# THE LANCET Diabetes & Endocrinology

## Supplementary appendix

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## Appendix

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#### Model overview

In the simulation, we simulated 100,000 people with type II diabetes based on the age-specific distribution of type II diabetes (**Appendix Table 1**), and assigned each individual baseline risk factor values by repeatedly sampling (with replacement) from the correlated probability distributions of risk factors among their cohort (**Appendix Table 2**),<sup>46</sup> where cohorts were defined by 10-year age group within the range 20 to 70 years old, sex, and either urban or rural residence. We updated risk factors annually to account for aging-related risk factor changes, secular trends in risk factor values, and the process of urbanization or migration to urban areas (**Appendix Table 1**), using a model coding approach that we previously validated and open-sourced.<sup>47</sup> We also used a rank stability coding procedure to update age-specific risk factors for each individual, to prevent survival bias (i.e., we keep an individual within the same quintile of their subgroup in

terms of each risk factor value, as individuals with a high risk factor value are likely to have a high value in the future without further treatment, and die in earlier years of the simulation).<sup>3</sup>

In each annual time step of the simulation, we calculated the annual risk for each of the five diabetes complications for each individual, estimated from previously-published UKPDS Outcomes Model 2 equations, which were chosen due to their extensive international validation, and inclusion of ethnicity-specific parameters.<sup>24,25</sup> Due to copyright restrictions, the equations themselves cannot be reproduced here, but are available online in the cited publication (see the statistical appendix for eTables 4-6 for the specific equations for CVD complications risk, microvascular complications risk, and associated mortality risk, respectively). The equations account for the risk of complications given a simulated individual's biomarker values, incorporating co-dependencies among complications such as the increased risk of cardiovascular complications given renal disease. We used a binomial probability function to simulate whether a person experienced a complication that year given their UKPDS-OM2 risk that year for each complication, and similarly computed mortality following a complication. Mortality from other causes was computed with a binomial probability function using probability of death estimates from the WHO Mortality Database, specific to each age, sex and country (Appendix Table 3).<sup>49</sup> Prior history of complications informed future risk of complications and mortality (e.g., we re-computed risk of CVD events and mortality if a patient experienced renal failure, to account for their heightened CVD risk). We subsequently calculated disability-adjusted life-years (DALYs) and total deaths from diabetes complications (accounting for healthcare service availability. Appendix Table 4).<sup>39</sup>

#### Medication choices and dose effects on biomarkers

#### Blood pressure therapy

For blood pressure agents, we simulated prescriptions following WHO guidelines,<sup>14</sup> which recommend a thiazide diuretic or angiotensin converting enzyme (ACE) inhibitor for people with diabetes, at standard WHO-recommended dosages (hydrochlorothiazide 25mg per day or enalapril 5mg per day), as dosage adjustment has

small effects on outcomes.<sup>50</sup> Initial drug choice and prescription order between the thiazide and the ACE inhibitor were randomly varied unless a person had microalbuminuria (in which case the ACE inhibitor was chosen first), and second-line choices of two additional agents (a calcium channel blocker [amlodipine 5mg daily], then a betablocker [bisoprolol 5mg daily] if needed) were simulated subsequently if necessary to achieve the target. The effect of each drug class on blood pressure was based on a prior meta-analysis of individual randomized trials, and suggested a typical effect of lowering systolic/diastolic blood pressure by 8.8/4.4 mmHg (thiazide, 95% CI: 8.3-9.4/4.0-4.8 mmHg), 8.5/4.7 mmHg (ACE inhibitor, 95% CI: 7.9-9.0/4.4-5.0 mmHg), 8.8/5.9 mmHg (calcium channel blocker, 95% CI: 8.3-9.2/5.6-6.2 mmHg), and 9.2/6.7 mmHg (betablocker, 95% CI: 8.3-9.2/5.6-6.2 mmHg).<sup>27</sup>

#### Statin therapy

Statin prescription was simulated based on a review of data from randomized trials, suggesting a 0.69 mmol/L (SD: 0.29) reduction in LDL with simvastatin 20mg daily, an additional 0.15 mmol/L (SD: 0.06) reduction with dose titration to simvastatin 40mg daily.<sup>32</sup> Atorvastatin and other alternative statins were not simulated given their lack of inclusion on the WHO Essential Medicine list<sup>51</sup>, and their corresponding lack of availability in most low- and middle-income countries.<sup>51</sup>

#### Glucose lowering therapy

For glucose lowering, metformin 500mg daily was uptitrated to as much as 1000mg twice daily for an A1c reduction ranging linearly with dose titration from 0.5% (SD: 0.2%) to 1.5% (SD: 0.5%), to which the sulfonylurea gliclazide (the sulfonylurea on the WHO Essential Medicine list<sup>51</sup>) was added with doses increasing from 80mg daily to 160mg twice daily for an additional A1c reduction ranging from 0.5% to 1.5% proportional to dose. If the A1c target of <7% was still not achieved, NPH insulin was substituted for the sulfonylurea to achieve the target, with a dose of 0.5 IU/kg body weight (SD: 0.1 IU/kg) to simulate the typical dose required for target achievement. <sup>52</sup>

#### **Risk reduction from therapy**

To modify the baseline risk of complications from these equations, we estimated the relative risk reduction from therapy based on meta-analyses of individual patient data from randomized controlled trials, specified below; this strategy was adopted instead of simply altering values of risk factors in the UKPDS OM2 equations, because full reversal of risk is not observed upon therapy.<sup>45</sup>

#### Blood pressure therapy

The relative risk reduction from blood pressure therapy for MI and stroke events was based on equations derived and validated previously from meta-analyses of individual patient data from blood pressure reduction trials, in which the relative risk of MI is given by equation 1 and the relative risk of stroke by equation 2 (where  $\triangle$ SBP is the change in systolic blood pressure [final minus initial blood pressure], and age is in years)<sup>29,53</sup>:

- [1]  $2^{\Delta SBP(-1.1009 \times 10^{-5} age^2 + 8.6305 \times 10^{-4} age + 3.5176 \times 10^{-2}}$
- $[2] \qquad 2^{\Delta SBP(-2.5946 \times 10^{-5} age^2 + 2.3052 \times 10^{-3} age + 2.2168 \times 10^{-2}}$

The relative risk reduction from blood pressure for microvascular events was 0.38 for a 10 mmHg decline in systolic blood pressure.<sup>2</sup>

#### Statin therapy

The relative risk reduction for MI and stroke events from statin therapy was 0.33 (95% CI: 0.27, 0.38) for simvastatin 20mg, an additional 0.07 for dose adjustment<sup>24</sup> from simvastatin 20mg to 40mg daily (95% CI: 0.05, 0.09).<sup>32</sup> The relative risk reduction from statin therapy for microvascular events was 0.03 for a 0.1 mmol/L reduction in LDL, with an effect on renal disease but not other microvascular complications.<sup>24</sup>

#### *Glucose lowering therapy*

The relative risk for diabetes complications from glucose lowering therapy was simulated as a log-linear relationship to be consistent with observed risk reductions.<sup>54</sup> Relative risk was based on a meta-analysis of randomized trial outcomes,<sup>19</sup> with an estimated relative risk of 0.87 for non-fatal MI (95% CI: 0.76, 1.00), 0.77 for retinal photocoagulation (95% CI: 0.61, 0.97), 0.64 for amputation of lower extremity (95% CI: 0.43, 0.95), and 0.78 for nephropathy (95% CI: 0.61, 0.99) for a 0.9% reduction in A1c.

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Estimated population size, distribution, and type II diabetes prevalence, years 2016 and 2025.<sup>20,21,23,38,55</sup> We simulated linear secular trends in each parameter across the simulation period. We estimated type II diabetes prevalence from overall prevalence based on the estimate that 95% of overall diabetes prevalence in the studied populations is type II.<sup>21</sup>

		Po	oulation siz	ze, thousa	nds	Rura	al, %	Urban/rural	Туре	II diabetes	s preval	ence, %
		20	16	20	25			T2DM	2	016	2	025
								prevalence				
Country	Age, yrs	Male	Female	Male	Female	2016	2025	ratio	Male	Female	Male	Female
China	0-4	44 734	38 730	36 568	32 130	57.1	68.9	1.14	0.0	0.0	0.0	0.0
	5-9	42 885	36 742	41 942	36 538				0.0	0.0	0.0	0.0
	10-14	40 624	35 057	44 479	38 399				0.0	0.0	0.0	0.0
	15-19	40 589	35 627	42 145	36 109				0.0	0.0	0.0	0.0
	20-24	52 641	47 064	40 001	34 615				0.5	0.3	0.6	0.3
	25-29	66 934	61 680	41 461	36 556				0.9	1.3	1.0	1.5
	30-34	53 975	50 911	55 268	49 741				2.3	1.8	2.6	2.1
	35-39	47 695	45 304	66 245	61 478				4.1	3.6	4.8	4.2
	40-44	58 690	55 871	50 341	47 774				6.9	6.5	8.0	7.6
	45-49	63 389	61 502	47 966	45 721				10.2	9.8	11.8	11.5
	50-54	53 089	51 277	59 383	57 005				14.1	13.8	16.3	16.2
	55-59	40 958	39 624	60 067	59 032				17.6	17.4	20.4	20.5
	60-64	39 522	38 936	47 054	46 248				19.6	19.8	22.7	23.3
	65-69	27 399	27 799	35 068	35 259				21.5	21.1	25.0	24.8
	70-74	17 284	17 700	30 739	32 449				23.0	22.0	26.7	25.9
	75-79	11 703	12 682	16 586	18 982				24.3	23.0	28.1	27.0
Ghana	0-4	2 116	2 025	2 192	2 099	54.8	60.8	1.10	0.0	0.0	0.0	0.0
	5-9	1 828	1 753	2 095	2 011				0.0	0.0	0.0	0.0
	10-14	1 610	1 542	2 006	1 923				0.0	0.0	0.0	0.0
	15-19	1 436	1 374	1 746	1 673				0.0	0.0	0.0	0.0

	20-24	1 323	1 271	1 529	1 468				0.2	0.1	0.3	0.2
	25-29	1 149	1 151	1 350	1 301				0.3	0.4	0.4	0.7
	30-34	971	1 046	1 236	1 202				0.8	0.6	1.1	1.0
	35-39	813	900	1 057	1 081				1.4	1.2	2.1	2.1
	40-44	678	740	887	978				2.4	2.2	3.5	3.8
	45-49	564	607	735	825				3.5	3.4	5.2	5.7
	50-54	446	478	601	669				4.9	4.8	7.1	8.0
	55-59	343	386	482	537				6.1	6.0	8.9	10.1
	60-64	248	284	359	405				6.8	6.8	9.9	11.5
	65-69	194	210	252	303				7.5	7.3	10.9	12.3
	70-74	123	136	158	192				8.0	7.6	11.6	12.8
	75-79	69	93	96	112				8.4	7.9	12.3	13.4
India	0-4	64 679	58 226	64 412	58 365	33.1	36.2	1.88	0.0	0.0	0.0	0.0
	5-9	66 672	59 810	64 683	58 306				0.0	0.0	0.0	0.0
	10-14	67 024	59 975	64 276	57 751				0.0	0.0	0.0	0.0
	15-19	65 366	58 702	66 304	59 405				0.0	0.0	0.0	0.0
	20-24	62 558	56 476	66 036	59 031				0.6	0.3	0.8	0.4
	25-29	59 341	54 525	63 757	57 353				1.0	1.5	1.2	1.7
	30-34	55 057	51 068	60 635	55 129				2.6	2.1	3.2	2.4
	35-39	48 318	45 201	57 091	53 138				4.8	4.2	5.7	4.8
	40-44	42 591	40 086	52 132	49 141				8.1	7.5	9.7	8.7
	45-49	37 259	35 343	44 930	42 966				11.9	11.4	14.3	13.2
	50-54	32 477	31 069	39 029	37 790				16.4	16.0	19.7	18.5
	55-59	27 416	26 535	33 114	32 628				20.6	20.3	24.6	23.4
	60-64	22 354	21 937	27 531	27 601				22.9	23.1	27.4	26.7
	65-69	14 994	15 548	21 422	21 921				25.2	24.6	30.1	28.4
	70-74	9 859	10 748	15 241	16 068				26.9	25.6	32.2	29.6
	75-79	6 269	7 284	8 350	9 530				28.3	26.8	34.0	30.9
Mexico	0-4	5 939	5 694	5 615	5 370	79.6	82.2	1.81	0.0	0.0	0.0	0.0
	5-9	5 916	5 654	5 786	5 542				0.0	0.0	0.0	0.0

	10-14	5 999	5 776	5 882	5 639		1		0.0	0.0	0.0	0.0
	-											
	15-19	6 049	5 870	5 849	5 611				0.0	0.0	0.0	0.0
	20-24	5 821	5 655	5 893	5 719				1.1	0.6	1.2	0.7
	25-29	5 409	5 282	5 874	5 759				1.7	2.5	2.0	2.8
	30-34	4 946	4 993	5 588	5 495				4.5	3.5	5.0	4.0
	35-39	4 598	4 783	5 170	5 137				8.1	7.1	9.2	8.0
	40-44	4 276	4 480	4 725	4 874				13.6	12.7	15.4	14.4
	45-49	3 738	3 872	4 390	4 648				20.1	19.3	22.8	21.9
	50-54	2 963	3 202	4 022	4 273				27.7	27.1	31.4	30.7
	55-59	2 405	2 643	3 403	3 592				34.6	34.2	39.2	38.8
	60-64	1 973	2 151	2 607	2 906				38.6	39.0	43.7	44.2
	65-69	1 412	1 482	2 059	2 325				42.4	41.6	48.0	47.1
	70-74	1 046	1 130	1 568	1 771				45.2	43.3	51.3	49.1
	75-79	692	801	999	1 106				47.7	45.2	54.1	51.3
South Africa	0-4	2 622	2 620	2 574	2 516	65.4	70.1	2.00	0.0	0.0	0.0	0.0
	5-9	2 838	2 728	2 656	2 607				0.0	0.0	0.0	0.0
	10-14	2 548	2 552	2 662	2 627				0.0	0.0	0.0	0.0
	15-19	2 811	2 431	2 731	2 652				0.0	0.0	0.0	0.0
	20-24	2 743	2 515	2 480	2 472				0.6	0.3	0.8	0.4
	25-29	2 765	2 602	2 791	2 381				1.0	1.2	1.3	1.5
	30-34	2 387	2 404	2 611	2 407				2.5	1.7	3.3	2.1
	35-39	1 747	1 899	2 528	2 340				4.6	3.5	5.9	4.3
	40-44	1 550	1 567	2 000	2 008				7.8	6.3	9.9	7.7
	45-49	1 435	1 374	1 416	1 534	1			11.5	9.6	14.7	11.7
	50-54	1 214	1 280	1 278	1 296	1			15.9	13.4	20.3	16.4
	55-59	881	1 131	1 135	1 154	1			19.8	16.9	25.3	20.7
		597	923	892	1 068	1			22.1	19.3	28.2	23.6
	65-69	347	707	571	892	1		24 25	24.3	20.6	31.0	25.2
	70-74	222	488	329	667	_			25.9	21.4	33.1	26.2
	75-79	172	339	151	447				27.3	22.4	34.9	27.4

Risk factor distribution ranges used for the simulation. For four of the parameters (white blood cell, haemoglobin, congestive heart failure, and peripheral vascular disease) we used the same range in the absence of country-specific data; variations in these covariates produce changes smaller than rounding error in outcome rates. PubMed and Google Scholar were searched with keywords corresponding to the "factor" column and the country name for English-language articles published from Jan 1, 1980, to July 31, 2016.

	Range of mean va	lues among age-, sex-, and un (range of sta	ˈban/rural-specific cohorts, ເ andard deviations within eac		s in each country
Factor	China <sup>25–31</sup>	Ghana <sup>25,27,32–34</sup>	India <sup>25–27,34–37</sup>	Mexico <sup>25,27,38,39</sup>	South Africa <sup>25,27,40</sup>
Tobacco smoking	0.02-0.74	0.03-0.40	0.04-0.73	0.02-0.58	0.07-0.48
(probability)	(0.12-0.53)	(0.04-0.51)	(0.19-0.63)	(0.14-0.70)	(0.25-0.71)
Body mass index	23.3-30.0	19.9-30.1	16.3-26.5	25.8-33.0	29.4-39.1
(kg/m^2)	(2.7-4.5)	(0.5-6.8)	(1.3-16.2)	(2.5-6.5)	(2.0-8.6)
Haemoglobin A1c	6.7-8.7	6.7-9.7	6.4-9.4	7.0-9.9	6.7-9.7
(%)	(1.5-5.4)	(1.5-1.5)	(1.0-1.5)	(1.5-2.5)	(1.5-1.5)
Systolic blood pressure	125.7-164.0	118.5-179.4	111.2-153.4	126.0-160.1	130.2-154.3
(mmHg)	(8.8-34.6)	(8.4-45.0)	(4.3-38.3)	(3.1-49.0)	(11.8-39.1)
High-density lipoprotein	0.9-2.0	0.9-1.5	1.0-1.4	0.9-1.5	0.9-1.5
(mmol/L)	(0.3-0.5)	(0.3-0.3)	(0.3-0.3)	(0.3-0.3)	(0.3-0.3)
Low-density lipoprotein	1.9-3.9	2.4-3.6	2.6-3.6	2.4-3.6	2.4-3.6
(mmol/L)	(0.6-1.0)	(0.6-0.6)	(0.6-0.7)	(0.6-0.6)	(0.6-0.6)
Heart rate	73.9-86.0	72.6-95.8	66.2-102.1	64.2-96.6	74.8-84.8
(beats/minute)	(8.9-23.5)	(9.1-27.5)	(5.0-18.8)	(4.8-18.2)	(2.7-16.0)
Glomerular filtration rate	65.7-112.3	62.5-92.5	62.5-100.2	62.5-92.5	62.5-92.5
(ml/min/1.73m^2)	(15.0-23.3)	(15.0-15.0)	(15.0-24.3)	(15.0-15.0)	(15.0-15.0)
White blood cell	5.0-8.6	5.0-8.6	5.0-8.6	5.0-8.6	5.0-8.6
(x10^9/L)	(1.8-1.8)	(1.8-1.8)	(1.8-1.8)	(1.8-1.8)	(1.8-1.8)
Haemoglobin	13.2-15.8	13.2-15.8	13.2-15.8	13.2-15.8	13.2-15.8
(g/dL)	(1.3-1.3)	(1.3-1.3)	(1.3-1.3)	(1.3-1.3)	(1.3-1.3)
Congestive heart failure	0.00-0.03	0.00-0.03	0.00-0.03	0.00-0.03	0.00-0.03
(probability)	(0.00-0.01)	(0.00-0.01)	(0.00-0.01)	(0.00-0.01)	(0.00-0.01)
Peripheral vascular disease	1.2-14.6	1.2-14.6	1.2-14.6	1.2-14.6	1.2-14.6
(probability)	(0.6-3.7)	(0.6-3.7)	(0.6-3.7)	(0.6-3.7)	(0.6-3.7)
Albuminuria	0.14-0.49	0.33-0.53	0.23-0.39	0.05-0.64	0.20-0.65
(probability)	(0.17-0.17)	(0.05-0.05)	(0.08-0.08)	(0.30-0.30)	(0.22-0.22)
Atrial fibrillation	0.000-0.010	0.000-0.007	0.000-0.001	0.000-0.015	0.000-0.007
(probability)	(0.000-0.002)	(0.000-0.002)	(0.000-0.001)	(0.000-0.003)	(0.000-0.002)

Probability of all-cause mortality by age and sex;<sup>49</sup> mortality specific to each diabetes complication was estimated by the UKPDS OM2 equations, using ethnicity-specific parameters as relevant for each country.<sup>24</sup> The equations account for both immediate and longer-term mortality from diabetes complications.

				Prot	oability o	f death by	age			
Age group, yrs	Cł	nina	Gł	nana	In	dia	Ме	xico	South	n Africa
	Male	Female	Male	Female	Male	Female	Male	Female	Male	Female
<1 year	0.011	0.012	0.042	0.052	0.043	0.042	0.012	0.015	0.029	0.036
1-4 years	0.002	0.002	0.023	0.024	0.014	0.011	0.002	0.002	0.011	0.012
5-9 years	0.002	0.002	0.017	0.017	0.006	0.006	0.001	0.001	0.005	0.007
10-14 years	0.001	0.001	0.010	0.010	0.004	0.004	0.001	0.002	0.004	0.007
15-19 years	0.002	0.002	0.011	0.014	0.007	0.006	0.003	0.006	0.008	0.010
20-24 years	0.003	0.003	0.014	0.019	0.009	0.010	0.003	0.010	0.019	0.014
25-29 years	0.003	0.003	0.017	0.020	0.009	0.012	0.003	0.012	0.036	0.026
30-34 years	0.003	0.004	0.019	0.022	0.010	0.015	0.004	0.014	0.049	0.043
35-39 years	0.004	0.005	0.024	0.027	0.012	0.021	0.006	0.016	0.057	0.068
40-44 years	0.007	0.009	0.027	0.031	0.015	0.027	0.008	0.019	0.044	0.077
45-49 years	0.011	0.015	0.033	0.039	0.022	0.038	0.014	0.025	0.045	0.091
50-54 years	0.017	0.024	0.044	0.055	0.032	0.055	0.022	0.036	0.052	0.103
55-59 years	0.029	0.043	0.057	0.070	0.053	0.081	0.035	0.052	0.067	0.125
60-64 years	0.051	0.074	0.085	0.102	0.090	0.128	0.056	0.076	0.092	0.178
65-69 years	0.089	0.123	0.132	0.151	0.142	0.194	0.082	0.111	0.134	0.249
70-74 years	0.150	0.199	0.209	0.229	0.224	0.270	0.127	0.170	0.196	0.338
75-79 years	0.244	0.306	0.323	0.346	0.315	0.373	0.195	0.252	0.277	0.437
80-84 years	0.397	0.469	0.490	0.520	0.432	0.474	0.288	0.344	0.404	0.457
85-89 years	0.573	0.637	0.701	0.716	0.534	0.563	0.416	0.462	0.508	0.558
90-94 years	0.782	0.826	0.930	0.947	0.642	0.654	0.577	0.609	0.638	0.677
95-99 years	0.898	0.916	0.969	0.975	0.743	0.739	0.761	0.775	0.780	0.798
100+ years	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000	1.000

Cost-effectiveness input data.<sup>19,39,40,71–75</sup> Costs are in 2016 US Dollars.

Parameter	Input values (95% Cl)
Blood pressure treatment	
Hydrochlorothiazide 25mg	\$3.43/person/yr (\$1.5, \$14.16)
Enalapril 5mg	\$6.02/person/yr (\$3.03, \$10.33)
Amlodipine 5mg	\$3.43/person/yr (\$1.17, \$14.86)
Bisoprolol 5mg	\$24.09/person/yr (\$18.18, \$30.04)
Statin treatment	
Simvastatin 20mg	\$8.94/person/yr (\$3.65, \$53.62)
Glucose treatment	
Metformin 1000mg	\$8.06/person/yr (\$7.81, \$25.11)
Gliclazide 80mg	\$16.61/person/yr (\$14.97, \$18.25)
NPH insulin + supplies*	\$326.42/person/yr (\$309.96, \$407.4)
Medical service costs	
blood pressure, monitoring and drug titration	\$12.00/person/yr (\$6, \$24)
lipid testing, monitoring and drug titration	\$30.00/person/yr (\$15, \$60)
haemoglobin A1c testing, monitoring and drug titration	\$105.00/person/yr (\$58, \$210)
MI acute event care	\$645.00/event (\$322.5, \$1290)
MI post-event annual care	\$79.00/person/yr (\$39.5, \$158)
Stroke acute event care	\$883.00/event (\$441.5, \$1766)
Stroke post-event annual care	\$795.00/person/yr (\$397.5, \$1590)
ESRD dialysis**	\$19,930.20/person/yr (\$16124.36, \$27270.07)
Photocoagulation services***	\$196.95/event (\$98.48, \$393.9)
Ulcer care and management**	\$585.60/event (\$292.8, \$1171.2)
Amputation care and management**	\$2,909.77/event (\$1406.87, \$7480.87)
Disability weights	
MI, days 1-2	0.422 (0.284, 0.560)
MI, days 3-28	0.056 (0.035, 0.082)
Stroke, mild <sup>†</sup>	0.021 (0.011, 0.037)
Stroke, moderate	0.076 (0.050, 0.110)
Stroke, moderate with cognitive involvement	0.312 (0.211, 0.433)
Stroke, severe	0.539 (0.363, 0.705)
Stroke, severe with cognitive involvement	0.567 (0.394, 0.738)
Distance vision blindness	0.195 (0.132, 0.272)
Near vision impairment <sup>‡</sup>	0.013 (0.006, 0.024)
End-stage renal disease	0.573 (0.397, 0.749)
Diabetic neuropathy <sup>§</sup>	0.099 (0.066, 0.145)
Amputation of one leg, long-term with treatment	0.021 (0.011, 0.035)
Amputation of one leg, long-term without treatment	0.164 (0.111, 0.229)

\* insulin supplies include syringes, needles, glucometer (last ~3yrs per meter), test strips, and lancets
\*\* proper long-term treatment available to approximately 10% of the affected population
\*\*\* available to approximately 35% of the affected population

<sup>1</sup> the distribution among stroke types was assumed to be equal <sup>2</sup> both near-vision and distance vision were assumed to be impaired among patients experiencing blindness <sup>§</sup> for ulcer, neuropathy disability was included, as well as a 10% probability of treatment, with progression to amputation if untreated

Lowering the threshold for treating microvascular risk under the BTT strategy from the base case of 5% lifetime risk to 3% lifetime risk. See **Appendix Figure 2** for an illustration of how microvascular complications prevented vary with BTT treatment threshold choices.

	Chi (type II c prevalenc	liabetes	(type II	hana diabetes nce ~2.2%)	(type II	idia diabetes ice ~8.8%)	Mex (type II d prevalence	liabetes	(type II	n Africa diabetes ace ~7.2%)
	TTT	BTT	TTT	BTT	ТТТ	BTT	TTT	BTT	TTT	BTT
Adults with type II diabetes	99.1 (99,	99.8	99.4	99.9 (99.9,	99.3 (99.2,	99.9 (99.9,	99.2 (99.2,	99.8	99.3 (99.2,	99.9 (99.9,
recommended any treatment,	99.1)	(99.8,	(99.3,	99.9)	99.4)	99.9)	99.3)	(99.8,	99.3)	99.9)
%:		99.9)	99.4)					99.8)		
Blood pressure treatment	80.5 (80.3,	82.5	86.4	81 (80.9,	85.4 (85.2,	84.4 (84.2,	84.1 (83.9,	82.3	84.1 (83.8,	82.8 (82.7,
	80.6)	(82.2, 82.7)	(86.3, 86.6)	81.1)	85.5)	84.7)	84.2)	(82.2, 82.6)	84.3)	82.9)
Lipid treatment	75.2 (75.1,	82.8	75.4	81.2 (81,	75.3 (75.1,	84.6 (84.3,	75.3 (75.2,	82.5	75.3 (75,	83 (82.8,
	75.5)	(82.5, 83)	(75.2, 75.6)	81.3)	75.6)	84.9)	75.5)	(82.4, 82.8)	75.5)	83.1)
Glycaemic treatment	80.7 (80.5,	99.7	80.7	99.8 (99.8,	80.7 (80.6,	99.9 (99.8,	80.7 (80.5,	99.7	80.8 (80.6,	99.8 (99.8,
	80.9)	(99.7, 99.7)	(80.6, 80.9)	99.8)	80.9)	99.9)	80.9)	(99.7, 99.7)	81)	99.8)
Insulin treatment		18.1	13.8					17.5		
	13.8 (13.7,	(18.0,	(13.7,	18.8 (18.6,	13.8 (13.7,	20.2 (20.1,	13.8 (13.5,	(17.3,	13.8 (13.7,	16.7 (16.6,
	13.9)	18.3)	14.0)	19.0)	14.0)	20.4)	13.9)	17.6)	14.0)	16.8)
number of medications, per	3.0 (3.0,	3.8 (3.8,	3.3 (3.3,	3.7 (3.7,	3.2 (3.2,	3.8 (3.8,	3.2 (3.2,	3.7 (3.7,	3.2 (3.2,	3.8 (3.8,
person recommended treatment	3.1)	3.8)	3.3)	3.7)	3.3)	3.8)	3.2)	3.8)	3.2)	3.8)
CVD events prevented per 100,	000 people wit	h type II diab	etes from 10	years of treatr	nent:					
MI	2098.4	3247.3	2206.5	3081.9	2290.4	3419.3	2201.1	3248.6	2200.8	3277.9
	(2005.4,	(3179.5,	(2133.2,	(3059.6,	(2229.6,	(3339.9,	(2125.5,	(3169.9,	(2111.3,	(3232.7,
	2146.1)	3342)	2268.7)	3241.8)	2356)	3493.6)	2311.4)	3354.8)	2309.9)	3348.8)
Stroke	1857.3	2863.5	1885.3	2603.5	2054.4	2991.5	1932 (1886,	2821.6	1941.5	2890.0
	(1771.5,	(2911,	(1790.5,	(2575.1,	(1986.8,	(2860.8,	1982.2)	(2777.4,	(1881.5,	(2858.5,
	1914.8)	2951.6)	1966.0)	2702.6)	2134.1)	3086.0)		2843.8)	1995.6)	2911.0)
Microvascular events prevented	d per 100,000 p	people with ty	/pe II diabete	s from 10 year	s of treatment	t:				
Blindness	229.4	306.9	244.1	309.1	238.2	321.5	225.2	300.3	222.3	299.1 (279,
	(214.2,	(298.8,	(228.0,	(287.5,	(219.6,	(297.9,	(205.6,	(274.6,	(204.9,	322.7)
	240.0)	329.4)	264.8)	335.7)	270.0)	338.0)	242.9)	364.8)	243.7)	

End-stage renal disease	764 (731.1,	888.4	833.5	967.1	973.7	1115.6	705.4	815.8	590.0 (559,	711.0
Ũ	799.2)	(844,	(813.3,	(927.9,	(936.2,	(1080.4,	(675.4,	(797.7,	614.6)	(672.3,
	,	936.8)	862.9)	997.4)	1020.1)	1164.6)	736.4)	919.4)	,	765.7)
Ulcer	265.3	265.7	261.8	252 (226.4,	220.6	202.5	306.1	307.5	411.9	412.8
	(238.7,	(247.1,	(239.1,	269.8)	(198.7,	(187.4,	(258.0,	(308.7,	(369.9,	(381.2,
	286.0)	300.5)	295.5)		256)	219.2)	345.1)	320.2)	442.6)	452.8)
Deaths averted per 100,000	1409.8	2056.3	1467.9	1965.1	1596.8	2227.8	1439.3	2021.5	1404.5	2025.4
people with type II diabetes	(1346.0,	(2040.4,	(1409.6,	(1935.5,	(1545.0,	(2148,	(1394.2,	(1982.2,	(1351.1,	(1989.4,
from 10 years of treatment:	1454.3)	2126.7)	1522.3)	2029)	1657.7)	2293.6)	1493.5)	2081.2)	1457.3)	2059.7)
Number needed to treat to	25 (24.4,	16.3	24.3	17.6 (16.8,	22.9 (22.1,	15.6 (15.2,	24 (23.1,	16.4	24 (23.1,	16.2 (16,
prevent one CVD event	26.2)	(15.9,	(23.5,	17.7)	23.5)	16.1)	24.7)	(16.1,	24.8)	16.4)
		16.4)	25.3)		-			16.8)		
Number needed to treat to	64 (60.8,	56.4	74.2	53 (50.6,	69.3 (64.3,	51.5 (49.2,	80.2 (74.9,	57.8	81.1 (76.3,	58.2 (53.8,
prevent one microvascular	67.8)	(52.8,	(69.8,	56.1)	73.3)	53.8)	87.1)	(51.5,	87.5)	62)
event		59.2)	77.6)					59.5)		
Cost and cost-effectiveness:										
Total costs, per capita per year,	\$891.1	\$888	\$725.4	\$725.8	\$952.6	\$953.1	\$1020.1	\$1014.9	\$517.6	\$513.5
\$US 2016	(\$876.6,	(\$879.5,	(\$717.4,	(\$718.7,	(\$946.8,	(\$952.8,	(\$1005.3,	(\$998.2,	(\$513.3,	(\$511,
	\$906.7)	\$906.8)	\$735.8)	\$743.7)	\$959)	\$963.4)	\$1035.6)	\$1040.8)	\$522.7)	\$518.9)
Total DALYs averted, per capita	0.085	0.123	0.043	0.06 (0.06,	0.063	0.089	0.093	0.128	0.031	0.048
per year	(0.083,	(0.121,	(0.042,	0.062)	(0.062,	(0.088,	(0.091,	(0.126,	(0.031,	(0.047,
	0.087)	0.126)	0.045)		0.065)	0.091)	0.095)	0.13)	0.032)	0.049)
\$/DALYs averted (average	\$10448.7	\$7248.6	\$16710.4	\$12034.2	\$15124.1	\$10652.0	\$11019.0	\$7961.4	\$16448.0	\$11073.9
cost-effectiveness, compared to	(\$10353.1,	(\$7123.4,	(\$16327,	(\$11791.4,	(\$14800.2,	(\$10555.0,	(\$10897.4,	(\$7814.0,	(\$16168.6,	(\$10892.2,
no treatment)	\$10514.3)	\$7303.1)	\$17094)	\$12222.8)	\$15385)	\$10796.6)	\$11062.4)	\$8045.9)	\$16728.4)	\$11096.1)
Incremental cost-effectiveness of shifting from TTT to BTT	\$-81.6 (-91.2,	-72.1)	\$23.5 (20, 2	6.7)	\$19.2 (17.2,	21.7)	\$-148.6 (-167	7.7, -133.3)	\$-241.2 (-273	.3, -227.8)

Increasing the threshold for treating microvascular risk under the BTT strategy from the base case of 5% lifetime risk to 7% lifetime risk. See **Appendix Figure 2** for an illustration of how microvascular complications prevented vary with BTT treatment threshold choices.

	Chi (type II c prevalenc	liabetes e ~9.3%)	(type II prevalen	Ghana (type II diabetes prevalence ~2.2%)		idia diabetes ice ~8.8%)	Mex (type II o prevalenc	liabetes e ~15.0%)	South Africa (type II diabetes prevalence ~7.2%)	
	TTT	BTT	TTT	BTT	TTT	BTT	TTT	BTT	TTT	BTT
Adults with type II diabetes recommended any treatment, %:	99.1 (99, 99.1)	93.3 (93.2, 93.4)	99.4 (99.3, 99.4)	93.2 (93.1, 93.4)	99.3 (99.2, 99.4)	95.2 (95.1, 95.3)	99.2 (99.2, 99.3)	92.6 (92.4, 92.8)	99.3 (99.2, 99.3)	92.2 (92, 92.4)
Blood pressure treatment	80.5 (80.3, 80.6)	82.5 (82.2, 82.7)	86.4 (86.3, 86.6)	81 (80.8, 81.1)	85.4 (85.2, 85.5)	84.4 (84.2, 84.5)	84.1 (83.9, 84.2)	82.3 (82.1, 82.5)	84.1 (83.8, 84.3)	82.7 (82.5, 82.8)
Lipid treatment	75.2 (75.1, 75.5)	82.8 (82.6, 83)	75.4 (75.2, 75.6)	81.2 (81, 81.4)	75.3 (75.1, 75.6)	84.5 (84.4, 84.7)	75.3 (75.2, 75.5)	82.5 (82.4, 82.7)	75.3 (75, 75.5)	82.9 (82.8, 83.2)
Glycaemic treatment	80.7 (80.5, 80.9)	79.4 (92.7, 92.9)	80.7 (80.6, 80.9)	81.4 (93.7, 94)	80.7 (80.6, 80.9)	84.5 (95, 95.2)	80.7 (80.5, 80.9)	77.6 (91.8, 92.1)	80.8 (80.6, 81)	76.5 (91.7, 92)
Insulin treatment	13.8 (13.7, 13.9)	14.4 (16.7, 17.1)	13.8 (13.7, 14)	15.3 (17.5, 17.9)	13.8 (13.7, 14)	17.1 (19.1, 19.4)	13.8 (13.5, 13.9)	13.6 (15.9, 16.3)	13.8 (13.7, 14)	12.8 (15.2, 15.5)
number of medications, per person recommended treatment	3.0 (3, 3.1)	3.7 (3.8, 3.8)	3.3 (3.3, 3.3)	3.6 (3.7, 3.7)	3.2 (3.2, 3.3)	3.8 (3.8, 3.8)	3.2 (3.2, 3.2)	3.6 (3.7, 3.8)	3.2 (3.2, 3.2)	3.7 (3.8, 3.8)
CVD events prevented per 100,0	000 people wit	h type II diab	etes from 10 y	ears of treatm	ent:	• •	• •			• •
МІ	2098.4 (2005.4, 2146.1)	3190.5 (3111.2, 3256.9)	2206.5 (2133.2, 2268.7)	3063.7 (2978.8, 3123.6)	2290.4 (2229.6, 2356)	3361.1 (3329.1, 3448.7)	2201.1 (2125.5, 2311.4)	3207.2 (3137.8, 3273)	2200.8 (2111.3, 2309.9)	3263.5 (3183.5, 3322.4)
Stroke	1857.3 (1771.5, 1914.8)	2819.3 (2715.3, 2814)	1885.3 (1790.5, 1966)	2586.7 (2502.9, 2645.3)	2054.4 (1986.8, 2134.1)	2943.9 (2853.7, 3042.8)	1932 (1886, 1982.2)	2746.4 (2685.9, 2801.5)	1941.5 (1881.5, 1995.6)	2801.3 (2714.7, 2858.4)
Microvascular events prevented	d per 100,000 j	people with t	ype II diabetes	from 10 years	of treatment:					
Blindness	229.4 (214.2, 240)	263 (236.7, 282.1)	244.1 (228, 264.8)	273.7 (254.4, 294.7)	238.2 (219.6, 270)	290.2 (267.5, 311.8)	225.2 (205.6, 242.9)	263 (244.5, 289)	222.3 (204.9, 243.7)	268.6 (235.8, 293)

End-stage renal disease	764 (731.1, 799.2)	875 (835.9, 904.0)	833.5 (813.3, 862.9)	936.3 (884, 961.7)	973.7 (936.2, 1020.1)	1105.4 (1050.6, 1147.0)	705.4 (675.4, 736.4)	791.5 (733.8, 823.8)	590 (559, 614.6)	664 (627.6, 697.3)
Ulcer	265.3 (238.7, 286)	252.1 (230.9, 268.3)	261.8 (239.1, 295.5)	233 (208, 247.6)	220.6 (198.7, 256)	197.7 (167.4, 218.1)	306.1 (258, 345.1)	275.1 (249.2, 295.6)	411.9 (369.9, 442.6)	366.6 (333.2, 398.5)
Deaths averted per 100,000 people with type II diabetes from 10 years of treatment:	1409.8 (1346.0, 1454.3)	2047 (1980, 2070.6)	1467.9 (1409.6, 1522.3)	1946.4 (1885.0, 1987.6)	1596.8 (1545.0, 1657.7)	2201.5 (2142.9, 2276.5)	1439.3 (1394.2, 1493.5)	1995.4 (1942.4, 2050.7)	1404.5 (1351.1, 1457.3)	1974.8 (1912.1, 2042.9)
Number needed to treat to prevent one CVD event	25 (24.4, 26.2)	15.5 (15.4, 16)	24.3 (23.5, 25.3)	16.5 (16.2, 17)	22.9 (22.1, 23.5)	15.1 (14.7, 15.4)	24 (23.1, 24.7)	15.6 (15.3, 15.9)	24 (23.1, 24.8)	15.2 (14.9, 15.6)
Number needed to treat to prevent one microvascular event	64.0 (60.8, 67.8)	59.4 (56.9, 63.1)	74.2 (69.8, 77.6)	56.2 (54.0, 60.0)	69.3 (64.3, 73.3)	53.0 (50.4, 56.7)	80.2 (74.9, 87.1)	61.9 (58.6, 66.9)	81.1 (76.3, 87.5)	63.7 (59.8, 69.1)
Cost and cost-effectiveness:										
Total costs, per capita per year, \$US 2016	\$891.1 (\$876.6, \$906.7)	\$885.6 (\$862.8, \$895.2)	\$725.4 (\$717.4, \$735.8)	\$723.4 (\$715.1, \$728.2)	\$952.6 (\$946.8, \$959)	\$950.3 (\$939.7, \$953.3)	\$1020.1 (\$1005.3, \$1035.6)	\$1009.8 (\$997.4, \$1015.5)	\$517.6 (\$513.3, \$522.7)	\$512.1 (\$504.2, \$515.6)
Total DALYs averted, per capita per year	0.085 (0.083, 0.087)	0.123 (0.120, 0.123)	0.043 (0.042, 0.045)	0.06 (0.059, 0.061)	0.063 (0.062, 0.065)	0.088 (0.087, 0.087)	0.093 (0.091, 0.095)	0.126 (0.124, 0.128)	0.031 (0.031, 0.032)	0.046 (0.045, 0.047)
\$/DALYs averted (average cost- effectiveness, compared to no treatment)	\$10448.7 (\$10314.3, \$10453.1)	\$7210.0 (\$7171.3, \$7281.8)	\$16710.4 (\$16327.0, \$17094.0)	\$12118.9 (\$12106.4, \$12206.8)	\$15124.1 (\$14800.2, \$15385)	\$10656.5 (\$10642.1, \$10766.2)	\$11019.0 (\$10897.4, \$11062.4)	\$8036.5 (\$7975.0, \$8085.6)	\$16448 (\$16168.6, \$16728.4)	\$11108.3 (\$11052.3, \$11116.2)
Incremental cost-effectiveness of shifting from TTT to BTT	\$-144.7 (-166		\$-117.6 (-142	.9, -105.3)	\$-92 (-104.5,	, -92)	\$-312.1 (-355	.2, -278.4)	\$-366.7 (-423	3.1, -343.8)

Using fasting plasma glucose (target <7mmol/L, per WHO guidance)<sup>14</sup> rather than haemoglobin A1c to guide TTT treatment.

	(type II o	ina diabetes ce ~9.3%)	(type II	Ghana (type II diabetes prevalence ~2.2%)		idia diabetes ice ~8.8%)	Mex (type II d prevalence	iabetes	South Africa (type II diabetes prevalence ~7.2%)	
	ТТТ	BTT	TTT	BTT	TTT	BTT	ттт	BTT	TTT	BTT
Adults with type II diabetes recommended any treatment, %:	99.1 (99, 99.1)	97 (97, 97.1)	99.4 (99.3, 99.4)	97.2 (97.1, 97.2)	99.3 (99.2, 99.4)	98.1 (98, 98.1)	99.2 (99.2, 99.3)	96.6 (96.4, 96.7)	99.3 (99.1, 99.2)	96.4 (96.4, 96.5)
Blood pressure treatment	80.5 (80.3, 80.6)	82.5 (82.2, 82.7)	86.4 (86.3, 86.6)	81 (80.9, 81.1)	85.4 (85.2, 85.5)	84.4 (84.2, 84.5)	84.1 (83.9, 84.2)	82.3 (82.2, 82.5)	84.1 (84, 84.4)	82.7 (82.5, 82.8)
Lipid treatment	75.2 (75.1, 75.5)	82.8 (82.5, 83)	75.4 (75.2, 75.6)	81.2 (81, 81.3)	75.3 (75.1, 75.6)	84.5 (84.3, 84.7)	75.3 (75.2, 75.5)	82.5 (82.4, 82.7)	75.3 (75.1, 75.5)	82.9 (82.7, 83)
Glycaemic treatment	85.6 (75.6, 85.8)	92.8 (92.7, 92.9)	85.7 (75.7, 85.8)	93.8 (93.7, 94)	85.6 (75.7, 85.8)	95.1 (95, 95.2)	85.6 (75.6, 85.8)	92 (91.8, 92.1)	85.7 (78.1, 78.4)	91.9 (91.7, 92)
Insulin treatment	14.6 (12.8, 14.7)	16.9 (16.7, 17.1)	14.7 (12.9, 14.8)	17.7 (17.5, 17.9)	14.7 (12.9, 14.8)	19.3 (19.1, 19.4)	14.6 (12.7, 14.8)	16.1 (15.9, 16.3)	14.7 (15.5, 15.9)	15.3 (15.2, 15.5)
number of medications, per person recommended treatment	3.2 (2.9, 3.2)	3.8 (3.8, 3.8)	3.4 (3.2, 3.4)	3.7 (3.7, 3.7)	3.4 (3.1, 3.4)	3.8 (3.8, 3.8)	3.3 (3.1, 3.3)	3.7 (3.7, 3.8)	3.3 (3.2, 3.2)	3.8 (3.8, 3.8)
CVD events prevented per 10	),000 people wi	th type II diab	petes from 10	years of treatm	ent:			•		•
MI	2098.4 (2005.4, 2146.1)	3218.9 (3145.3, 3299.4)	2206.5 (2133.2, 2268.7)	3080.9 (3021.6, 3197.7)	2290.4 (2229.6, 2356)	3390.2 (3334.5, 3471.1)	2201.1 (2125.5, 2311.4)	3232.2 (3153.8, 3343.7)	2200.8 (2149.3, 2303.1)	3270.7 (3208.1, 3335.6)
Stroke	1857.3 (1771.5, 1914.8)	2841.4 (2813.1, 2882.8)	1885.3 (1790.5, 1966)	2595.1 (2539, 2677.6)	2054.4 (1986.8, 2134.1)	2967.7 (2857.3, 3085)	1932 (1886, 1982.2)	2784 (2731.7, 2822.7)	1941.5 (1900.8, 2005.4)	2850 (2791.2, 2906)
Microvascular events prevent	ed per 100,000	people with t	ype II diabetes	s from 10 years	of treatment:	:				
Blindness	231.1 (212.6, 241.8)	303.5 (286.5, 327.1)	245.9 (226.3, 266.7)	305.7 (285.4, 328.8)	240 (218, 272)	310.1 (284.6, 329)	226.9 (204.1, 244.7)	295.9 (274.5, 336.8)	223.9 (216.1, 242.6)	295.1 (266.8, 319.9)
End-stage renal disease	769.6 (725.7, 805.1)	881.7 (840, 920.7)	839.7 (807.3, 869.3)	955 (917.6, 989.4)	980.9 (929.3, 1027.6)	1110.5 (1065.5, 1155.8)	710.6 (670.4, 741.9)	810.3 (785.6, 871.6)	594.4 (565.2, 636)	687.5 (649.9, 731.5)

Ulcer	267.3	260.4	263.7	245.1	222.2	200.1	308.4	291.3	414.9	389.7
	(236.9,	(243,	(237.4,	(217.5,	(197.2,	(177.4,	(256.1,	(278.9,	(353.1,	(357.2,
	288.1)	284.4)	297.7)	262.8)	257.8)	218.7)	347.6)	307.9)	457.5)	425.7)
Deaths averted per 100,000	1399.2	2051.7	1447.8	1957.7	1602.9	2214.7	1426.9	2008.8	1415	2000.1
people with type II diabetes	(1358.2,	(2010.2,	(1399.6,	(1910.3,	(1550.1,	(2145.5,	(1381.3,	(1963.7,	(1368.0,	(1950.8,
from 10 years of treatment:	1441.1)	2098.6)	1510.7)	2025.7)	1651.8)	2291.7)	1478.0)	2069.1)	1467.6)	2051.3)
Number needed to treat to	25 (24.4,	16 (15.7,	24.3 (23.5,	17.1 (16.5,	22.9 (22.1,	15.4 (15,	24.7 (15.9,	16.1	24 (23,	15.8 (15.5,
prevent one macrovascular event	26.2)	16.3)	25.3)	17.5)	23.5)	15.8)	16.6)	(15.7, 16.4)	24.5)	16.1)
Number needed to treat to	63.5 (60.4,	57.1 (54,	73.6 (69.3,	64.5 (61.5,	68.8 (63.8,	60.5 (57.6,	87.7 (67.3,	69.1	80.5 (74.2,	70.3 (65.4,
prevent one microvascular event	68.3)	60.1)	78.2)	68.4)	73.8)	64.2)	75.2)	(63.8, 72)	87.4)	75.7)
Cost and cost-effectiveness:	1	1	1	1	L		1	L	1	
Total costs, per capita per year,	\$890.8	\$886.8	\$725.1	\$724.6	\$952.4	\$952.5	\$1019.8	\$1012.4	\$517.3	\$512.8
\$US 2016	(\$876.9,	(\$871.2,	(\$717.6,	(\$717.7,	(\$947.1,	(\$946.3,	(\$1005.5,	(\$997.8,	(\$508.5,	(\$507.6,
	\$906.5)	\$901)	\$735.5)	\$736)	\$958.8)	\$958.3)	\$1035.4)	\$1028.1)	\$531)	\$517.3)
Total DALYs averted, per capita	0.085	0.123	0.043	0.06 (0.059,	0.063	0.088	0.093	0.127	0.031	0.047
per year	(0.083,	(0.121,	(0.042,	0.061)	(0.062,	(0.087,	(0.091,	(0.125,	(0.031,	(0.046,
	0.087)	0.124)	0.045)		0.065)	0.089)	0.095)	0.129)	0.032)	0.048)
\$/DALYs averted (average	\$10581.2	\$7215.9	\$16995.3	\$12038.8	\$15142.6	\$10769.1	\$11149.3	\$7941.9	\$16298.9	\$10928.4
cost-effectiveness, compared to	(\$10531.9,	(\$7209.5,	(\$16798.3,	(\$11978.3,	(\$15009,	(\$10728.3,	(\$11013.8,	(\$7933.1,	(\$16266.4,	(\$10754.1,
no treatment)	\$10593.7)	\$7254.9)	\$17073.9)	\$12106.3)	\$15289.5)	\$10840.7)	\$11150.0)	\$7966)	\$16409.8)	\$11017.3)
Incremental cost-effectiveness of shifting from TTT to BTT	\$-102.6 (-117	.6, -97.6)	\$-29.4 (-35.7,	-26.3)	\$4 (3.7, 4.5)		\$-217.6 (-246	.7, -194.7)	\$-281.3 (-321	1.4, -264.7)

Modifying the BTT treatment thresholds to match the same total population size treated as the TTT strategy. The minimal proportionate change in each BTT threshold (CVD/microvascular) from the base case (10% 10-year risk/5.0% lifetime risk) was found to match the total population size. CVD/microvascular treatment thresholds to match the TTT population size treated, rounded to the nearest 0.5%, were 8.0% for 10-year CVD risk and 4.0% for lifetime microvascular risk.

	(type II d	China (type II diabetes prevalence ~9.3%)		Ghana (type II diabetes prevalence ~2.2%)		dia diabetes ce ~8.8%)	Mex (type II o prevalenc	liabetes	(type II	Africa diabetes ce ~7.2%)
	TTT	BTT	TTT	BTT	TTT	BTT	TTT	BTT	TTT	BTT
Adults with type II diabetes recommended any treatment, %:	99.1 (99.0, 99.1)	99.1 (99.0, 99.1)	99.4 (99.3, 99.4)	99.4 (99.3, 99.4)	99.3 (99.2, 99.4)	99.3 (99.2, 99.4)	99.2 (99.2, 99.3)	99.2 (99.2, 99.3)	99.3 (99.2, 99.3)	99.3 (99.2, 99.3)
Blood pressure treatment	80.5 (80.3,	87.7 (87.6,	86.4 (86.3,	86.7 (86.5,	85.4 (85.2,	87.2 (87,	84.1 (83.9,	91.3 (91.1,	84.1 (83.8,	86.7 (86.6,
	80.6)	87.8)	86.6)	86.8)	85.5)	87.3)	84.2)	91.4)	84.3)	86.9)
Lipid treatment	75.2 (75.1,	88 (87.9,	75.4 (75.2,	86.8 (86.7,	75.3 (75.1,	87.4 (87.2,	75.3 (75.2,	91.5 (91.4,	75.3 (75,	86.9 (86.8,
	75.5)	88.1)	75.6)	87)	75.6)	87.5)	75.5)	91.6)	75.5)	87.1)
Glycaemic treatment	80.7 (80.5,	96.1 (96,	80.7 (80.6,	97.1 (97,	80.7 (80.6,	96.8 (96.8,	80.7 (80.5,	97.4 (97.3,	80.8 (80.6,	95.3 (95.2,
	80.9)	96.2)	80.9)	97.1)	80.9)	96.9)	80.9)	97.5)	81)	95.4)
Insulin treatment	13.8 (13.7,	18.8 (18.6,	13.8 (13.7,	19.6 (19.5,	13.8 (13.7,	20.2 (19.9,	13.8 (13.5,	20 (19.9,	13.8 (13.7,	16.6 (16.4,
	13.9)	19.1)	14)	19.8)	14)	20.4)	13.9)	20.2)	14)	16.8)
number of medications, per	3 (3, 3.1)	3.8 (3.8,	3.3 (3.3,	3.7 (3.7,	3.2 (3.2,	3.9 (3.9,	3.2 (3.2,	3.9 (3.8,	3.2 (3.2,	3.8 (3.8,
person recommended treatment		3.8)	3.3)	3.7)	3.3)	3.9)	3.2)	3.9)	3.2)	3.8)
CVD events prevented per 100,0	000 people with	n type II diabe	etes from 10 y	ears of treatm	ient:					
MI	2098.4	3276.7	2206.5	3122.4	2290.4	3417.2	2201.1	3293.9	2200.8	3397
	(2005.4,	(3167.9,	(2133.2,	(3067.8,	(2229.6,	(3362.6,	(2125.5,	(3242.4,	(2111.3,	(3336.2,
	2146.1)	3296)	2268.7)	3150.4)	2356)	3532.7)	2311.4)	3365.9)	2309.9)	3390.6)
Stroke	1857.3	2850.7	1885.3	2656.9	2054.4	2999.7	1932	2815.2	1941.5	2873.2
	(1771.5,	(2729.1,	(1790.5,	(2586.3,	(1986.8,	(2893.8,	(1886,	(2772.8,	(1881.5,	(2825.7,
	1914.8)	2899.7)	1966)	2754.1)	2134.1)	3099.5)	1982.2)	2855.8)	1995.6)	2945.1)
Microvascular events prevented	l per 100,000 p	eople with ty	pe II diabetes	from 10 years	s of treatment:					
Blindness	229.4 (214.2, 240)	309.4 (275.3, 328.3)	244.1 (228, 264.8)	308.4 (287.9, 331.6)	238.2 (219.6, 270)	315.3 (282.2, 338.3)	225.2 (205.6, 242.9)	303.7 (272, 326.2)	222.3 (204.9, 243.7)	311.4 (287.9, 331.7)

End-stage renal disease	764 (731.1,	885.7	833.5	957.1	973.7	1124.3	705.4	810.8	590 (559,	702.9
C C	799.2)	(852.6,	(813.3,	(896.4,	(936.2,	(1081.9,	(675.4,	(786.1,	614.6)	(678.6,
	,	902.9)	862.9)	995.6)	1020.1)	1166.4)	736.4)	872.2)	,	772.5)
Ulcer	265.3	262.2	261.8	249.5	220.6	209.7	306.1 (258,	291.5	411.9	394.8
	(238.7, 286)	(241.3,	(239.1,	(212.4,	(198.7,	(193.3,	345.1)	(279.1,	(369.9,	(360.7,
		282.5)	295.5)	277.3)	256)	236)		308.1)	442.6)	429.2)
Deaths averted per 100,000	1409.8	2068.7	1467.9	1990.1	1596.8	2237.4	1439.3	2032.1	1404.5	2034.9
people with type II diabetes from	(1346.0,	(1988.5,	(1409.6,	(1829.7,	(1545.0,	(2171.2,	(1394.2,	(1994.4,	(1351.1,	(1958.0,
10 years of treatment:	1454.3)	2097.5)	1522.3)	2046.3)	1657.7)	2314.4)	1493.5)	2078.9)	1457.3)	2099.0)
Number needed to treat to	25 (24.4,	16.3 (15.7,	24.3 (23.5,	17.3 (17,	22.9 (22.1,	15.6 (15.1,	24 (23.1,	16.3 (16,	24 (23.1,	16.1 (16,
prevent one CVD event	26.2)	16.3)	25.3)	17.7)	23.5)	16)	24.7)	16.5)	24.8)	16.4)
Number needed to treat to	64.0 (60.8,	69.4 (67.2,	74.2 (69.8,	66.2 (62.5,	69.3 (64.3,	60.6 (57.5,	80.2 (74.9,	70.6 (65.9,	81.1 (76.3,	71.8 (65.9,
prevent one microvascular	67.8)	70.5)	77.6)	71.8)	73.3)	64.2)	87.1)	74.2)	87.5)	76.2)
event										
Cost and cost-effectiveness:										
Total costs, per capita per year,	\$891.1	\$899.4	\$725.4	\$735.1	\$952.6	\$962.9	\$1020.1	\$1015	\$517.6	\$526
\$US 2016	(\$876.6,	(\$881.9,	(\$717.4,	(\$727.2,	(\$946.8,	(\$953.1,	(\$1005.3,	(\$1003.8,	(\$513.3,	(\$517.3,
	\$906.7)	\$905.2)	\$735.8)	\$741.9)	\$959)	\$972.5)	\$1035.6)	\$1022.9)	\$522.7)	\$533.2)
Total DALYs averted, per capita	0.085	0.124	0.043	0.061 (0.06,	0.063	0.09	0.093	0.129	0.031	0.047
per year	(0.083,	(0.121,	(0.042,	0.063)	(0.062,	(0.087,	(0.091,	(0.127,	(0.031,	(0.046,
	0.087)	0.126)	0.045)	-	0.065)	0.092)	0.095)	0.13)	0.032)	0.048)
\$/DALYs averted (average cost-	\$10448.7	\$7269.4	\$16710.4	\$12009.8	\$15124.1	\$10755	\$11019	\$7891.1	\$16448.0	\$11075.4
effectiveness, compared to no	(\$10314.3,	(\$7158.5,	(\$16327,	(\$11812.2,	(\$14800.2,	(\$10586.9,	(\$10897.4,	(\$7861.4,	(\$16168.6,	(\$11010.0,
treatment)	\$10453.1)	\$7318.0)	\$17094)	\$12100.7)	\$15385)	\$10964.5)	\$11062.4)	\$7901.5)	\$16728.4)	\$11320.0)
Incremental cost-effectiveness of shifting from TTT to BTT	\$212.8 (193, 2	244.1)	\$538.9 (461	.9, 646.7)	\$381.5 (343.	3, 468.2)	\$-141.7 (-159	9.4, -130.8)	\$525 (494.1,	600)

Treatment outcomes if insulin were unavailable.

	Chi (type II o prevalenc	liabetes	(type II	iana diabetes ice ~2.2%)	(type II	dia diabetes ce ~8.8%)	Mex (type II c prevalenc	liabetes	(type II	n Africa diabetes nce ~7.2%)
	TTT	BTT	TTT	BTT	ТТТ	BTT	ттт	BTT	ТТТ	BTT
Adults with type II diabetes recommended any treatment, %:	99.1 (99.0, 99.1)	97.0 (97.0, 97.1)	99.4 (99.3, 99.4)	97.2 (97.1, 97.2)	99.3 (99.2, 99.4)	98.1 (98, 98.1)	99.2 (99.2, 99.3)	96.6 (96.4, 96.7)	99.3 (99.2, 99.3)	96.4 (96.4, 96.5)
Blood pressure treatment	80.5 (80.3, 80.6)	82.5 (82.2, 82.7)	86.4 (86.3, 86.6)	81 (80.9, 81.1)	85.4 (85.2, 85.5)	84.4 (84.2, 84.5)	84.1 (83.9, 84.2)	82.3 (82.2, 82.5)	84.1 (83.8, 84.3)	82.7 (82.5, 82.8)
Lipid treatment	75.2 (75.1, 75.5)	82.8 (82.5, 83)	75.4 (75.2, 75.6)	81.2 (81, 81.3)	75.3 (75.1, 75.6)	84.5 (84.3, 84.7)	75.3 (75.2, 75.5)	82.5 (82.4, 82.7)	75.3 (75, 75.5)	82.9 (82.7, 83)
Glycaemic treatment	80.8 (80.5, 81)	92.8 (92.7, 92.9)	80.7 (80.5, 80.9)	93.8 (93.8, 93.9)	80.8 (80.5, 81)	95.1 (95, 95.2)	80.7 (80.7, 80.8)	92.1 (92, 92.3)	80.8 (80.5, 80.9)	91.9 (91.7, 92)
Insulin treatment	-	-	-	-	-	-	-	-	-	-
number of medications, per person recommended treatment	3.0 (3.0, 3.0)	3.5 (3.5, 3.5)	3.2 (3.2, 3.2)	3.4 (3.4, 3.4)	3.2 (3.2, 3.2)	3.6 (3.6, 3.6)	3.1 (3.1, 3.1)	3.5 (3.5, 3.5)	3.1 (3.1, 3.1)	3.5 (3.5, 3.5)
CVD events prevented per 100	),000 people wi	th type II dial	petes from 10	years of treatr	nent:					
MI	2076.6 (2016.7, 2148)	3217.1 (3133.1, 3340.3)	2195.6 (2145.1, 2246.8)	3079.0 (2996.6, 3132.0)	2350 (2304.8, 2398.9)	3419.7 (3302.2, 3537.1)	2190.8 (2111.1, 2269.5)	3204.7 (3095.4, 3273.8)	2220 (2136.8, 2317.4)	3268.5 (3220.4, 3337.2)
Stroke	1830.3 (1761.8, 1917.4)	2834.0 (2735.5, 2872.5)	1893.6 (1856.9, 1937.8)	2803.5 (2706.5, 2806.2)	2029.7 (1965.9, 2131.5)	2964.6 (2951.8, 3050.2)	1900.5 (1861.9, 1977.5)	2775.9 (2738.5, 2829.8)	1931.3 (1856.7, 1990.6)	2805.3 (2767.7, 2852.3)
Microvascular events prevent	ed per 100,000	people with t	ype II diabetes	s from 10 year	s of treatment:	:				
Blindness	200.2 (180.9, 218.1)	170.9 (156.2, 187.8)	207 (189.8, 220.6)	178.2 (154.9, 190.8)	207.7 (192, 223.8)	171.9 (154.9, 189)	205.4 (180.7, 222.8)	167.8 (155.5, 187)	205.6 (186.6, 224.1)	174.5 (159.9, 188)
End-stage renal disease	732.7 (678.9, 783.5)	516.5 (484, 549.1)	768.8 (723, 804.9)	542.3 (498.2, 602.5)	914.1 (866, 950.7)	641.2 (588.5, 680.1)	654.8 (632.5, 670.3)	456.2 (407.8, 495.9)	569.9 (538.2, 598.4)	395.0 (373.6, 451.9)
Ulcer	262.4 (243.2, 288.9)	189.4 (170.9, 209.3)	245.9 (230.7, 258.8)	188.4 (177.2, 208.6)	217.1 (195.9, 233.5)	158.3 (144.6, 179.2)	290.6 (263.8, 314.5)	223.3 (206.7, 238.2)	388.9 (365.4, 405.9)	296.3 (264.5, 316.7)

Deaths averted per 100,000 people with type II diabetes from 10 years of treatment: Number needed to treat to prevent one CVD event	1384.0 (1326.3, 1450.1) 25.4 (24.4, 26.2)	1915.8 (1849.5, 1968.4) 16.0 (15.6, 16.5)	1445.0 (1404.0, 1485.4) 24.3 (23.8, 24.8)	1884.4 (1815.1, 1918.8) 17.0 (16.7, 17.5)	1579.0 (1528.2, 1640.4) 22.4 (21.9, 22.9)	2050.6 (2001.5, 2121.5) 15.3 (14.8, 15.8)	1407.0 (1367.1, 1458.3) 24.3 (23.4, 25)	1871.2 (1816.4, 1920.3) 16.2 (15.8, 16.6)	1397.0 (1339.9, 1450.2) 23.9 (23, 24.8)	1875.8 (1843.2, 1928.6) 15.9 (15.6, 16.1)
Number needed to treat to prevent one microvascular event Cost and cost-effectiveness:	67.3 (62.5, 72.8)	94.1 (87.4, 101.4)	81.3 (77.4, 86.9)	106.9 (97, 116.9)	74.2 (70.5, 79.1)	101.0 (93.6, 110.4)	86.2 (82.2, 92.1)	114.0 (105, 125.5)	85.2 (80.8, 91)	111.5 (101.0, 120.8)
Total costs, per capita per year, \$US 2016	\$899 (\$891.3, \$915.4)	\$924.3 (\$914.2, \$938.5)	\$729.7 (\$724.1, \$735.8)	\$752.5 (\$745, \$760.6)	\$960.7 (\$950.3, \$968.9)	\$991.2 (\$980.5, \$1000.1)	\$1026.6 (\$1017.5, \$1036)	\$1052 (\$1042, \$1058.1)	\$521.7 (\$514.4, \$533.1)	\$536 (\$528, \$548.5)
Total DALYs averted, per capita per year	0.084 (0.081, 0.086)	0.114 (0.111, 0.116)	0.043 (0.042, 0.044)	0.057 (0.055, 0.059)	0.063 (0.062, 0.065)	0.083 (0.081, 0.086)	0.091 (0.088, 0.093)	0.118 (0.117, 0.12)	0.031 (0.03, 0.032)	0.045 (0.044, 0.045)
\$/DALYs averted (average cost-effectiveness, compared to no treatment)	\$10747.2 (\$10663.7, \$10942.3)	\$8131.5 (\$8101.1, \$8216.0)	\$17056.2 (\$16834.9, \$17235.8)	\$13185.3 (\$12975.3, \$13569.1)	\$15203.0 (\$14910.9, \$15409.1)	\$11892.1 (\$11649.1, \$12064.9)	\$11342.4 (\$11111.7, \$11516.0)	\$8907.0 (\$8843.3, \$8938.6)	\$16869.4 (\$16721.6, \$16998.6)	\$12019.5 (\$11946.8, \$12108.6)
Incremental cost-effectiveness of shifting from TTT to BTT	\$843.3 (722.9, 1012)		\$1628.6 (1341.2, 1753.8)		\$1525 (1270.8, 1906.3)		\$940.7 (793.8, 1058.3)		\$1021.4 (953.3, 1100)	

Treatment outcomes if BTT microvascular treatment guidelines had 10% lower adherence from practitioners than the TTT approach.

	China (type prevalenc			e II diabetes ice ~2.2%)		e II diabetes ce ~8.8%)		e II diabetes e ~15.0%)	diabetes p	ica (type II prevalence 2%)
	TTT	BTT	ттт	BTT	TTT	BTT	ттт	BTT	ттт	BTT
Adults with type II diabetes recommended any treatment, %:	99.1 (99, 99.1)	97.0 (97.0, 97.1) 82.5	99.4 (99.3, 99.4)	97.2 (97.1, 97.2)	99.3 (99.2, 99.4)	98.1 (98, 98.1)	99.2 (99.2, 99.3)	96.6 (96.4, 96.7)	99.3 (99.2, 99.3)	96.4 (96.4, 96.5)
Blood pressure treatment	80.5 (80.3, 80.6)	(82.2, 82.7) 82.8	86.4 (86.3, 86.6)	81.0 (80.9, 81.1)	85.4 (85.2, 85.5)	84.4 (84.2, 84.5)	84.1 (83.9, 84.2)	82.3 (82.2, 82.5)	84.1 (83.8, 84.3)	82.7 (82.5, 82.8)
Lipid treatment	75.2 (75.1, 75.5)	(82.5, 83.0) 92.8	75.4 (75.2, 75.6)	81.2 (81, 81.3)	75.3 (75.1, 75.6)	84.5 (84.3, 84.7)	75.3 (75.2, 75.5)	82.5 (82.4, 82.7)	75.3 (75, 75.5)	82.9 (82.7, 83.0)
Glycaemic treatment	80.7 (80.5, 80.9)	(92.7, 92.9) 16.9	80.7 (80.6, 80.9)	93.8 (93.7, 94.0)	80.7 (80.6, 80.9)	95.1 (95, 95.2)	80.7 (80.5, 80.9)	92 (91.8, 92.1)	80.8 (80.6, 81.0)	91.9 (91.7, 92.0)
Insulin treatment	13.8 (13.7, 13.9)	(16.7, 17.1)	13.8 (13.7, 14.0)	17.7 (17.5, 17.9)	13.8 (13.7, 14.0)	19.3 (19.1, 19.4)	13.8 (13.5, 13.9)	16.1 (15.9, 16.3)	13.8 (13.7, 14.0)	15.3 (15.2, 15.5)
number of medications, per	3.0 (3.0,	3.8 (3.8,	3.3 (3.3,	3.7 (3.7,	3.2 (3.2,	3.8 (3.8,	3.2 (3.2,	3.7 (3.7,	3.2 (3.2,	3.8 (3.8,
person recommended treatment	3.1)	3.8)	3.3)	3.7)	3.3)	3.8)	3.2)	3.8)	3.2)	3.8)
CVD events prevented per 100,0	000 people wit	h type II diab	etes from 10	years of treatn	nent:					
MI	2098.4 (2005.4, 2146.1)	3025.8 (2956.6, 3101.5)	2206.5 (2133.2, 2268.7)	2896 (2840.3, 3005.9)	2290.4 (2229.6, 2356.0)	3186.8 (3134.4, 3262.8)	2201.1 (2125.5, 2311.4)	3038.3 (2964.6, 3143.1)	2200.8 (2111.3, 2309.9)	3074.5 (3015.6, 3135.4)
Stroke	1857.3 (1771.5, 1914.8)	2670.9 (2644.3, 2709.8)	1885.3 (1790.5, 1966.0)	2439.4 (2386.7, 2516.9)	2054.4 (1986.8, 2134.1)	2789.6 (2685.8, 2899.9)	1932.0 (1886.0, 1982.2)	2617.0 (2567.8, 2653.3)	1941.5 (1881.5, 1995.6)	2679.0 (2623.7, 2731.6)
Microvascular events prevented	l per 100,000 p	eople with ty	/pe II diabete	s from 10 years	s of treatment:	:				
Blindness	229.4 (214.2, 240.0)	273.2 (257.8, 294.4) 793.5	244.1 (228.0, 264.8) 833.5	275.1 (256.8, 295.9) 859.5	238.2 (219.6, 270.0) 973.7	279.1 (256.1, 296.1) 999.5	225.2 (205.6, 242.9) 705.4	266.3 (247.0, 303.1) 729.3	222.3 (204.9, 243.7)	265.6 (240.1, 287.9) 618.8
End-stage renal disease	764 (731.1, 799.2)	(756.0, 828.6)	(813.3, 862.9)	(825.8, 890.5)	(936.2, 1020.1)	(958.9, 1040.2)	(675.4, 736.4)	(707.0, 784.4)	590 (559.0, 614.6)	(584.9, 658.4)

Ulcer	265.3 (238.7, 286.0)	234.4 (218.7, 256.0)	261.8 (239.1, 295.5)	220.6 (195.8, 236.5)	220.6 (198.7, 256.0)	180.1 (159.6, 196.8)	306.1 (258.0, 345.1)	262.2 (251.0, 277.1)	411.9 (369.9, 442.6)	350.7 (321.4, 383.1)
Deaths averted per 100,000 people with type II diabetes from 10 years of treatment:	1409.8 (1346.0,145 4.3)	1915.6 (1877.2, 1959.2)	1467.9 (1409.6, 1522.3)	1826.2 (1782.3, 1889.6)	1596.8 (1545.0, 1657.7)	2065.6 (2001.3, 2137.4)	1439.3 (1394.2, 1493.5)	1876.3 (1834.3, 1932.1)	1404.5 (1351.1, 1457.3)	1869.8 (1824.0, 1917.2)
Number needed to treat to prevent one CVD event	25.0 (24.4, 26.2)	17.0 (16.7, 17.3)	24.3 (23.5, 25.3)	18.2 (17.6, 18.6)	22.9 (22.1, 23.5)	16.4 (15.9, 16.8)	24.0 (23.1, 24.7)	17.1 (16.7, 17.4)	24.0 (23.1, 24.8)	16.8 (16.5, 17.1)
Number needed to treat to prevent one microvascular event	64.0 (60.8, 67.8)	63.4 (60.0, 66.7)	74.2 (69.8, 77.6)	71.7 (68.3, 76.0)	69.3 (64.3, 73.3)	67.2 (64.0, 71.3)	80.2 (74.9, 87.1)	76.8 (70.9, 80.0)	81.1 (76.3, 87.5)	78.1 (72.6, 84.1)
Cost and cost-effectiveness:										
Total costs, per capita per year, \$US 2016	\$891.1 (\$876.6, \$906.7)	\$894.7 (\$878.7, \$909.4)	\$725.4 (\$717.4, \$735.8)	\$732.4 (\$725.0, \$744.3)	\$952.6 (\$946.8, \$959.0)	\$960.6 (\$953.8, \$966.9)	\$1020.1 (\$1005.3, \$1035.6)	\$1020.1 (\$1005.0, \$1036.7)	\$517.6 (\$513.3, \$522.7)	\$520.5 (\$514.7, \$525.5)
Total DALYs averted, per capita per year	0.085 (0.083, 0.087)	0.104 (0.102, 0.105)	0.043 (0.042, 0.045)	0.051 (0.050, 0.052)	0.063 (0.062, 0.065)	0.075 (0.074, 0.076)	0.093 (0.091, 0.095)	0.108 (0.106, 0.110)	0.031 (0.031, 0.032)	0.04 (0.039, 0.041)
\$/DALYs averted (average cost- effectiveness, compared to no treatment)	\$10448.7 (\$10453.1, \$10514.3)	\$8587 (\$8575.1, \$8639.2)	\$16710.4 (\$16327, \$17094)	\$14362.9 (\$14299.6, \$14432.3)	\$15124.1 (\$14800.2, \$15385.0)	\$12816 (\$12774.4, \$12891.4)	\$11019 (\$10897.4, \$11062.4)	\$9437.4 (\$9348.9, \$9461.4)	\$16448 (\$16168.6, \$16728.4)	\$13079.5 (\$12886.6, \$13168)
Incremental cost-effectiveness of shifting from TTT to BTT	\$189.5 (163.6	6, 240)	\$875 (1000,	1400)	\$666.7 (571.4	1, 888.9)	\$0 (-15.8, 10	0)	\$322.2 (290,	414.3)

Combining the BTT approach for preventing CVD complications with the TTT approach for preventing micro-vascular complications.

	China (type II diabetes prevalence ~9.3%)	Ghana (type II diabetes prevalence ~2.2%)	India (type II diabetes prevalence ~8.8%)	Mexico (type II diabetes prevalence ~15.0%)	South Africa (type II diabetes prevalence ~7.2%)
Adults with type II diabetes recommended any treatment, %:	98.3 (98.2, 98.4)	97.8 (97.7, 97.9)	98.8 (98.6, 98.8)	98.1 (98.1, 98.2)	98.3 (98.2, 98.4)
Blood pressure treatment	82.6 (82.4, 82.7)	81.9 (81.8, 82.0)	84.4 (84.2, 84.5)	82.4 (82.2, 82.5)	82.8 (82.7, 82.9)
Lipid treatment	82.8 (82.7, 83.0)	82.0 (81.9, 82.1)	84.6 (84.4, 84.7)	82.5 (82.4, 82.7)	83.0 (82.9, 83.1)
Glycemic treatment	80.8 (80.7, 80.9)	80.8 (80.7, 80.9)	80.7 (80.6, 81)	80.7 (80.5, 80.9)	80.7 (80.6, 80.9)
Insulin treatment	13.9 (13.8, 14)	13.9 (13.7, 14)	13.8 (13.6, 14)	13.8 (13.6, 13.9)	13.8 (13.7, 14)
number of medications, per person recommended reatment	3.7 (3.7, 3.7)	3.6 (3.6, 3.6)	3.7 (3.7, 3.7)	3.6 (3.6, 3.6)	3.6 (3.6, 3.6)
CVD events prevented per 100,000 people with type II diabetes from 10 years of treatment:					
MI		2909.3 (2891.1, 3009.6)		3167.1 (2983.2, 3251.5)	3114.2 (3055, 3274.2)
Stroke	2719.1 (2676.6, 2852.4)	2439.7 (2301.8, 2560)	2843.1 (2764.5, 2994.3)	2658.7 (2532.3, 2780.3)	2758.3 (2603.1, 2808)
Microvascular events prevented per 100,000 people with type II diabetes from 10 years of treatment:					
Blindness	262.8 (223.5, 302.7)	279.6 (250.1, 299.0)	,	260.3 (239.0, 288.3)	268.3 (237.6, 291.8)
End-stage renal disease	867.4 (835.2, 910.8)	920.6 (883.7, 953.1)	1080.2 (1026.6, 1133.0)	775.3 (747.1, 807.9)	661.5 (642.1, 687.6)
Ulcer	264.7 (248.9, 306.0)	257.6 (246.7, 307.0)	210.6 (206.5, 252.6)	297.3 (292.7, 336.1)	390.3 (380.9, 456.2)
Deaths averted per 100,000 people with type II liabetes from 10 years of treatment:	1774.4 (1732.8, 1853.0)	1642 (1575.9, 1715.4)	1798.5 (1737.3, 1903.7)	1766.1 (1672.1, 1839.7)	1791 (1709.8, 1852.5)
Number needed to treat to prevent one CVD event	16.9 (3.8, 17.2)	18.3 (17.6, 18.8)	17.1 (16.2, 17.6)	16.8 (16.3, 17.8)	16.7 (16.2, 17.4)
Number needed to treat to prevent one microvascular event	70.5 (64.8, 75.1)	67.1 (62.8, 70.8)	63 (58.2, 66.4)	73.6 (68.6, 76.7)	74.5 (68.5, 77.9)
Cost and cost-effectiveness					
Total costs, per capita per year, \$US 2016	\$888.2 (880.0, 896.7)	\$724.8 (719.8, 729.6)	\$952.5 (948.7, 954.9)	\$1014.9 (1007.7, 1025.5)	\$514.4 (513.1, 519.6)

Total DALYs averted, per capita per year	0.110 (0.108, 0.112)	0.055 (0.054, 0.056)	0.080 (0.079, 0.081)	0.116 (0.114, 0.118)	0.042 (0.041, 0.043)
\$/DALYs averted (average cost-effectiveness,	\$8048.6 (7877.8,	\$13277 (12856.6,	\$11912.6 (11690.5,		\$12314.5 (11976.7,
compared to no treatment)	8275.9)	13635.5)	12133.1)	\$8761.6 (8541.6, 9011.7)	12690.9)
Incremental cost-effectiveness of shifting from TTT to BTT					

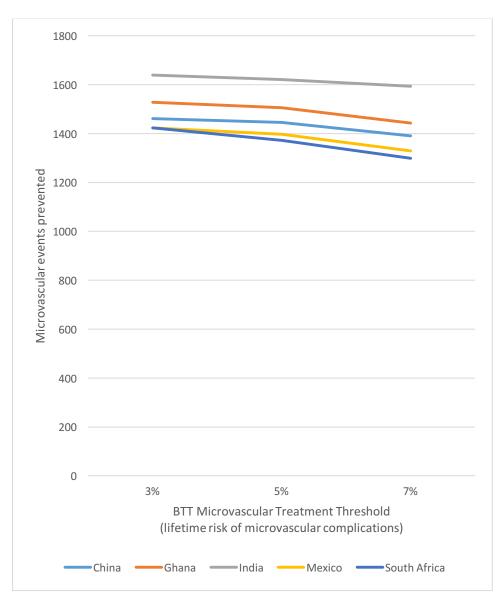
#### Appendix Figure 1

Example of a risk chart for lifetime risk of blindness for males newly diagnosed with type II diabetes in China. Lifetime risk is based on the study model. Note that lifetime risk decreases among the 70+ age group due to low life expectancy (i.e., less time left to develop blindness, rather than die of another cause).

			A1c			
Age (years)	6	7	8	9	10	SBP (mmHg)
(years)	2.6	3.1	3.7	4.3	5.1	180
	2.3	2.7	3.2	3.8	4.5	160
70	2.0	2.4	2.8	3.3	3.9	140
	1.7	2.1	2.5	2.9	3.4	120
	5.4	6.4	7.6	8.9	10.5	180
	4.8	5.6	6.6	7.8	9.2	160
60	4.2	4.9	5.8	6.9	8.1	140
	3.7	4.3	5.1	6.0	7.1	120
	5.8	6.8	8.0	9.5	11.1	180
	5.1	6.0	7.1	8.3	9.8	160
50	4.4	5.2	6.2	7.3	8.6	140
	3.9	4.6	5.4	6.4	7.6	120
	5.1	6.1	7.1	8.4	9.9	180
	4.5	5.3	6.3	7.4	8.7	160
40	3.9	4.7	5.5	6.5	7.6	140
	3.4	4.1	4.8	5.7	6.7	120
	4.2	4.9	5.8	6.9	8.1	180
	3.6	4.3	5.1	6.0	7.1	160
30	3.2	3.8	4.5	5.3	6.2	140
	2.8	3.3	3.9	4.6	5.5	120
	3.2	3.8	4.5	5.3	6.3	180
20	2.8	3.3	3.9	4.6	5.5	160
	2.5	2.9	3.4	4.1	4.8	140
	2.1	2.5	3.0	3.6	4.2	120

#### Appendix Figure 2

Variations in microvascular complications prevented under different thresholds for BTT treatment. Data are from Table 1 and Appendix Tables 5 and 6.



#### CHEERS Checklist Items to include when reporting economic evaluations of health interventions

The **ISPOR CHEERS Task Force Report**, *Consolidated Health Economic Evaluation Reporting Standards* (*CHEERS*)—*Explanation and Elaboration: A Report of the ISPOR Health Economic Evaluations Publication Guidelines Good Reporting Practices Task Force*, provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <u>http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp</u>

Section/item	Item No	Recommendation	Reported on page No/ line No
Title and abstract			
Title	1	Identify the study as an economic evaluation or use more specific terms such as "cost-effectiveness analysis", and describe the interventions compared.	1
Abstract	2	Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.	2
Introduction			
Background and objectives	3	Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or	
		practice decisions.	3
Methods			
Target population and	4	Describe characteristics of the base case population and	
subgroups		subgroups analysed, including why they were chosen.	4-5
Setting and location	5	State relevant aspects of the system(s) in which the decision(s) need(s) to be made.	6
Study perspective	6	Describe the perspective of the study and relate this to the costs being evaluated.	7
Comparators	7	Describe the interventions or strategies being compared and state why they were chosen.	6
Time horizon	8	State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate.	7
Discount rate	9	Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.	7
Choice of health outcomes	10	Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of	
		analysis performed.	5
Measurement of	11a	Single study-based estimates: Describe fully the design	
effectiveness		features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.	n/a



	11b	Synthesis-based estimates: Describe fully the methods used for	
		identification of included studies and synthesis of clinical effectiveness data.	5-6
Measurement and	10		3-0
valuation of preference	12	If applicable, describe the population and methods used to elicit preferences for outcomes.	
based outcomes		enen preferences for outcomes.	7
Estimating resources	13a	Single study-based economic evaluation: Describe approaches	<u> </u>
and costs	15a	used to estimate resource use associated with the alternative	
		interventions. Describe primary or secondary research methods	
		for valuing each resource item in terms of its unit cost.	
		Describe any adjustments made to approximate to opportunity	
		costs.	n/a
	13b	Model-based economic evaluation: Describe approaches and	
		data sources used to estimate resource use associated with	
		model health states. Describe primary or secondary research	
		methods for valuing each resource item in terms of its unit	
		cost. Describe any adjustments made to approximate to	
		opportunity costs.	7
Currency, price date,	14	Report the dates of the estimated resource quantities and unit	
and conversion		costs. Describe methods for adjusting estimated unit costs to	
		the year of reported costs if necessary. Describe methods for	
		converting costs into a common currency base and the	_
		exchange rate.	7
Choice of model	15	Describe and give reasons for the specific type of decision-	
		analytical model used. Providing a figure to show model	5
Assumptions	16	structure is strongly recommended. Describe all structural or other assumptions underpinning the	<u> </u>
Assumptions	10	decision-analytical model.	5
Analytical methods	17	Describe all analytical methods supporting the evaluation. This	<u> </u>
T mary floar moulous	17	could include methods for dealing with skewed, missing, or	
		censored data; extrapolation methods; methods for pooling	
		data; approaches to validate or make adjustments (such as half	
		cycle corrections) to a model; and methods for handling	
		population heterogeneity and uncertainty.	5-6
Results			
Study parameters	18	Report the values, ranges, references, and, if used, probability	
• •		distributions for all parameters. Report reasons or sources for	
		distributions used to represent uncertainty where appropriate.	
		Providing a table to show the input values is strongly	
		recommended.	5-6
Incremental costs and	19	For each intervention, report mean values for the main	
outcomes		categories of estimated costs and outcomes of interest, as well	
		as mean differences between the comparator groups. If	_
	20	applicable, report incremental cost-effectiveness ratios.	<u> </u>
Characterising	20a	Single study-based economic evaluation: Describe the effects	
uncertainty		of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact	n/a
		incremental effectiveness parameters, together with the impact	



	20ь	of methodological assumptions (such as discount rate, study perspective). <i>Model-based economic evaluation:</i> Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.	9-10
Characterising heterogeneity	21	If applicable, report differences in costs, outcomes, or cost- effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or	
		other observed variability in effects that are not reducible by more information.	9-10
Discussion			
Study findings, limitations, generalisability, and current knowledge	22	Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.	13-14
Other			
Source of funding	23	Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.	15
Conflicts of interest	24	Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.	15

For consistency, the CHEERS Statement checklist format is based on the format of the CONSORT statement checklist

The **ISPOR CHEERS Task Force Report** provides examples and further discussion of the 24-item CHEERS Checklist and the CHEERS Statement. It may be accessed via the *Value in Health* link or via the ISPOR Health Economic Evaluation Publication Guidelines – CHEERS: Good Reporting Practices webpage: <u>http://www.ispor.org/TaskForces/EconomicPubGuidelines.asp</u>

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