Type 2 diabetes: Which interventions best reduce absolute risks of adverse events?

The Archimedes risk engine shows that many patients are likely to benefit more from aspirin and exercise than all other interventions combined.

Practice recommendations
- The program Diabetes PHD, powered by Archimedes software, estimates absolute risk and absolute risk reductions for individual patients and is a useful decision-support tool (C).
- For most patients with type 2 diabetes who are older than 50 years, recommend aspirin and exercise as first-line interventions (C).

Strength of recommendation (SOR)
A Good-quality patient-oriented evidence
B Inconsistent or limited-quality patient-oriented evidence
C Consensus, usual practice, opinion, disease-oriented evidence, case series

Abstract
Background Benefits of interventions are usually reported as relative risk reductions. Absolute risk reductions (ARRs)—most relevant to individual patients—are reported less often.

Objectives Estimate ARRs for interventions in a patient with diabetes mellitus.

Methods We used the Archimedes Risk Assessment Tool to estimate 10-year risks of myocardial infarction (MI), cerebrovascular accident (CVA), end-stage renal disease (ESRD), blindness, foot ulceration, and amputation, and to estimate the ARRs associated with controlling blood pressure (BP), blood sugar, and low-density lipoprotein (LDL) cholesterol levels; moderate exercise; and taking aspirin and a beta-blocker. Our hypothetical base case was a 65-year-old white man. Three other hypothetical patients were a 50-year-old white man, a 65-year-old white woman, and a 65-year-old black man. Each patient had a 5-year history of diabetes mellitus, a sedentary lifestyle, body mass index (BMI) of 28 kg/m², BP of 140/90 mm Hg, LDL of 120 mg/dL, high-density lipoprotein (HDL) of 45 mg/dL, and glycosylated hemoglobin (HbA1c) of 10%.

Results For the base case, the risks of MI (22.3%) and CVA (14.4%) far exceeded the risks of ESRD, blindness, and amputation. ARRs for interventions to reduce MI risk were: aspirin, 6.8%; HbA1c to 7%, 5.1%; moderate exercise, 2.7%; BP to 130/80 mm Hg, 1.4%; and LDL to 100 mg/dL, 1.4%. The female patient had a lower ARR for aspirin and a greater
ARR for exercise. The black male patient had greater ARRs for both aspirin and exercise. Estimates were similar for CVA.

**Conclusion** Patients resembling our base case and its variations would probably benefit more from aspirin and moderate exercise than from all other interventions combined.

If you’re accustomed to telling patients with diabetes how different interventions may reduce their risk of macro- and microvascular complications, our study’s findings may alter your approach to the next patient.

Standard guidelines recommend controlling hyperglycemia, hypertension, and dyslipidemia, advocating moderate exercise and weight control, and treating with aspirin, angiotensin-converting enzyme (ACE) inhibitors, and β-blockers.\(^1\)\(^-\)\(^3\) Published benefits of these interventions most commonly come from clinical trials and are usually reported as relative risk reductions (RRR). However, the true benefit for an individual—the absolute risk reduction (ARR)—depends on that person’s baseline risk, the duration of a selected treatment, and the RRR associated with the treatment. Because RRR is often numerically larger than ARR, some patients may mistakenly perceive an intervention’s benefit to be greater than it actually is.

The purpose of this study was 2-fold: (1) to estimate the ARR for common diabetes interventions by analyzing a model case and variations of the case, thereby giving physicians a better sense of potential outcomes with these interventions; and (2) to demonstrate the potential utility of our evaluation method for practice.

**Methods**

**How we estimated RRR and ARR**

Diabetes risk engines use customized software designed to calculate the probable occurrence of different disease complications and how certain interventions might decrease those probabilities. Among the better known risk engines are the United Kingdom Prospective Diabetes Study (UKPDS) Risk Engine,\(^4\) the CDC/RTI Diabetes Cost-Effectiveness Model,\(^5\) and the Global Diabetes Model (GDM).\(^6\)

**Risk engines are generally of 1 of 2 types.** The first type uses regression equations to analyze data from a single study. An example is the UKPDS Risk Engine, based on data from the United Kingdom Prospective Diabetes Study.

The second type uses Markov modeling, a method that describes the progression of diabetes through transition states. A simulated patient moves from 1 state of a disease to another at defined intervals based on transitional probabilities. Treatment impacts are analyzed according to their effects on these probabilities. Examples are the CDC/RTI Diabetes Cost-Effectiveness Model and the GDM.

**The unique risk engine we used.** We obtained absolute risk estimates for adverse events in a simulated patient using Diabetes PHD (Personal Health Decisions), a risk engine available online through the American Diabetes Association (ADA) Web site.\(^7\) The Diabetes PHD engine uses a software program called Archimedes, which differs from all other engines in several important ways.

First, it represents as continuous variables the physiologic and other processes that are continuous in reality—unlike, say, the Markov model that introduces progressions abruptly at specified intervals.

Second, it is more comprehensive, containing more than 100 variables: biologic factors, symptoms, tests, treatments, and outcomes.

Third, because it is written with differential equations and object-oriented programming at a level that represents physiologic processes, it more accurately depicts comorbidities and the multiple possible effects of treatments.\(^8\)\(^,\)\(^9\)

Fourth, the accuracy of a model’s
Type 2 diabetes absolute risk reductions

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How we applied Diabetes PHD to our study. To use Diabetes PHD, we entered sociodemographic information for our hypothetical patient (described below); patient and family health histories; blood pressure, cholesterol, fasting glucose, and glycosylated hemoglobin (HbA1c) levels; and medications the patient was taking for diabetes or for blood pressure or cholesterol reduction. The Archimedes software creates 1000 simulated patients identical to the profile entered by the user. The outcomes for these 1000 patients are simulated over the lifespan of each patient, and each run can be thought of as a clinical trial with 1000 participants.

Results are reported as absolute risk (AR) projections out to >30 years for myocardial infarction (MI), cerebrovascular accident (CVA), end-stage renal disease (ESRD), retinopathy, blindness, foot ulceration, and foot amputation. Once risk projections have been generated, the user can choose from a variety of interventions. Archimedes recalculates the risks, displaying the size of the ARRs graphically.

Our hypothetical base case

The Mount Hood Challenge, established in 2000, is a periodic gathering of university research teams for the purpose of cross-validating diabetes simulation models. In the first 3 Mount Hood Challenges, the number of models increased with each gathering, as did the rigor of model validation. In the fourth Mount Hood Challenge, held in 2005, 5 diabetes risk engines were compared using 2 published patient data sets and 1 hypothetical case (Patient 3 from the third Mount Hood Challenge). This simulated patient is the one we used in our study.

The patient is a 65-year old Caucasian man with a 5-year history of type 2 diabetes mellitus, an HbA1c of 10%, blood pressure of 140/90 mm Hg, low-density lipoprotein (LDL) cholesterol level of 120 mg/dL, high-density lipoprotein (HDL) of 45 mg/dL, and a body mass index (BMI) of 27 kg/m². This profile is not substantially different from the “average” patient enrolled in several primary care-based studies: mean age 58 to 59.5 years; BMI 30-33 kg/m²; HbA1c 8.1%; BP 136-140/76-90 mm Hg; and LDL cholesterol 109-118 mg/dL.

Archimedes assumes that an intervention occurs at the beginning of a simulation. We used this feature of the model to analyze the impact of various interventions on the ARs for MI, CVA, ESRD, blindness, foot ulceration, and lower extremity amputation. The interventions we examined were moderate exercise, reduction of BMI to 25, reduction of HbA1c to 7.0% and 6.5%, reduction of systolic BP to 130 and 120 mm Hg, reduction of LDL cholesterol to 100 and 70 mg/dL, and treatment with low-dose aspirin, an ACE inhibitor, and a β-blocker (TABLE 1).

We examined the benefits of these interventions for our base case and for 3 other cases in which a single factor changed (sex, race, age). We chose to examine ARs and ARRs at 10 years from baseline because the trial-to-trial variability of these estimates was much more stable than the 30-year estimates. For example, over the course of 10 separate runs using the same input, estimated 10-year risks of MI varied by an average of 0.8%, while the 30-year risk estimates varied by an average of 9.8%.

Unfortunately, Archimedes does not allow the user to adjust the exercise level without entering a new patient profile. We did so, realizing that we were comparing 2 different sets of 1000 simulated patients while assuming the only difference between them was level of exercise.
### Results

**TABLE 1** lists 10-year ARs for adverse events for the base case and the ARRs for each intervention. Macrovascular complications were projected to occur at much higher rates than microvascular complications. The 10-year AR estimates for MI and CVA for the model case were 22.3% and 14.4%, respectively, whereas those for ESRD, blindness, and amputation were less than 1%. The risk of MI was greater than the risk of all other complications combined.

**BASE CASE**

### Aspirin, exercise clearly worthwhile

For the base case, aspirin was the most effective way to reduce the risk of MI (ARR=6.8%). Moderate exercise reduced the risk of MI by only 2.7%, but it reduced the risk of CVA by 6.8%, more than any other intervention. Combining aspirin and moderate exercise reduced the risk of MI by 8.9% and CVA by 7.8% (data not shown).

Reducing HbA1c from 10% to 6.5% reduced MI risk by 6.4%; reducing systolic BP from 140 to 120 mm Hg reduced MI risk by 5%. Reducing the LDL level from 120 to 70 mg/dL reduced risk of MI by 3.5%, but it had little effect on risk of CVA.

Glycemic control and exercise were the only interventions that had any meaningful effect on risk of foot ulceration. Weight reduction and use of an ACE inhibitor did not
affect outcomes. The maximum possible risk reduction for MI using all available interventions was 15.2% (10-year risk reduced from 22.3% to 7.1%), and for stroke was 11.1% (risk reduced from 14.4% to 3.3%).

**CASE VARIATION—WHITE WOMAN**

**Exercise reduces MI risk even further**

The 10-year AR estimates for the female case (TABLE 2) were similar to those of the base case, with a slightly lower risk for foot ulceration. Treatment effects were also similar, except that exercise more effectively reduced MI risk (ARR = 10% vs 2.7%). Aspirin was slightly less effective for reducing MI risk (ARR 5.9% vs 6.8%), but similarly effective for reducing stroke risk. Weight loss alone and use of an ACE inhibitor had no effect on any outcome.

**CASE VARIATION—BLACK MAN**

**Greater benefit from aspirin**

For the black male (TABLE 3), risk of foot ulceration was substantially less than with the base case (ARR = 0.7% vs 5.2%). Both aspirin and exercise were more effective for reducing risk of MI (ARRs = 9.4% and 7.0% vs 6.8% and 2.7%). Tight control of BP (120) and LDL (70) were also somewhat more effective (ARRs = 6.9% and 5.7% vs 5.0% and 3.5%). Weight loss and use of an ACE inhibitor did not affect outcomes.
**TABLE 3**

**Absolute risk reduction predicted by Archimedes risk engine**

65-year-old black male, sedentary, non-smoker with a 5-year history of diabetes mellitus; BMI 27 kg/m2; BP 140/90 mm Hg; HbA1c 10%; LDL 120 mg/dL; HDL 45 mg/dL

<table>
<thead>
<tr>
<th>MI</th>
<th>CVA</th>
<th>ESRD</th>
<th>BLINDNESS</th>
<th>FOOT ULCERATION</th>
<th>FOOT AMPUTATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>10-year risks before interventions</td>
<td>24.9%</td>
<td>14.1%</td>
<td>0%</td>
<td>0.8%</td>
<td>0.7%</td>
</tr>
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**INTERVENTIONS* | RISK (ARR) | RISK (ARR) | RISK (ARR) | RISK (ARR) | RISK (ARR) | RISK (ARR) |
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<thead>
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</thead>
<tbody>
<tr>
<td>Aspirin, 81 mg/d</td>
<td>15.5% (9.4%)</td>
<td>11.7% (2.4%)</td>
<td>0% (0%)</td>
<td>0.8% (0%)</td>
<td>0.7% (0%)</td>
<td>0.7% (0%)</td>
</tr>
<tr>
<td>Moderate aerobic exercise</td>
<td>17.9% (7.0%)</td>
<td>9.2% (4.9%)</td>
<td>0% (0%)</td>
<td>0.7% (0.1%)</td>
<td>1.2% (-0.5%)</td>
<td>0.7% (0%)</td>
</tr>
<tr>
<td>Reduce HbA1c to 7.0%</td>
<td>19.8% (5.1%)</td>
<td>11.1% (3.0%)</td>
<td>0% (0%)</td>
<td>0.5% (0.3%)</td>
<td>0% (0.7%)</td>
<td>0% (0.7%)</td>
</tr>
<tr>
<td>Reduce HbA1c to 6.5%</td>
<td>19.0% (5.9%)</td>
<td>10.4% (3.7%)</td>
<td>0% (0%)</td>
<td>0.5% (0.3%)</td>
<td>0% (0.7%)</td>
<td>0% (0.7%)</td>
</tr>
<tr>
<td>Reduce SBP to 130 mm Hg</td>
<td>21.0% (3.9%)</td>
<td>12.0% (2.1%)</td>
<td>0% (0%)</td>
<td>0.6% (0.2%)</td>
<td>0.7% (0%)</td>
<td>0.5% (0.2%)</td>
</tr>
<tr>
<td>Reduce SBP to 120 mm Hg</td>
<td>18.0% (6.9%)</td>
<td>10.6% (3.5%)</td>
<td>0% (0%)</td>
<td>0.6% (0.2%)</td>
<td>0.7% (0%)</td>
<td>0.5% (0.2%)</td>
</tr>
<tr>
<td>Reduce LDL to 100 mg/dL</td>
<td>22.5% (2.4%)</td>
<td>14.0% (0.1%)</td>
<td>0% (0%)</td>
<td>0.6% (0.2%)</td>
<td>0.6% (0.1%)</td>
<td>0.6% (0.1%)</td>
</tr>
<tr>
<td>Reduce LDL to 70 mg/dL</td>
<td>19.2% (5.7%)</td>
<td>13.8% (0.3%)</td>
<td>0% (0%)</td>
<td>0.4% (0.4%)</td>
<td>0.5% (0.2%)</td>
<td>0.5% (0.2%)</td>
</tr>
<tr>
<td>β-Blocker</td>
<td>20.9% (4.0%)</td>
<td>13.1% (1.0%)</td>
<td>0% (0%)</td>
<td>0.6% (0.2%)</td>
<td>0.5% (0.2%)</td>
<td>0.7% (0%)</td>
</tr>
<tr>
<td>All of the above</td>
<td>3.6% (21.3%)</td>
<td>4.1% (10.0%)</td>
<td>0% (0%)</td>
<td>0.4% (0.4%)</td>
<td>0% (0.7%)</td>
<td>0% (0.7%)</td>
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AR, absolute risk; ARR, absolute risk reduction; BMI, body mass index; BP, blood pressure; CVA, cerebrovascular accident; ESRD, end-stage renal disease; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MI, myocardial infarction; SBP, systolic blood pressure.

*Weight loss alone and use of an ACE inhibitor had no effect on any outcome.

**CASE VARIATION—50-YEAR-OLD WHITE MAN**

**Better reductions than for 65 year old**

For the 50-year-old man (TABLE 4), risk for CVA was substantially lower and the risk for foot ulceration was somewhat higher than for the base case (ARs 7.1% and 8.6% vs 14.4% and 5.2%, respectively). Risk reductions for MI associated with aspirin and moderate exercise were greater at age 50 than at age 65 (ARRs = 9.6% and 10.1% vs 6.8% and 2.7%, respectively). This was also true, but to a lesser extent, for tight control of BP and LDL (ARRs = 7.1% and 4.9% vs 5.0% and 3.5%, respectively). Weight loss had only a minimal effect on risk of MI, CVA, and foot ulceration. Using an ACE inhibitor did not affect risk of any of the outcomes.

**Discussion**

Based on projections derived from Archimedes, patients with diabetes who are older than 50 years are at far less risk for microvascular complications than for macrovascular complications. Older patients are 20 times more likely to experience heart attack and stroke than ESRD, blindness, or amputation.

It’s important to keep in mind here that comparisons between various interventions in these test cases depend entirely on the initial values of the risk factors. So, for example, we are comparing a 3%
reduction in HbA1c with a 20 mg/dL reduction in LDL and a 20 mm Hg reduction in BP.

Our estimates differ substantially from those reported by Eastman and colleagues, who used Monte Carlo techniques to model outcomes for a representative sample of patients with type 2 diabetes using data from several epidemiologic studies.\textsuperscript{15,16} They projected lifetime risks of 17% for ESRD and amputation and a lifetime risk of 39% for cardiovascular events. These differences can probably be accounted for by the inclusion of a number of younger patients in the Eastman sample, a longer projected time frame (lifetime vs 10 years), and a different modeling technique. The Archimedes projections of these complications are actually higher than those reported in a recently published longitudinal study based on Medicare claims.\textsuperscript{17}

**Benefit of aspirin and exercise together.** Of the available interventions to reduce risk of MI and CVA, the least expensive ones, aspirin and moderate exercise, appear to be at least as effective as the others. In fact, even in the base case, in which exercise was somewhat less effective than in the variations, the combination of as-

### TABLE 4

**Absolute risk reduction predicted by Archimedes risk engine**

50-year-old white male, sedentary, nonsmoker with a 5-year history of diabetes mellitus; BMI 27 kg/m\(^2\); BP 140/90 mm Hg; HbA1c 10%; LDL 120 mg/dL; HDL 45 mg/dL

<table>
<thead>
<tr>
<th>INTERVENTIONS*</th>
<th>MI</th>
<th>CVA</th>
<th>ESRD</th>
<th>BLINDNESS</th>
<th>FOOT ULCERATION</th>
<th>FOOT AMPUTATION</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>10-year AR before interventions</strong></td>
<td>22.2%</td>
<td>7.1%</td>
<td>0%</td>
<td>0%</td>
<td>8.6%</td>
<td>0%</td>
</tr>
<tr>
<td><strong>INTERVENTIONS</strong></td>
<td><strong>RISK (ARR)</strong></td>
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</tr>
<tr>
<td>Moderate aerobic exercise</td>
<td>12.1% (10.1%)</td>
<td>3.7% (3.4%)</td>
<td>0% (0%)</td>
<td>0.1% (-0.1%)</td>
<td>8.8% (-0.2%)</td>
<td>0% (0%)</td>
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<tr>
<td>Reduce BMI to 25 kg/m(^2)</td>
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<td>7.0% (0.1%)</td>
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<td>0% (0%)</td>
<td>8.5% (0.1%)</td>
<td>0% (0%)</td>
</tr>
<tr>
<td>Reduce HbA1c to 7.0%</td>
<td>17.2% (5.0%)</td>
<td>5.5% (1.6%)</td>
<td>0% (0%)</td>
<td>0% (0%)</td>
<td>3.4% (5.2%)</td>
<td>0% (0%)</td>
</tr>
<tr>
<td>Reduce HbA1c to 6.5%</td>
<td>16.1% (6.1%)</td>
<td>5.2% (1.9%)</td>
<td>0% (0%)</td>
<td>0% (0%)</td>
<td>3.4% (5.2%)</td>
<td>0% (0%)</td>
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<tr>
<td>Reduce SBP to 130 mm Hg</td>
<td>17.8% (4.4%)</td>
<td>5.9% (1.2%)</td>
<td>0% (0%)</td>
<td>0% (0%)</td>
<td>8.6% (0%)</td>
<td>0% (0%)</td>
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<tr>
<td>Reduce SBP to 120 mm Hg</td>
<td>15.1% (7.1%)</td>
<td>5.2% (1.9%)</td>
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<td>0% (0%)</td>
<td>8.6% (0%)</td>
<td>0% (0%)</td>
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<tr>
<td>Reduce LDL to 100 mg/dL</td>
<td>20.1% (2.1%)</td>
<td>7.1% (0%)</td>
<td>0% (0%)</td>
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<td>8.5% (0.1%)</td>
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<tr>
<td>Reduce LDL to 70 mg/dL</td>
<td>17.3% (4.9%)</td>
<td>5.2% (1.9%)</td>
<td>0% (0%)</td>
<td>0% (0%)</td>
<td>8.3% (0.3%)</td>
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<td>6.5% (0.6%)</td>
<td>0% (0%)</td>
<td>0% (0%)</td>
<td>8.6% (0%)</td>
<td>0% (0%)</td>
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<tr>
<td><strong>All of the above</strong></td>
<td>2.0% (20.2%)</td>
<td>1.3% (5.8%)</td>
<td>0% (0%)</td>
<td>0% (0%)</td>
<td>3.1% (5.5%)</td>
<td>0% (0%)</td>
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</table>

AR, absolute risk; ARR, absolute risk reduction; BMI, body mass index; BP, blood pressure; CVA, cerebrovascular accident; ESRD, end-stage renal disease; HbA1c, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MI, myocardial infarction; SBP, systolic blood pressure.

*Use of an ACE inhibitor had no effect on any outcome
Aspirin and exercise reduced the risk of MI by 8.9% (59% of the maximum possible ARR) and reduced the risk of CVA by 7.8% (70% of the maximum ARR).

Is aspirin's benefit for MI and CVA amplified in diabetes patients? Multiple clinical trials have confirmed the benefits of aspirin for secondary prevention of cardiovascular events and mortality for both men and women.\(^{19}\) The average RRR seen in clinical trials of aspirin has been between 15% and 18%.\(^{19}\) Relative risk reductions predicted by Archimedes were approximately twice that (30%-35%, data not shown). We have no explanation for this other than that all of the patients analyzed had diabetes mellitus, and so were different from most patients included in the clinical trials.

Aerobic exercise reduces the risk of fatal MIs. Studies examining the cardiovascular benefits of aerobic exercise have looked primarily at intermediate outcomes, such as reductions in BP or lipid levels and improved endothelium-dependent vasodilatation.\(^{20,21}\) The effect of aerobic exercise on risk of cardiovascular events has primarily been investigated in the context of cardiac rehabilitation programs, which also offer other forms of lifestyle counseling and tend to include patients who have already suffered a cardiac event. In a meta-analysis of 48 clinical trials, Taylor et al found that cardiac rehabilitation programs reduced all-cause mortality and cardiac mortality, but they found no difference in the rates of nonfatal MI or need for revascularization.\(^{22}\) Two other meta-analyses have documented that such programs significantly reduce fatal reinfarction rates, sudden deaths, and overall mortality, but not nonfatal reinfarctions.\(^{23,24}\)

LDL reduction's surprisingly negligible effect on risk of stroke. An overview of lipid-lowering trials conducted before 1995 found that reducing LDL levels by 22% to 30% decreased the incidence of strokes by 29%.\(^{25}\) A separate systematic review conducted by Crouse et al concluded that, in patients with coronary artery disease, statin therapy reduced risk of stroke by 27%.\(^{26}\) Again, the initial LDL level for our cases was only 120 mg/dL, so a 25% reduction would have lowered it to 90 mg/dL, and an RRR of 29% would have resulted in an ARR of 4% in the base case. Our simulated reduction of LDL to 70 mg/dL yielded an ARR of just 0.4%. However, our cases did not have a history of coronary artery disease, which makes them very different from the participants in most of the clinical trials.

HbA1c control is important for MI and CVA prevention. Controlling hyperglycemia was the most effective way to lower risk of foot ulceration. It was also quite effective at reducing risk of MI and CVA—comparable to, or better than, BP and LDL control. However, the HbA1c for the base case was 10%, so our intervention (3% reduction) was more substantial than in most clinical trials. Though early clinical trials were unable to demonstrate an effect of HbA1c control on macrovascular outcomes, except when metformin was used, newer trials are confirming a benefit of glycemic control on macrovascular disease and events.\(^{27}\) Interestingly, Archimedes predicted that very tight control of HbA1c to 6.5%, BP to 120/80 mm Hg, and LDL to 70 mg/dL would be substantially more effective than control to standard targets.

Unanticipated lack of effect with ACE inhibitors. Another surprising finding of this study was that using ACE inhibitors had no effect on risk of MI or CVA. This is inconsistent with the literature, which has shown that ACE inhibitors significantly reduce all-cause mortality, cardiovascular mortality, nonfatal MI, strokes, and need for revascularization in patients at high risk for these events.\(^{28-30}\) Reduction of BMI alone had no effect on risk of adverse events. However, in these simulations the BMI was not very high to begin with.

Clinical recommendations. Though we did our best to choose cases that physicians would consider typical, each
patient with diabetes will have a unique clinical profile. Patients with clinical profiles similar to our cases would probably benefit more from aspirin and moderate exercise than from all other interventions combined.

The Archimedes diabetes risk engine is a well-validated tool that can be used to enhance shared decision-making in primary care settings, though for some interventions it seems to be in conflict with the results of clinical trials.

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Disclosure
The authors reported no potential conflicts of interest relevant to this article.

References

In a simulated black male 65 years of age, aspirin and exercise reduced risk of MI even more effectively than in the base case.


