

Supplementary Table S1. Population characteristics derived from the Program ACTIVE II trial at 15 months after randomization and for the initiation of model simulation

Variable name and definition			Trial-derived data				Model-simulated data			
			UC	EXER	CBT	EXER+CB T	UC	EXER	CBT	EXER+CB T
Demographics										
Age (years)		Mean (SD)	57.3 (10.7)	57.3 (10.7)	57.3 (10.7)	57.3 (10.7)	57.3 (10.7)	57.3 (11.2)	57.3 (10.6)	57.3 (10.6)
Male		%	23.6	23.6	23.6	23.6	23.6	23.6	23.6	23.6
Race	White	%	70.7	70.7	70.7	70.7	70.7	70.7	70.7	70.7
	Black	%	22.1	22.1	22.1	22.1	29.3	29.3	29.3	29.3
	Native American	%	1.4	1.4	1.4	1.4	0	0	0	0
	Multiple races	%	1.4	1.4	1.4	1.4	0	0	0	0
	Unknown/refused	%	4.3	4.3	4.3	4.3	0	0	0	0
Duration of diabetes (years)		Mean (SD)	13.1 (8.4)	13.1 (8.4)	13.1 (8.4)	13.1 (8.4)	13.3 (7.7)	13.1 (8.0)	13.3 (7.9)	13.3 (8.1)
BMI (kg/m²)		Mean (SD)	36.7 (7.1)	36.7 (7.1)	36.7 (7.1)	36.7 (7.1)	36.6 (7.0)	36.6 (7.0)	36.6 (7.2)	36.6 (7.3)
Risk factors and health utilities										
HbA1c (%)		Mean (SD)	7.90 (1.7)	7.83 (1.6)	7.78 (1.9)	7.48 (1.1)	7.91 (1.8)	7.83 (1.66)	7.76 (1.93)	7.50 (1.1)
Total cholesterol (mmol/L)		Mean (SD)	5.19 (1.45)	4.73 (1.11)	5.00 (1.00)	4.84 (0.59)	5.19 (1.45)	4.73 (1.10)	5.00 (0.98)	4.84 (0.59)
HDL cholesterol (mmol/L)		Mean (SD)	1.22 (0.30)	1.06 (0.23)	1.17 (0.30)	1.19 (0.27)	1.22 (0.30)	1.06 (0.23)	1.17 (0.29)	1.19 (0.27)
LDL cholesterol (mmol/L)		Mean (SD)	2.81 (0.77)	2.55 (0.88)	2.57 (1.00)	2.58 (0.67)	2.81 (0.77)	2.55 (0.87)	2.57 (0.98)	2.58 (0.63)
Triglycerides (mmol/L)		Mean (SD)	1.95 (2.22)	2.04 (1.06)	2.13 (2.25)	1.88 (0.53)	1.95 (2.21)	2.03 (1.03)	2.12 (2.08)	1.88 (0.50)
SBP (mmHg)		Mean (SD)	127.1 (14.7)	125.3 (13.4)	130.3 (19.0)	132.3 (12.3)	127.3 (14.7)	125.3 (13.5)	130.3 (19.3)	132.3 (12.3)
DBP (mmHg)		Mean (SD)	76.4 (8.8)	76.4 (8.8)	76.4 (8.8)	76.4 (8.8)	76.5 (7.8)	76.4 (7.9)	76.4 (8.0)	76.4 (7.8)
Current smoker		%	8.6	8.6	8.6	8.6	8.6	8.6	8.6	8.6
History of atrial fibrillation		%	24.3	24.3	24.3	24.3	24.3	24.3	24.3	24.3
Health utility (SF-12)		Mean (SD)	0.606 (0.117)	0.654 (0.114)	0.643 (0.121)	0.694 (0.148)	0.606 (0.117)	0.654 (0.114)	0.643 (0.121)	0.694 (0.148)
Disease status										
History of angina		%	18.6	18.6	18.6	18.6	18.6	18.6	18.6	18.6
History of heart failure with no MI		%	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4
History of revascularization procedure (CABG or PCI)		%	3.6	3.6	3.6	3.6	3.6	3.6	3.6	3.6

with no MI									
History of MI with no heart failure	%	6.4	6.4	6.4	6.4	6.4	6.4	6.4	6.4
History of MI and heart failure	%	0	0	0	0	0	0	0	0
History of stroke	%	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Microalbuminuria (30 mg/g \leq UACR < 300 mg/g)	%	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Proteinuria (UACR \geq 300 mg/g)	%	6.4	6.4	6.4	6.4	6.4	6.4	6.4	6.4
ESRD – dialysis	%	1.4	1.4	1.4	1.4	1.4	1.4	1.4	1.4
ESRD – transplant	%	0	0	0	0	0	0	0	0
Clinical neuropathy	%	40.0	40.0	40.0	40.0	40.0	40.0	40.0	40.0
Amputation due to diabetic neuropathy	%	0.7	0.7	0.7	0.7	0.7	0.7	0.7	0.7
Non-proliferative retinopathy (left eye)	%	6.4	6.4	6.4	6.4	6.4	6.4	6.4	6.4
Proliferative retinopathy or macular edema (left eye)	%	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Blindness (left eye)	%	11.4	11.4	11.4	11.4	11.4	11.4	11.4	11.4
Non-proliferative retinopathy (right eye)	%	6.4	6.4	6.4	6.4	6.4	6.4	6.4	6.4
Proliferative retinopathy or macular edema (right eye)	%	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
Blindness (right eye)	%	11.4	11.4	11.4	11.4	11.4	11.4	11.4	11.4
Medications									
Diet and exercise only	%	6.4	6.4	6.4	6.4	6.4	6.4	6.4	6.4
Single non-insulin med (e.g., metformin only)	%	32.1	32.1	32.1	32.1	32.1	32.1	32.1	32.1
Two or more non-insulin meds	%	24.4	24.4	24.4	24.4	24.4	24.4	24.4	24.4
Basal insulin only (basal insulin or NPH)	%	15.4	15.4	15.4	15.4	15.4	15.4	15.4	15.4
Intensive bolus insulin	%	21.8	21.8	21.8	21.8	21.8	21.8	21.8	21.8
Beta-blocker (whether a subject is taking beta-blocker)	%	29.5	29.5	29.5	29.5	30.0	29.3	30.0	30.0
ACE inhibitor (whether a subject is taking ACE inhibitor)	%	51.9	51.9	51.9	51.9	52.3	52.2	52.2	52.3
Statin (whether a subject is taking statin)	%	29.5	29.5	29.5	29.5	30.0	29.3	30.0	30.0
Aspirin (whether a subject is taking aspirin)	%	30.8	30.8	30.8	30.8	30.5	30.5	30.5	30.5

Abbreviations: UC, usual care; EXER, exercise; CBT, cognitive behavioral therapy; SD, standard deviation; BMI, body mass index; HbA1c, glycated hemoglobin; HDL, high density lipoprotein; LDL, low density lipoprotein; SBP, systolic blood pressure; DBP, diastolic blood pressure; SF-12, 12-item short form health survey; MI, myocardial infarction; CABG, coronary artery bypass grafting; PCI, percutaneous coronary intervention; UACR, urine albumin-to-creatinine ratio; ESRD, end-stage renal disease; NPH, neutral protamine Hagedorn; ACE, angiotensin-converting enzyme.

Supplementary Table S2. Intervention-related costs over the 15-month study period in the Program ACTIVE II trial

Cost component	Per-participant cost (2014 US\$)			
	UC	EXER	CBT	EXER+CBT
Formal healthcare sector				
PA2 intervention (resource utilization and cost incurred by the PA2 interventions)				
CBT intervention				
Cost of training CBT therapists (including time and material costs) ¹	NA	NA	NC	NC
Cost of time that CBT therapists spent on interventions ²	NA	NA	694.3	738.4
Cost of time that CBT therapists spent on remote communications for health counseling ³	NA	NA	DU	DU
EXER intervention				
Cost of training exercise trainers (including time and material costs) ⁴	NA	None	NA	None
Cost of time that exercise trainers spent on interventions ⁵	NA	190.8	NA	165.2
Cost of passes/memberships to fitness facilities ⁶	NA	129.0	NA	129.0
Cost of time that exercise trainers spent on remote communications for health counseling ³	NA	DU	NA	DU
<i>Sub-total cost of the PA2 interventions</i>	<i>0</i>	<i>319.8</i>	<i>694.3</i>	<i>1,032.6</i>
Resource utilization and cost of medical care outside the PA2 ⁷	1,615.2	1,026.0	1,062.7	703.7
<i>Sub-total cost of the PA2 interventions and resource utilization of medical care outside the PA2</i>	<i>1,615.2</i>	<i>1,345.8</i>	<i>1,757.0</i>	<i>1,736.3</i>
Informal healthcare sector				
Participant time				
Cost of time spent on participation in CBT sessions ⁸	NA	NA	226.0	240.3
Cost of time spent on participation in EXER sessions ⁹	NA	186.5	NA	161.4
<i>Sub-total cost of participant time spent on participation in intervention sessions</i>	<i>0</i>	<i>186.5</i>	<i>226.0</i>	<i>401.7</i>
Total cost	1,615.2	1,532.3	1,983.0	2,138.0

Abbreviations: PA2, Program ACTIVE II; UC, usual care; EXER, exercise; CBT, cognitive behavioral therapy; NA, not applicable; NC, not considered; DU, data unavailable.

¹Each CBT therapist was paid for the 6-hour training. However, the per-participant fixed start-up cost for training CBT therapists in the PA2 could vary extensively by the number of participants enrolled in the PA2 for CBT therapists' interventions. Moreover, considering 1) CBT therapists would probably give interventions to more participants in a real-world practice than they did in the PA2, 2) CBT therapists who were partnered with the PA2 were already available to the public, and 3) CBT therapists were well qualified and trained, we would assume that the PA2 is an ongoing program and thus we would not consider the fixed start-up cost for training CBT therapists in the base-case cost-effectiveness analysis.

²CBT therapists were paid at the hourly rate of \$70 for 90 minutes per CBT session, and it was inflated to the hourly rate of \$73.4 in year 2014 cost. Thus, it was \$110.2 in year 2014 cost for 90 minutes per CBT session. On average, a CBT participant and a CBT+EXER participant attended 6.3 and 6.7 CBT sessions, respectively, over the 12-week intervention period.

³Remote communications may include phone calls, e-mails, or other electronic communications (e.g., text messages, portal messages, etc.), or mails.

⁴Exercise trainers have already worked in the fitness facilities that were partnered with the PA2, and thus there would be no cost of training exercise trainers.

⁵Exercise trainers were paid at the hourly rate of \$35 for a 60-minute exercise session, and it was inflated to \$36.7 in year 2014 cost per exercise session. On average, an EXER participant and a CBT+EXER participant attended 5.2 and 4.5 exercise sessions, respectively, over the 12-week intervention period.

⁶The cost of passes/memberships to fitness facilities was \$123 per participant, and it was inflated to \$129.0 in year 2014 cost.

⁷To estimate the resource utilization and cost of medical care outside the PA2, we surveyed participants and estimated the cost of using outpatient, urgent care, emergency room, and hospitalization services, and laboratory testing, and self-monitoring of blood glucose.

⁸The total participant time spent on participating in CBT sessions with CBT therapists in the PA2 trial was 6.3 hours (6.3 sessions x 60 minutes/session) and 6.7 hours (6.7 sessions x 60 minutes/session) for the CBT and CBT+EXER group, respectively. Based on year 2014 data from the US Bureau of Labor Statistics (<https://www.bls.gov/bls/blswage.htm>), these times were valued using the US nonfarm workers with a total hourly rate of \$35.87, consisting of the hourly wage of \$24.57 plus the fringe benefits of \$11.30 (fringe rate: 46%).

⁹The total participant time spent on participating in EXER sessions with exercise trainers in the PA2 trial was 5.2 hours (5.2 sessions x 60 minutes/session) and 4.5 hours (4.5 sessions x 60 minutes/session) for the EXER and CBT+EXER group, respectively. Based on year 2014 data from the US Bureau of Labor Statistics (<https://www.bls.gov/bls/blswage.htm>), these times were valued using the US nonfarm workers with a total hourly rate of \$35.87, consisting of the hourly wage of \$24.57 plus the fringe benefits of \$11.30 (fringe rate: 46%).

Supplementary Table S3. Impact inventory for components considered in the cost-effectiveness analyses

Type of impact	Included in the reference case analysis from each perspective		Notes on sources of evidence
	Healthcare sector	Societal	
Formal healthcare sector			
Health			
Health outcomes (effects)			
Longevity effects	Yes	Yes	Program ACTIVE II trial, MMD
Health-related quality-of-life effects	Yes	Yes	Program ACTIVE II trial (utilities derived from SF-12), MMD (utilities from published literature)
Other health effects	No	No	
Medical costs			
Paid for by third-party payers	Yes	Yes	Program ACTIVE II trial (intervention-related costs), MMD (outcome costs from published literature)
Paid for by patients out-of-pocket	Not available	Not available	
Future related medical costs	Yes	Yes	MMD (outcome costs from published literature)
Future unrelated medical costs	Not available	Not available	
Informal healthcare sector			
Health			
Patient-time costs	Not applicable	Yes	Program ACTIVE II trial
Unpaid caregiver-time costs	Not applicable	Not available	
Transportation costs	Not applicable	Not available	
Non-healthcare sectors			
Productivity	Not applicable	Not available	
Consumption	Not applicable	Not available	
Social services	Not applicable	Not available	
Legal or criminal justice	Not applicable	Not available	
Education	Not applicable	Not available	
Housing	Not applicable	Not available	
Environment	Not applicable	Not available	

Abbreviations: MMD, Michigan Model for Diabetes; SF-12, 12-item short form health survey.

Supplementary Table S4. Base-case and sensitivity analyses for cost-effectiveness of the EXER and EXER+CBT interventions vs. the CBT intervention, and of the EXER+CBT intervention vs. the EXER intervention

	EXER vs. CBT			EXER+CBT vs. CBT			EXER+CBT vs. EXER		
	Incremental total cost, \$	Incremental QALY	ICER, \$	Incremental total cost, \$	Incremental QALY	ICER, \$	Incremental total cost, \$	Incremental QALY	ICER, \$
Base-case analysis ¹	-908	0.092	Cost-saving	-192	0.401	Cost-saving	716	0.308	2,323
Perspective									
Societal perspective	-948	0.092	Cost-saving	-16.7	0.401	Cost-saving	931	0.308	3,021
Time horizon									
5-year simulation time horizon	-813	0.051	Cost-saving	-207	0.224	Cost-saving	605	0.173	3,496
Effectiveness									
Persistent intervention effects	-1,561	0.098	Cost-saving	-5,645	0.426	Cost-saving	-4,084	0.328	Cost-saving
Cost									
400% increase of the cost for passes/memberships to fitness facilities ²	-392	0.092	Cost-saving	324	0.401	808	716	0.308	2,323
50% increase of the hourly rate for CBT therapists	-1,255	0.092	Cost-saving	-170	0.401	Cost-saving	1,085	0.308	3,520
50% increase of the hourly rate for exercise trainers	-813	0.092	Cost-saving	-110	0.401	Cost-saving	703	0.308	2,281
400% increase of the cost for passes/memberships to fitness facilities, ² and 50% increase of the hourly rate for both CBT therapists and exercise trainers	-644	0.092	Cost-saving	428	0.401	1,070	1,072	0.308	3,478

Abbreviations: EXER, exercise; CBT, cognitive behavioral therapy; QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio.

¹The base-case analysis was from the healthcare sector perspective over a 10-year simulation time horizon for the cost-effectiveness of the Program ACTIVE II interventions assuming the diminishing intervention effects after the end of the trial.

²The cost of passes/memberships to fitness facilities was assumed to increase by 400%, which would provide participants with free access to fitness facilities for the first 3 months of the study period (\$129 per participant in the base-case analysis) versus for the total 15 months of the study period (\$645 per participant in the sensitivity analysis).