Appendix 1. Sensitivity analysis on the persistency of treatment effect
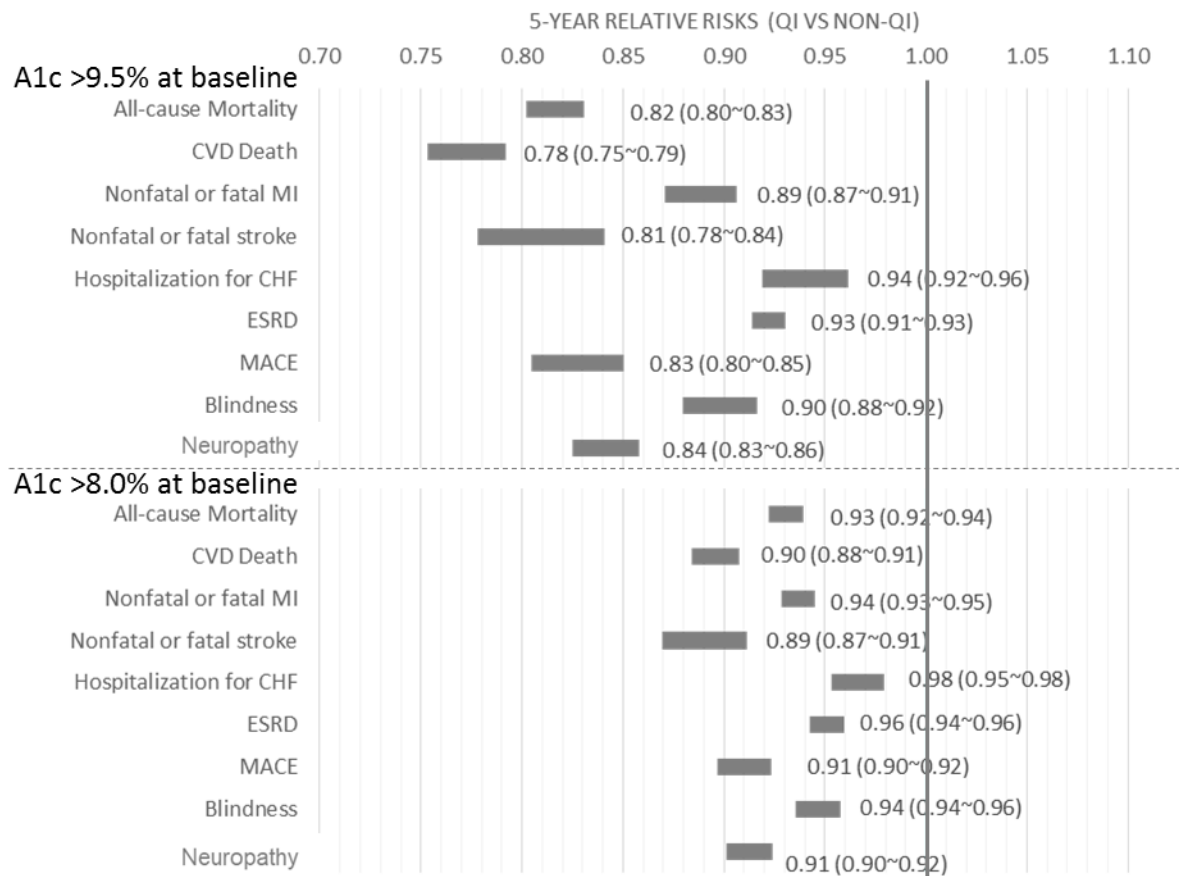

Figure A.1. 5-year relative risk of diabetes-related complications (QI vs non-QI).

Notes: CVD: cardiovascular disease; MI: myocardial infarction; CHF: congestive heart failure; ESRD: end-stage renal disease; MACE: major adverse cardiovascular events. Numbers at end of columns denote relative risks (QI vs non-QI), with 95% confidence interval in the brackets.

Fig A.1 shows the 5-year projected risk reduction of clinical outcomes following the QI intervention. Among patients with baseline HbA1c >8% (64 mmol/mol), the model estimated the QI program to significantly reduce the 5-year risk of all-cause mortality (hazard ratio (HR): 0.93, 95% confidence interval (CI) 0.92-0.94), CVD death (HR: 0.90, 95% CI: 0.88-0.91), nonfatal or fatal MI (HR: 0.94, 95% CI:0.93-0.95), nonfatal or fatal stroke (HR:0.89, 95% CI:0.87-0.91), hospitalization for CHF (HR:0.95, 95% CI:0.95-0.98), ESRD (HR:0.96, 95% CI:0.94-0.96), major cardiovascular adverse event (HR:0.91, 95% CI: 0.90-0.92), blindness (HR:0.94, 95% CI: 0.94-0.96), and neuropathy (HR:0.91, 95% CI: 0.91-0.92).

Individuals with HBA1C > 9.5% (80 mmol/mol) at baseline experienced even larger predicted clinical benefits over 5 years following the QI intervention than those with with baseline HbA1c >8% (64 mmol/mol). In these patients the model estimated the QI program to significantly reduce the 5-year risk of all-cause mortality (HR:0.82, 95% CI: 0.80-0.83), CVD death (HR: 0.78, 95% CI: 0.75-0.79), nonfatal or fatal MI (HR: 0.89, 95% CI:0.87-0.91), nonfatal or fatal stroke (HR:0.81, 95% CI:0.78-0.84), hospitalization for CHF (HR:0.94, 95% CI:0.92-0.96), ESRD (HR:0.93, 95% CI:0.91-0.93), major cardiovascular adverse event (HR:0.83, 95% CI: 0.80-0.85), blindness (HR:0.90, 95% CI: 0.88-0.92), and neuropathy (HR:0.84, 95% CI: 0.83-0.86).
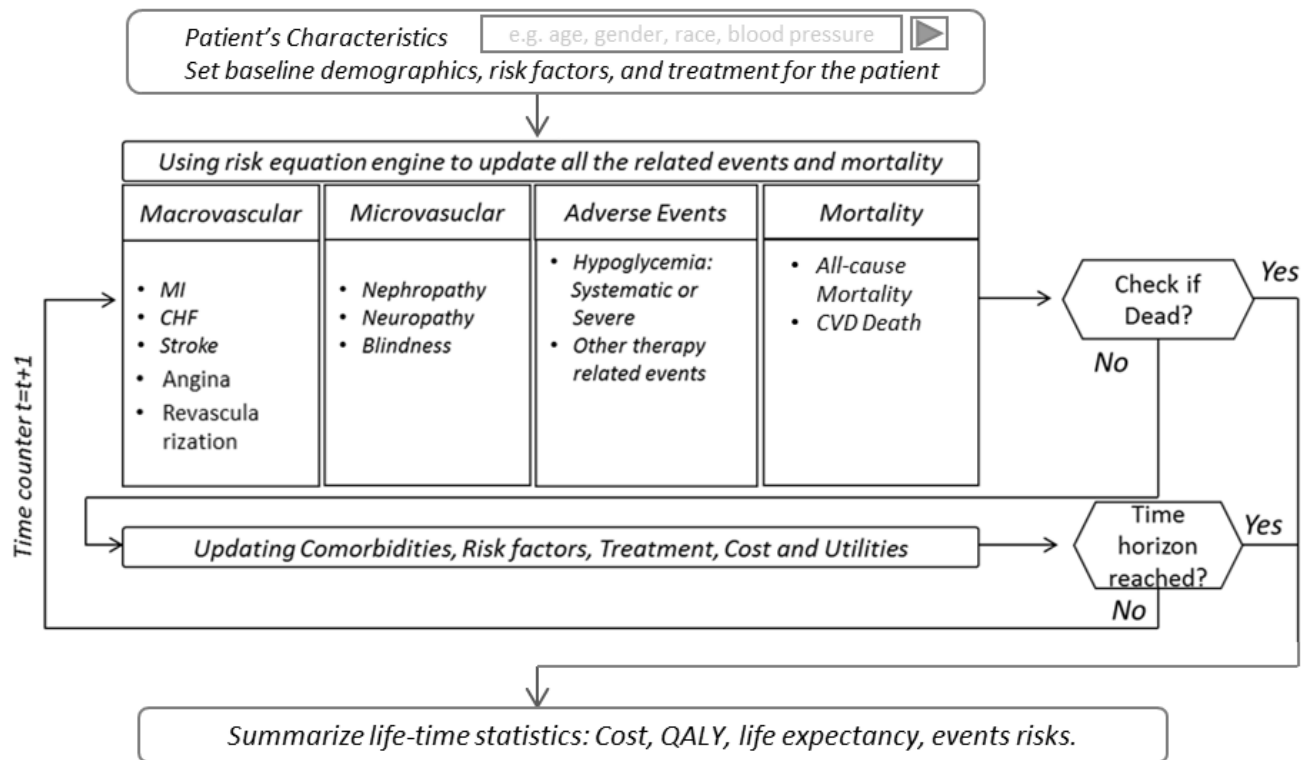
Appendix 2. Description of the BRAVO model

Figure A.2. The BRAVO model's Simulation Flow Chart

We've summarized the flow chart of the BRAVO model in Figure A2. The simulation process was conducted at a personal level, instead of a traditional Markov-based cohort level. An annual cycle was adopted in the simulation, and each cycle, complications were examined at random order. To determine the occurrence of each complication, we estimated the probability of encountering each complication using the BRAVO risk equations. This set of equations utilized the patient's characteristics and value of the biomarkers (presented in table 1) to estimate the likelihood of the complication. After that, the estimated probability was compared with a random number drawn from a uniform distribution (0-1). If the random number was lower than the estimated probability, we counted the person as encountering the corresponding complication. After all the complications were concluded, a check on death events was performed. If survived, the simulation process will be carried on to the next cycle, and this process kept going until a death event encountered, or the 5-year time horizon reached.