

# Strategies to reduce complications of type 2 diabetes

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## Practice recommendations

- Control blood pressure to at least 150/80 mm Hg or lower to reduce mortality for patients with type 2 diabetes (A). Strongly consider the use of an angiotensin-converting enzyme (ACE) inhibitor to reduce the incidence of myocardial infarction (MI) and total mortality (A).
- In obese patients with type 2 diabetes, consider the use of metformin, unless contraindicated (A).
- Consider the use of a statin for patients with diabetes, even when their cholesterol level is normal (A).
- Screen patients with type 2 diabetes for peripheral neuropathy and peripheral vascular disease to reduce the risk of major amputation (B).

Diabetes need not automatically sentence patients to the well-known ravages of the disease. Evidence-supported preventive strategies can forestall complications.

Increasing evidence suggests diabetes can be prevented by a combination of lifestyle changes and

medications. Key interventions for patients with established type 2 diabetes include tight control of blood glucose levels, reduction of blood pressure and lipid levels, and early identification of diabetes-related neuropathy, nephropathy, and retinopathy. Antiplatelet therapy may also be beneficial.

## ■ PRIMARY PREVENTION: SHOULD INTERVENTION BEGIN WITH PREDIABETES STATES?

Treatment of risk factors for diabetes (eg, obesity) and management of prediabetes (eg, impaired glucose tolerance) has suggested early intervention can forestall the development of type 2 diabetes (Table 1). Three trials addressed intensive lifestyle/diet modification. Though the onset of clinically diagnosed diabetes was delayed while patients adhered to these strategies, long-term studies of lifestyle modification have not been performed.<sup>1-3</sup>

Several other investigations have looked at whether prescription medications achieve similar benefit. Metformin,<sup>3</sup> acarbose,<sup>4</sup> and orlistat<sup>5</sup> have been studied in populations with prediabetes. These interventions appear to delay the onset of diabetes (number needed to treat [NNT]=33–88 patient-years) and to reduce blood sugar levels by 5% to 10%. A post-hoc analysis of the Heart Outcomes Prevention Evaluation (HOPE) trial<sup>6</sup> also suggests a favorable effect with the ACE inhibitor, ramipril (NNT=250 patient-years). However, patient-oriented outcomes—development of microvascular or macrovascular

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TABLE 1

### Treating prediabetes conditions delays onset of diabetes, but affect on patient-oriented outcomes is unknown

| Study                         | N    | Intervention  | Control | Outcome measured    | RRR | 95% CI  | NNT       | LOE |
|-------------------------------|------|---------------|---------|---------------------|-----|---------|-----------|-----|
| Eriksson et al <sup>1</sup>   | 216  | Diet/exercise | None    | Fasting blood sugar | —*  | —†      | —‡        | 2b  |
| Pan et al <sup>2</sup>        | 259  | Diet/exercise | None    | New-onset diabetes  | 45% | (36–53) | 28 pt-yrs | 1b  |
| DPPRG <sup>3</sup>            | 3234 | Diet/exercise | Placebo | New-onset diabetes  | 58% | (48–66) | 45 pt-yrs | 1b  |
| Chiasson et al <sup>4</sup>   | 1368 | Acarbose      | Placebo | New-onset diabetes  | 25% | (10–37) | 33 pt-yrs | 1b  |
| Heymsfield et al <sup>5</sup> | 474  | Orlistat      | Placebo | New-onset diabetes  | 61% | —†      | 56 pt-yrs | 2b  |
| DPPRG <sup>3</sup>            | 3234 | Glucophage    | Placebo | New-onset diabetes  | 31% | (17–43) | 88 pt-yrs | 1b  |

\* This study reduced blood sugar by 8%, but a RRR cannot be calculated.

† These trials did not provide the 95% CI.

‡ NNT can not be calculated from a continuous variable like blood sugar, but only from dichotomous outcomes like “onset of diabetes.”

RRR, relative risk reduction; CI, confidence interval; NNT, number needed to treat; LOE, level of evidence; DPPRG, Diabetes Prevention Program Research Group.

disease—were not assessed in these trials. Consequently, the ultimate benefit of treating prediabetes states remains uncertain.

#### ■ SECONDARY PREVENTION: DOES EARLY DETECTION OF DIABETES HELP DELAY COMPLICATIONS?

No randomized trial of screening has reported any patient-oriented benefits. However, based on consensus opinion, the American Diabetes Association (ADA) recommends screening every person aged 45 years and older every 3 years (strength of recommendation [SOR]: **C**).<sup>7</sup>

The characteristics of a clinically recognized disease like diabetes, however, may differ significantly from the characteristics of the subclinical states that would be recognized with screening. Therefore, though the US Preventive Health Services Task Force<sup>8</sup> has concluded there is no evidence to recommend screening average risk individuals for diabetes, it does recommend screening individuals at increased risk of macrovascular changes (eg, those with hypertension) (SOR: **B**).

This is based in part on indirect evidence that tighter blood pressure targets may be beneficial for patients with diabetes. (See the Clinical Inquiry, “Does screening for diabetes in at-risk patients improve long-term outcomes?,” page 401.)

#### ■ TERTIARY PREVENTION: PREVENTING COMPLICATIONS OF EXISTING DIABETES

Patient-oriented outcomes in diabetes can be significantly improved with numerous interventions (Table 2).

##### Tight glycemic control warranted

The United Kingdom Prospective Diabetes Study<sup>14</sup> (UKPDS) randomized participants to usual diabetic care or intensive glycemic control with insulin or sulfonylureas over 10 years. Intensive control reduced average hemoglobin A<sub>1c</sub> from 7.9% to 7.0%; it also reduced aggregate microvascular complications, mainly a relative 39% decreased need for photocoagulation for diabetic retinopathy (NNT=320 patient-years). No other

TABLE 2

## Patient-oriented outcomes improve with interventions

| Mortality Intervention                           | Control        | Study                        | N    |
|--|----------------|------------------------------|------|
| Intensive glycemic control with metformin        | Usual care     | UKPDS 34 <sup>9</sup>        | 753  |
| Diastolic blood pressure goal of 85 mm Hg        | Usual care     | UKPDS 38 <sup>10</sup>       | 1148 |
| Diastolic blood pressure goal of 80 mm Hg        | Goal 85        | HOT <sup>11</sup>            | 1501 |
| Tighter blood pressure control with ramipril     | Looser control | HOPE <sup>12</sup>           | 3577 |
| Tighter blood pressure control with nitrendipine | Looser control | Syst-Eur <sup>13</sup>       | 492  |
| Macrovascular endpoints Intervention             | Control        | Study                        | N    |
| Intense glycemic control (insulin/sulfonylurea)  | Usual care     | UKPDS 33 <sup>14</sup>       | 3867 |
| Intensive glycemic control with metformin        | Usual care     | UKPDS 34 <sup>9</sup>        | 753  |
| Diastolic blood pressure goal 85                 | Usual care     | UKPDS 38 <sup>10</sup>       | 1148 |
| Simvastatin                                      | Placebo        | 4S (with CAD) <sup>15</sup>  | 202  |
| Simvastatin                                      | Placebo        | HPS (with CAD) <sup>16</sup> | 2006 |
| Simvastatin                                      | Placebo        | HPS (w/o CAD) <sup>16</sup>  | 972  |
| Microvascular endpoints Intervention             | Control        | Study                        | N    |
| Intense glycemic control (insulin/sulfonylurea)  | Usual care     | UKPDS 33 <sup>14</sup>       | 3867 |
| Foot screening and referral                      | Usual care     | McCabe et al <sup>17</sup>   | 2001 |

\*Mean age and percentage of participants who were male were not provided in these reports. †Confidence interval was not evidence; CAD, coronary artery disease.

individual endpoint was independently affected.

The UKPDS suggested a trend toward 16% fewer relative MIs in the intensive control group; however, the results did not reach statistical significance ( $P=.052$ ). In addition an increase in major hypoglycemic episodes was noted, worse with insulin than sulfonylureas (relative risk [RR]=257%; number needed to harm [NNH]=1110 patient-years).

**Approach to obese patients.** The UKPDS also studied intensive control with metformin among a subgroup of obese patients with diabetes

(>120% ideal body weight).<sup>9</sup> Metformin lowered average hemoglobin A<sub>1c</sub> only from 8.0% to 7.4%, but reduced relative total mortality by 36% (NNT=142 patient-years). Metformin also reduced the relative chance of MI by 39% (NNT=143 patient-years).

These benefits were reversed, however, in a separate UKPDS subgroup placed first on a sulfonylurea, then receiving metformin if glycemic control was inadequate. Total mortality was relatively *increased* by 60% (NNH=89 patient-years).<sup>9</sup> This adverse outcome disappeared when

**Patient-oriented outcomes improve with interventions (continued)**

|  | Mean age | % Male | Outcome                  | RRR | 95% CI         | NNT         | LOE |
|--|----------|--------|--------------------------|-----|----------------|-------------|-----|
|  | 53       | 47     | Total mortality          | 36% | (9–55)         | 142 pt-yrs  | 1b  |
|  | 56       | 54     | Diabetic mortality       | 32% | (6–51)         | 150 pt-yrs  | 1b  |
|  | 62       | 53     | Cardiovascular mortality | 67% | (22–86)        | 154 pt-yrs  | 1b  |
|  | 65       | 63     | Total mortality          | 24% | (8–37)         | 140 pt-yrs  | 1b  |
|  | —*       | —*     | Cardiovascular mortality | 70% | (1–89)         | 100 pt-yrs  | 1b  |
|  | Mean age | % Male | Outcome                  | RRR | 95% CI         | NNT         | LOE |
|  | 54       | 61     | Myocardial infarction    | 16% | (0–29)         | 370 pt-yrs  | 1b  |
|  | 53       | 47     | Myocardial infarction    | 39% | (11–59)        | 143 pt-yrs  | 1b  |
|  | 56       | 44     | Stroke                   | 44% | (11–65)        | 196 pt-yrs  | 1b  |
|  | 60       | 72     | Major cardiac event      | 55% | (25–63)        | 22.5 pt-yrs | 1b  |
|  | 40-80    | 75     | Major cardiac event      | 26% | (16–38)        | 104 pt-yrs  | 1b  |
|  | 40-80    | 75     | Major cardiac event      | 12% | (1–26)         | 114 pt-yrs  | 2b  |
|  | Mean age | % Male | Outcome                  | RRR | 95% CI         | NNT         | LOE |
|  | 54       | 61     | Retinal photocoagulation | 39% | (4–47)         | 320 pt-yrs  | 1b  |
|  | —*       | —*     | Major amputations        | 92% | — <sup>†</sup> | 180 pt-yrs  | 2b  |

provided in this report, but  $P < .01$ . RRR, relative risk reduction; CI, confidence interval; NNT, number needed to treat; LOE, level of

adjustment was made for age, sex, ethnic group, and glycemic control.

Other potential risks of metformin include lactic acidosis, but 1 recent systematic review found no associated cases of this condition with metformin prescribed in published studies.<sup>17</sup>

**Applying the evidence.** Initial treatment of patients with diabetes over 120% of ideal body weight should include tight glucose control with metformin, unless contraindicated (SOR: **A**). For leaner patients, therapy with a sulfonylurea or insulin is supported by evidence (SOR: **B**).

### **Control blood pressure to below 150/80 mm Hg**

The UKPDS also compared tight blood pressure control (aiming at systolic <150 mm Hg and diastolic <80) with usual treatment. Tight control reduced relative deaths attributed to diabetes by 32% (NNT=150 patient-years), and demonstrated a trend toward reduced total mortality that was not statistically significant (relative risk reduction [RRR]=18%; 95% confidence interval [CI], –0.8% to 37%). Both stroke (NNT=196 patient-years) and the aggregate endpoint of “all microvascular

TABLE 3

## Effect of ACE inhibitors/ARBs on patient-oriented outcomes

| Total mortality                                |      |     |        |              |                           |      |             |            |       |
|--|------|-----|--------|--------------|---------------------------|------|-------------|------------|-------|
| Study  | N    | Age | % Male | Intervention | Control                   | RRR  | 95% CI      | NNT        | LOE** |
| UKPDS 39 <sup>26</sup>                         | 1148 | 56  | 54%    | Captopril    | Atenolol                  | -14% | (-61 to 19) | NS         | 2     |
| CAPP <sup>27</sup>                             | 572  | 55  | 62%    | Captopril    | Diuretic/<br>beta-blocker | 46%  | (5-69)      | 96 pt-yrs  | 1b    |
| ABCD <sup>28</sup>                             | 470  | 57  | 67%    | Enalapril    | Nisoldipine               | 23%  | (-67 to 64) | NS         | 2b    |
| FACET <sup>29</sup>                            | 189  | 63  | 60%    | Fosinopril   | Amlodipine                | 20%  | *           | NS         | 2b    |
| LIFE <sup>30</sup>                             | 1195 | 67  | 47%    | Losartan     | Atenolol                  | 40%  | (18-66)     | 167 pt-yrs | 2b    |
| Lewis et al <sup>31</sup>                      | 1715 | 59  | 64%    | Irbesartan   | Amlodipine                | -4%  | (-40 to 23) | NS         | 2b    |
| Major cardiovascular events/myocardial infarct |      |     |        |              |                           |      |             |            |       |
| Study  | N    | Age | % Male | Intervention | Control                   | RRR  | 95% CI      | NNT        | LOE   |
| UKPDS 39 <sup>26</sup>                         | 1148 | 56  | 54%    | Captopril    | Atenolol                  | -20% | (-76 to 18) | NS         | 2b    |
| CAPP <sup>27</sup>                             | 572  | 55  | 62%    | Captopril    | Diuretic/<br>beta-blocker | 66%  | (33-83)     | 96 pt-yrs  | 1b    |
| ABCD <sup>28</sup>                             | 470  | 57  | 67%    | Enalapril    | Nisoldipine               | 80%  | (52-93)     | 25 pt-yrs  | 1b    |
| FACET <sup>29</sup>                            | 189  | 63  | 60%    | Fosinopril   | Amlodipine                | 51%  | (5-74)      | 146 pt-yrs | 1b    |
| LIFE <sup>30</sup>                             | 1195 | 67  | 47%    | Losartan     | Atenolol                  | -7%  | (-31 to 12) | NS         | 2b    |
| Lewis et al <sup>31</sup>                      | 1715 | 59  | 64%    | Irbesartan   | Amlodipine                | -3%  | (-31 to 19) | NS         | 2b    |

\*No confidence interval was given in this particular trial. RRR, relative risk reduction; CI, confidence interval; NNT, number needed to treat; LOE, level of evidence; CAD, coronary artery disease.

disease" (NNT=139 patient-years) were significantly reduced by tight blood pressure control.<sup>10</sup>

The Hypertension Optimal Treatment (HOT) Study Group<sup>11</sup> compared various levels of blood pressure control. A reduction in cardiovascular mortality was significant even between those treated with a goal of 80 and 85 mm Hg diastolic (RRR=67%; NNT=133 patient-years). The trend toward reduction in total mortality in this trial also approached statistical significance ( $P=.068$ ; RRR=42%).

The Syst-Eur trial<sup>13</sup> compared tight blood pressure control on nitrendipine with looser control with a variety of agents. Cardiovascular mortality

was reduced by 30% with tight control (NNT=100 patient-years).

The Heart Outcomes Prevention Evaluation (HOPE) study<sup>6</sup> included patients with diabetes, of which only 56% had a diagnosis of hypertension. It randomized participants to receive ramipril or placebo, in addition to any off-study antihypertensive agents they were already using. The intervention group had both lower average blood pressures as well as lower total mortality by 24% (NNT=140 patient-years).

**Choice of agent important.** Lower blood pressure goals have consistently demonstrated

benefit across multiple studies. The choice of anti-hypertensive agent may also affect outcomes (Table 3). The UKPDS blood pressure analysis was also stratified to evaluate whether the results of blood pressure treatment differed between captopril and atenolol. Though compliance was slightly better with captopril, there were no differences in patient-oriented outcomes between the groups.<sup>26</sup>

The Captopril Prevention Project (CAPPP)<sup>27</sup> compared captopril with diuretics and beta-blockers alone or in combination. While blood pressure control was about the same in all study groups, the captopril group realized a 66% reduction in MI (NNT=96 patient-years) and a total mortality 46% less than that seen with the other agents (NNT=96 patient-years).

The Appropriate Blood Pressure Control in Diabetes (ABCD) trial<sup>28</sup> compared nisoldipine and enalapril. Participants randomized to receive the ACE inhibitor had an 80% decreased risk of MI (NNT=25 patient-years).

In the Fosinopril versus Amlodipine Cardiovascular Events Trial (FACET),<sup>29</sup> blood pressure was better controlled with amlodipine, but major vascular events were 51% fewer with the ACE inhibitor (NNT=146 patient-years), again supporting the superior performance of ACE inhibitors.

Angiotensin receptor blockers (ARBs) may have comparable effects to ACE inhibitors. The Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) trial<sup>30</sup> studied patients with left ventricular hypertrophy, diabetes, and hypertension, comparing losartan with atenolol. Total mortality with losartan was reduced by a relative 40% compared with atenolol (NNT=167 patient-years). Another study<sup>31</sup> of patients with diabetes, hypertension, and nephropathy compared irbesartan with amlodipine. This trial demonstrated no differences in patient-oriented outcomes between the calcium-channel blocker and the ARB.

**Applying the evidence.** The goals for blood pressure control in type 2 diabetes should be less than 150 mm Hg systolic and 80 mm Hg diastolic (SOR: **A**). Evidence also strongly supports the use of an ACE inhibitor, or possibly ARB, as first-line

## Impact of type 2 diabetes

**Type 2 diabetes** is the second most common problem seen by family physicians, and represents over 4% of office visits.<sup>19</sup> The cost to society is staggering: in the United States, \$100 billion was spent in 1997 alone.<sup>20</sup> Its toll in clinical outcomes is also dramatic, leading to over 150,000 annual deaths in the US.<sup>20</sup>

Left unchecked, diabetes leads to microvascular and macrovascular complications. Cardiovascular disease occurs 2 to 3 times more often among patients with diabetes than healthy individuals,<sup>21,22</sup> and is also linked to impaired glucose tolerance.<sup>23</sup> Cardiovascular events are responsible for over half of deaths in patients with diabetes.<sup>20</sup>

Each year, neuropathy contributes to ulcers in 2% of patients with diabetes, and amputation in 0.6%.<sup>24</sup> Proteinuria occurs in 20% to 40% of all patients with diabetes<sup>7</sup>; of those, 20% rapidly develop end-stage renal disease.<sup>25</sup> Retinopathy is treated at a rate of 1% per year among patients with diabetes.<sup>14</sup>

treatment for hypertension in diabetes (SOR: **A**). Many authorities recommend even more aggressive blood pressure goals.

### Lipid management: statins improve outcomes

Lowering elevated triglycerides has not been independently associated with an improvement in patient-oriented outcomes. In the Helsinki Heart Study<sup>22</sup> and the St. Mary's, Ealing, Northwick Park Diabetes Cardiovascular Disease Prevention (SENDCAP) trial,<sup>32</sup> a fibric acid derivative was compared with placebo. The average triglyceride concentration was decreased, but no significant effect on coronary events was noted. However, elevated triglycerides are associated with the metabolic syndrome, which may warrant lifestyle changes or medication (based on expert opinion).

Treatment with hydroxymethyl glutaryl coenzyme A reductase inhibitors (statins) has better supporting evidence. In the Scandinavia Simvastatin Survival Study (4S),<sup>15</sup> 202 patients with diabetes, coronary artery disease, and elevated cholesterol were randomized to receive simvastatin or placebo. Major coronary events were reduced by 55% with simvastatin (NNT=22.5 patient-years). Total mortality was reduced, but not to a statistically significant extent ( $P=.087$ ; RRR=43%).

The Air Force/Texas Coronary Atherosclerosis Prevention Study<sup>33</sup> (AFCAPS/TexCAPS) compared lovastatin with placebo for patients with diabetes and healthy individuals with normal cholesterol levels. Though the overall population demonstrated a 37% reduction in first coronary events, the diabetes subgroup had insufficient power to confirm this trend independently.

The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial<sup>34</sup> (ALLHAT-LLT) randomized 3638 patients with diabetes to receive pravastatin 40 mg or placebo. No changes were seen in total mortality or cardiovascular events. These results may have been confounded by off-study prescription for statins, given to 32% of those randomized to the placebo group.

The best independent evidence for use of statins in diabetes comes from the Heart Protection Study<sup>16</sup> of 3982 patients with diabetes with a total cholesterol level >135 mg/dL and no evidence of coronary disease. They were randomized to receive 40 mg simvastatin or placebo for 5 years. First major vascular events (MI or stroke) were decreased in the simvastatin group by 26% over 5 years (NNT=104 patient-years).

**Applying the evidence.** Reducing elevated triglycerides in type 2 diabetes is not supported by clear evidence, although elevated triglycerides may be associated with the metabolic syndrome and may warrant lifestyle change (SOR: C).

However, statins—even for those with a normal cholesterol level—reduce macrovascular outcomes (SOR: A), a measure now endorsed by the American College of Physicians.

### Anti-platelet therapy

Aspirin prophylaxis in diabetes has weaker support. The Early Treatment Diabetic Retinopathy Study<sup>35</sup> (ETDRS) randomized 3711 patients with diabetes to receive aspirin 650 mg or placebo. No benefit in mortality or cardiovascular event rates was documented after 5 years. However, the results did suggest a nonsignificant trend toward reduction of MI (RRR=17%; 95% CI, -4% to 34%; NNT=333).

In the Physician's Health Study,<sup>36</sup> 22,071 participants (most of whom did not have diabetes) were randomized to receive aspirin 325 mg every other day or placebo. MI was reduced by 44% with aspirin (NNT=500). The risk of MI in the subgroup of 533 individuals with diabetes paralleled this reduction (RRR=39%), though, independently, the reduction in the subgroup did not reach statistical significance. Bleeding problems were the most common adverse effect of the aspirin, and were increased by 32% (NNH=78 person-years).

In the HOT study,<sup>11</sup> a subgroup of 1501 patients with diabetes was randomized to receive aspirin 75 mg or placebo daily. The rate of MI trended downward with aspirin but was not statistically significant. Among the 18,790 patients in this study (most of whom did not have diabetes), MI was 36% less likely to occur with aspirin (NNT=770).

**Applying the evidence.** Overall, there is some suggestion that persons with cardiac risk factors, like type 2 diabetes, benefit by taking low-dose aspirin to avoid macrovascular complications. No study has confirmed this in a population of individuals with diabetes, but the trends suggest a possible benefit (SOR: C). The decision to use aspirin should be made in consultation with an informed patient.

### ■ SCREENING FOR NEUROPATHY

One trial<sup>17</sup> has been conducted on screening for neuropathy. It compared monofilament testing and palpation of pedal pulses with “no special care.” Patients with an original positive screen result received a calculation of their ankle-

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brachial index, foot x-rays, and other measurements, and were referred to a high-risk podiatry clinic if the second level testing showed abnormal results. Major amputations were decreased in the screened group by 92% over 2 years (NNT=180 patient-years). This evidence of benefit is sufficient to recommend screening patients with diabetes for peripheral neuropathy or peripheral vascular disease, and appropriate referral (SOR: **B**). (See the Clinical Inquiry, "What is the best treatment for diabetic neuropathy?," page 403.)

### ■ SCREENING FOR NEPHROPATHY

One systematic review<sup>37</sup> found no randomized trials of screening for urinary microalbumin and how it might affect overt nephropathy. However, several studies have looked at treatment of gross proteinuria, and have demonstrated some benefit in patient-oriented outcomes. Improved blood pressure control has reduced progression of nephropathy to end-stage renal disease.<sup>38,39</sup> Other studies have suggested that an ACE inhibitor or ARB might provide benefit.<sup>30,39</sup>

The ADA recommends annual screening for microalbumin based on expert consensus (SOR: **C**).<sup>7</sup> Though early detection of microalbumin might optimize the treatment of nephropathy, it is also possible that screening may detect a population whose disease would have remained subclinical indefinitely. No clear evidence suggests that screening for microalbumin reduces the incidence of patient-oriented outcomes.

### ■ SCREENING FOR RETINOPATHY

Several trials have evaluated interventions in the diagnosis and prevention of visual loss. As discussed previously, intensive glucose control with sulfonylureas or insulin reduced the need for retinal photocoagulation by 39% in the UKPDS (NNT=320 patient-years).<sup>14</sup> Similarly in this trial, tight blood pressure control reduced the progression of retinopathy, compared with usual care.<sup>10</sup>

Specific treatments for retinopathy include photocoagulation, which has been demonstrated to significantly reduce severe visual loss by 58%

(NNT=30 patient-years).<sup>40</sup> One cohort study suggests that screening for retinopathy coupled with appropriate treatment may reduce the onset of visual loss.<sup>41</sup> The ADA recommends annual screening for retinopathy with a dilated eye exam based on indirect evidence of its benefit (SOR: **B**).<sup>7</sup>

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**DRUG BRAND NAMES**

|             |                     |
|-------------|---------------------|
| Acarbose    | Prandase, Precose   |
| Amlodipine  | Norvasc             |
| Atenolol    | Tenoretic; Tenormin |
| Captopril   | Capoten             |
| Enalapril   | Vasotec             |
| Fosinopril  | Monopril            |
| Irbesartan  | Avapro              |
| Losartan    | Cozaar              |
| Lovastatin  | Mevacor             |
| Metformin   | Glucophage          |
| Nisoldipine | Sular               |
| Orlistat    | Xenical             |
| Pravastatin | Pravachol           |
| Ramipril    | Altace              |
| Simvastatin | Zocor               |