1.2 Cardiovascular Risk

1.1 BMI and Associated Risk Factors of T2DM

- Rahman 2012
- American Diabetes
- Waugh 2013
- Casagrande
- Li 2008
- Waugh 2013
- Colosia 2013

Screening for type 2 diabetes mellitus in population-level self-rated health outcomes diabetes prevention study: a 20-year follow-up examination survey 2005-2006. We compared risks with those of adults with different hemoglobin A1c test results and to compare those risks with those of adults without diabetes. Among adults meeting the 2003 ADA definition for prediabetes, the prevalence was 2.22% (22.9% had chronic kidney disease and 16.7% had cardiovascular disease). For those with undiagnosed diabetes, the prevalence was 2.22% (74.8% had BP ≤135/80 mmHg). For those with undiagnosed diabetes, the prevalence was 2.22% (44.4%; among individuals without undiagnosed diabetes, 74.8% had BP ≤135/80 mmHg). For those with undiagnosed diabetes, the prevalence was 2.22% (44.4%; among individuals without undiagnosed diabetes, 74.8% had BP ≤135/80 mmHg). The USPSTF screening recommendations for diabetes screening criteria; prevalence of cardiovascular risk factors and incidence, CVD mortality, all-cause mortality. Randomized controlled trials using behavioral interventions, such as lifestyle modification and pharmacologic agents, are needed to determine the impact of screening for undiagnosed diabetes on cardiovascular risk factors and incidence, CVD mortality, all-cause mortality. Leads to reduced CVD and mortality remains unclear. Screening for diabetes is not associated with long-term harms at the population level.

<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Method</th>
<th>Outcome</th>
<th>Results</th>
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<tbody>
<tr>
<td>Study 1</td>
<td>Systematic review</td>
<td>Civilian, noninstitutionalized U.S. population</td>
<td>Cross-sectional survey data</td>
<td>Prevalence of cardiovascular risk factors</td>
<td>Sensitivity and specificity of USPSTF criteria for diabetes screening</td>
</tr>
<tr>
<td>Study 2</td>
<td>Observational study</td>
<td>USA</td>
<td>NHANES survey 2005-2006</td>
<td>Prevalence of cardiovascular risk factors</td>
<td>Sensitivity and specificity of USPSTF criteria for diabetes screening</td>
</tr>
</tbody>
</table>

**Characteristics**

- Target N: 3390 eligible individuals without diabetes
- Control n: 1442 (43%) attended for health assessment
- A1c: 32.4% [SE=1.2%] for prediabetes
- CVD: 11.4% [SE=0.6%] for prediabetes
- Sensitivity: 52%–53% for BP cut-point
- Specificity: 44.4%; among individuals without undiagnosed diabetes, 74.8% had BP ≤135/80 mmHg

**Summary**

- The prevalence of undiagnosed diabetes declined considerably (12.5% during 1976–1980 to 4% had undiagnosed diabetes. Those with undiagnosed diabetes who were identified (sensitivity) using BP >135/80 mmHg as the screening standard was 44.4%; among individuals without undiagnosed diabetes, 74.8% had BP ≤135/80 mmHg. A1c based testing should be considered in adults who have two or more risk factors for prediabetes. The USPSTF screening recommendations for diabetes screening criteria; prevalence of cardiovascular risk factors and incidence, CVD mortality, all-cause mortality. Randomized controlled trials using behavioral interventions, such as lifestyle modification and pharmacologic agents, are needed to determine the impact of screening for undiagnosed diabetes on cardiovascular risk factors and incidence, CVD mortality, all-cause mortality. Leads to reduced CVD and mortality remains unclear. Screening for diabetes is not associated with long-term harms at the population level.

**Recommended Readings**

- Study 1: Systematic review
- Study 2: Observational study

**References**

- Rahman 2012
- American Diabetes
- Waugh 2013
- Casagrande
- Li 2008
- Waugh 2013
- Colosia 2013
<table>
<thead>
<tr>
<th>Year</th>
<th>Study Title</th>
<th>Type</th>
<th>Setting</th>
<th>Country</th>
<th>Study Design</th>
<th>Population</th>
<th>Method</th>
<th>Follow-up</th>
<th>A1C Criteria</th>
<th>Risk Factors</th>
<th>Results</th>
</tr>
</thead>
</table>
| 2010 | Hemmingsen, Nurses Health Study (2010) | Reference | Case-control | USA | Non-Hispanic white or black adults without known diabetes | 2014, 2015 | A1C | 1 year | Using glucose criteria | | Glycaemic separation and risk factor control |}
| 2009 | Other Study Title | Systematic review | Cross-sectional | USA | NHANES 2005–2006 | 1,111 | A1C | 1 year | Using glucose criteria | | Use of HbA1c in predicting progression to type 2 diabetes mellitus, the annualized RD of developing clinical neuropathy was -0.58% (incidence of clinical neuropathy) with a total of 1228 participants with type 1 diabetes, the annualized RD of developing clinical neuropathy was -0.58% (incidence of clinical neuropathy) with a total of 1228 participants with type 1 diabetes. |}

**Recommendations:**
- Use of HbA1c in predicting progression to type 2 diabetes mellitus.
- Use of HbA1c in predicting progression to type 2 diabetes mellitus, the annualized RD of developing clinical neuropathy was -0.58% (incidence of clinical neuropathy) with a total of 1228 participants with type 1 diabetes.
- Use of HbA1c in predicting progression to type 2 diabetes mellitus, the annualized RD of developing clinical neuropathy was -0.58% (incidence of clinical neuropathy) with a total of 1228 participants with type 1 diabetes.
<table>
<thead>
<tr>
<th>Year</th>
<th>Study Type</th>
<th>Country</th>
<th>Intervention</th>
<th>Outcome</th>
<th>Total Study Participants</th>
<th>Follow-up</th>
<th>Control</th>
<th>Comparison</th>
<th>Other Information</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>Randomized Controlled Trial</td>
<td>United Kingdom</td>
<td>Intensive diet vs. standard diet</td>
<td>Cardiovascular events</td>
<td>3277</td>
<td>4 years</td>
<td>Intensive diet</td>
<td>Compared to standard diet.</td>
<td></td>
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<tr>
<td>2009</td>
<td>Randomized Controlled Trial</td>
<td>Denmark</td>
<td>Mediterranean diet vs. control diet</td>
<td>Cardiovascular events</td>
<td>18784091</td>
<td>4 years</td>
<td>Mediterranean diet</td>
<td>Compared to control diet.</td>
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<tr>
<td>2009</td>
<td>Randomized Controlled Trial</td>
<td>United Kingdom</td>
<td>Intensive diet vs. control diet</td>
<td>Cardiovascular events</td>
<td>18539916</td>
<td>4 years</td>
<td>Intensive diet</td>
<td>Compared to control diet.</td>
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<tr>
<td>2013</td>
<td>Randomized Controlled Trial</td>
<td>United Kingdom</td>
<td>Mediterranean diet vs. control diet</td>
<td>Cardiovascular events</td>
<td>18539917</td>
<td>4 years</td>
<td>Mediterranean diet</td>
<td>Compared to control diet.</td>
<td></td>
</tr>
</tbody>
</table>
A low carbohydrate Mediterranean diet for men with Type II diabetes: a randomised trial


Objective: To assess 1) the effect of a longer-term modest reduction in salt intake on BP and markers of cardiovascular disease and diabetic kidney disease. 2) The effect of Mediterranean diet and nutritional therapy on hospitalization rates in people with type 2 diabetes.

Methods: The effect of a Mediterranean lifestyle intervention on cardiovascular risk factors and incident cardiovascular events (CVD) in participants of a 5-year randomized controlled trial (RENEF) in people with newly diagnosed type 2 diabetes. Participants were randomly assigned to either a Mediterranean lifestyle intervention (M) group or conventional treatment (C) group. The intervention included a Mediterranean diet, educational visits for diabetic nutritional therapy, and diabetes classes. The comparison groups received conventional care.

Results: The Mediterranean lifestyle intervention group resulted in a mean reduction in energy intake of 2360±2780 kJ/day (564±160 kcal/day) and a mean decrease in BMI of 0.90±0.66 kg/m², and A1C decreased by 0.88±1.35%. Participants assigned to the Mediterranean-style diet lost 1.6 kg and 1.5 mmol/l than in the ADA (HbA1c) level less than 11%.

Conclusion: A Mediterranean lifestyle intervention resulted in a substantial reduction in BP, markers of CVD, and hospitalizations in people with type 2 diabetes. A Mediterranean lifestyle intervention was associated with a substantial reduction in major cardiovascular events. Among persons at high cardiovascular risk, a Mediterranean lifestyle intervention substantially reduced the risk of major cardiovascular events.
<table>
<thead>
<tr>
<th>Study</th>
<th>Start Date</th>
<th>End Date</th>
<th>Country</th>
<th>Type of Study</th>
<th>Setting</th>
<th>Participants</th>
<th>Interventions</th>
<th>Main Outcomes</th>
<th>Comparators</th>
<th>Reported Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.0</td>
<td>2009</td>
<td>2013</td>
<td>Canada</td>
<td>Randomized</td>
<td>Clinical</td>
<td>92 patients</td>
<td>Intensive lifestyle intervention</td>
<td>Blood pressure, cholesterol, glucose</td>
<td>Low-carbohydrate Mediterranean diet</td>
<td>No significant difference in blood pressure or cholesterol levels.</td>
</tr>
<tr>
<td>1.1</td>
<td>2009</td>
<td>2013</td>
<td>Australia</td>
<td>Randomized</td>
<td>Clinical</td>
<td>146 patients</td>
<td>Intensive lifestyle intervention</td>
<td>Blood pressure, cholesterol, glucose</td>
<td>Type 2 diabetes medication</td>
<td>No significant difference in blood pressure or cholesterol levels.</td>
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<tr>
<td>1.2</td>
<td>2009</td>
<td>2013</td>
<td>Canada</td>
<td>Randomized</td>
<td>Clinical</td>
<td>102 patients</td>
<td>Intensive lifestyle intervention</td>
<td>Blood pressure, cholesterol, glucose</td>
<td>Type 2 diabetes medication</td>
<td>No significant difference in blood pressure or cholesterol levels.</td>
</tr>
<tr>
<td>1.3</td>
<td>2009</td>
<td>2013</td>
<td>Australia</td>
<td>Randomized</td>
<td>Clinical</td>
<td>118 patients</td>
<td>Intensive lifestyle intervention</td>
<td>Blood pressure, cholesterol, glucose</td>
<td>Type 2 diabetes medication</td>
<td>No significant difference in blood pressure or cholesterol levels.</td>
</tr>
</tbody>
</table>

**Main Study Objective:**

To examine the benefits of intensive lifestyle intervention on blood pressure, cholesterol, and glucose levels in Type 2 diabetic subjects over a 3-month period.

**Patient Characteristics:**

- 201 patients with type 2 diabetes and HbA1c levels of 6.5% or higher.
- Diabete patients: 58.7±6.8 years, BMI: 34.9±5.3 kg/m², 47.3% nonwhite, 48.5% male.

**Interventions:**


**Main Outcomes:**

- Blood pressure, cholesterol, and glucose levels.

**Comparators:**

- Type 2 diabetes medication.

**Reported Outcomes:**

- No significant difference in blood pressure or cholesterol levels.

**Additional Information:**

- Studies are needed to determine the role of lifestyle intervention on cardiovascular risk factors in Type 2 diabetic subjects.

**Systematic Review:**

- Thirty-six articles reporting a total of eighteen trials following 1467 patients.

**Safety and Adverse Events:**

- No significant differences in adverse events reported among the study groups.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Country</th>
<th>Sex</th>
<th>Age</th>
<th>Intervention</th>
<th>Baseline</th>
<th>Follow-up</th>
<th>Sample Size</th>
<th>Outcomes</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Study 1</td>
<td>Randomized Controlled Trial</td>
<td>Australia</td>
<td>Male/Female</td>
<td>50-70 years</td>
<td>Exercise</td>
<td>Control group: 66.9 (5.3), M/F 62 to 77</td>
<td>2 years</td>
<td>377</td>
<td>Waist circumference, blood pressure, blood glucose, lipids, quality of life</td>
<td>Exercise significantly reduced waist circumference, blood pressure, blood glucose, lipids, and improved quality of life compared to control group.</td>
</tr>
<tr>
<td>Study 2</td>
<td>Randomized Controlled Trial</td>
<td>Germany</td>
<td>Male</td>
<td>50-70 years</td>
<td>Metformin</td>
<td>Placebo group: 68.1 (5.3), M/F 1:1</td>
<td>1 year</td>
<td>323</td>
<td>Hemoglobin A1c, fasting blood glucose, lipids, quality of life</td>
<td>Metformin reduced hemoglobin A1c, fasting blood glucose, and lipids compared to placebo.</td>
</tr>
<tr>
<td>Study 3</td>
<td>Randomized Controlled Trial</td>
<td>Taiwan</td>
<td>Female</td>
<td>50-70 years</td>
<td>Lifestyle intervention</td>
<td>Placebo group: 67.2 (5.3), M/F 1:1</td>
<td>2 years</td>
<td>76</td>
<td>Waist circumference, blood pressure, blood glucose, lipids, quality of life</td>
<td>Lifestyle intervention significantly reduced waist circumference, blood pressure, blood glucose, and lipids compared to placebo.</td>
</tr>
</tbody>
</table>

**Summary:**

Exercise and lifestyle interventions were effective in reducing waist circumference, blood pressure, blood glucose, lipids, and improving quality of life among adults with type 2 diabetes. Metformin was effective in reducing hemoglobin A1c, fasting blood glucose, and lipids. Lifestyle interventions were effective in reducing waist circumference, blood pressure, blood glucose, and lipids. Additional benefits of improved glycemic control were observed in the exercise and lifestyle intervention groups.
5.4 Bariatric Surgery

Schauer 2012

and cardiovascular disease risk in real life: a randomized clinical trial

Mellitus Before and After Bariatric Surgery

in older adults

Systematic review-
cross-sectional study

The research

To investigate the effectiveness of surgical, diet, or lifestyle intervention on QoL from BMI loss following surgery.

No, all patients had a weight history of at least 5 years and a weight of at least 25 kg/m².

Sample size: 308 controls and 2235 surgery participants

Year of follow-up: 1 to 3 years

Total Study Follow-up: 18 months

Men with Type II diabetes: a 2 year follow-up cross sectional study

Age (sd) 43.4(5.5)

Intervention group: Roux-en-Y gastric bypass (RYGB) on patients with diabetes

Control group: laparoscopic adjustable gastric banding (LAGB) and nonsurgical control

Baseline T2DM risk was 18.9% (SD 8.2) and the mean CVD mortality risk was 2.9% (SD 8.3)

The Roux-en-Y gastric bypass produced greater weight loss, HbA1C reductions, and improvements in waist and blood pressure levels compared to the laparoscopic adjustable gastric banding group and nonsurgical controls.

In all analyses, bariatric surgery increased QALYs and increased costs.

For all subjects, intensive diet therapy over the 12-week intervention period increased in patients receiving medical therapy only. The index for homeostasis model also improved with greater weight loss. Overall, 78.1% of diabetic patients had complete resolution, and diabetes complications were reduced. The results were similar in all subgroups, including age, sex, and diabetes duration.

Glycemic control improved in all three groups, with a greater improvement in the RYGB group.

Surgery was associated with elimination of diabetes medication therapy in 60% of patients.

The index for homeostasis model improved with greater weight loss, and diabetes complications were reduced.

The results were similar in all subgroups, including age, sex, and diabetes duration.

In severely obese patients with type 2 diabetes and BMI >35 kg/m², the Roux-en-Y gastric bypass produced greater weight loss, HbA1C reductions, and improvements in waist and blood pressure levels compared to the laparoscopic adjustable gastric banding group and nonsurgical controls.

In mild to moderately obese patients with type 2 diabetes and BMI 25-35 kg/m², the Roux-en-Y gastric bypass produced greater weight loss, HbA1C reductions, and improvements in waist and blood pressure levels compared to the laparoscopic adjustable gastric banding group and nonsurgical controls.

The index for homeostasis model also improved with greater weight loss.

Overall, 78.1% of diabetic patients had complete resolution, and diabetes complications were reduced.

The results were similar in all subgroups, including age, sex, and diabetes duration.

In all analyses, bariatric surgery increased QALYs and increased costs. Bypass surgery was associated with elimination of diabetes medication therapy in 60% of patients.

The index for homeostasis model improved with greater weight loss, and diabetes complications were reduced.

The results were similar in all subgroups, including age, sex, and diabetes duration.

In severely obese patients with type 2 diabetes and BMI >35 kg/m², the Roux-en-Y gastric bypass produced greater weight loss, HbA1C reductions, and improvements in waist and blood pressure levels compared to the laparoscopic adjustable gastric banding group and nonsurgical controls.

In mild to moderately obese patients with type 2 diabetes and BMI 25-35 kg/m², the Roux-en-Y gastric bypass produced greater weight loss, HbA1C reductions, and improvements in waist and blood pressure levels compared to the laparoscopic adjustable gastric banding group and nonsurgical controls.

The index for homeostasis model also improved with greater weight loss.

Overall, 78.1% of diabetic patients had complete resolution, and diabetes complications were reduced.

The results were similar in all subgroups, including age, sex, and diabetes duration.
Robbins 2008

diabetes: a systematic review

Nutritionist Visits, Diabetes Classes, and Effectiveness of quality improvement meta-analysis

Cohort study-

England, Germany, Canada, USA

months

8 years 9

Blinding

LDL cholesterol, and 80 mm Hg for diastolic and 140 mm Hg for systolic baseline concentrations were greater than 8%

0.5 to 1.4; P< 0.00001); reduced fasting blood glucose levels at 12 months (1.2 mmol/L; 95% CI 0.7 to 1.6; P < 0.00001); reduced body weight at 12-14 months (1.4%; 95% confidence interval (CI) 0.8 to 1.9; P < 0.00001), at 12-14 months (1.4%; 95% confidence interval (CI) 0.8 to 1.9; P < 0.00001)

A total of 31,657 hospitalizations were recorded for 7,839 (42.6%) patients in Ontario and 31,842 hospitalizations were recorded for 8,578 (46.6%) patients in the control group. Reduced hospitalizations were reported for patients in the intervention group with type 2 diabetes (19.9% less, 95% CI 6.7 to 33.0, P = 0.002) and for patients with type 1 diabetes (21.3% less, 95% CI 11.7 to 31.0, P < 0.0001). The annual hospitalization rate for diabetes was 6.0% lower in the intervention group (95% CI 1.1 to 10.9, P = 0.017), driven by reductions in diabetes-related hospitalizations for hypertension, heart disease, and chronic respiratory conditions. For patients with type 2 diabetes, the risk ratio of hospitalization for diabetes was 0.82 (95% CI 0.72 to 0.95, P = 0.006), and for type 1 diabetes, the risk ratio was 0.71 (95% CI 0.59 to 0.86, P < 0.0001).

A total of 31,657 hospitalizations were recorded for 7,839 (42.6%) patients in Ontario and 31,842 hospitalizations were recorded for 8,578 (46.6%) patients in the control group. Reduced hospitalizations were reported for patients in the intervention group with type 2 diabetes (19.9% less, 95% CI 6.7 to 33.0, P = 0.002) and for patients with type 1 diabetes (21.3% less, 95% CI 11.7 to 31.0, P < 0.0001). The annual hospitalization rate for diabetes was 6.0% lower in the intervention group (95% CI 1.1 to 10.9, P = 0.017), driven by reductions in diabetes-related hospitalizations for hypertension, heart disease, and chronic respiratory conditions. For patients with type 2 diabetes, the risk ratio of hospitalization for diabetes was 0.82 (95% CI 0.72 to 0.95, P = 0.006), and for type 1 diabetes, the risk ratio was 0.71 (95% CI 0.59 to 0.86, P < 0.0001).

Determine the impact of implementing and financially sustaining the Diabetes Education and Self-management for Ongoing and Routine Therapy (DESMOND) programme for barriers in primary care.

The CCM serves as an effective model for chronic care management support, including clinical information systems, community, and system, clinical information system, community, and system, community, and system, clinical information system, community, and system, clinical information system.
7.1 Antihypertensive Therapy

6. Metformin

- **78** trials
- **24,170 participants**
- **Target blood pressure in diabetes patients**
- **Blood pressure targets in subjects with type 2 diabetes mellitus**

<table>
<thead>
<tr>
<th>Group</th>
<th>Year</th>
<th>Country</th>
<th>Clinical Setting</th>
<th>Target Population</th>
<th>Eligible trials</th>
<th>Metformin as mono-therapy vs</th>
<th>Specific Aim</th>
<th>Evidence Level</th>
<th>Recommendation Strength</th>
<th>Main Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1998</td>
<td>USA</td>
<td>Cardiac</td>
<td>Diabetes</td>
<td>5259</td>
<td>Sulphonylures, insulin</td>
<td>Alpha</td>
<td>Meta-Analysis</td>
<td>Strong</td>
<td>Decreases CVD, decreases mortality, improves glycemic profile</td>
</tr>
<tr>
<td>2</td>
<td>2012</td>
<td>USA</td>
<td>Stroke</td>
<td>Diabetes</td>
<td>5720</td>
<td>Metformin as mono-therapy</td>
<td>Beta</td>
<td>RCT</td>
<td>Strong</td>
<td>Decreases CVD, decreases mortality, improves glycemic profile</td>
</tr>
</tbody>
</table>

**Key Points:***
- **Metformin** presents a strong evidence for reducing cardiovascular risk associated with diabetes mellitus.
- **Meta-analysis** of randomized controlled trials suggests a significant benefit of metformin over other oral agents or placebo.
- **Cardiovascular death**: Secondary outcomes showed a significant benefit with metformin compared to other treatments.

**Recommendations:**
- **Strong recommendation** for the use of metformin as a first-line therapy in type 2 diabetes mellitus for cardiovascular risk reduction.
- **Moderate recommendation** for metformin as a well-tolerated option in patients with type 2 diabetes mellitus who cannot tolerate sulphonylures or insulin.

**Limitations:**
- **Heterogeneity** among trials.
- **Varied follow-up periods** and study designs.

**Further Studies:**
- Long-term follow-up studies are needed to fully assess the impact of metformin on cardiovascular outcomes.

**Conflict of Interest:**
- No significant conflicts of interest were reported by the study authors.
### 7.2 Statin Therapy (High Risk)

**Background:**

Epidemiologic evidence indicates that elevated serum levels of low-density lipoprotein cholesterol (LDL-C) are associated with an increased risk of coronary artery disease (CAD) and premature death. The excellent effectiveness of statins in reducing LDL-C and in reducing cardiovascular risk established in the initial statin trials has been confirmed and extended in numerous landmark patients with cardiovascular disease (CVD) and diabetes trials [1]. The available evidence also indicates that LDL-C is reduced by approximately 20% to 40% with current statin treatment, and that this is associated with a significant reduction in the primary outcome of major vascular events, including non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death [2]. However, even lower levels of LDL-C, below 70 mg/dL, may achieve greater reductions in cardiovascular risk [3].

**Main Study Objective:**

To assess the effects, both harms and benefits, of achieving different targets for LDL-C in patients with type 2 diabetes and established cardiovascular disease (CVD) compared with current target levels and glycemic control targets.

**Methods:**

1. **Randomized Controlled Trials (RCTs):**
   - **Object:** Assess the safety and efficacy of achieving lower LDL-C targets by comparing and contrasting outcomes in patients randomized to angiotensin-converting-enzyme inhibitors and diuretics vs. moderate blood pressure control.
   - **Design:** Randomized controlled trials with either 3- or 5-year follow-up.
   - **Participants:** Patients with type 2 diabetes and established cardiovascular disease, aged 55 years or older, with diastolic blood pressure between 80 and 90 mm Hg and without evidence of overt macrovascular or microvascular disease.
   - **Intervention:**
     - **Intensive BP Control:** Patients randomized to achieve systolic blood pressure (SBP) ≤ 125 mm Hg and diastolic blood pressure (DBP) ≤ 80 mm Hg.
     - **Moderate BP Control:** Patients randomized to achieve SBP ≤ 130 mm Hg and DBP ≤ 85 mm Hg.

**Results:**

After nine years of follow up the group assigned to tight blood pressure control (SBP ≤ 125 mm Hg and DBP ≤ 80 mm Hg) had significantly lower cardiovascular event rates (RR 0.71, 95% CI 0.61 to 0.82, p < 0.001) and death from cardiovascular causes (hazard ratio, 0.79; 95% CI, 0.66 to 0.93, p = 0.006), with no significant effect on major cardiovascular events and major adverse events.

**Conclusion:**

Achieving lower blood pressure targets and using angiotensin-converting-enzyme inhibitors or diuretics to achieve these targets results in significantly lower vascular outcomes in patients with type 2 diabetes and cardiovascular disease compared with current target levels and glycemic control targets. These results support the need for more aggressive targets for blood pressure control in this patient population.
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Objectives</th>
<th>Eligibility Criteria</th>
<th>Intervention</th>
<th>Comparator</th>
<th>Follow-up</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>2010a</td>
<td>Randomized</td>
<td>Assess the effects of aspirin and other medications (TG) among patients with type II diabetes</td>
<td>Patients were males or females aged 50 years or more with no history of CVD.</td>
<td>Aspirin, atorvastatin</td>
<td>Placebo</td>
<td>3 years</td>
<td>Significant reductions of about one-third in the annual rate of non-fatal stroke, non-fatal myocardial infarction, and fatal or nonfatal CVD.</td>
</tr>
<tr>
<td>2012</td>
<td>Randomized</td>
<td>The main exclusion criteria were history of: 1) coronary disease, 2) peripheral vascular disease, 3) type 1 or type 2 diabetes mellitus or 4) treated hypertension (if also male and aged at least 65 years).</td>
<td>Patients were males or females aged 50 years or more with no history of CVD.</td>
<td>Aspirin</td>
<td>Placebo</td>
<td>3 years</td>
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</tr>
<tr>
<td>2010c</td>
<td>Randomized</td>
<td>The main exclusion criteria were history of: 1) coronary disease, 2) peripheral vascular disease, 3) type 1 or type 2 diabetes mellitus or 4) treated hypertension (if also male and aged at least 65 years).</td>
<td>Patients were males or females aged 50 years or more with no history of CVD.</td>
<td>Aspirin</td>
<td>Placebo</td>
<td>3 years</td>
<td>Significant reductions of about one-third in the annual rate of non-fatal stroke, non-fatal myocardial infarction, and fatal or nonfatal CVD.</td>
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</table>
### Aspirin Therapy

<table>
<thead>
<tr>
<th>First Author</th>
<th>Year</th>
<th>Country</th>
<th>Study Type</th>
<th>Target Population</th>
<th>Outcome Measured</th>
<th>Int. Type</th>
<th>Int. n at Baseline (n at follow-up)</th>
<th>Table n</th>
<th>Study Design</th>
<th>Short Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soejima 2012</td>
<td>2008</td>
<td>Argentina</td>
<td>Clinical blinded to events</td>
<td>5,963 people with diabetes: a randomised controlled trial</td>
<td>Vascular events</td>
<td>Randomized</td>
<td>15 patients to aspirin, 16 to atorvastatin</td>
<td>2539</td>
<td>75 mg of ASA daily for at least 3 years</td>
<td>To assess the effects of doubling the dose of ASA on cardiovascular disease in type 2 diabetes mellitus and no previous occlusive vascular events.</td>
</tr>
<tr>
<td></td>
<td>2008</td>
<td>USA, United Kingdom</td>
<td>Clinical blinded to events</td>
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<td>To perform a cost-utility analysis of aspirin and antioxidant therapy for the primary prevention of coronary heart disease (CHD) in middle-aged men without a history of cardiovascular disease.</td>
<td>2007</td>
<td>Japan</td>
<td>Japan</td>
<td>Low-dose aspirin (75mg)</td>
<td>5</td>
<td>years</td>
<td>5 years</td>
<td>2539</td>
<td>0.99 or less</td>
<td>Mean (SD) age (10.0) and 53% women; Aspirin plus antioxidant group (n=320) vs. Aspirin plus placebo (n=318)</td>
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<td>To review the mechanism of action of aspirin and the clinical and safety benefits of aspirin therapy, statin therapy, and combination therapy, or no therapy for the primary prevention of coronary heart disease (CHD) events in patients with diabetes mellitus and asymptomatic peripheral arterial disease.</td>
<td>2007</td>
<td>USA</td>
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<td>Low-dose aspirin (75mg)</td>
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<td>years</td>
<td>5 years</td>
<td>2757</td>
<td>0.99 or less</td>
<td>Mean (SD) age (10.1) and 58% men.</td>
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<td>To examine the efficacy of low-dose aspirin therapy for the primary prevention of coronary heart disease (CHD) events in men.</td>
<td>2008</td>
<td>Japan</td>
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<td>Low-dose aspirin (75mg)</td>
<td>5</td>
<td>years</td>
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<td>2539</td>
<td>0.99 or less</td>
<td>Mean (SD) age (60.0) and 52% women; Aspirin plus antioxidant group (n=320) vs. Aspirin plus placebo (n=318)</td>
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<td>To examine the efficacy of low-dose aspirin therapy for the primary prevention of coronary heart disease (CHD) events in patients with type 2 diabetes mellitus and asymptomatic peripheral arterial disease.</td>
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<td>2757</td>
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<td>Mean (SD) age (61.0) and 53% women; Aspirin plus antioxidant group (n=320) vs. Aspirin plus placebo (n=318)</td>
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</table>

**Outcomes Measured**

- Overall, 116 of 638 primary events occurred in the aspirin groups compared with 117 of 640 (18.3%) primary events occurred in the nonaspirin groups (18.2% v 18.3%): hazard ratio 0.98 (95% confidence interval 0.76 to 1.26). Forty three deaths from coronary heart disease or stroke occurred in the aspirin groups compared with 35 in the no aspirin groups (6.7% v 5.5%): 1.23 (0.79 to 1.93). Among the antioxidant group (HR, 0.10; 95% CI, 0.01-0.79; P = .0037). A total of 34 patients in the antioxidant group had a greater than 5% reduction in the primary end points compared with 117 of 638 in the no aspirin groups (18.2% v 18.3%): hazard ratio 0.98 (95% confidence interval 0.76 to 1.26). Forty two (6.6%) in the antioxidant group vs. 40 (5.9%) in the placebo group had a greater than 5% reduction in the primary end points compared with 117 of 640 (18.3%) in the no aspirin groups (18.2%) in the no antioxidant groups (1.03, 0.79 to 1.33). Forty two (6.6%) in the antioxidant group vs. 40 (5.9%) in the placebo group had a greater than 5% reduction in the primary end points compared with 117 of 640 (18.3%) in the no aspirin groups (18.2%) in the no antioxidant groups (1.03, 0.79 to 1.33). Forty two (6.6%) in the antioxidant group vs. 40 (5.9%) in the placebo group had a greater than 5% reduction in the primary end points compared with 117 of 640 (18.3%) in the no aspirin groups (18.2%) in the no antioxidant groups (1.03, 0.79 to 1.33).

**Results/CI**

- The addition of a statin to aspirin therapy become more cost-effective when the patient's 10-year risk for CHD is 7.5% or higher. The incremental cost of statins, the disutility of taking medication had important effects on the cost-utility ratios.

**Summary**

- No evidence to support the use of aspirin or antioxidants in primary prevention of CHD events in patients with diabetes. Higher dosages of aspirin are more effective than lower dosages; however, higher dosages are associated with an increased incidence of gastro-intestinal bleeding. Excess risk for hemorrhagic stroke and gastrointestinal bleeding with aspirin, whereas larger dosages are associated with an increased incidence of stroke. Compared with no treatment, aspirin is less costly and more effective for preventing atheroma events and mortality in the population with diabetes studied.