persons at High Risk

The DPP Research Group

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Central Resources

Lifestyle core	Univ. Pittsburgh
Medication resource group	Albert Einstein
Central biochemistry lab	Univ. Washington
ECG reading center	Wake Forest Univ.
Carotid US reading center	New England Medical Center
CT scan reading center	Univ. of Colorado Health Sciences Center
Nutrition coding center	Univ. South Carolina
Quality of well being center	Univ. California San Diego
Drug distribution center	McKesson Biosciences
Community outreach/media	Matthews Media Group
Clinical monitoring group	ACRN

Sponsors

- National Institute of Diabetes & Digestive & Kidney Diseases
- Other NIH Institutes, Offices
  - National Center on Minority Health and Health Disparities
  - National Institute of Child Health and Human Development
  - National Institute on Aging
  - National Center for Research Resources, GCRC Program
  - Office of Research on Women's Health
- Other Federal Agencies
  - Indian Health Service
  - Centers for Disease Control and Prevention
- American Diabetes Association

Sponsors

- Industrial grant support
  - Bristol-Myers Squibb
  - Warner-Lambert.
- Additional Support

LifeScan, Inc
Health O Meter
Hoechst Marion Roussel, Inc.
Merck-Medco Managed Care, Inc
Merck & Co.
Nike Sports Marketing
Slim Fast Foods Co.
Quaker Oats Co.

Feasibility of Preventing Type 2 Diabetes

- There is a long period of glucose intolerance that precedes the development of diabetes
- Screening tests can identify persons at high risk
- There are safe, potentially effective interventions that can address modifiable risk factors

Modifiable Risk Factors for Type 2 Diabetes

- Obesity
- Body fat distribution
- Physical inactivity
- Elevated fasting and 2 hr glucose levels

DPP Primary Goal

- To prevent or delay the development of type 2 diabetes in persons with impaired glucose tolerance (IGT)

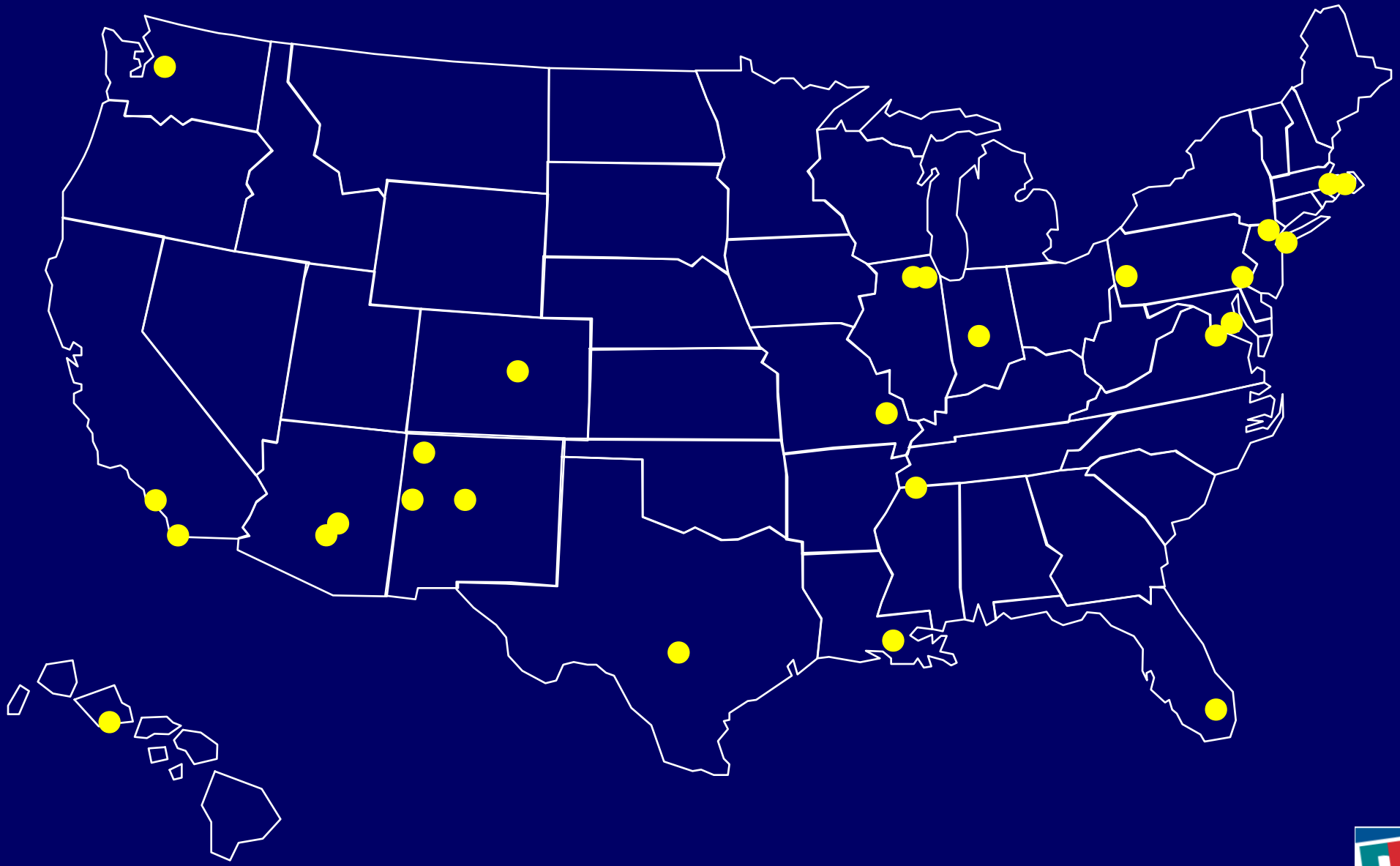
DPP Secondary Goals

- Reduce cardiovascular disease (CVD) events
- Reduce CVD risk factors
- Reduce atherosclerosis

Study Design

- 3-group randomized clinical trial
- 27 clinical sites
- Standardized across clinics:
  - Common protocol and procedures manual
  - Staff training
  - Data quality control program

Diabetes Prevention Program Clinics



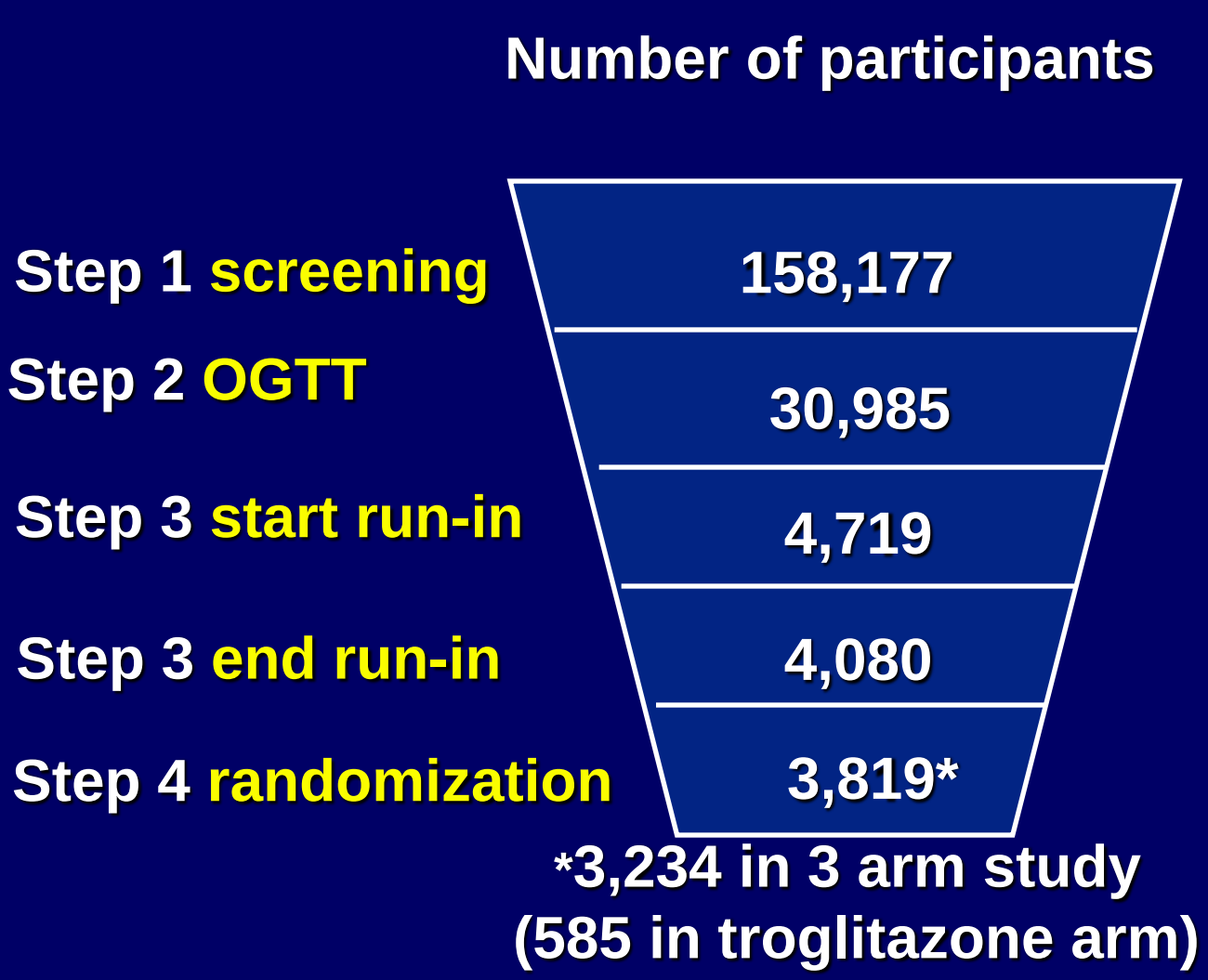
Eligibility Criteria

- Age ≥ 25 years
- Plasma glucose
  - 2 hour glucose 140-199 mg/dl (7.8- <11.1 mmol/L)

    and
  - Fasting glucose 95-125 mg/dl (5.3- <7.0 mmol/L)
- Body mass index ≥ 24 kg/m^2
- All ethnic groups

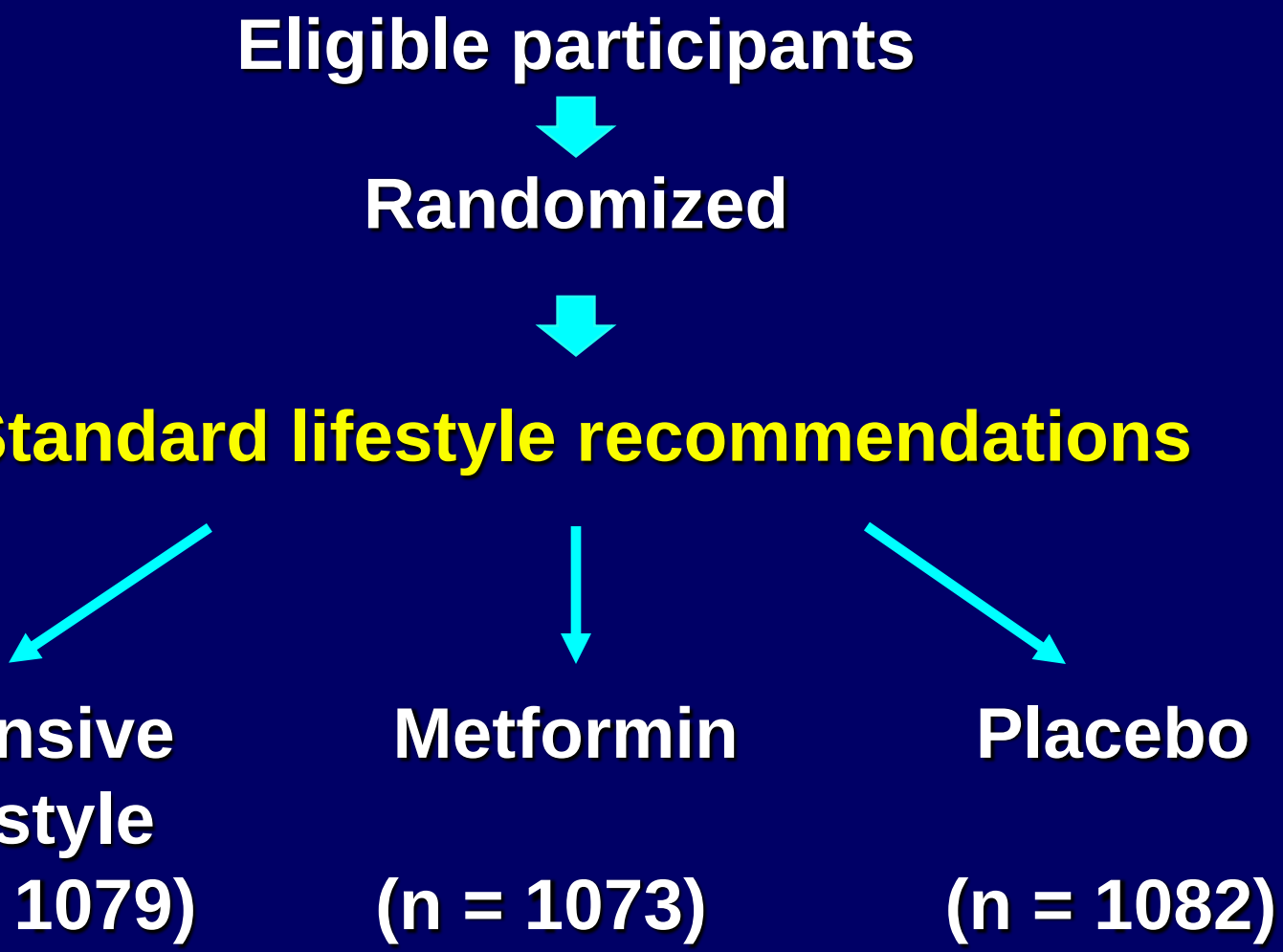
  goal of up to 50% from high risk populations

Screening and Recruitment



The DPP Research Group, *Controlled Clin Trials* (in press)

Study Interventions



Primary Outcome: Diabetes

- Annual fasting plasma glucose (FPG) and 75 gm Oral Glucose Tolerance Test
  - FPG ≥ 126 mg/dL (7.0 mmol/L) or
  - 2-hr ≥ 200 mg/dL (11.0 mmol/L),
  - Either confirmed with repeat test
- Semi-annual FPG
  - ≥ 126 mg/dL, confirmed

Lifestyle Intervention

An intensive program with the following specific goals:

- ≥ 7% loss of body weight and maintenance of weight loss
  - Dietary fat goal -- <25% of calories from fat
  - Calorie intake goal -- 1200-1800 kcal/day
- ≥ 150 minutes per week of physical activity

Lifestyle Intervention Structure

- 16 session core curriculum (over 24 weeks)
- Long-term maintenance program
- Supervised by a case manager
- Access to lifestyle support staff
  - Dietitian
  - Behavior counselor
  - Exercise specialist

The Core Curriculum

- 16 session course conducted over 24 weeks
- Education and training in diet and exercise methods and behavior modification skills
- Emphasis on:
  - Self monitoring techniques
  - Problem solving
  - Individualizing programs
  - Self esteem, empowerment, and social support
  - Frequent contact with case manager and DPP support staff

Post Core Program

- Self-monitoring and other behavioral strategies
- Monthly visits
  - Must be seen in person at least every two months
- Supervised exercise sessions offered
- Periodic group classes and motivational campaigns
- Tool box strategies
  - Provide exercise videotapes, pedometers
  - Enroll in health club or cooking class

DPP Study Interventions: Criteria for Drug Treatment

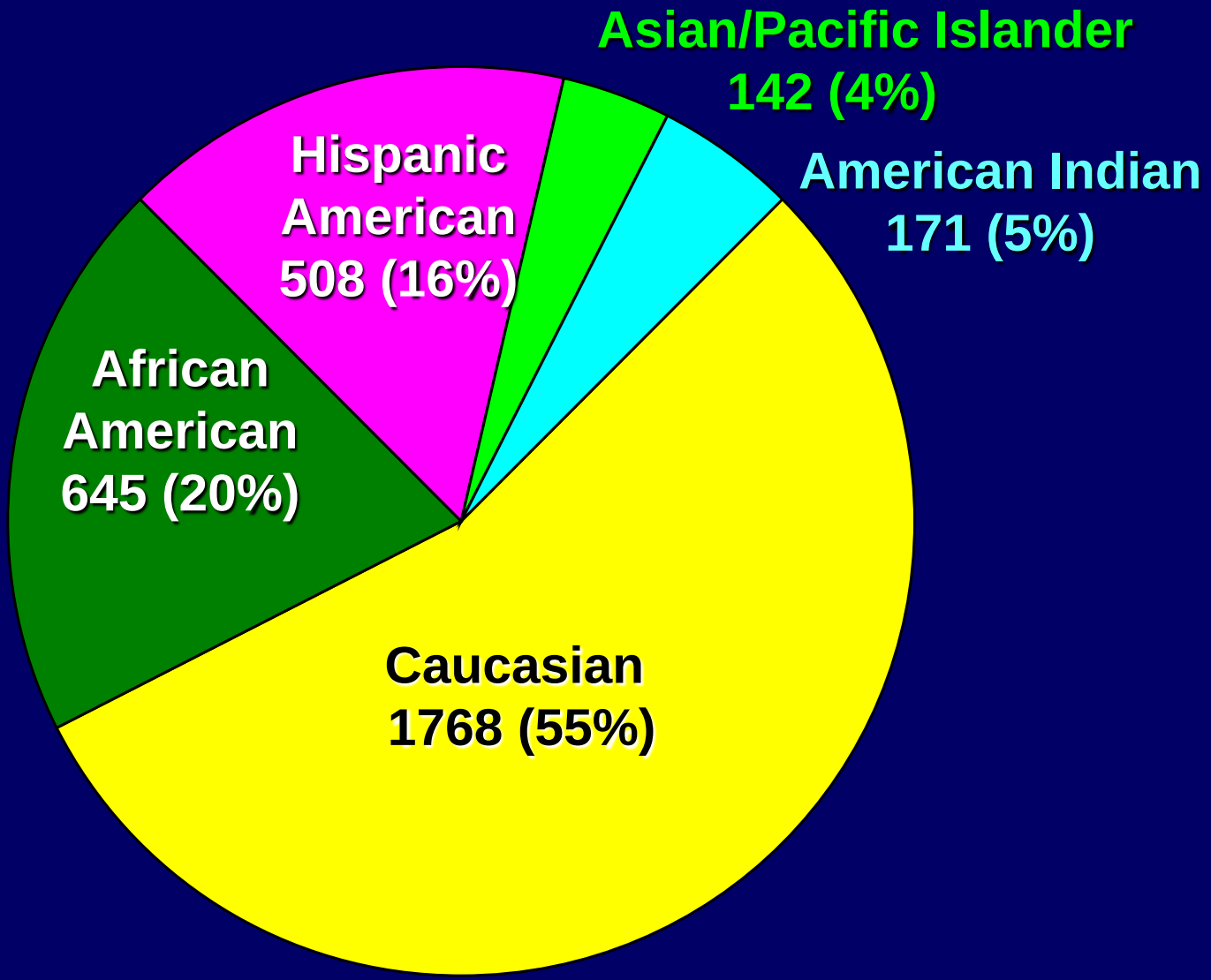
- Efficacy
- Safety
- Tolerability - minimal side effects
- Acceptability - dose frequency

Interventions: Medications

Metformin- 850 mg per day escalating after 4 weeks to 850 mg twice per day

Placebo- Metformin placebo adjusted in parallel with active drugs

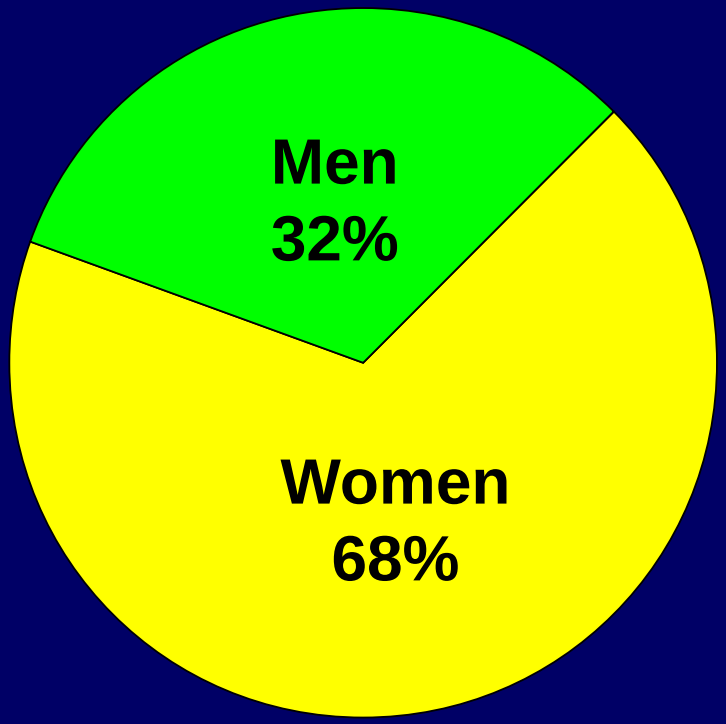
DPP Population



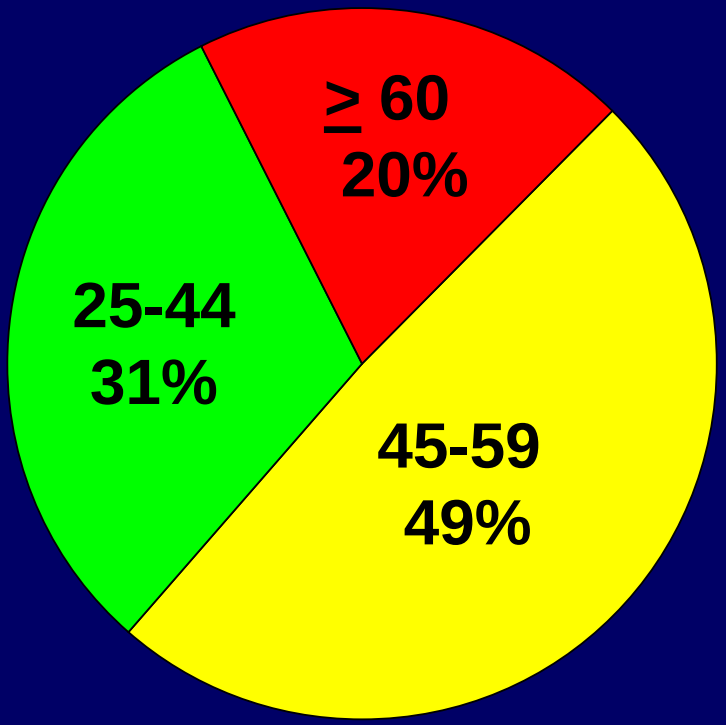
The DPP Research Group, *Diabetes Care* 23:1619-29, 2000

DPP Population

Sex Distribution



Age Distribution



The DPP Research Group, *Diabetes Care* 23:1619-29, 2000

Retention and Participation

- 99.6% of the study cohort alive at study end
- 93% completed study
- 93% of annual visits completed
- Average follow-up 2.8 years (range 1.8 - 4.6)

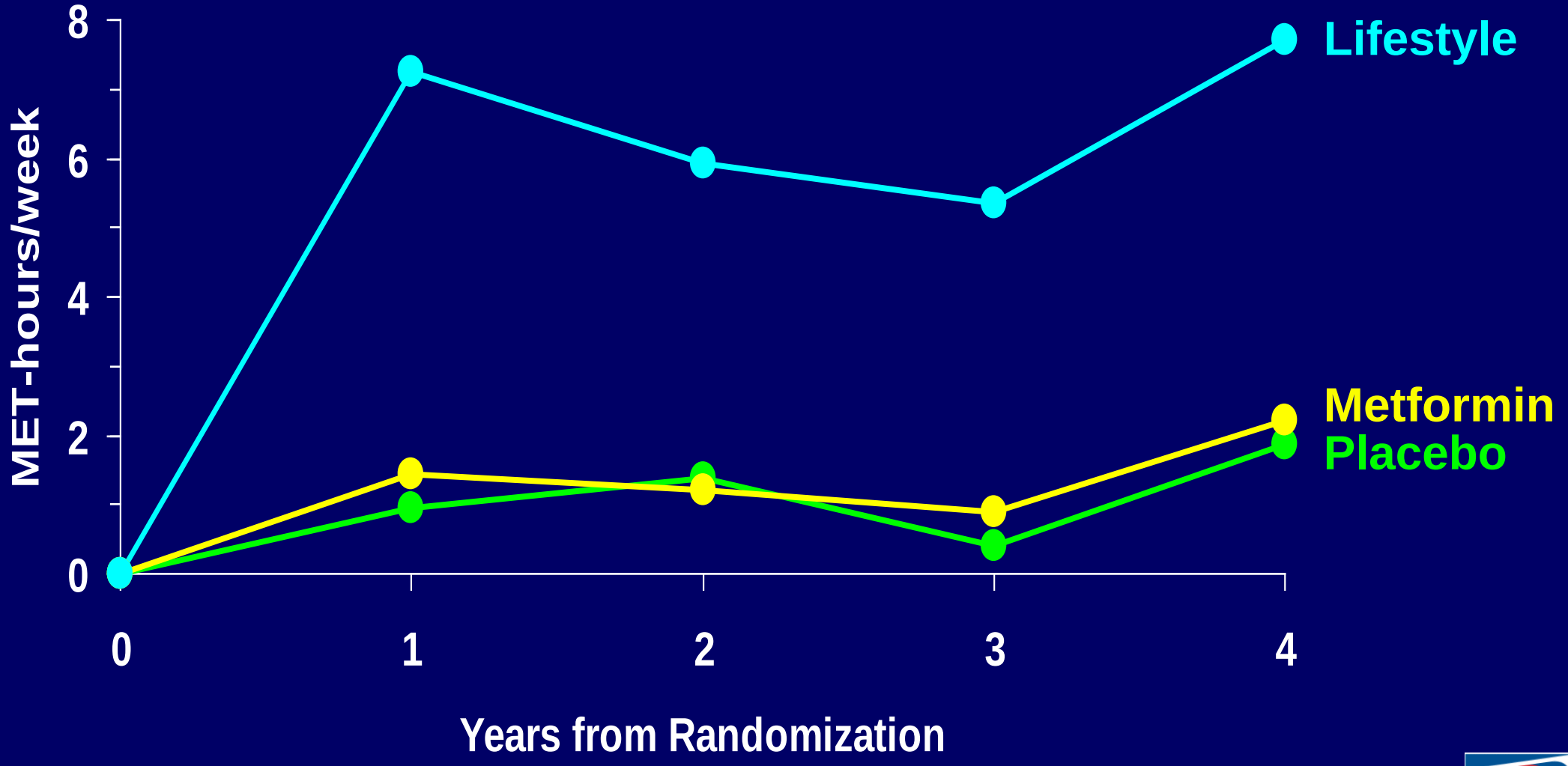
The DPP Research Group, *NEJM 346*:393-403, 2002

Lifestyle Intervention: Physical Activity Results

- 74% of volunteers assigned to intensive lifestyle achieved the study goal of ≥ 150 minutes of activity per week at 24 weeks

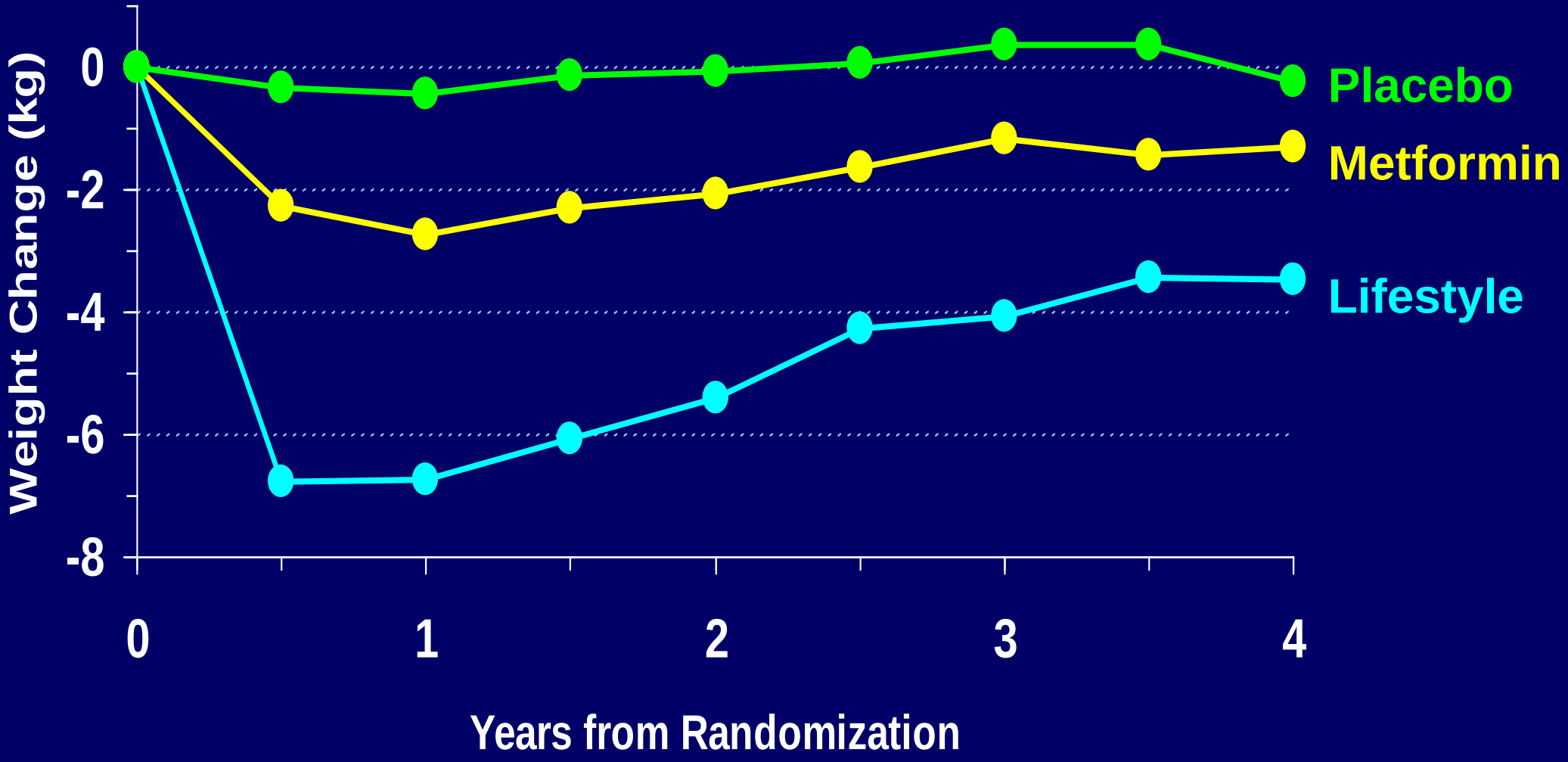
The DPP Research Group, *NEJM 346*:393-403, 2002

Mean Change in Leisure Physical Activity



The DPP Research Group, *NEJM 346*:393-403, 2002

Mean Weight Change



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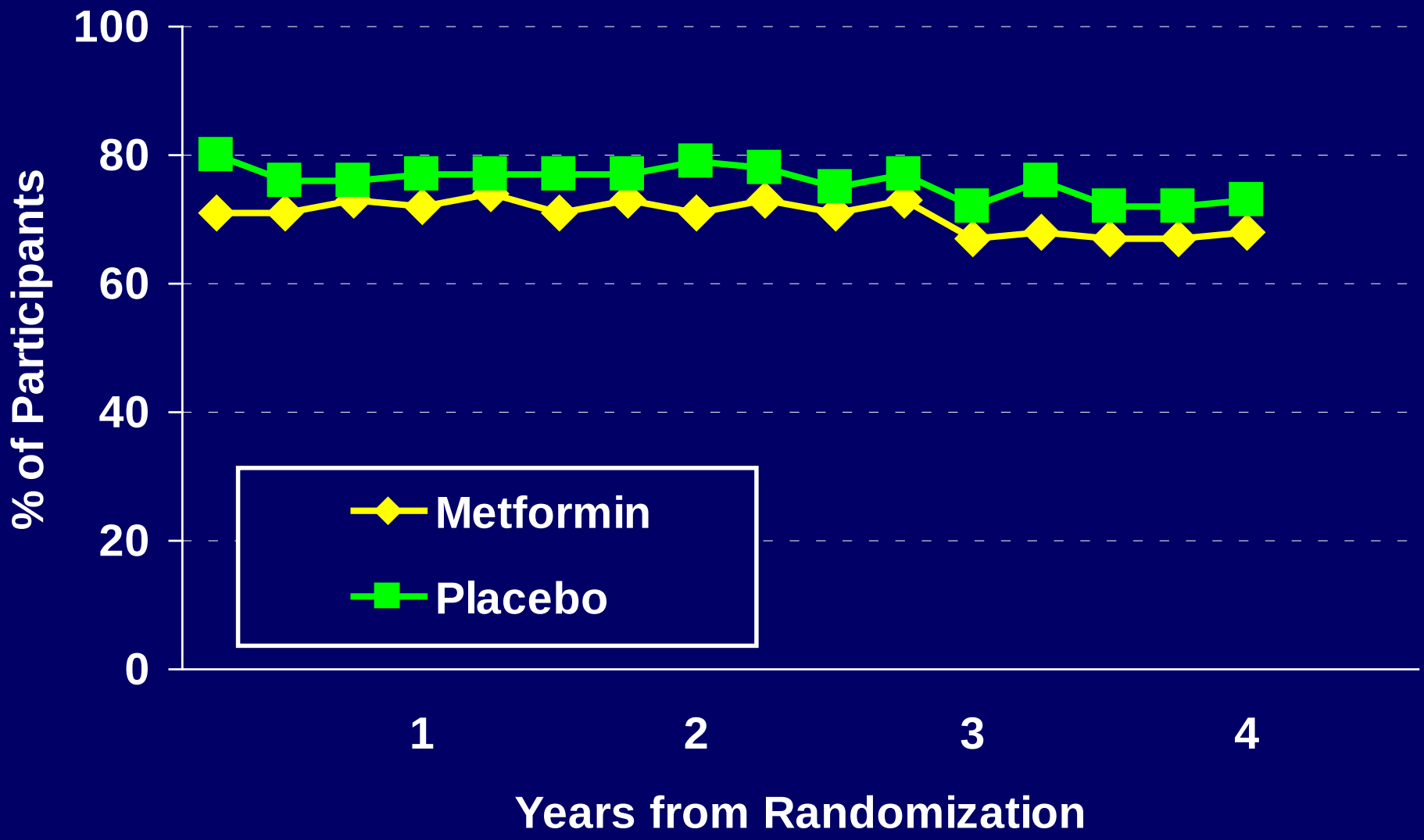
Percent Taking ≥ 80% of Prescribed Dose of Coded Medication



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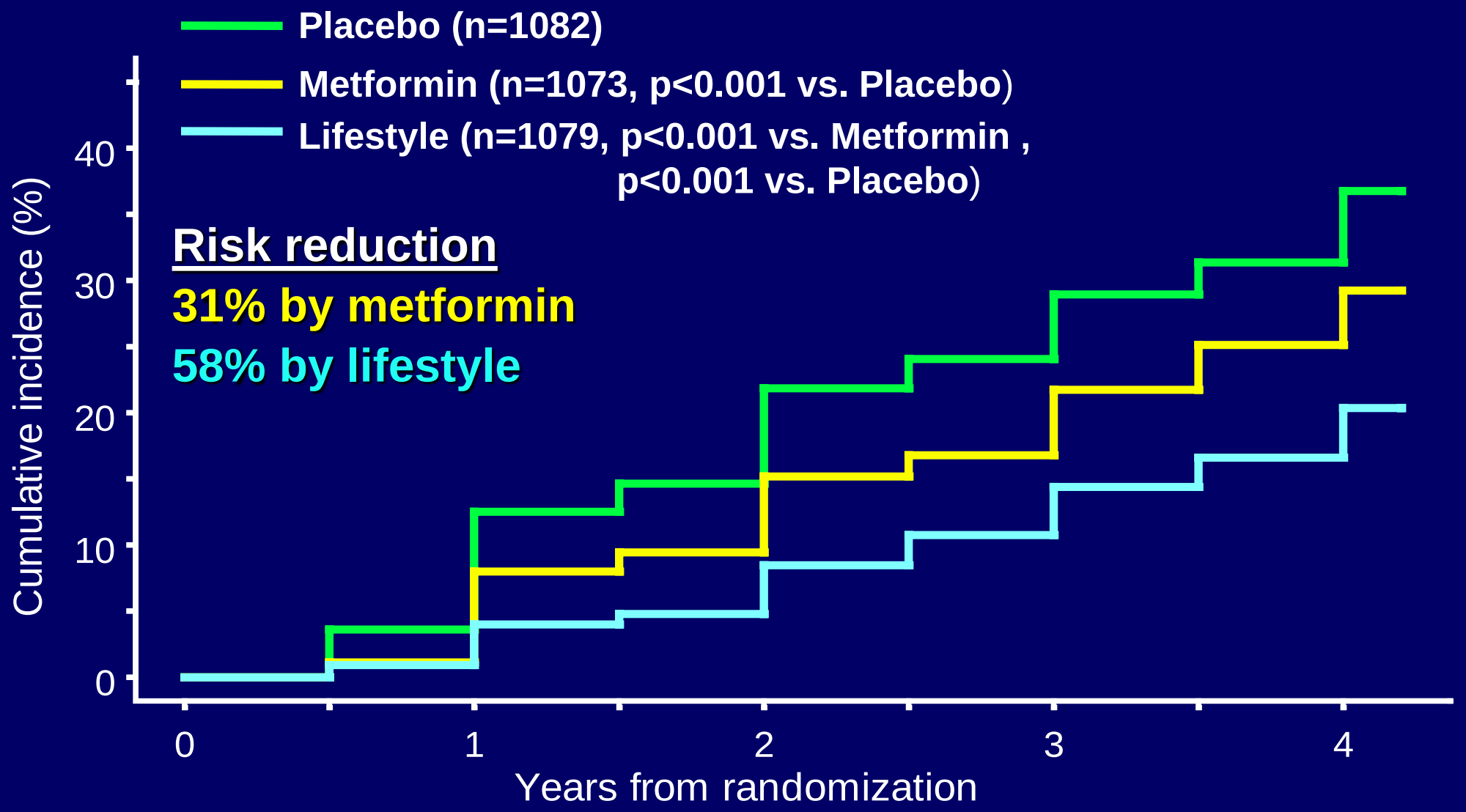
Incidence of Diabetes



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Effect of Treatment on Incidence of Diabetes

	Placebo	Metformin	Lifestyle
Incidence of diabetes (percent per year)	11.0%	7.8%	4.8%
Reduction in incidence compared with placebo	----	31%	58%
Number needed to treat to prevent 1 case in 3 years	----	13.9	6.9

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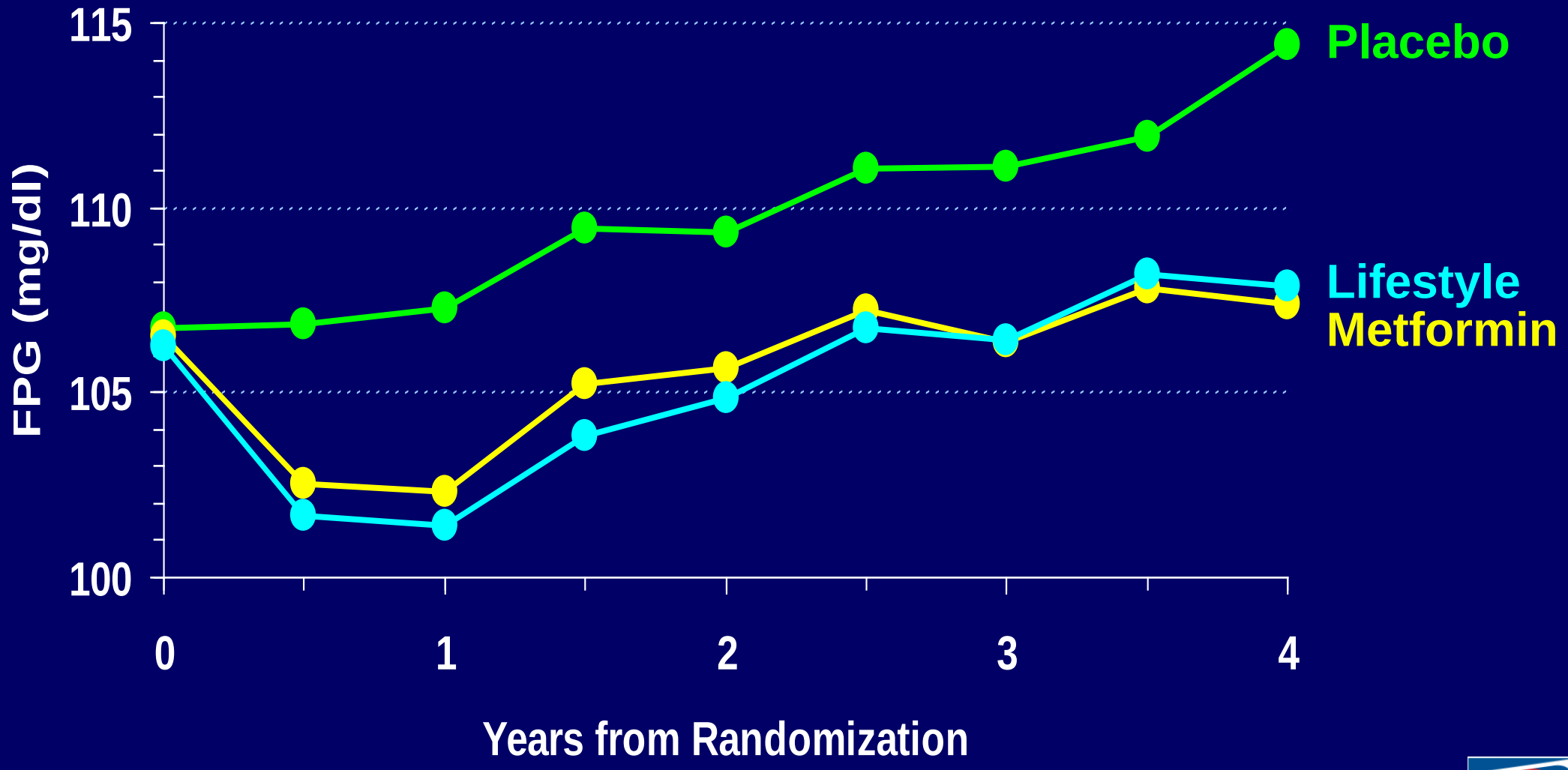
Mean Change in Fasting Plasma Glucose



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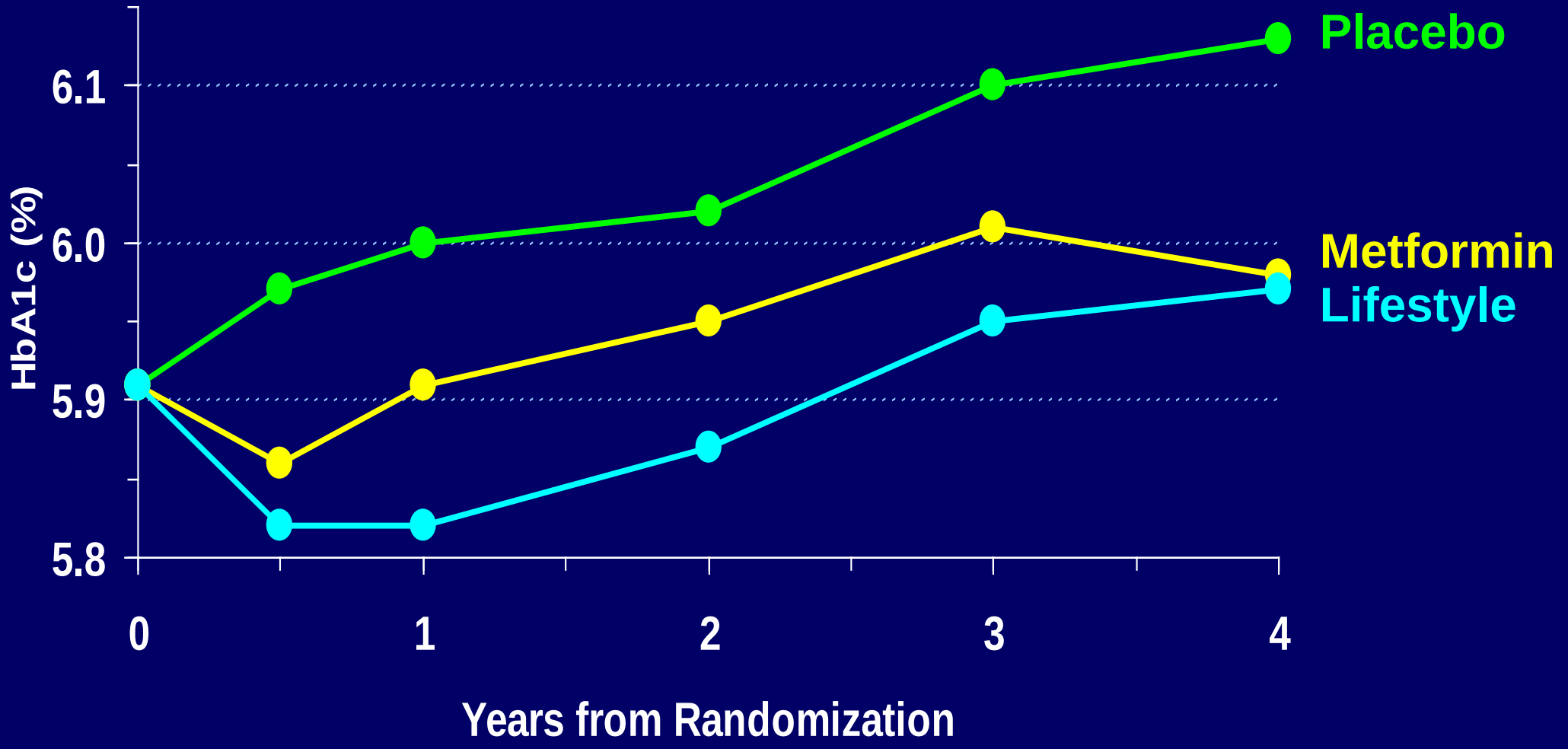
Mean Change in HbA_{1c}



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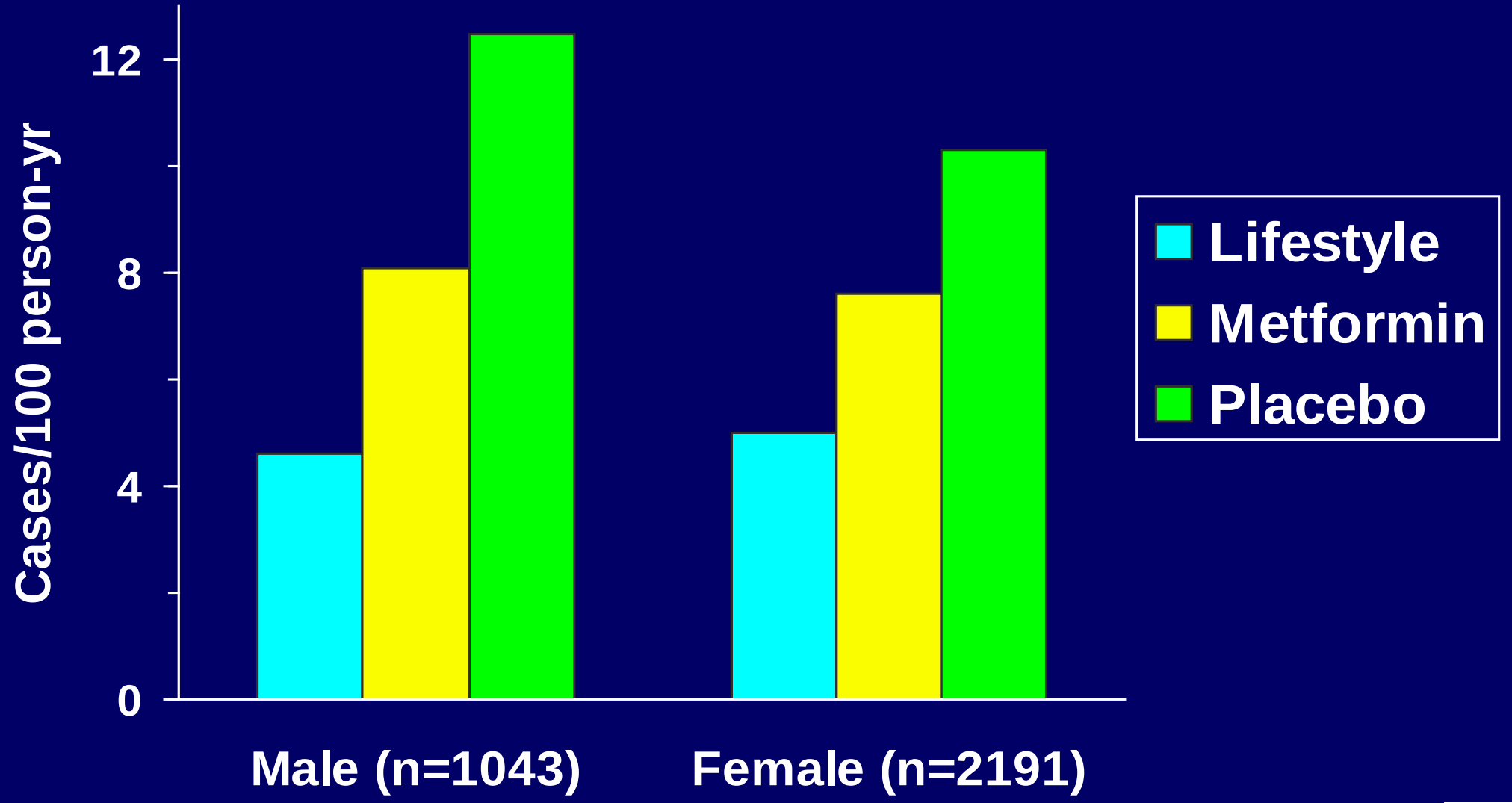
Diabetes Incidence Rates by Sex



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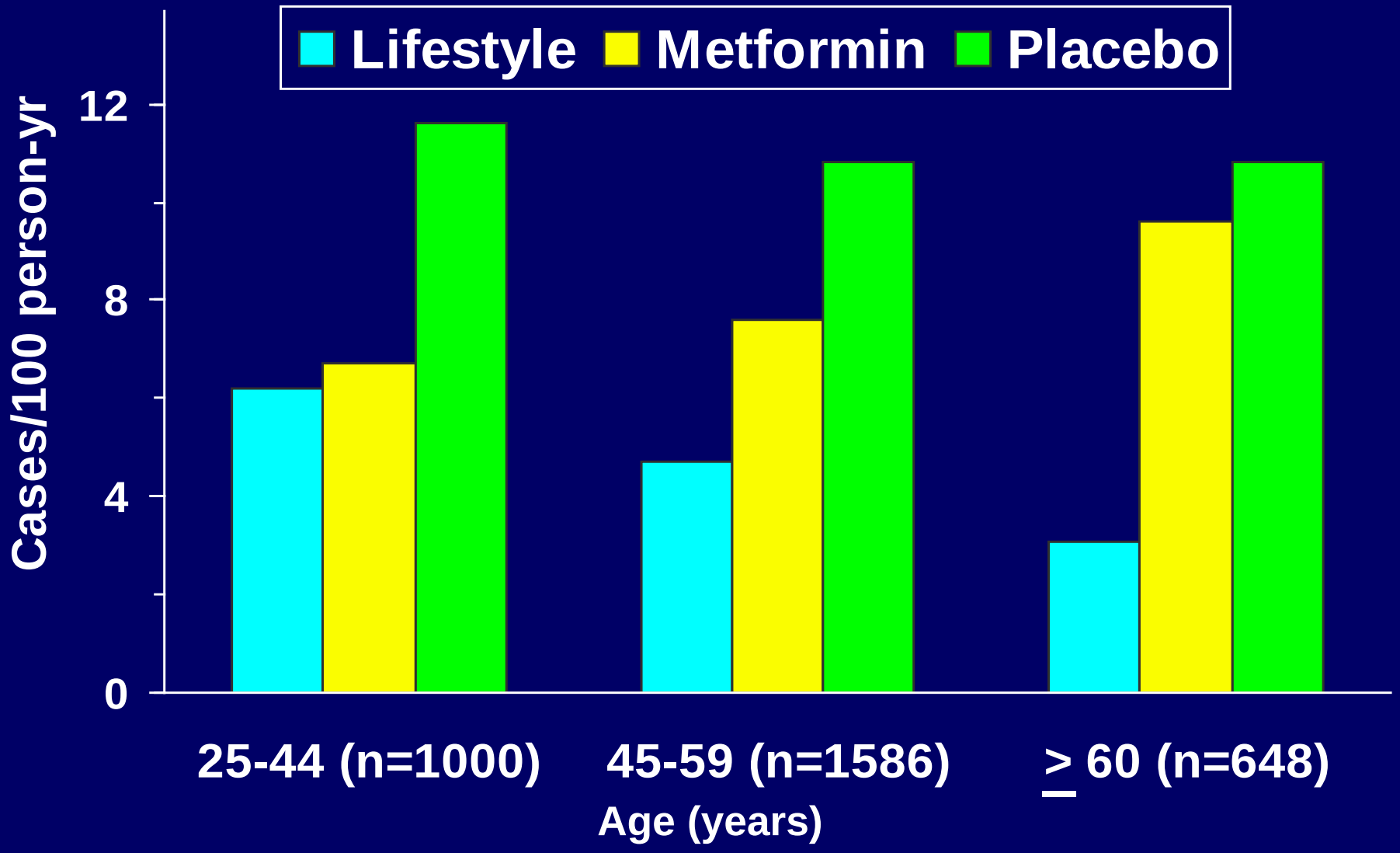
Diabetes Incidence Rates by Age



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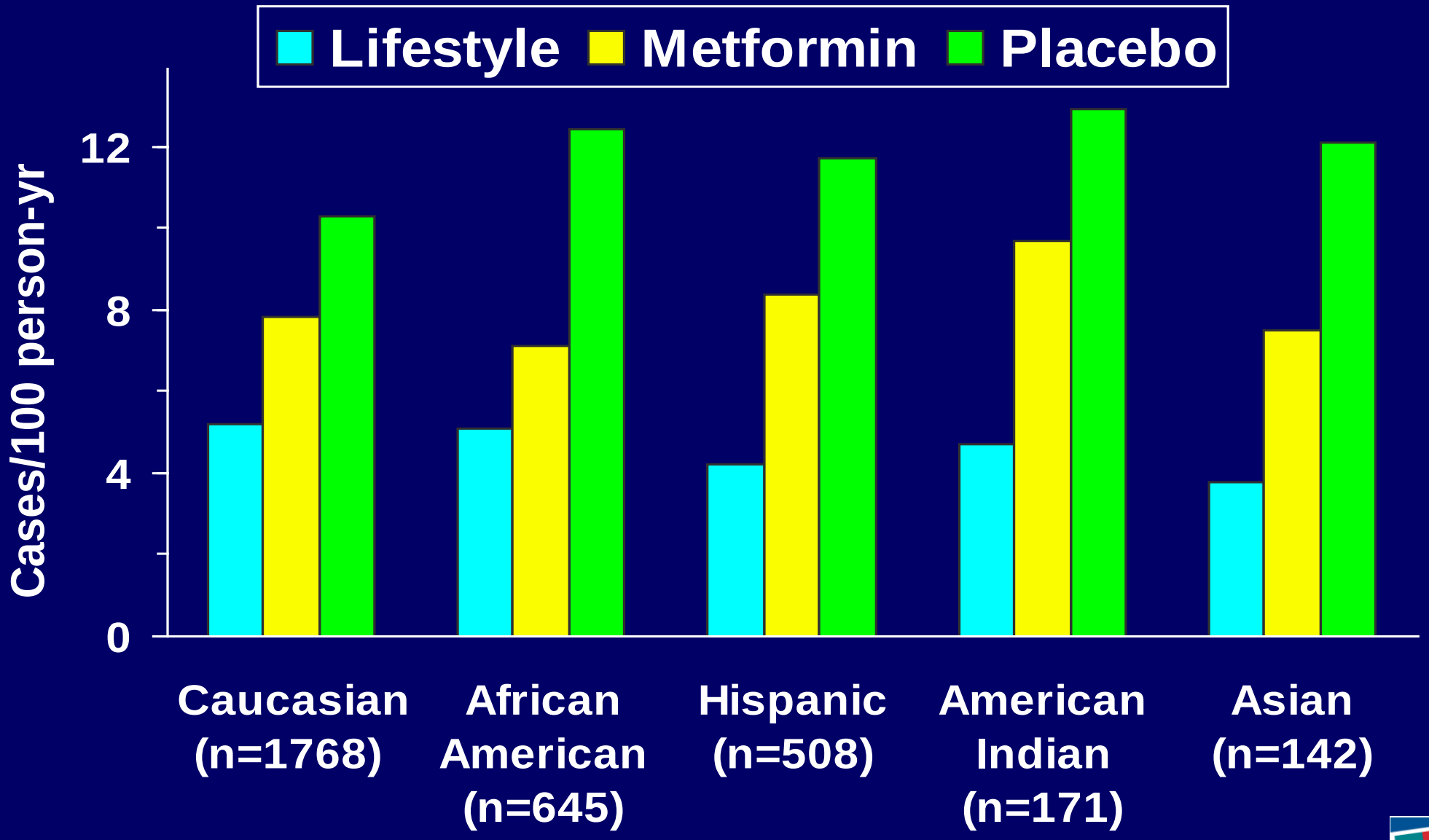
Diabetes Incidence Rates by Ethnicity



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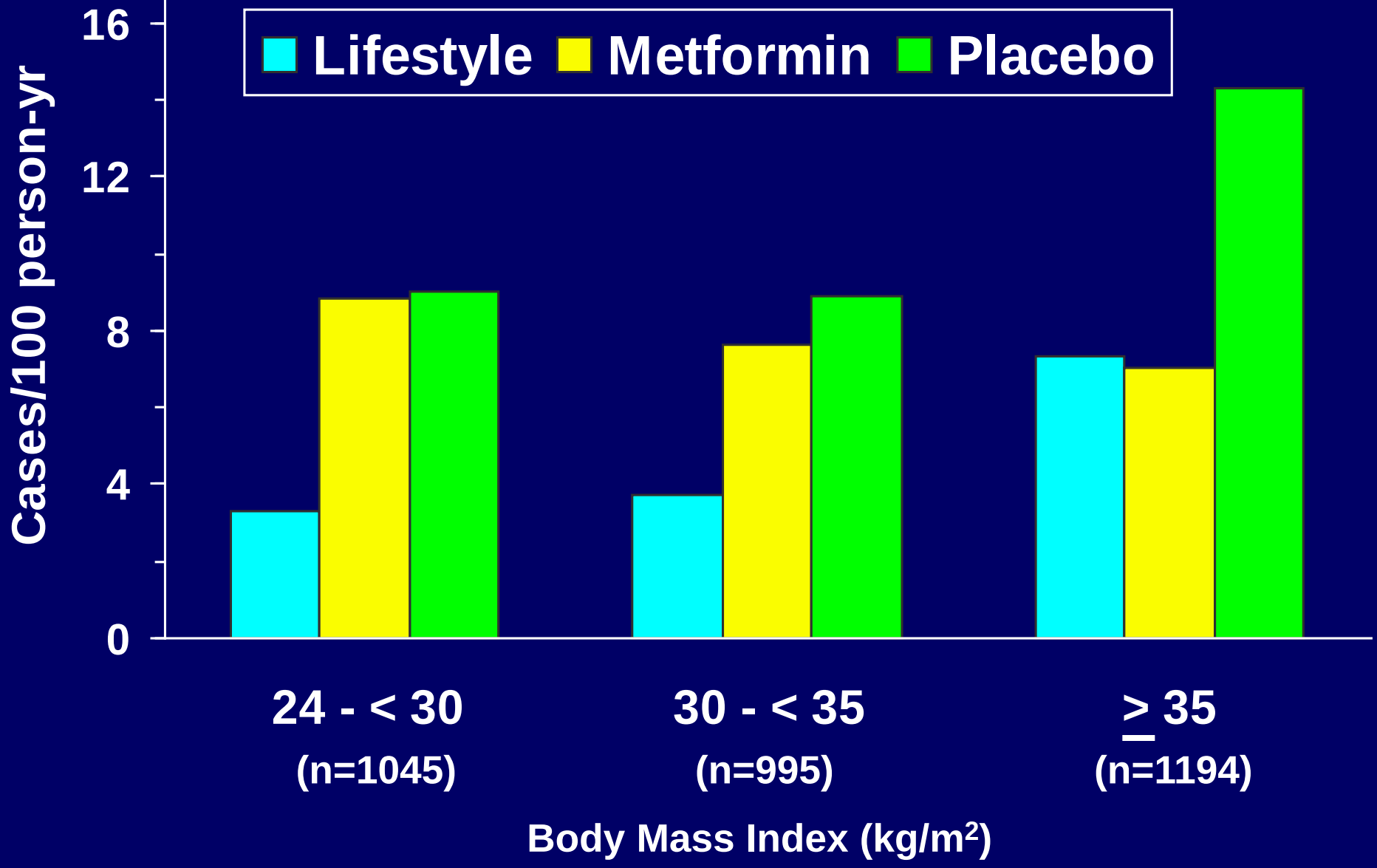
Diabetes Incidence Rates by BMI



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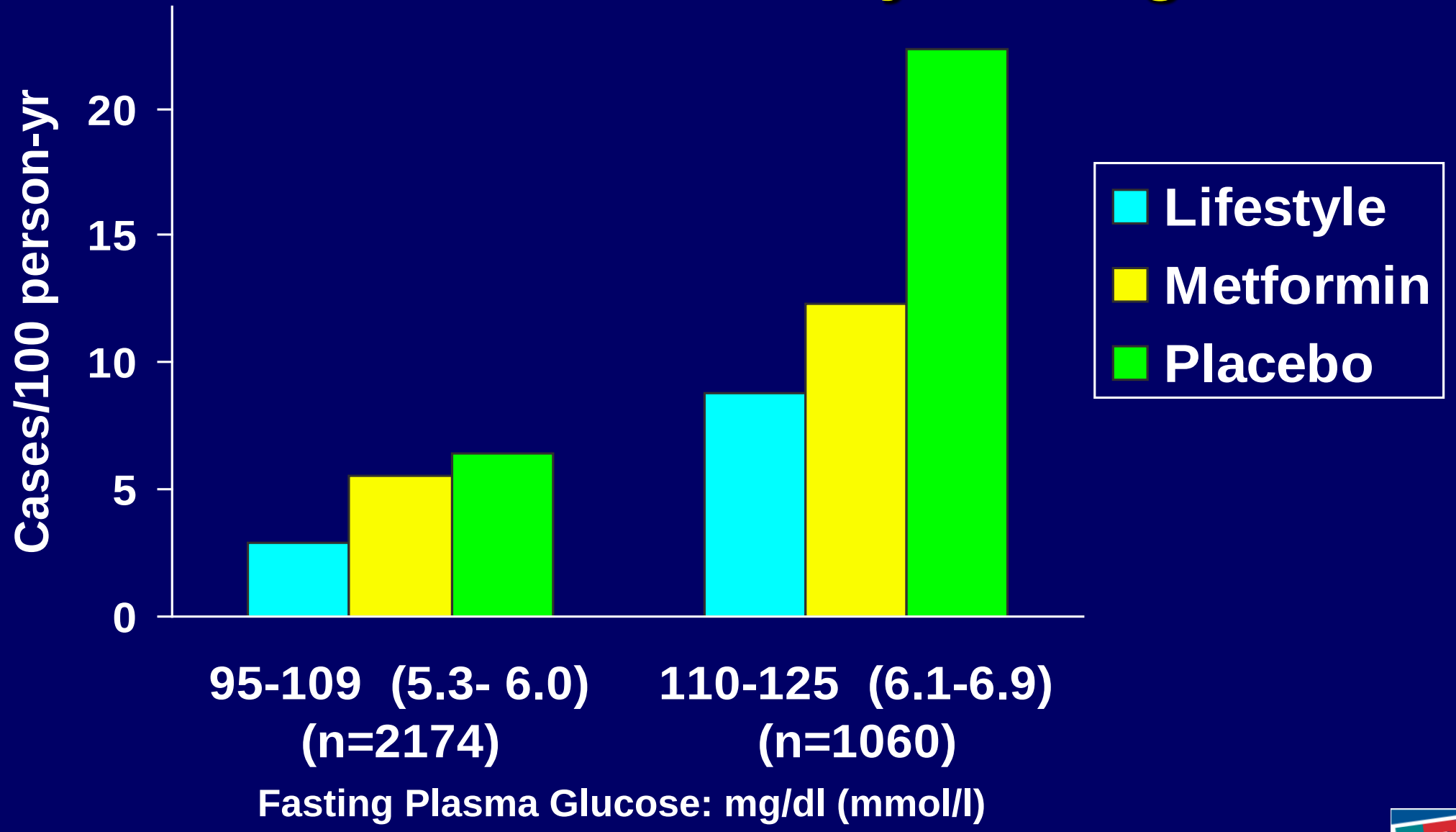
Diabetes Incidence Rates by Fasting Glucose



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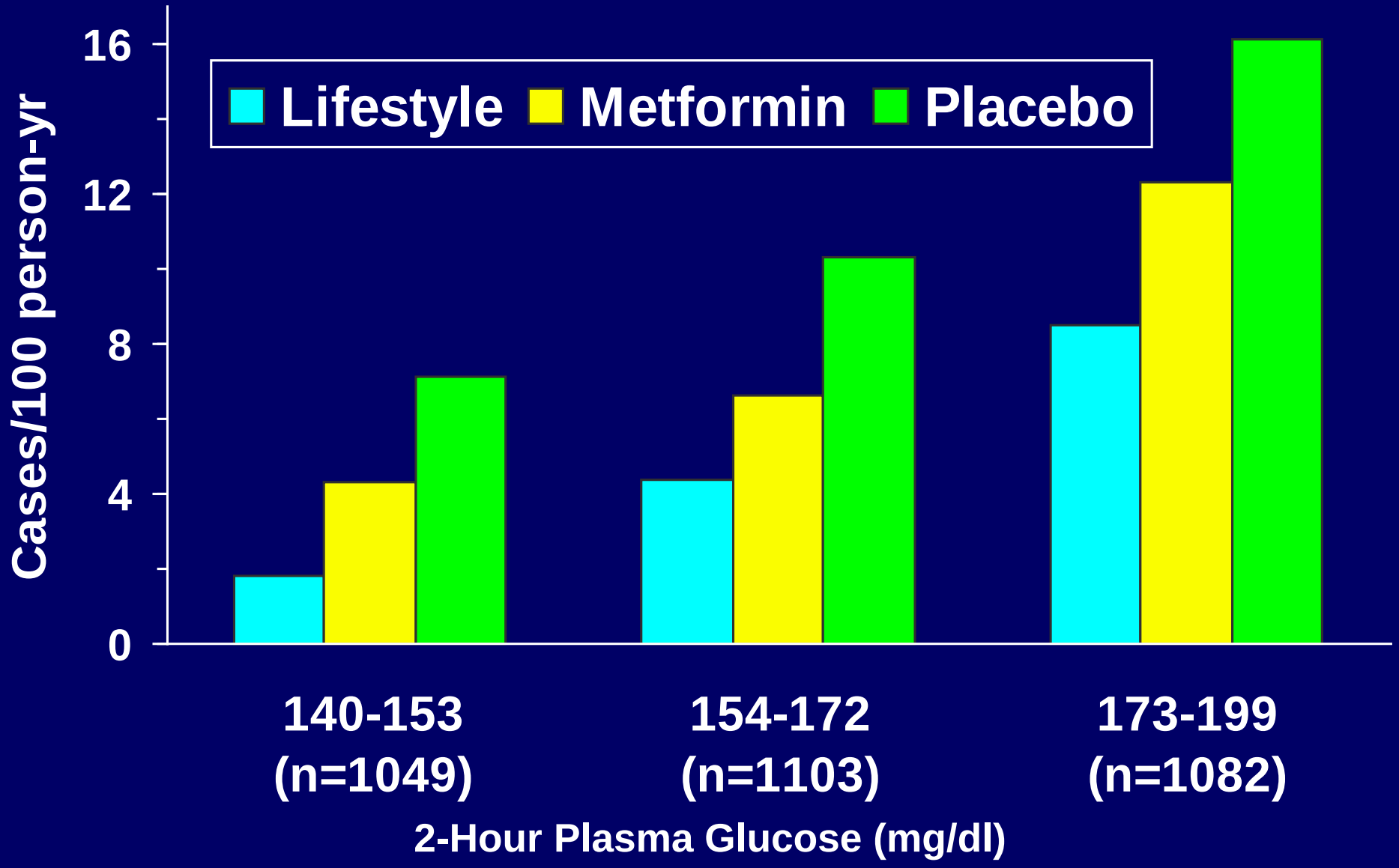
Diabetes Incidence Rates by 2-hr Glucose

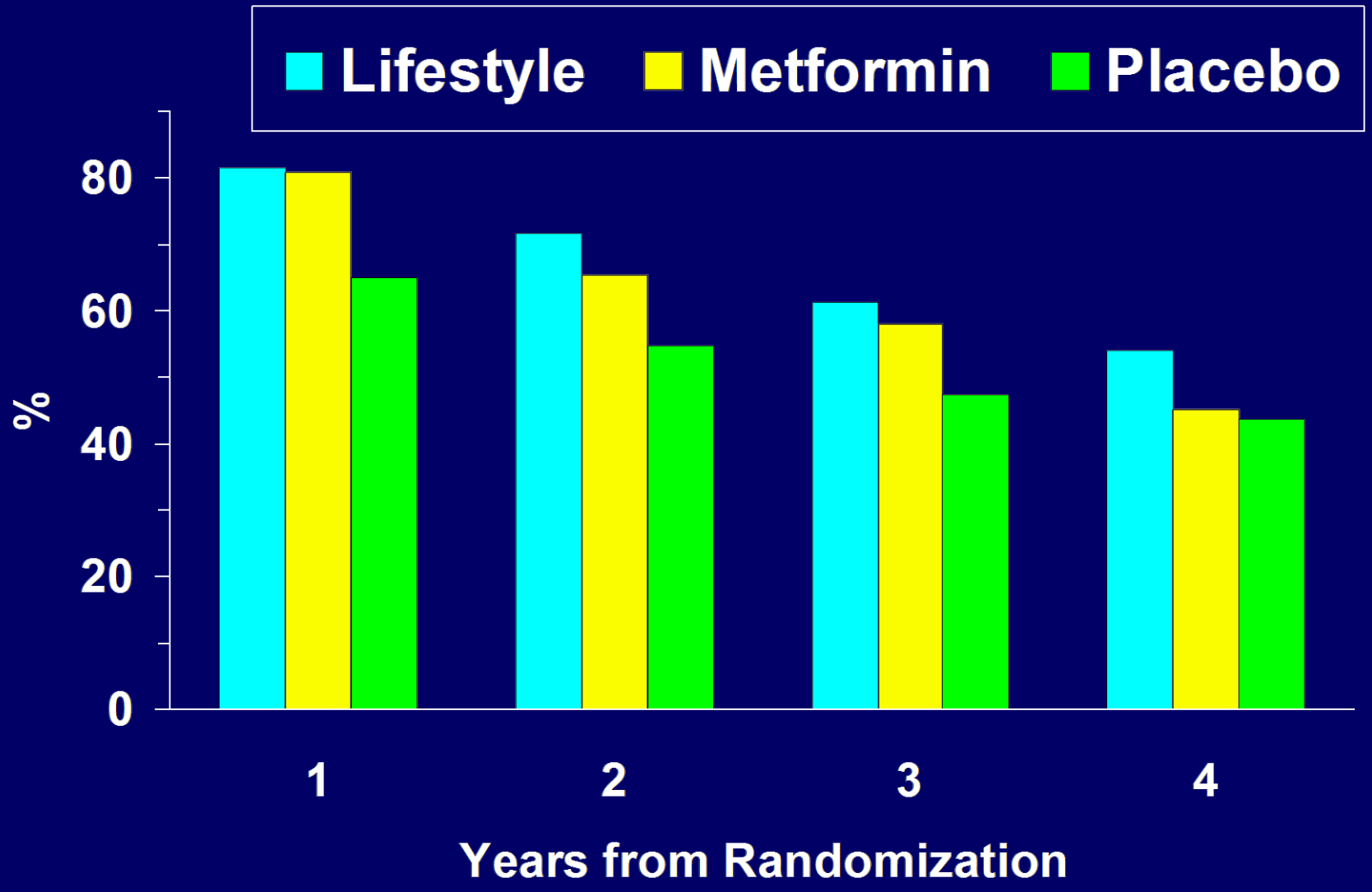


The DPP Research Group, *NEJM 346*:393-403, 2002

Consistency of Treatment Effects

- Lifestyle intervention was beneficial regardless of ethnicity, age, BMI, or sex
- The efficacy of lifestyle relative to metformin was greater in older persons and in those with lower BMI
- The efficacy of metformin relative to placebo was greater in those with higher baseline fasting glucose and BMI

Normal Fasting Glucose at Annual Visits



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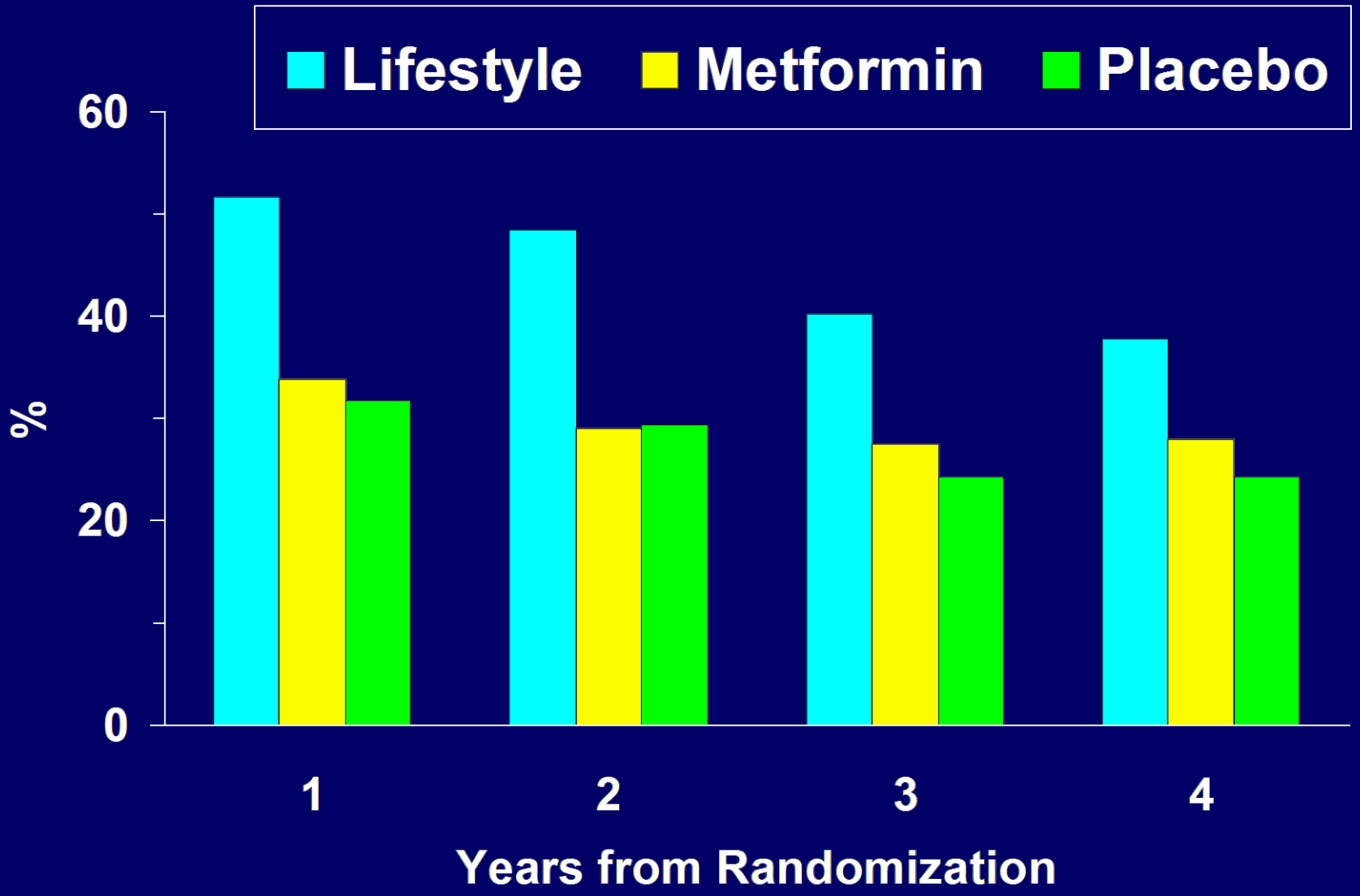
Normal 2-hr Glucose at Annual Visits



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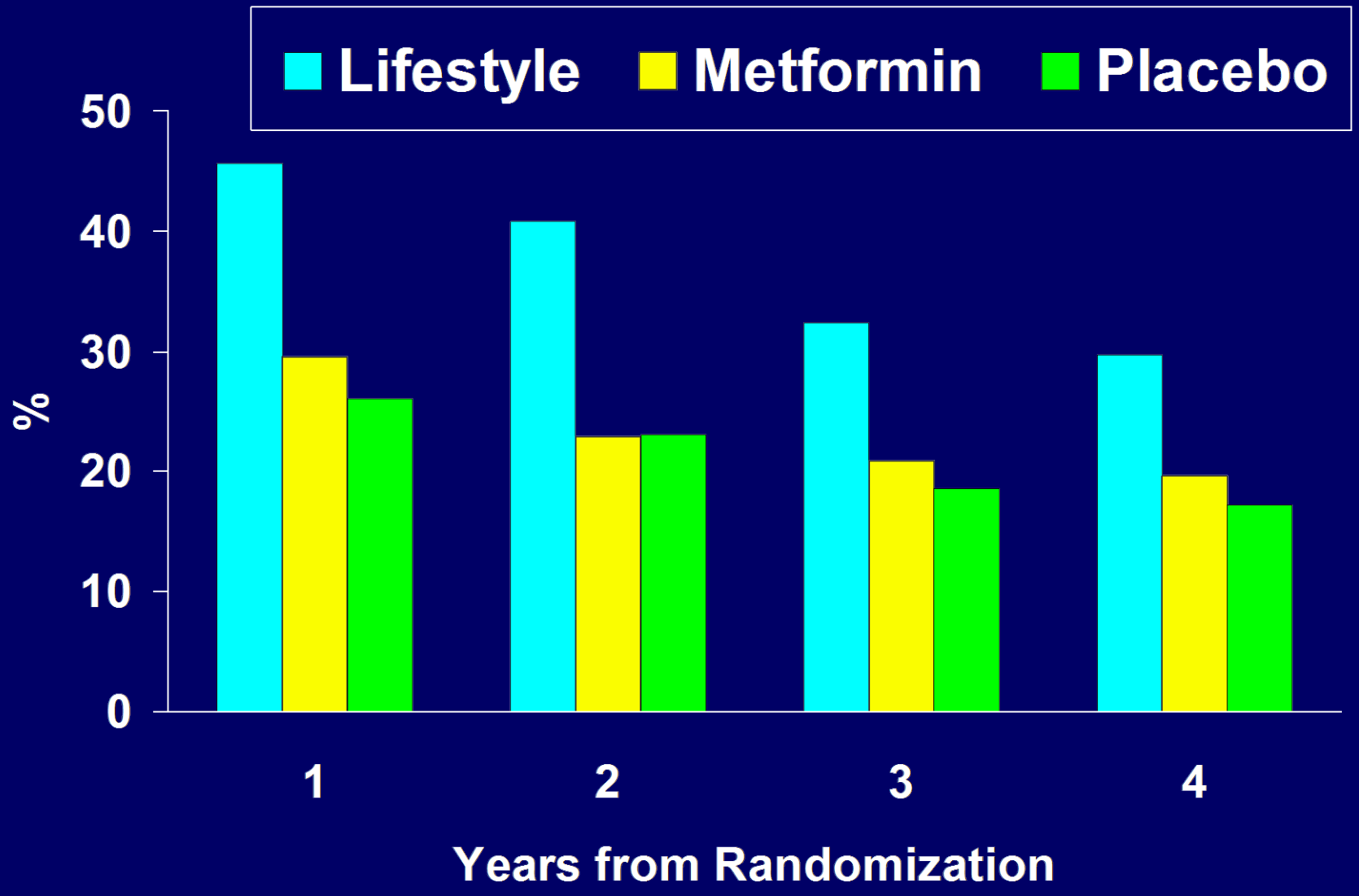
Normal Fasting & 2-hr Glucose at Annual Visits



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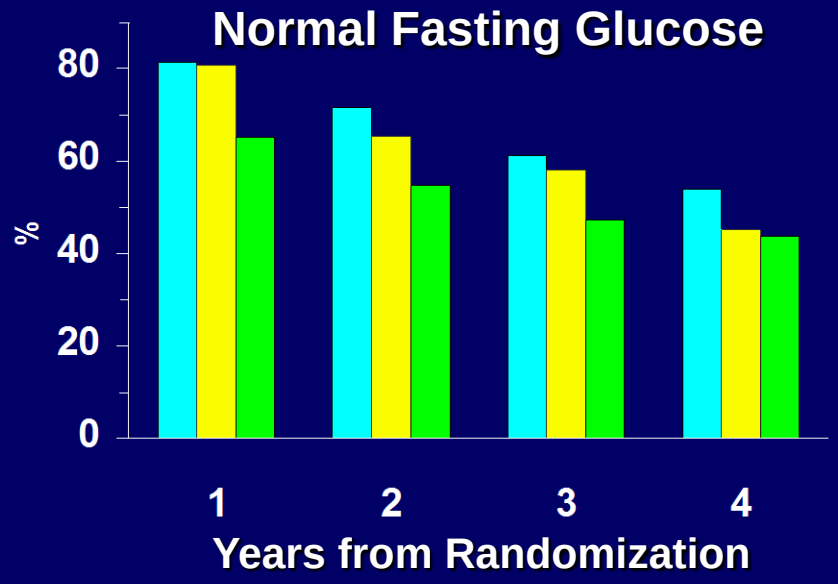
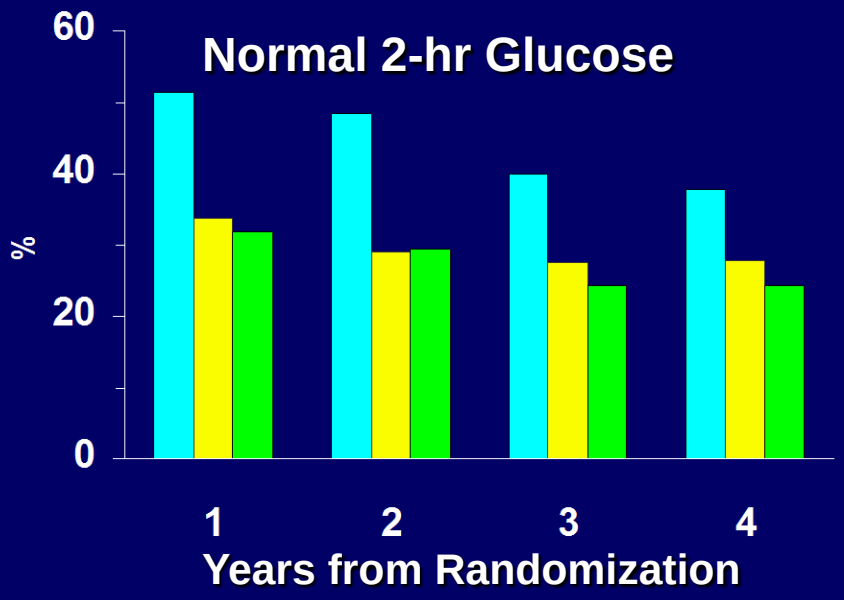
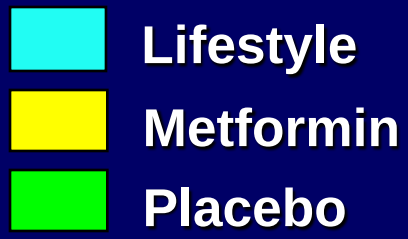
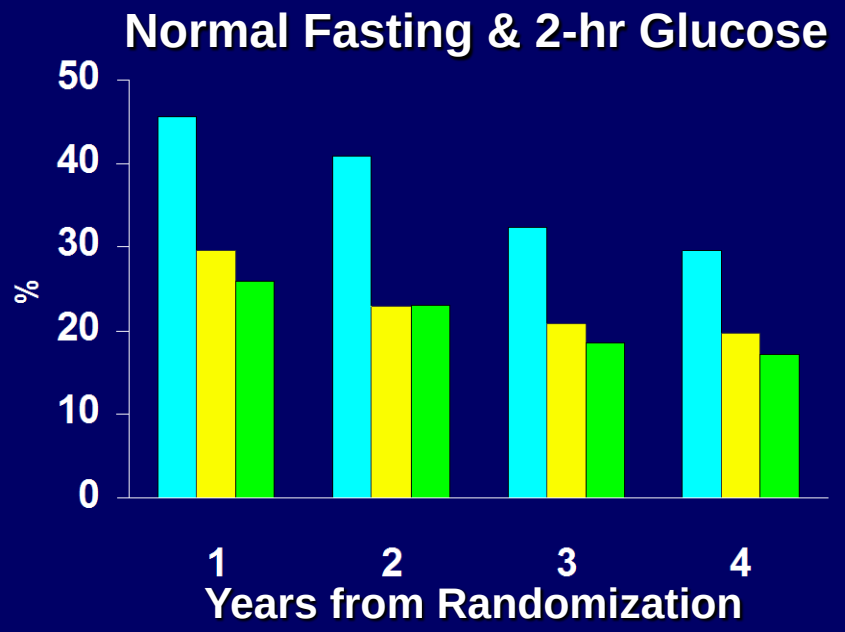
Normal Glucose at Annual Visits









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Adverse Events
(rates per 100 person years)

	Placebo	Metformin	Lifestyle
Death	0.16	0.20	0.10
Hospitalization	7.9	8.4	8.0
GI Symptoms	30.7	77.8*	12.9*
Musculoskeletal Symptoms	21.1	20.0	24.1*

* significantly different from placebo

The DPP Research Group, *NEJM 346*:393-403, 2002

Summary-1

- Both interventions were well accepted and safe
- Intensive lifestyle resulted in weight loss and increased activity level for the duration of the study

Summary-2

- Both interventions were effective in men and women and all ethnic groups

- Intensive lifestyle intervention was effective in all age groups, including those ≥ 60 years of age

Summary-3

- Intensive lifestyle intervention reduced the development of diabetes by 58%
- Metformin reduced the development of diabetes by 31%
- Lifestyle was more effective than metformin

THANK YOU

Diabetes Prevention Program

Baseline Characteristics

Participant Characteristics by Treatment Group Assignment (1)

	Overall	ILS	Metformin	Placebo
n	3,234	1,079	1,073	1,082
Age (years)*	50.6 ± 10.7	50.6 ± 11.3	50.9 ± 10.3	50.3 ± 10.4
Sex**				
Male	1043 (32%)	345 (32%)	363 (34%)	335 (31%)
Female	2191 (68%)	734 (68%)	710 (66%)	747 (69%)
Ethnicity				
Caucasian	1768 (55%)	580 (54%)	602 (56%)	586 (54%)
African-American	645 (20%)	204 (19%)	221 (21%)	220 (20%)
Hispanic	508 (16%)	178 (17%)	162 (15%)	168 (16%)
American Indian	171 (5%)	60 (6%)	52 (5%)	59 (6%)
Asian-American	142 (4%)	57 (5%)	36 (3%)	49 (4%)

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*Mean ± SD; ** *n*, (%)

Participant Characteristics by Treatment Group Assignment (2)

	Overall	*ILS*	*Metformin*	*Placebo*
n	3,234	1,079	1,073	1,082
FPG (mmol/L) *	5.9 ± 0.5	5.9 ± 0.4	5.9 ± 0.5	5.9 ± 0.5
BMI (kg/m^2)	34.0 ± 6.7	33.9 ± 6.8	33.9 ± 6.6	34.2 ± 6.8
BP (mm Hg)				
Systolic	124 ± 15	124 ± 15	124 ± 15	124 ± 14
Diastolic	78 ± 9	79 ± 9	78 ± 10	78 ± 9

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*Mean ± SD

Demographic and Socioeconomic Characteristics by Sex (1)

	Overall	*Male*	*Female*
n	3,234	1,043	2,191
Age (years) *			
25 to <40	505 (16%)	113 (11%)	392 (18%)
40 to <50	1137 (35%)	286 (27%)	851 (39%)
50 to <60	945 (29%)	325 (31%)	620 (28%)
≥60	647 (20%)	319 (31%)	328 (15%)
Race/Ethnicity			
Caucasian	1768 (55%)	608 (58%)	1160 (53%)
African-American	645 (20%)	165 (16%)	480 (22%)
Hispanic	508 (16%)	167 (16%)	341 (16%)
American Indian	171 (5%)	20 (2%)	151 (7%)
Asian American	142 (4%)	83 (8%)	59 (3%)

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** n, (%)*

Demographic and Socioeconomic Characteristics by Sex (2)

	Overall	*Male*	*Female*
n	3,234	1,043	2,191
Employment Status *			
Employed	2401 (74.2%)	771 (73.9%)	1630 (74.4%)
Retired	420 (13.0%)	217 (20.8%)	203 (9.3%)
Homemaker	204 (6.3%)	1 (0.1%)	203 (9.3%)
Not employed	121 (3.7%)	33 (3.2%)	88 (4.0%)
Seasonally employed	25 (0.8%)	8 (0.8%)	17 (0.8%)
Student	21 (0.6%)	2 (0.2%)	19 (0.9%)
Other	37 (1.1%)	11 (1.1%)	26 (1.2%)
Never worked	5 (0.2%)	0 (0.0%)	5 (0.2%)

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* *n*, (%)

Demographic and Socioeconomic Characteristics by Sex (3)

	Overall	*Male*	*Female*
n	3,234	1,043	2,191
Education in years *			
<13	834 (26%)	221 (21%)	613 (28%)
13 to 16	1556 (48%)	488 (47%)	1068 (49%)
17 or more	844 (26%)	334 (32%)	510 (23%)
Annual family income			
< $20,000	446 (14%)	110 (11%)	336 (15%)
$20,000 to <$35,000	561 (17%)	146 (14%)	415 (19%)
$35,000 to <$50,000	641 (20%)	207 (20%)	434 (20%)
$50,000 to <$75,000	646 (20%)	218 (21%)	428 (20%)
> $75,000	682 (21%)	281 (27%)	401 (18%)
Refused	257 (8%)	81 (8%)	176 (8%)

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* *n*, (%)

Demographic and Socioeconomic Characteristics by Sex (4)

	Overall	Male	Female
n	3,234	1,043	2,191
Marital status *			
Married	1999 (62%)	765 (73%)	1234 (56%)
Divorced	448 (14%)	75 (7%)	373 (17%)
Never married	420 (13%)	115 (11%)	305 (14%)
Widowed	151 (5%)	31 (3%)	120 (6%)
Living together	125 (4%)	31 (3%)	94 (4%)
Separated	91 (3%)	26 (3%)	65 (3%)
Smoking			
Never	1897 (59%)	497 (48%)	1400 (64%)
Former	1111 (34%)	471 (45%)	640 (29%)
Current	226 (7%)	75 (7%)	151 (7%)

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* *n*, (%)

Self-reported Characteristics by Sex and Ethnicity

	Overall	Caucasian	African American	Hispanic	American Indian	Asian American
No. of MEN	1,043	608	165	167	20	83
Fam hx type 2 diabetes *	690 (66%)	390 (64%)	117 (71%)	112 (67%)	13 (65%)	58 (70%)
Hx of high cholesterol	389 (37%)	234 (39%)	65 (39%)	53 (32%)	3 (15%)	34 (41%)
Hx of hypertension	302 (29%)	171 (28%)	58 (35%)	49 (29%)	5 (25%)	19 (23%)
No. of WOMEN	2,191	1,160	480	341	151	59
Fam hx type 2 diabetes	1553 (71%)	799 (69%)	360 (75%)	243 (71%)	116 (77%)	35 (60%)
Hx of gest. diabetes	353 (16%)	191 (17%)	63 (13%)	55 (16%)	36 (24%)	8 (14%)
Hx of high cholesterol	730 (33%)	429 (37%)	147 (31%)	114 (33%)	22 (15%)	17 (29%)
Hx of hypertension	569 (26%)	303 (26%)	144 (30%)	68 (20%)	40 (27%)	15 (26%)

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** n, (%)*

Body Mass Index by Sex and Ethnicity

	Overall	Caucasian	African American	Hispanic	American Indian	Asian American
No. of MEN	1,043	608	165	167	20	83
BMI (kg/m^2) *	32.0 ± 5.7	32.5 ± 5.8	32.5 ± 6.0	31.7 ± 5.0	31.2 ± 4.1	28.3 ± 3.7
range	22.7 - 70.9	24.0 - 70.9	24.4 - 64.9	24.4 - 54.4	24.3 - 40.1	22.7 - 44.0
<30 **	453 (43%)	246 (41%)	66 (40%)	72 (43%)	8 (40%)	61 (74%)
30 to <40	505 (48%)	305 (50%)	84 (51%)	84 (50%)	11 (55%)	21 (25%)
≥40	85 (8%)	57 (9%)	15 (9%)	11 (7%)	1 (5%)	1 (1%)
No. of WOMEN	2,191	1,160	480	341	151	59
BMI (kg/m^2)	34.9 ± 7.0	35.0 ± 7.1	36.3 ± 7.1	34.0 ± 6.0	33.9 ± 6.3	30.7 ± 6.5
range	22.1 - 71.5	23.9 - 71.5	24.1 - 65.1	22.6 - 64.9	24.0 - 55.4	22.1 - 50.4
<30	593 (27%)	325 (28%)	101 (21%)	94 (28%)	38 (25%)	35 (59%)
30 to <40	1134 (52%)	585 (50%)	248 (52%)	194 (57%)	90 (60%)	16 (29%)
≥40	464 (21%)	250 (22%)	131 (27%)	53 (16%)	23 (15%)	7 (12%)

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*Mean ± SD; **n, (%)

Glycemia by Sex and Ethnicity

	Overall	Caucasian	African American	Hispanic	American Indian	Asian American
No. of MEN	1,043	608	165	167	20	83
FPG (mmol/L) *	6.0 ± 0.5	6.0 ± 0.5	6.0 ± 0.4	6.0 ± 0.5	5.8 ± 0.4	6.0 ± 0.4
range	5.2 - 7.7	5.3 - 7.7	5.3 - 7.3	5.3 - 7.7	5.2 - 6.6	5.3 - 7.5
2-hr PG (mmol/L)	9.1 ± 0.9	9.2 ± 0.9	9.1 ± 1.0	9.1 ± 1.0	9.1 ± 0.9	9.1 ± 0.9
range	7.8 - 11.0	7.8 - 11.0	7.8 - 11.0	7.8 - 11.0	7.9 - 10.5	7.8 - 11.0
HbA_{1c} (%)	5.9 ± 0.5	5.8 ± 0.4	6.2 ± 0.7	5.9 ± 0.5	5.8 ± 0.5	6.0 ± 0.4
range	4.0 - 7.7	4.0 - 7.2	4.2 - 7.7	4.4 - 7.2	4.5 - 6.7	4.8 - 6.8
> 6.1% **	316 (30%)	133 (22%)	105 (64%)	47 (28%)	5 (25%)	26 (31%)
No. of WOMEN	2,191	1,160	480	341	151	59
FPG (mmol/L)	5.9 ± 0.4	5.9 ± 0.4	6.0 ± 0.5	5.8 ± 0.4	5.5 ± 0.5	5.9 ± 0.4
range	4.2 - 7.7	5.3 - 7.7	5.3 - 7.5	5.3 - 7.3	4.2 - 6.8	5.3 - 6.8
2-hr PG (mmol/L)	9.1 ± 0.9	9.2 ± 0.9	9.1 ± 1.0	9.1 ± 0.9	9.1 ± 1.0	9.4 ± 0.9
range	7.8 - 11.0	7.8 - 11.0	7.8 - 11.0	7.8 - 11.0	7.8 - 11.0	7.8 - 11.0
HbA_{1c} (%)	5.9 ± 0.5	5.8 ± 0.4	6.2 ± 0.6	5.9 ± 0.5	6 ± 0.4	5.9 ± 0.4
range	3.2 - 8.5	3.6 - 7.4	3.2 - 8.5	4.4 - 7.5	5.0 - 7.6	4.5 - 7.1
> 6.1%	616 (28%)	215 (19%)	259 (54%)	76 (22%)	52 (34%)	15 (25%)

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*Mean ± SD; **_n_, (%)

Insulinemia by Sex and Ethnicity

INSULIN (pmol/L)	Overall	Caucasian	African American	Hispanic	American Indian	Asian American
No. of MEN	1,043	608	165	167	20	83
Fasting *	158 ± 99	157 ± 101	148 ± 74	178 ± 118	151 ± 70	155 ± 88
range	26 - 1104	27 - 684	26 - 510	43 - 1104	48 - 288	36 - 480
30-min	590 ± 423	555 ± 424	527 ± 317	711 ± 414	820 ± 760	661 ± 441
range	27 - 4854	31 - 4854	66 - 1812	27 - 2190	294 - 3480	78 - 2280
No. of WOMEN	2,191	1,160	480	341	151	59
Fasting	158 ± 86	151 ± 80	167 ± 91	168 ± 91	170 ± 89	148 ± 103
range	14 - 720	14 - 552	18 - 576	32 - 720	34 - 534	36 - 576
30-min	607 ± 368	557 ± 323	617 ± 416	681 ± 378	810 ± 444	569 ± 276
range	18 - 3600	36 - 3600	18 - 3024	52 - 2100	78 - 2436	132 - 1248

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*Mean ± SD

Lipids by Sex and Ethnicity

Lipids (mmol/L)	Overall	Caucasian	African American	Hispanic	American Indian	Asian American
No. of MEN	1,043	608	165	167	20	83
Total cholesterol *	5.2 ± 0.9	5.2 ± 0.9	5.2 ± 0.9	5.2 ± 0.9	4.9 ± 1.0	5.4 ± 1.0
HDL cholesterol	1.0 ± 0.2	1.0 ± 0.2	1.1 ± 0.2	1.0 ± 0.2	1.0 ± 0.1	1.1 ± 0.2
LDL cholesterol	3.3 ± 0.8	3.2 ± 0.8	3.4 ± 0.9	3.2 ± 0.9	2.9 ± 1.0	3.4 ± 0.8
Trigylcerides	2.0 ± 1.1	2.1 ± 1.1	1.5 ± 0.9	2.2 ± 1.2	2.1 ± 1.1	2.0 ± 1.1
No. of WOMEN	2,191	1,160	480	341	151	59
Total cholesterol	5.3 ± 1.0	5.4 ± 0.9	5.2 ± 1.0	5.2 ± 0.9	4.8 ± 1.0	5.4 ± 0.9
HDL cholesterol	1.2 ± 0.3	1.2 ± 0.3	1.3 ± 0.3	1.2 ± 0.3	1.2 ± 0.3	1.3 ± 0.3
LDL cholesterol	3.2 ± 0.9	3.2 ± 0.8	3.3 ± 0.9	3.2 ± 0.9	2.8 ± 0.8	3.2 ± 0.9
Trigylcerides	1.7 ± 0.9	1.9 ± 1.0	1.2 ± 0.6	1.8 ± 0.9	1.7 ± 0.8	2.0 ± 1.2

*Mean ± SD

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