

# CARDIOLOGY AND DIABETES MELLITUS

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HOSKINSON HEALTH AND WELLNESS

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Daniel Davidovich, MD- None

Disclosure of Relevant Financial Relationships and Mechanism to Identify and Mitigate Conflicts of Interest: No conflicts of interest

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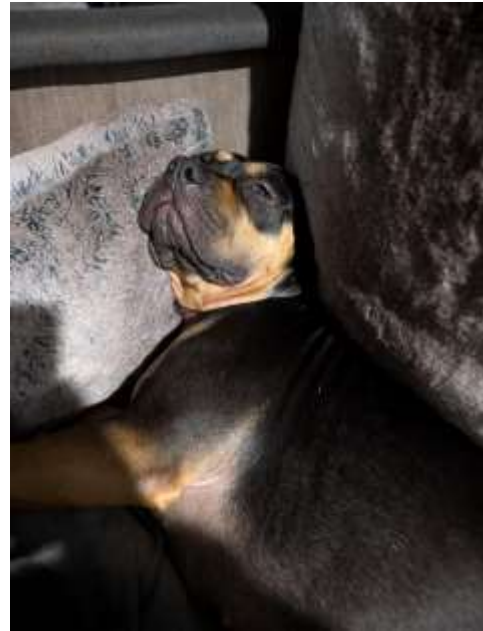
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## STATISTICS

- Higher incidence of disease
- Greater extent of CAD
- Higher incidence of multi-vessel or severe disease
- More often asymptomatic
- Higher BG level, higher incidence of CAD
- More myocardial infarctions

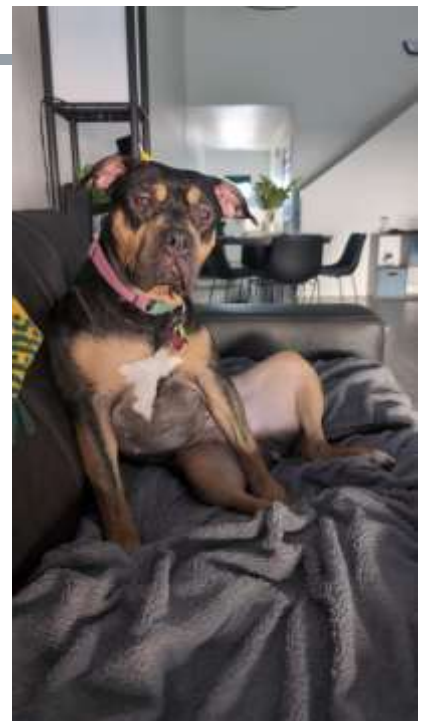


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## WHY?

- Endothelial dysfunction (can be acute, is reversible)
- Increased thrombosis (platelet aggregation and activation, coag abnormalities)
- Plaque characteristics (type 1 vs type 2)



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# CALCIUM SCORING?

Screening of asymptomatic patients with type 2 diabetes mellitus for silent coronary artery disease: combined use of stress myocardial perfusion imaging and coronary calcium scoring

Screening of asymptomatic patients with type 2 diabetes mellitus for silent coronary artery disease: combined use of stress myocardial perfusion imaging and coronary calcium scoring

Author: J. A. Gidding, MD, PhD, et al. (2014)

### Abstract

Diabetes and coronary artery disease modification are common clinical complications. Rates of and mortality in a result of cardiovascular complications are high in patients with type 2 diabetes. Screening for silent coronary artery disease to detect the disease in an early stage able to initiate early appropriate treatment, has recently become an important focus of attention. Recent prospective studies have shown that the overall prevalence of silent coronary disease in type 2 diabetes mellitus patients is about 20% to 30%. It is of clinical importance to explore just to screen for the target population, in the era of view the relative value of stress radiolabeled myocardial perfusion imaging and calcium scoring are evaluated. The two investigations appear to have complementary benefits in asymptomatic individuals with diabetes mellitus, a scoring algorithm, separate use of coronary calcium scoring and subsequent stress radiolabeled myocardial imaging is presented.

# Coronary Calcium Score and Prediction of All-Cause Mortality in Diabetes

The Diabetes Heart Study

Author: J. A. Gidding, MD, PhD, et al. (2014)

**OBJECTIVE**—To determine if coronary calcium scoring (CCS) can provide additional prognostic information beyond traditional risk factors. **RESEARCH DESIGN AND METHODS**—A total of 1,031 participants aged 45–65 years in the Diabetes Heart Study (DHS) were selected for 7-year follow-up and screened for the presence of coronary artery disease (CAD) using a 64-slice CT scan. The mean age was 54.1 years (SD 6.1 years), 50% were female, and 80% were African American. The mean HbA1c was 7.5% (SD 1.2%). The mean systolic blood pressure was 130/70 mm Hg. The mean LDL cholesterol was 170 mg/dL. The mean waist circumference was 100 cm. The mean duration of diabetes was 10 years. The mean duration of diabetes was 10 years. The mean duration of diabetes was 10 years.

**RESULTS**—At baseline, 11% (118 of 1,031) participants had coronary artery disease (CAD) as defined by a stenosis of ≥50% in any of the major coronary arteries. The mean age of those with CAD was 54.1 years (SD 6.1 years), 50% were female, and 80% were African American. The mean HbA1c was 7.5% (SD 1.2%). The mean systolic blood pressure was 130/70 mm Hg. The mean LDL cholesterol was 170 mg/dL. The mean waist circumference was 100 cm. The mean duration of diabetes was 10 years. The mean duration of diabetes was 10 years.

**CONCLUSIONS**—In patients with type 2 diabetes, the presence of CAD at baseline was associated with an increased risk of all-cause mortality. The addition of CCS to traditional risk factors improved the prediction of all-cause mortality. The addition of CCS to traditional risk factors improved the prediction of all-cause mortality.

**RESEARCH DESIGN AND METHODS**—The Diabetes Heart Study (DHS) is a 7-year study to assess the impact of intensive glucose control on the risk of cardiovascular complications in patients with type 2 diabetes. The study includes a baseline assessment of cardiovascular risk factors, including coronary calcium scoring and myocardial perfusion imaging. The DHS design has been described in detail previously (1). The study protocol is available at <http://www.nhlbi.nih.gov/health/studies/dhs/>.

# Value of Coronary Artery Calcium Scanning by Computed Tomography for Predicting Coronary Heart Disease in Diabetic Subjects

Author: J. A. Gidding, MD, PhD, et al. (2014)

Abstract

**OBJECTIVE**—The intent of this study is to evaluate the value of coronary artery calcium scoring (CAC) in predicting the risk of cardiovascular complications in patients with type 2 diabetes. **RESEARCH DESIGN AND METHODS**—A total of 1,031 participants aged 45–65 years in the Diabetes Heart Study (DHS) were selected for 7-year follow-up and screened for the presence of coronary artery disease (CAD) using a 64-slice CT scan. The mean age was 54.1 years (SD 6.1 years), 50% were female, and 80% were African American. The mean HbA1c was 7.5% (SD 1.2%). The mean systolic blood pressure was 130/70 mm Hg. The mean LDL cholesterol was 170 mg/dL. The mean waist circumference was 100 cm. The mean duration of diabetes was 10 years. The mean duration of diabetes was 10 years.

**CONCLUSIONS**—The addition of CAC to traditional risk factors improved the prediction of all-cause mortality. The addition of CAC to traditional risk factors improved the prediction of all-cause mortality.

with diabetes (13.5%) had risk stratification using a risk ratio between 0.5 and 1.5.

Participants were screened for the presence of coronary artery disease and the extent of atherosclerosis using a 64-slice CT scanner. The mean age was 54.1 years (SD 6.1 years), 50% were female, and 80% were African American. The mean HbA1c was 7.5% (SD 1.2%). The mean systolic blood pressure was 130/70 mm Hg. The mean LDL cholesterol was 170 mg/dL. The mean waist circumference was 100 cm. The mean duration of diabetes was 10 years. The mean duration of diabetes was 10 years.

**RESEARCH DESIGN AND METHODS**

Subjects and study design

# Absence of Coronary Artery Calcium Identifies Asymptomatic Diabetic Individuals at Low Near-Term But Not Long-Term Risk of Mortality

A 10-Year Follow-Up Study of 8718 Patients

Abstract

Author: J. A. Gidding, MD, PhD, et al. (2014)



https://www.nhlbi.nih.gov/health/studies/dhs/

MESA The Multi-Ethnic Study of Atherosclerosis

Back to MESA LWC

Input your age, select your gender and race/ethnicity, age (approximately) your observed calcium score and risk calculator

Age (years)

Gender

Race/Ethnicity

Observed Calcium Score (approx)

Calculate

The estimated probability of a nonfatal calcium event for a black female of age 50 is **12%**.

Percentiles and Calcium Scores for: Black female of age 50

25th	50th	75th	90th
2	2	3	3

The observed calcium score of 12 is at percentile **10** for subjects of the same age, gender, and race/ethnicity who are free of clinical cardiovascular disease and treated diabetes.

Chart 1: Percentiles





# MEDICATIONS

- Daily low dose ASA
- Statins
- Other lipid lowering agents
- SGLT2 inhibitor
- GLP-1 Receptor agonist
- Metformin



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**Journal of the American Heart Association**  
 Original Article  
**Effects of Aspirin for Primary Prevention in Persons with Diabetes Mellitus**  
 The ASCEND Study Collaborators Group<sup>1</sup>  
 Abstract  
**Background**  
 Diabetes mellitus is associated with an increased risk of cardiovascular events. Aspirin use reduces the risk of ischemic vascular events but increases the risk of bleeding. The balance of benefits and harms for the prevention of first cardiovascular events in persons with diabetes is unclear.  
**Objective**  
 We randomly assigned adults who had diabetes but no other cardiovascular disease to receive aspirin at a dose of 80 mg daily or matching placebo. The primary efficacy outcome was the first stroke (ischemic stroke or fatal stroke), stroke or myocardial infarction, stroke or myocardial infarction, or death from any vascular cause, including any confirmed anatomical heart failure. The primary safety outcome was the first major bleeding event (ie, intracranial hemorrhage, gastrointestinal bleeding event in the not gastrointestinal bleeding, or other serious bleeding). Secondary outcomes included gastrointestinal tract cancer.  
**Results**  
 A total of 35,446 participants underwent randomization. During a mean follow-up of 6.2 years, serious vascular events occurred in a significantly lower percentage of participants in the aspirin group than in the placebo group (50 participants [0.14%] vs 543 [1.54%]; risk ratio, 0.09; 95% confidence interval [CI], 0.07 to 0.10; P<0.001). In addition, major bleeding events occurred in 584 participants (1.74%) in the aspirin group, as compared with 697 (2.01%) in the placebo group (hazard ratio, 0.86; 95% CI, 0.76 to 0.97; P=0.008), with most of the events being gastrointestinal bleeding and other external bleeding. There was no significant difference between the aspirin group and the placebo group in the incidence of gastrointestinal tract cancer (117 participants [0.34%] and 138 [0.40%], respectively) or all-cause mortality (111,492 and 107,123 [0.34%] respectively) during the mean 6.2 years of follow-up.  
**Conclusions**  
 Aspirin use prevented serious vascular events in persons who had diabetes and no other cardiovascular disease at 80 mg daily, but it also caused major bleeding events. The absolute benefits were largely counterbalanced by the bleeding harms, (funded by the Robert Wood Johnson Foundation and others. ASCEND ClinicalTrials.gov Identifier: NCT01260958; ClinicalTrials.gov Identifier: NCT01260958).  
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**Journal of the American Heart Association**  
 Original Research  
**Aspirin Use and Cardiovascular Outcome in Patients With Type 2 Diabetes Mellitus and Heart Failure: A Population-Based Cohort Study**  
 Chakraborti R, PhD, PhD, FACC, FAMA, et al. Circulation. 2019;140:1421-1430.  
**Background**  
 Aspirin is of uncertain benefit for primary prevention in patients with type 2 diabetes mellitus (T2D). We assessed whether primary prevention with aspirin is beneficial in patients with T2D and heart failure (HF).  
**Methods and Results**  
 Data from the Health Improvement Network, a UK medication prospective primary care database, were analyzed. Those with T2D and HF, age ≥65 years, and no previous history of myocardial infarction, stroke, coronary artery disease, peripheral artery disease, or atrial fibrillation were included. We compared outcomes for those not aspirin to an aspirin algorithm of HF and T2D and assessed the role of a 100-mg daily. The primary outcome was a composite of all-cause mortality and hospitalization for HF. Secondary outcomes were cardiac stroke, nonfatal myocardial infarction, or major bleeding. There were 5877 participants on aspirin and 8027 not on aspirin. The mean age (SD) was 75.1 (8.6) years, 53.8% were men, and the mean follow-up (SD) was for 5.1 (4.2) years. After propensity score matching and further multivariate adjustment, aspirin use significantly decreased with a decrease in the primary outcome and all-cause mortality (hazard ratio: 0.92; 95% confidence interval [CI], 0.88, 0.95; P<0.001), myocardial infarction (hazard ratio: 0.88; 95% CI, 0.82, 0.94; P<0.001), stroke (hazard ratio: 0.87; 95% CI, 0.81, 0.93; P<0.001), and hospitalization for HF was not significantly higher with aspirin (hazard ratio: 0.94; 95% CI, 0.87, 1.01; P=0.15). There was no additional benefit for a dose >75 mg.  
**Conclusions**  
 Primary prevention with aspirin in patients with T2D and HF is associated with lower all-cause mortality.  
**Key Words:** aspirin • death • diabetes mellitus • heart failure  
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**ASAP Aspirin Use**  
**Recommendations for Aspirin Use**  
 Referenced studies that support recommendations are summarized in Online Data Supplement 17 and 18.

CDE	IOK	Recommendations
Stroke	IOK	1. Low-dose aspirin (75-100 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk. <sup>16a,16b</sup>
MI	IOK	2. Low-dose aspirin (75-100 mg orally daily) should not be administered as a routine basis for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding. <sup>16a,16b</sup>
MI	IOK	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding. <sup>16a,16b</sup>

**Recommendations for Adults With Type 2 Diabetes Mellitus**  
 Referenced studies that support recommendations are summarized in Online Data Supplement 17 and 18.

CDE	IOK	Recommendations
Stroke	IOK	1. For adults with T2DM, a reduced-dose aspirin (75 mg orally daily) might be considered for the primary prevention of ASCVD among select adults 40 to 70 years of age who are at higher ASCVD risk but not at increased bleeding risk. <sup>16a,16b</sup>
MI	IOK	2. Low-dose aspirin (75-100 mg orally daily) should not be administered as a routine basis for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding. <sup>16a,16b</sup>
MI	IOK	3. Low-dose aspirin (75-100 mg orally daily) should not be administered for the primary prevention of ASCVD among adults of any age who are at increased risk of bleeding. <sup>16a,16b</sup>

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**11.7%** Current 10 Year ASCVD Risk

Lifetime ASCVD Risk: 50%    Duration ASCVD Risk: 2.1%

App should be used for primary prevention patients (those without ASCVD only)

Current Age: 75    Sex: Male    Race: White

Systolic Blood Pressure: 117    Diastolic Blood Pressure: 82

Total Cholesterol: 170    HDL Cholesterol: 50    LDL Cholesterol: 120

History of Diabetes: No    History of MI: No    History of Stroke: No

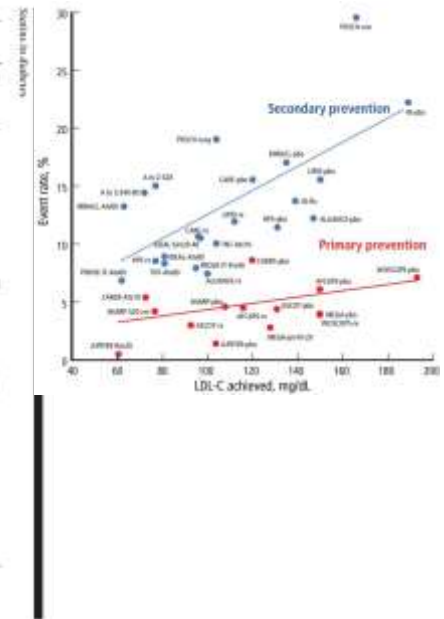
Are you currently taking any cholesterol-lowering drugs? No

[Estimate Therapy Impact](#)    [View Advice](#)

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Table 1—Primary prevention trials and meta-analysis of statin use in diabetic individuals with no other CVD risk factors

Intervention	n	Primary outcome comparison	Results
Heart Protection Study (2)	5,000	Five major coronary events, stroke, or revascularization	22% (95% CI 13–30) reduction in the event rate ( $P < 0.0001$ ); 19% reduction in event rate (95% CI 13–26, $P = 0.0002$ ) among the 2,512 diabetic without CVD at entry, and 27% reduction in event rate (95% CI 13–40, $P = 0.0002$ ) among 2,488 diabetic participants whose pre-treatment LDL cholesterol concentration was $< 3.0$ mmol/L
Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in Statin-naïve, dependent diabetes mellitus (ASPEN) (3)	2,818	Cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, revascularization, coronary artery bypass surgery, revascularized cardiac arrest, and occurring or fatal acute myocardial infarction requiring hospitalization	Composite primary end point favor statin 13.7 risk reduction vs 15.1% in the placebo group (based on 0.90 95% CI 0.73–1.12). Among 1,405 subjects without prior myocardial infarction or interventional procedure, 0.4% of atorvastatin-treated and 0.8% of placebo-treated subjects experienced a primary end point (0.87 [0.78–1.24])
Cholesterol Treatment Project (CTP) Collaborative meta-analysis (4)	38,888 (14 randomized trials)	All-cause mortality and major vascular events (myocardial infarction or coronary death, stroke, or coronary revascularization)	0% reduction in all-cause mortality per mmol/L LDL cholesterol reduction (RR 0.91, 95% CI 0.92–1.01, $P = 0.02$ ); 20% in major vascular events per mmol/L LDL cholesterol reduction (0.79, 95% CI 0.72–0.86, $P < 0.0001$ )
Steg Achieves Increase in HbA1c Diabetes Study (SANDHUS) (5)	408	Progression of subclinical atherosclerosis measured by carotid-intimal artery-mechanical thickness	Intimal medial thickness progressed in the aggressive group and regressed in the standard group ( $-0.011$ vs $0.008$ mm, $P < 0.005$ )



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THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes

Steven P. Marso, M.D., Stephen C. Bain, M.D., Agostino Cerami, M.D., ...

ABSTRACT

Background Semaglutide specifies the need to establish cardiovascular safety of new diabetes therapies in patients with type 2 diabetes in order to use for more cardiovascular risk.

Methods We randomly assigned 10,001 patients with type 2 diabetes who were at a moderate-to-high risk to receive once-weekly semaglutide, 0.5 mg or 1.0 mg or placebo for 52 weeks.

Results At baseline, 57% of the patients (5094) had established cardiovascular disease. The primary composite outcome was the first occurrence of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke.

Conclusions Semaglutide significantly reduced the risk of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke in patients with type 2 diabetes.



DOI: 10.1056/NEJMoa2102009. Copyright © 2021 Massachusetts Medical Society. All rights reserved.

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Empagliflozin, Cardiovascular Outcomes, and Mortality in Type 2 Diabetes

Michael E. Zelnick, M.D., Michael J. Blum, M.D., ...

ABSTRACT

Background Empagliflozin, an inhibitor of sodium-glucose cotransporter 2, in addition to standard care, can reduce cardiovascular morbidity and mortality in patients with type 2 diabetes or high cardiovascular risk.

Methods We randomly assigned patients to receive 10 mg or 25 mg of empagliflozin or placebo once daily. The primary composite outcome was death from cardiovascular causes.

Results A total of 7608 patients were treated (mean duration, 3.3 years). The primary outcome occurred in 40% of 3681 patients (50%) in the placebo group and in 28% of 3927 patients (22%) in the empagliflozin group.

Conclusions Empagliflozin significantly reduced the risk of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke in patients with type 2 diabetes.

Background Semaglutide specifies the need to establish cardiovascular safety of new diabetes therapies in patients with type 2 diabetes in order to use for more cardiovascular risk.

THE NEW ENGLAND JOURNAL OF MEDICINE

ORIGINAL ARTICLE

Canagliflozin and Cardiovascular and Renal Events in Type 2 Diabetes

Michael E. Zelnick, M.D., Michael J. Blum, M.D., ...

ABSTRACT

Background Canagliflozin, an inhibitor of sodium-glucose cotransporter 2, in addition to standard care, can reduce cardiovascular morbidity and mortality in patients with type 2 diabetes or high cardiovascular risk.

Methods We randomly assigned patients to receive 100 mg or 300 mg of canagliflozin or placebo once daily. The primary composite outcome was death from cardiovascular causes.

Results A total of 7608 patients were treated (mean duration, 3.3 years). The primary outcome occurred in 40% of 3681 patients (50%) in the placebo group and in 28% of 3927 patients (22%) in the canagliflozin group.

Conclusions Canagliflozin significantly reduced the risk of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke in patients with type 2 diabetes.

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Canagliflozin in Patients with Heart Failure and Reduced Ejection Fraction

Michael E. Zelnick, M.D., Michael J. Blum, M.D., ...

Background Canagliflozin, an inhibitor of sodium-glucose cotransporter 2, in addition to standard care, can reduce cardiovascular morbidity and mortality in patients with type 2 diabetes or high cardiovascular risk.

Methods We randomly assigned patients to receive 100 mg or 300 mg of canagliflozin or placebo once daily. The primary composite outcome was death from cardiovascular causes.

Results A total of 7608 patients were treated (mean duration, 3.3 years). The primary outcome occurred in 40% of 3681 patients (50%) in the placebo group and in 28% of 3927 patients (22%) in the canagliflozin group.

Conclusions Canagliflozin significantly reduced the risk of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke in patients with type 2 diabetes.

ARTICLE

### Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34)

UK Prospective Diabetes Study (UKPDS 34)\*

#### Summary

**Background:** Intensive control with metformin in overweight patients with newly diagnosed type 2 diabetes, mean age 55 years, had modest benefits on glucose control and microvascular complications.

**Methods:** In 4071 patients recruited to UKPDS in 18 centres, 1783 overweight (>25% above bodyweight) patients with newly diagnosed type 2 diabetes, mean age 55 years, had random fasting plasma glucose 9.0–12.0 mmol/L without insulin therapy. Patients who 2 months later did not have diabetes in a randomised controlled trial between insulin and 1 year of intensive glucose control with oral glucose control (IGC) were included in the primary outcome (microvascular complications) and secondary outcome (all-cause mortality). The primary outcome included the 3073 patients who had complete data on microvascular complications. The primary outcome included the 3073 patients who had complete data on microvascular complications. The primary outcome included the 3073 patients who had complete data on microvascular complications.

**Results:** In the primary outcome, intensive control with metformin reduced the risk of microvascular complications by 33% (95% CI 19–47, p<0.001) compared with standard control. The primary outcome included the 3073 patients who had complete data on microvascular complications. The primary outcome included the 3073 patients who had complete data on microvascular complications.

intensive control with metformin reduced the risk of microvascular complications by 33% (95% CI 19–47, p<0.001) compared with standard control. The primary outcome included the 3073 patients who had complete data on microvascular complications. The primary outcome included the 3073 patients who had complete data on microvascular complications.

**Conclusion:** The UK Prospective Diabetes Study reported that intensive blood glucose control with metformin in newly diagnosed type 2 diabetes patients with newly diagnosed type 2 diabetes, mean age 55 years, had modest benefits on glucose control and microvascular complications. The primary outcome included the 3073 patients who had complete data on microvascular complications.



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## HOW ABOUT DIET AND EXERCISE?



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## QUESTIONS?

