

Appendix Table. Base-Case Model Assumptions

| Definition | Base-Case Values | | | Study, Year (Reference) |
|--|---|----------------------|--------------------|----------------------------|
| Patient population | | | | |
| Demographic characteristics | | | | |
| Age groups, age at onset of simulation | 60–64, 65–69, 70–74, 75–79 (uniform distributions) | | | -- |
| Duration of diabetes groups, years at onset of simulation | 0, 0–5, 5–10, 10–15 (uniform distributions) | | | -- |
| Men, % | 47 | | | Robbins et al., 2001 (34) |
| Ethnic distribution, % | White | 71 | | Robbins et al., 2001 (34) |
| | Black | 13 | | |
| | Latino | 10 | | |
| | Asian | 2.5 | | |
| | Native American | 2.5 | | |
| Comorbidity and functional status | | | | |
| Mortality index scores at onset of simulation | Age group | Men | Women | Lee et al., 2006 (21) |
| | 60–64 | 3–17 | 1–15 | |
| | 65–69 | 4–18 | 2–16 | |
| | 70–74 | 5–19 | 3–17 | |
| | 75–79 | 6–20 | 4–18 | |
| Cardiovascular risk factor distributions (Age-, race-, and sex-specific levels for patients with diabetes [normal distributions]) – below risk factors for 65- to 85-year-old white female patients | | | | |
| Mean systolic blood pressure (SD), <i>mm Hg</i> | 145 (33) | | | Robbins et al., 2001 (34) |
| Mean diastolic blood pressure (SD), <i>mm Hg</i> | 61 (16) | | | Robbins et al., 2001 (34) |
| Mean total cholesterol (SD), <i>mmol/L</i> | 5.30 (1.29) | | | Robbins et al., 2001 (34) |
| | <i>mg/dl</i> | | | |
| Mean HDL cholesterol (SD), <i>mmol/L</i> | 1.29 (0.34) | | | Robbins et al., 2001 (34) |
| | <i>mg/dl</i> | | | |
| Smoking, %* | 8 | | | Robbins et al., 2001 (34) |
| Treatment assumptions | | | | |
| ACE inhibitor utilization, % | 26 | | | Grant et al., 2004 (38) |
| Aspirin utilization, % | 12 | | | Stafford et al., 2005 (39) |
| Antihypertensive therapy, % | 44 | | | Saydah et al., 2004 (37) |
| Diabetes-related complication modules | | | | |
| Retinopathy | | | | |
| No retinopathy to blindness in one eye | Functional form: Weibull† | | | Clarke et al., 2004 (23) |
| | Parameter | Coefficient | | |
| | λ | –6.464 | | |
| | γ | 1.154 | | |
| | Age (Age at diagnosis – 52.59) | 0.069 | | |
| | HbA _{1c} (A _{1c} – 7.09) | 0.221 | | |
| Nephropathy | | | | |
| No nephropathy to microalbuminuria | Baseline event rate | | | UKPDS, 1998 (3) |
| | Functional form for complication free survival with moderate glucose control: $\text{Exp}(-\text{exp}(\beta_0) \times (\text{Duration of diabetes}^{\beta_1}) \times (\text{HbA}_{1c})^{\alpha})$ | | | DCCT, 1993 (2) |
| | Parameter | Coefficient | | CDC, 2002 (19) |
| | β_0 | 1.348 | | Huang et al., 2007 (26) |
| | β_1 | 3.622 | | |
| | α | –11.959 | | |
| | Multiplier to calculate event rate with lower sugar levels (HbA _{1c} with moderate glucose control/HbA _{1c} with intensive glucose control) ^β | | | |
| | Parameter | Coefficient | | |
| | β | 4.28 | | |
| | Microalbuminuria to gross proteinuria | Baseline event rate | | |
| Functional form for complication free survival with moderate glucose control: $\text{Exp}(-\text{exp}(\beta_0) \times (\text{Duration of diabetes}^{\beta_1}) \times (\text{HbA}_{1c})^{\alpha})$ | | | | DCCT 1993 (2) |
| Parameter | | Coefficient | | CDC 2002 (19) |
| β_0 | | 1.495 | | Huang et al., 2007 (26) |
| β_1 | | 5.727 | | |
| α | | 17.810 | | |
| Multiplier to calculate event rate with lower sugar levels (HbA _{1c} with moderate glucose control/HbA _{1c} with intensive glucose control) ^β | | | | |
| Parameter | | Coefficient | | |
| β | | 2.33 | | |
| Gross proteinuria to end-stage renal disease | | Duration of diabetes | Annual probability | |
| | 0–11 years | 0.004 | | |
| | 12–24 years | 0.039 | | |
| | 25 years | 0.074 | | |

Neuropathy

| | | | | |
|---|---|-------|-------------|--------------------------|
| No neuropathy to lower extremity amputation | Functional form: Weibull† | | | Clarke et al., 2004 (23) |
| | Parameter | | Coefficient | |
| | λ | | -8.718 | |
| | γ | | 1.451 | |
| | HbA _{1c} ($A_{1c} - 7.09$) | | 0.435 | |
| | Systolic blood pressure ($[SBP - 135.09]/10$) | | 0.228 | |
| Peripheral vascular disease | | 2.436 | | |
| Blind | | 1.812 | | |

Cardiovascular complications

Base-case models with UKPDS equations

| | | | | |
|------------------------|---|-------|-------------|---------------------------|
| Coronary heart disease | Functional form: Cox Proportional Hazards† | | | Stevens et al., 2001 (20) |
| | Parameter | | Coefficient | |
| | Intercept | | 0.011 | |
| | Age (Age at diagnosis - 55) | | 1.059 | |
| | Female sex | | 0.525 | |
| | Smoking | | 1.350 | |
| | HbA _{1c} ($A_{1c} - 6.72$) | | 1.183 | |
| | Systolic blood pressure ($SBP - 135.7/10$) | | 1.088 | |
| | Cholesterol (natural log total cholesterol/HDL cholesterol) | | 3.845 | |
| Duration of diabetes | | 1.078 | | |

Stroke

| | | | | |
|--|--|-------|-------------|---------------------------|
| Stroke | Functional form: Cox Proportional Hazards† | | | Kothari et al., 2002 (24) |
| | Parameter | | Coefficient | |
| | Intercept | | 0.002 | |
| | Duration of diabetes | | 1.145 | |
| | Age (Age at diagnosis - 55) | | 1.092 | |
| | Female sex | | 0.700 | |
| | Smoking | | 1.547 | |
| | Atrial fibrillation | | 8.554 | |
| | Systolic blood pressure ($SBP - 135.5/10$) | | 1.122 | |
| Cholesterol ($[\text{total cholesterol}/\text{HDL cholesterol}] - 5.11$) | | 1.138 | | |

Sensitivity analysis using Framingham equations

| | | | | | | |
|---|--|-------|----------|-------------|--------------------------|--|
| Coronary heart disease | Functional form: Cox Proportional Hazards† | | | | Wilson et al., 1998 (48) | |
| | Parameter | | | Coefficient | | |
| | | | Men | Women | | |
| | Age | | 0.048 | 0.338 | | |
| | Age ² | | - | 0.003 | | |
| | Total cholesterol | | | | | |
| | <4.14 mmol/L (<160 mg/dl) | | -0.659 | -0.261 | | |
| | 4.14-5.16 mmol/L (160-199 mg/dl) | | Referent | Referent | | |
| | 5.17-6.19 mmol/L (200-239 mg/dl) | | 0.177 | 0.208 | | |
| | 6.20-7.22 mmol/L (240-279 mg/dl) | | 0.505 | 0.243 | | |
| | ≥7.23 mmol/L (≥280 mg/dl) | | 0.657 | 0.535 | | |
| | HDL cholesterol | | | | | |
| | <0.91 mmol/L (<35 mg/dl) | | 0.49744 | 0.843 | | |
| | 0.91-1.15 mmol/L (35-44 mg/dl) | | 0.24310 | 0.378 | | |
| | 1.16-1.28 mmol/L (45-49 mg/dl) | | Referent | 0.198 | | |
| | 1.29-1.53 mmol/L (50-59 mg/dl) | | -0.05107 | Referent | | |
| | 1.54 mmol/L (≥60 mg/dl) | | -0.48660 | -0.430 | | |
| | Blood pressure, mm Hg | | | | | |
| | <120 and <80 | | 0.002 | 0.534 | | |
| | 120-129 or 80-84, | | Referent | Referent | | |
| | 130-139 or 85-89 | | 0.283 | 0.068 | | |
| | 140-159 or 90-99 | | 0.522 | 0.263 | | |
| | ≥160 or ≥100 | | 0.619 | 0.466 | | |
| | Diabetes | | 0.428 | 0.596 | | |
| Smoker | | 0.523 | 0.292 | | | |
| Baseline survival function at 10 years† | | 0.900 | 0.962 | | | |

Stroke

| | | | | | | |
|--------|--|--|-------|-------------|-----------------------|--|
| Stroke | Functional form: Cox Proportional Hazards† | | | | Wolf et al., 1991(49) | |
| | Parameter | | | Coefficient | | |
| | | | Men | Women | | |
| | Age | | 0.051 | 0.066 | | |
| | Systolic blood pressure | | 0.014 | 0.020 | | |
| | Antihypertensive therapy | | 0.326 | 2.543 | | |
| | Blood pressure × therapy interaction | | 0 | -0.013 | | |
| | Diabetes | | 0.338 | 0.542 | | |
| | Smoker | | 0.515 | 0.529 | | |
| | Cardiovascular disease | | 0.520 | 0.433 | | |
| | Atrial fibrillation | | 0.606 | 1.150 | | |
| | Left ventricular hypertrophy | | 0.842 | 0.849 | | |

For cardiovascular probabilities after incident event, please see Eastman et al., 1997 (22), and Huang et al., 2007 (26)

Treatment effects

ACE inhibitor effect

| | | |
|---|------|---|
| Hazard ratio for no nephropathy to microalbuminuria | 0.32 | Rosen et al., 2005 (44) HOPE 1999 (57) |
| Hazard ratio for microalbuminuria to gross proteinuria | 0.24 | Rosen et al., 2005 (44) HOPE 1999 (57) |
| Hazard ratio for proteinuria to end-stage renal disease | 0.61 | Rosen et al., 2005 (44) HOPE 1999 (57) |
| Hazard ratio for coronary heart disease | 0.75 | Rosen et al., 2005 (44) HOPE 1999 (57) |
| Hazard ratio for stroke | 0.67 | Rosen et al., 2005 (44) HOPE 1999 (57) |
| Aspirin effect | | |
| Hazard ratio for coronary heart disease | 0.64 | Hansson et al., 1998 (58) |

Background mortality rate assumptions

| | | | |
|--|---|---------------------------------|--------------------------------|
| Overall mortality rates used to calculate background mortality rates | Mortality Index Score | Annual probability of mortality | Lee et al., 2006 (21) |
| | 1 | 0.005 | |
| | 2 | 0.004 | |
| | 3 | 0.009 | |
| | 4 | 0.016 | |
| | 5 | 0.020 | |
| | 6 | 0.245 | |
| | 7 | 0.040 | |
| | 8 | 0.054 | |
| | 9 | 0.053 | |
| | 10 | 0.079 | |
| | 11 | 0.141 | |
| | 12 | 0.136 | |
| | 13 | 0.200 | |
| | ≥14 | 0.225 | |
| Cardiovascular mortality rate subtracted from overall mortality rate with general population risk factor levels (NHANES 1999-2002) | Functional form: Weibull† Parameter | Coefficient | Anderson et al., 1990 (30) |
| | θ_0 | 0.821 | |
| | θ_1 | -0.435 | |
| | β_0 | -0.504 | |
| | Female | 0.224 | |
| | Log (age) | 8.237 | |
| | (Log (age)) ² | -1.211 | |
| | Log (SBP) | -0.838 | |
| | Smoking | -0.162 | |
| | Log (Total cholesterol/HDL cholesterol) | -0.349 | |
| | Diabetes | -0.083 | |
| | Diabetes × female | -0.207 | |
| | Left ventricular hypertrophy | 0.295 | |
| Background mortality rate multiplier | | 2.75 | Eastman et al., 1997 (22) |
| Other assumptions* | | | |
| Prevalence of peripheral vascular disease, % | | 14.5 | Selvin and Erlinger, 2004 (59) |
| Prevalence of atrial fibrillation | Sex- and age-specific prevalence from Kaiser population | | Go et al., 2001(60) |

Utilities

| | | |
|---------------------------------|------|---------------------------|
| Blindness | 0.69 | Dasbach et al., 1992(41) |
| End-stage renal disease | 0.61 | DCCT, 1996 (27) |
| Lower extremity amputation | 0.68 | Redekop et al., 2004 (42) |
| Myocardial infarction or arrest | 0.88 | CDC, 2002 (19) |
| Angina | 0.97 | CDC, 2002 (19) |
| Stroke | 0.64 | Rosen et al., 2005 (44) |

ACE = angiotensin-converting enzyme; CDC = Centers for Disease Control and Prevention; DCCT = Diabetes Control and Complication Trial; HbA_{1c} = hemoglobin A_{1c}; HDL = high-density lipoprotein; HOPE = Heart Outcomes Prevention Evaluation Study; NHANES = National Health and Nutrition Examination Surveys; SBP = systolic blood pressure; UKPDS = United Kingdom Prospective Diabetes Study.

* Analyses assumed no uncertainty surrounding proportion of patients smoking, hazard ratios for ACE inhibitors and aspirin, or utility weights. Prevalences of peripheral vascular disease and atrial fibrillation did not differ by duration of diabetes.

† Please use technical approach described in the original publications to calculate annual probabilities. Analyses assumed no uncertainty surrounding model coefficients.