

eAppendix Table.

Cohort Characteristics

Required values	All patients		Units/Range	References/Notes
PATIENT DEMOGRAPHICS	Mean	SD		
Start age	57.9	11.9	years	
Duration of Diabetes	3	3.6	years	GE Centricity ¹
Prop. Male	0.518		[0-1]	
All patients				
BASELINE RISK FACTORS	Mean	SD		
HbA1c	8.37	1.84	%-points	GE Centricity ¹
SBP	130.94	16.90	mmHg	
T-CHOL	181.79	42.81	mg/dL	Merck Data on File ²
HDL	42.94	11.52	mg/dL	GE Centricity ¹
LDL	99.53	37.21	mg/dL	Merck Data on File ²
TRIG	143.34	80.88	mg/dL	
BMI	34.40	7.87	kg/m ²	GE Centricity ¹
eGFR	87.200	18.500	ml/min/1.73m ²	Merck Data on File ²
HAEM	13.827	1.237	gr/dl	Merck Data on File ²
WBC	7.437	1.913	10 ⁶ /ml	
Heart rate	70.502	10.698	bpm	Merck Data on File ²
Alcohol consumption	7.54		oz/week	WHO Global status report on alcohol and health 2014 ³
All patients				
RACIAL CHARACTERISTICS	Mean			
Prop. White	0.659		[0-1]	
Prop. Black	0.0126		[0-1]	
Prop. Hispanic	0.00		[0-1]	GE Centricity ¹
Prop. Native American	0.0034		[0-1]	
Prop. Asian/Pacific Islander	0.02		[0-1]	
All patients				
BASELINE CVD COMPLICATIONS	Mean			
Prop. MI	0.029		[0-1]	
Prop. Angina	0.034		[0-1]	
Prop. PVD	0.003		[0-1]	
Prop. stroke	0.011		[0-1]	Merck Data on File ²
Prop. HF	0.008		[0-1]	
Prop. Atrial fibrillation	0.015		[0-1]	
Prop. LVH	0.005		[0-1]	
All patients				

BASELINE RENAL COMPLICATIONS			
	Mean		
Prop. MA	0.017	[0-1]	Merck Data on File ²
Prop. GRP	0.006	[0-1]	
Prop. ESRD	0.000	[0-1]	
All patients			
BASELINE RETINOPATHY COMPLICATIONS			
	Mean		
Prop. BDR	0.038	[0-1]	Merck Data on File ²
Prop. PDR	0.000	[0-1]	
Prop. SVL	0.004	[0-1]	
All patients			
BASELINE MACULAR EDEMA			
	Mean		
Prop. ME	0.0	[0-1]	Merck Data on File ² ; none reported
All patients			
BASELINE CATARACT			
	Mean		
Prop. cataract	0.063	[0-1]	Merck Data on File ²
All patients			
BASELINE FOOT ULCER COMPLICATIONS			
	Mean		
Prop. uninfected ulcer	0.000	[0-1]	Merck Data on File ² (0= not reported)
Prop. infected ulcer	0.000	[0-1]	
Prop. healed ulcer	0.000	[0-1]	
Prop. history of amputation	0.002	[0-1]	
All patients			
BASELINE NEUROPATHY			
	Mean		
Prop. neuropathy	0.125	[0-1]	Merck Data on File ²
All patients			
BASELINE DEPRESSION			
	Mean		
Prop. depression	0.054	[0-1]	Merck Data on File ²

Clinical inputs (non-treatment specific)

	Required values	Units/Range	References/Notes
HbA1c adjustments - Type 2 diabetes			
Risk Reduct for 1%-point lower HbA1c MI T2	14	[0-100]	Stratton et al 2000 ⁴
Risk Reduct for 1%-point lower HbA1c micro T2	37	[0-100]	Stratton et al 2000 ⁴
Risk Reduct for 1%-point lower HbA1c PVD T2	22	[0-100]	Adler et al 2002 ⁵
Risk Reduct for 1%-point lower HbA1c Cataract T2	19	[0-100]	Stratton et al 2000 ⁴
Risk Reduct for 1%-point lower HbA1c HF T2	16	[0-100]	Stratton et al 2000 ⁴
Risk Reduct for 1%-point lower HbA1c stroke type 2	12	[0-100]	Stratton et al 2000 ⁴
Risk Reduct for 1%-point lower HbA1c angina type 2	12	[0-100]	Clarke et al 2004 ⁶
HbA1c adjustments - Type 1 and -2 diabetes			
Risk Reduct for 1%-point lower HbA1c HD Mort	12	[0-100]	Morioka et al 2001 ⁷
Risk Reduct for 1%-point lower HbA1c PD Mort	12	[0-100]	Morioka et al 2001 ⁷
Risk Reduct for 1%-point lower HbA1c RT Mort	0	[0-100]	Wiesbauer et al 2010 ⁴
Risk Reduct for 1%-point lower HbA1c 1st ulcer	17	[0-100]	Monami et al 2009 ⁸
SBP adjustments			
Risk Reduct for 10mmHg lower SBP all micro T2	13	[0-100]	Adler et al 2000 ⁹
Risk Reduct for 10mmHg lower SBP SVL T2	0	[0-100]	Assumption (No data)
MI			
Prop. init CHD event MI Female	0.361	[0-1]	D'Agostino et al 2000 ¹⁰
Prop. init CHD event MI Male	0.522	[0-1]	D'Agostino et al 2000 ¹⁰
Prop. subseq CHD event MI female	0.474	[0-1]	D'Agostino et al 2000 ¹⁰
Prop. subseq CHD event MI Male	0.451	[0-1]	D'Agostino et al 2000 ¹⁰
Increased Risk MI if MA	1.00	Multiplier	Assumption (No data)
Increased Risk MI if GPR	1.00	Multiplier	Assumption (No data)
Increased Risk MI if ESRD	1.00	Multiplier	Assumption (No data)
Multiplier for Risk rec MI if DIGAMI intensive control	1.00	Multiplier	Assumption (No data)
Multiplier for Risk pot MI mort if DIGAMI intensive control	1.00	Multiplier	Assumption (No data)
Multiplier Aspirin 1° MI	0.82	Multiplier	Antithrombotic Trialists' (ATT) Collaboration 2009 ¹¹
Multiplier Aspirin 2° MI	0.80	Multiplier	Antithrombotic Trialists' (ATT) Collaboration 2009 ¹¹
Multiplier Statins 1° MI	0.70	Multiplier	Brugts et al 2009 ¹²
Multiplier Statins 2° MI	0.81	Multiplier	Shepherd et al 2002 ¹³
Risk Reduct with ACE 1st MI	0.78	[0-1]	Heart Outcomes Prevention Evaluation (HOPE) Study Investigators 2000 ¹⁴
Risk Reduct with ACE rec MI	0.78	[0-1]	Heart Outcomes Prevention Evaluation (HOPE) Study Investigators 2000 ¹⁴
MI mortality			
p sudden death 1st MI male	0.393	[0-1]	Sonke et al 1996 ¹⁵
p sudden death 1st MI female	0.364	[0-1]	Sonke et al 1996 ¹⁵
p sudden death rec MI male	0.393	[0-1]	Sonke et al 1996 ¹⁵

p sudden death rec MI female	0.364	[0-1]	Sonke et al 1996 ¹⁵
Multiplier 12 month mortality MI convent treatment	1.45	Multiplier	Malmberg et al 1995 ¹⁶
Multiplier Aspirin mortality 1st year MI	0.88	Multiplier	Antiplatelet Trialists' Collaboration 1994 ¹⁷
Multiplier Aspirin mortality 2nd+ years MI	0.88	Multiplier	Antiplatelet Trialists' Collaboration 1994 ¹⁷
Multiplier Statins mortality 1st year MI	0.75	Multiplier	Stenstrand et al 2001 ¹⁸
Multiplier Statins mortality 2nd+ years MI	1.00	Multiplier	Assumption (No data)
Multiplier Aspirin sudden death MI	1.00	Multiplier	Assumption (No data)
Multiplier Statin sudden death MI	1.00	Multiplier	Briel et al 2006 ¹⁹
Multiplier ACE sudden death MI	1.00	Multiplier	Assumption (No data)
Risk Reduct with ACE MI long-term mort	0.64	[0-1]	Gustafsson et al 1999 ²⁰
Risk Reduct with ACE MI 12 month mort	0.64	[0-1]	Gustafsson et al 1999 ²⁰
Stroke			
Mult Stroke MA	1.00	Multiplier	Assumption (no data)
Mult Stroke GRP	1.00	Multiplier	Assumption (no data)
Mult Stroke ESRD	1.00	Multiplier	Assumption (no data)
Multiplier Aspirin 1° stroke	0.86	Multiplier	Antithrombotic Trialists' (ATT) Collaboration 2009 ¹¹
Multiplier Aspirin 2° stroke	0.78	Multiplier	Antithrombotic Trialists' (ATT) Collaboration 2009 ¹¹
Multiplier Statins 1° stroke	0.81	Multiplier	Brugts et al 2009 ¹²
Multiplier Statins 2° stroke	0.84	Multiplier	The Stroke Prevention by Aggressive Reduction in Cholesterol Levels (SPARCL) Investigators 2006 ²¹
Risk Reduct with ACE 1st stroke	0.67	[0-1]	Heart Outcomes Prevention Evaluation (HOPE) Study Investigators 2000 ¹⁴
Risk Reduct with ACE rec stroke	0.72	[0-1]	PROGRESS Collaborative Group 2001 ²²
Stroke mortality			
p 30-day death 1st stroke male	0.124	[0-1]	Eriksson et al 2001 ²³
p 30-day death 1st stroke female	0.124	[0-1]	Eriksson et al 2001 ²³
p 30-day death rec stroke male	0.422	[0-1]	Eriksson et al 2001 ²³
p 30-day death rec stroke female	0.422	[0-1]	Eriksson et al 2001 ²³
Multiplier Aspirin mortality 1st year stroke	0.84	Multiplier	Antiplatelet Trialists' Collaboration 1994 ¹⁷
Multiplier Aspirin mortality 2nd+ years stroke	0.84	Multiplier	Antiplatelet Trialists' Collaboration 1994 ¹⁷
Multiplier Statins mortality 1st year stroke	1.00	Multiplier	Manktelow et al 2009 ²⁴
Multiplier Statins mortality 2nd+ years stroke	1.00	Multiplier	Manktelow et al 2009 ²⁴
Multiplier Aspirin sudden death stroke	0.95	Multiplier	Sandercock et al 2008 ²⁵
Multiplier Statin sudden death stroke	1.00	Multiplier	Briel et al 2006 ¹⁹
Multiplier ACE sudden death stroke	0.49	Multiplier	Chitravas et al 2007 ²⁶
Risk Reduct with ACE stroke long-term mort	1.000	[0-1]	Asberg et al 2010 ²⁷
Risk Reduct with ACE stroke 12 month mort	1.000	[0-1]	Asberg et al 2010 ²⁷
Angina			
Prop. init CHD event angina Female	0.621	[0-1]	D'Agostino et al 2000 ¹⁰

Prop. init CHD event angina Male	0.420	[0-1]	D'Agostino et al 2000 ¹⁰
Prop. subseq CHD event angina Female	0.359	[0-1]	D'Agostino et al 2000 ¹⁰
Prop. subseq CHD event angina Male	0.301	[0-1]	D'Agostino et al 2000 ¹⁰
Mult Angina MA	1.00	Multiplier	Assumption (No data)
Mult Angina GRP	1.00	Multiplier	Assumption (No data)
Mult Angina ESRD	1.00	Multiplier	Assumption (No data)
Congestive heart failure			
Increased Risk HF if MAU	1.00	Multiplier	Assumption (No data)
Increased Risk HF if GPR	1.00	Multiplier	Assumption (No data)
Increased Risk HF if ESRD	1.00	Multiplier	Assumption (No data)
Risk reduct HF if Aspirin	1.00	[0-1]	Assumption (No data)
Risk reduct HF if Statin	1.00	[0-1]	Assumption (No data)
Risk reduct HF if ACE	0.80	[0-1]	Heart Outcomes Prevention Evaluation (HOPE) Study Investigators 2000 ¹⁴
Risk reduct HF death if ACE	0.80	[0-1]	Ascencao et al 2008 ²⁸
Multiplier HF death diab male	1.00	Multiplier	Ho et al 1993 ²⁹
Multiplier HF death diab female	1.70	Multiplier	Ho et al 1993 ²⁹
ACE inhibitor adjustments for microvascular complications			
Risk Reduct with ACE BDR T2	0.75	[0-1]	Chaturvedi et al 1998 ³⁰
Risk Reduct with ACE PDR T2	0.19	[0-1]	Chaturvedi et al 1998 ³⁰
Risk Reduct with ACE ME T2	1.00	[0-1]	Assumption (No data)
Risk Reduct with ACE SVL T2	1.00	[0-1]	Assumption (No data)
Risk Reduct with ACE Neuropathy T2	1.00	[0-1]	Assumption (No data)
Probabilities for ACE side effects			
p SEs stopping ACE 1st year	0.000	[0-1]	Assumption (No data)
p SEs stopping ACE 2nd+ years	0.000	[0-1]	Assumption (No data)
Adverse events			
p die major hypo T2	0.000	[0-1]	Ben-Ami et al 1999 ³¹
p die ketoacidosis	0.027	[0-1]	MacIsaac et al 2002 ³²
p die after lactic acidosis	0.430	[0-1]	Campbell 1985 ³³
Increased Risk hypo with ACE T2	1.00	Multiplier	Assumption (No data)
Foot ulcer and amputation			
p gangrene to amp with gang	0.181800	[0-1] monthly based	Persson et al 2000 ³⁴
p gangrene to healed amp	0.308200	[0-1] monthly based	Persson et al 2000 ³⁴
p death following onset gangrene	0.009800	[0-1] monthly based	Persson et al 2000 ³⁴
p death with history amputation	0.004000	[0-1] monthly based	Persson et al 2000 ³⁴

p death following healed ulcer	0.004000	[0-1] monthly based	Persson et al 2000 ³⁴
p developing recurrent uninfected ulcer	0.039300	[0-1] monthly based	Persson et al 2000 ³⁴
p amputation following infected ulcer	0.003700	[0-1] monthly based	Persson et al 2000 ³⁴
p infect ulcer->amp healed	0.044500	[0-1] monthly based	Persson et al 2000 ³⁴
p infect ulcer->death	0.009800	[0-1] monthly based	Persson et al 2000 ³⁴
p infect ulcer->gangrene	0.007500	[0-1] monthly based	Persson et al 2000 ³⁴
p infect ulc->uninfect ulc	0.139700	[0-1] monthly based	Persson et al 2000 ³⁴
p recurrent amp	0.008451	[0-1] monthly based	Borkosky et al 2012 ³⁵
p uninfect ulc->death	0.004000	[0-1] monthly based	Persson et al 2000 ³⁴
p uninfect ulc->infect ulc	0.047300	[0-1] monthly based	Persson et al 2000 ³⁴
p uninfect ulc->healed ulc	0.078700	[0-1] monthly based	Persson et al 2000 ³⁴
p developing ulcer with neither neur or PVD	0.000250	[0-1] monthly based	Ragnarson Tennvall et al 2001 ³⁶
p developing ulcer with either neur or PVD	0.006092	[0-1] monthly based	Ragnarson Tennvall et al 2001 ³⁶
p developing ulcer with both neur or PVD	0.006092	[0-1] monthly based	Ragnarson Tennvall et al 2001 ³⁶
Depression			
Mult for all cause death if depression	1.33	Multiplier	Egede et al 2005 ³⁷
Mult for CHF if depression	1.00	Multiplier	Assumption (No data)
Mult for MI if depression	1.00	Multiplier	Assumption (No data)
Mult for depression if neuropathy	3.10	Multiplier	Yoshida et al 2009 ³⁸
Mult for depression if stroke	6.30	Multiplier	Whyte et al 2004 ³⁹
Mult for depression if amp.	1.00	Multiplier	Assumption (No data)
Other			
p BDR->SVL	0.0148	[0-1]	Javitt et al 1994 ⁴⁰
p reversal of neuropathy	0.000	[0-1]	Assumption (No data)

Other management relevant inputs

	Required values	Units/ Range	References/Notes
Concomitant medication			
	Mean		
Prop 1° prevention ASP	0.575	[0-1]	VanWormer 2014 ⁴¹
Prop 2° prevention ASP	0.575	[0-1]	
Prop 1° prevention Statins	0.404	[0-1]	Gamboia 2014 ⁴²
Prop 2° prevention Statins	0.215	[0-1]	Abdallah 2014 ⁴³
Prop 1° prevention ACE-I	0.64	[0-1]	Ali 2013 ⁴⁴
Prop 2° prevention ACE-I	0.64	[0-1]	
Screening and patient management proportions			
Prop on foot ulcer prevention program	0.714	[0-1]	Ali 2013 ⁴⁴
Prop screened eye disease	0.734	[0-1]	
Prop screened for renal disease	0.477	[0-1]	Anabtawi 2013 ⁴⁵
Prop receiving intensive insulin after MI	0.877	[0-1]	McMullin 2004 ⁴⁶
Prop treated with extra ulcer treatment	0.570	[0-1]	Lyon 2008 ⁴⁷
Prop screened for depression - no complications	0.830	[0-1]	Jones 2007 ⁴⁸
Prop screened for depression - complications	0.830	[0-1]	
Other			
Reduction in incidence FU with Prev Program	0.310	[0-1]	O'Meara 2000 ⁴⁹
Improvement in ulcer healing rate with extra ulcer treatment	1.390	Multiplier	Kantor 2001 ⁵⁰
Reduction in amputation rate with footcare	0.340	[0-1]	O'Meara 2000 ⁴⁹
Sensitivity eye screening	0.934	[0-1]	Wilson 2010 ⁵¹
Specificity eye screening	0.858	[0-1]	
Sensitivity GRP screening	0.989	[0-1]	White 2011 ⁵²
Sensitivity MA screening	0.87	[0-1]	Wu 2014 ⁵³
Specificity MA screening	0.88	[0-1]	

Economic inputs

	Required values	Units / Range	References/notes
DISCOUNT RATES			
Discount Clinical	3.0	%	Sanders 2016 ⁵⁴
Discount Costs	3.0	%	
SAMPLING FOR PROBABILISTIC SENSITIVITY ANALYSIS			
Percent variation direct costs	20.0	%	Assumed
Percent variation indirect costs	20.0	%	Assumed
MANAGEMENT COSTS			
c statins	47.67	\$	PriceRx 2017 ⁵⁵
c aspirin	2.82	\$	
c ACE	33.22	\$	
c screening for MA	28.39	\$	
c screening for GRP	25.49	\$	
c eye screening	66.75	\$	
DIRECT COSTS CVD COMPLICATIONS			
c MI 1st year	16,556.91	\$	Yeaw 2014 ⁵⁶
c MI 2nd+ years	2,004.75	\$	
c angina 1st year	3,625.33	\$	
c angina 2nd+ years	507.00	\$	
c CHF 1st year	12,523.77	\$	
c CHF 2nd+ years	6,394.86	\$	
c stroke 1st year	7,223.48	\$	
c stroke 2nd+ years	1,010.65	\$	
c stroke death within 30 days	7,343.84	\$	
c PVD 1st year	5,496.51	\$	
c PVD 2nd+ years	2,128.86	\$	
DIRECT COSTS RENAL COMPLICATIONS			
HD costs 1st year	20,204.70	\$	Yeaw 2014 ⁵⁶
annual costs HD 2+ years	15,302.76	\$	
PD costs 1st year	30,901.02	\$	
annual costs PD 2+ years	22,241.36	\$	
RT costs 1st year	10,149.04	\$	
annual costs RT 2+ years	7,166.74	\$	
DIRECT COSTS ACUTE EVENTS			
c severe hypo requiring non-medical third party intervention	75.26	\$	Foos 2013 ⁵⁷
c severe hypo requiring medical third party intervention	1,311.30	\$	
c non-severe hypo	10.23	\$	CMS PFS 2017 ⁵⁸
c keto event	290.78	\$	Yeaw 2014 ⁵⁶
c lactic acid event	12,889.02	\$	
DIRECT COSTS EYE DISEASE			
c laser treatment	982.27	\$	CMS PFS 2017 ⁵⁸

c cataract operation	627.67	\$	Yeaw 2014 ⁵⁶
c following cataract operation	154.85	\$	
c blindness - year of onset	1,241.15	\$	
c blindness - following years	302.60	\$	

DIRECT COSTS NEUROP/FOOT ULCER/AMP

c Neurop 1st year	2,101.68	\$	Yeaw 2014 ⁵⁶
c Neurop 2nd+ years	709.23	\$	
c Amputation (event based)	7,304.32	\$	
c Amp Prosthesis (event based)	21,720.47	\$	
c Gangrene treatment	15,552.16	\$	
c after healed ulcer	3,898.29	\$	
c infected ulcer	7,833.17	\$	
c standard uninfected ulcer	7,833.17	\$	
c healed ulcer history of amputation	3,898.29	\$	

QUALITY OF LIFE	Mean		
QoL utility T2 no complications	0.7850	[0-1]	Clarke et al 2002 ⁵⁹
QoL disutility MI event	-0.0550	[-1-0]	
QoL utility post MI	0.7300	[0-1]	
QoL utility angina	0.6950	[0-1]	
QoL utility CHF	0.6770	[0-1]	
QoL disutility stroke event	-0.1640	[-1-0]	
QoL utility post Stroke	0.6210	[0-1]	
QoL utility PVD	0.7240	[0-1]	Bagust et al 2005 ⁶⁰
QoL utility MA	0.7850	[0-1]	Assumed to be asymptomatic
QoL utility GRP	0.7370	[0-1]	Bagust et al 2005 ⁶⁰
QoL utility HD	0.6210	[0-1]	Wasserfallen et al 2004 ⁶¹
QoL utility PD	0.5810	[0-1]	
QoL utility RT	0.7620	[0-1]	Kiberd 1995 ⁶²
QoL utility BDR	0.7450	[0-1]	Fenwick et al 2012 ⁶³
QoL utility BDR wrongly treated	0.7450	[0-1]	
QoL utility PDR laser treated	0.7150	[0-1]	
QoL utility PDR no Laser	0.7150	[0-1]	
QoL utility ME	0.7450	[0-1]	
QoL utility SVL	0.7110	[0-1]	Clarke et al 2002 ⁵⁹
QoL utility cataract	0.7690	[0-1]	Lee et al 2012 ⁶⁴
QoL utility neuropathy	0.7010	[0-1]	Bagust et al 2005 ⁶⁰
QoL utility healed ulcer	0.7850	[0-1]	Assumed not to have impact on QoL
QoL utility active ulcer	0.6150	[0-1]	Bagust et al 2005 ⁶⁰
QoL disutility amp event	-0.2800	[-1-0]	Clarke et al 2002 ⁵⁹
QoL utility post amputation	0.5050	[0-1]	
QoL disutility for major hypo events, non-medical third party assistance	-0.0183	[-1-0]	Marrett et al 2011 ⁶⁵
QoL disutility for major hypo events, medical third party assistance	-0.055	[-1-0]	Evans et al 2013 ⁶⁶
QoL for minor hypo events	Lauridsen diminishing disutilities function selected		Lauridsen et al 2014 ⁶⁷ [model autocalculates per line of therapy based on annual rate]

eAppendix References

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eAppendix Figure. PSA Scatterplot and Cost-Effectiveness Acceptability Curve

