Updated cost utility analysis for statins

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Pharmac estimates the cost-utility of providing statins to everyone with dyslipidaemia and > 10% 5-year absolute risk of cardiovascular events, at a proposed price of $0.45/day, is $1,630/QALY if statins are used over patients' remaining lifetimes, or $1,445/QALY if statins are used for 5 years and then use is reassessed.

In particular, those with established coronary heart disease (CHD) and total cholesterol > 5.5 mmol/l are estimated to have remaining lifetime and 5-year cost/QALYs of $1,285/QALY and $1,155 respectively. Others with a >10% 5-year absolute cardiovascular risk and total cholesterol > 5.5 mmol/l have $2,110 and $1,860 cost/QALYs for the same analyses. Only one group has cost/QALYs greater than $5,000 - those with <10% 5-year absolute risk (giving less value with much higher cost/QALYs at >$13-15,000/QALY):

Cost/QALYS for statins Rx, lifetime use at 10% discount rate

discount rate:	10.0%								
population group			Undiscounted values	Discounted 5-year costs, QALYs per patient					
group	5-year absolute CHD risk	potential no. pts	undiscounted QALYs	**discounted QALYs**	Rx costs	net other Vote:Health costs	% offsets	cost/QALYs	
Average daily cost/patient (ADC)					$0.60 current price simvastatin	$0.60	$0.60	**$0.60**	$0.45 future contracted price simv
Average cost/patient/year (AYC)					$219	$219	$219	**$219**	$164
past CHD >=7.5	61.6%	16,388	3.73	**1.09**	$1,362	-$397	29%	**$888**	**$575**
past CHD 6.5-7.4	43.9%	39,281	3.49	**0.93**	$1,450	-$447	31%	**$1,076**	**$688**
past CHD 5.5-6.4	31.7%	66,949	2.53	**0.54**	$1,501	-$383	25%	**$2,090**	**$1,389**
past CHD <5.5	23.8%	54,690	1.34	**0.26**	$1,502	-$236	16%	**$4,950**	**$3,482**
genetic LDs	35.3%	2,936	5.13	**0.66**	$1,843	-$1,149	62%	**$1,047**	**$352**
at risk >=20%	22.5%	25,369	1.92	**0.54**	$1,472	-$387	26%	**$2,010**	**$1,329**
at risk 15-19%	17.5%	46,187	1.80	**0.45**	$1,562	-$362	23%	**$2,661**	**$1,795**
at risk 10-14%	12.5%	107,860	1.64	**0.36**	$1,683	-$311	18%	**$3,815**	**$2,645**
low risk <10%	3.6%	1,319,776	1.05	**0.10**	$2,034	-$168	8%	**$18,768**	**$13,654**
past CHD	32.6%	177,308	2.49	**0.59**	$1,477	-$353	24%	**$1,913**	**$1,285**
others >10% risk	10.3%	182,352	1.77	**0.41**	$1,626	-$348	21%	**$3,096**	**$2,111**
total	21.3%	359,660	2.13	**0.50**	$1,552	-$350	23%	**$2,409**	**$1,631**

Note that the above estimates for using statins over patients' remaining lifetimes are based on undiscounted QALY gains (for everyone with dyslipidaemia and >10% risk) of 2.1 extra quality-adjusted life years (falling to 0.5 years after discounting at 10%), and discounted savings elsewhere in the Health Sector offsetting statin costs by 23%.

Cost/QALYS for statins Rx, 5-year use at 10% discount rate

discount rate:	10.0%								
population group			Undiscounted values	Discounted 5-year costs, QALYs per patient					
group	5-year absolute CHD risk	potential no. pts	undiscounted QALYs	**discounted QALYs**	Rx costs	net other Vote:Health costs	% offsets	cost/QALYs	
Average daily cost/patient (ADC)					$0.60 current price simvastatin	$0.60	$0.60	**$0.60**	$0.45 future contracted price simv
Average cost/patient/year (AYC)					$219	$219	$219	**$219**	$164
past CHD >=7.5	61.6%	16,388	1.49	**0.63**	$758	-$243	32%	**$823**	**$520**
past CHD 6.5-7.4	43.9%	39,281	1.28	**0.51**	$770	-$263	34%	**$986**	**$612**
past CHD 5.5-6.4	31.7%	66,949	0.78	**0.28**	$773	-$228	29%	**$1,948**	**$1,257**
past CHD <5.5	23.8%	54,690	0.39	**0.13**	$773	-$141	18%	**$4,746**	**$3,294**
genetic LDs	35.3%	2,936	1.52	**0.41**	$800	-$467	58%	**$817**	**$326**
at risk >=20%	22.5%	25,369	0.75	**0.30**	$771	-$223	29%	**$1,806**	**$1,171**
at risk 15-19%	17.5%	46,187	0.63	**0.24**	$783	-$202	26%	**$2,405**	**$1,595**
at risk 10-14%	12.5%	107,860	0.52	**0.18**	$797	-$166	21%	**$3,475**	**$2,378**
low risk <10%	3.6%	1,319,776	0.14	**0.04**	$825	-$72	9%	**$21,129**	**$15,343**
past CHD	32.6%	177,308	0.83	**0.32**	$771	-$210	27%	**$1,760**	**$1,155**
others >10% risk	10.3%	182,352	0.60	**0.22**	$790	-$188	24%	**$2,769**	**$1,861**
total	21.3%	359,660	0.71	**0.27**	$781	-$199	25%	**$2,176**	**$1,446**

Note that the above estimates for using statins over 5 years are based on undiscounted QALY gains for everyone with dyslipidaemia and >10% risk of 0.7 extra quality-adjusted life years (lower than occurs with lifetime statin use), falling to 0.27 years after discounting at 10%, and discounted savings elsewhere in the Health Sector offsetting statin costs by 25% (similar to offsets with lifetime statin use).

Pharmac's analysis is based on clinical trial data on the effectiveness of statin treatment (i.e. treated versus untreated patients), applied to models of natural history of cardiovascular disease (deaths rates, rates of non-fatal events, and calculations of life expectancy), quality of life scores for each health state, and costs of treating with pharmaceuticals and to other parts of the health sector of treating or not treating with statins.

The updated model involves a number of cohorts based on age, gender, 5-year absolute CHD risk, and total cholesterol levels. These groups relate to those defined in the updated guidelines published by New Zealand's National Heart Foundation (NHF) in 1996[1], i.e.:

- clinically proven ischaemic heart disease (NHF risk group A1:1)
- post coronary artery bypass graft (CABG) or angioplasty (A1:2)
- post heart transplant
- proven ischaemic stroke or unequivocal history of transient ischaemic attack due to arteriosclerosis (A1:3)
- unequivocal history of intermittent claudication (A1:4)
- genetic lipid disorders (familial hypercholesterolaemia, familial defective Apo B, familial combined dyslipidaemia, combined dyslipidaemia (type III)) (A2)
- insulin and non-insulin dependent diabetes with established nephropathy (albumin excretion greater than 300 mg/day) total cholesterol (A3)
- > 20% 5-year cardiovascular disease risk (B)
- 15-20% 5-year cardiovascular disease risk (C)

[1] NHF Guidelines for the assessment and management of dyslipidaemia. NZ Med J 1996;109:224-32.

- 10-15% 5-year cardiovascular disease risk (D)
- < 10% 5-year cardiovascular disease risk (E)

Pharmac has done similar analysis previously, and the methods and results have been described in some detail (see Pharmac documents #26723 and #26220 of June 1997, available on Pharmac's website at http://www.pharmac.govt.nz/download/statin97methods.pdf and http://www.pharmac.govt.nz/download/statin97results.pdf or freephone 0800 66 00 50). The current analysis differs from those of May 1997 and subsequently by the following features:

- Use of both 5-year and remaining lifetime timespans (previously had used 5-year horizon only).

- Inclusion of cerebrovascular (stroke) and peripheral vascular disease (PVD) outcomes (previously only CHD deaths and non-fatal events). Stroke and PVD event rates (a) for each cohort are derived from 4S[2] placebo event rates (b), 4S placebo CHD events (b) and the cohort's baseline CHD event rate (d), where $a = b \times d \div c$. Patients with stroke are assigned a quality of life score of 0.72 (from NZBD[3] disability weight of 0.285, a case-weighted average including no sequelae of Netherlands BD weights[4]).

- Updated absolute risk estimates for genetic lipid disorders (familial hyperlipidaemia etc) - see Pharmac document #31473 of November 1997, available on Pharmac's website at http://www.pharmac.govt.nz/download/statin97A2FH.pdf .

- Updated relative risk reductions, now constant across all categories of age, gender and baseline cardiovascular risk (La Rosa 1999[5], HTA meta-analysis 1999[6], preliminary results from the MRC/BHF Heart Protection Study (HPS)[7]) at 42% for fatal (CHD death), 30% for non-fatal major CHD events, 37% for coronary surgery or angioplasty, 11% for non-MI acute CHD, 36% for both fatal and non-fatal stroke, and 27% for peripheral vascular disease events, from the 4S trial (had previously varied according to age, gender, and baseline cardiovascular risk). Note that stratification according to baseline total cholesterol levels still occurs for those with established CHD as previously, particularly affecting those with TC < 5.5 mmol/l (consistent with 4S[8], CARE[9] and LIPID[10] relative risk reduction patterns).

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[2] Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian simvastatin survival study (4S). Lancet 1994;344:1383-9.
[3] Tobias M. The Burden of Disease and Injury in New Zealand. Public Health Intelligence Occasional Bulletin No. 1. Wellington: Ministry of Health, 2001.
[4] Stouthard MEA, Essink-Bot M, Bonsel GJ, Barendregt PGN, et al. Disability weights for diseases in the Netherlands. Rotterdam: Department of Public Health, Erasmus University, 1997.
[5] LaRosa JC, He J, Vupputuri S. Effect of statins on risk of coronary disease: a meta-analysis of randomized controlled trials. JAMA. 1999;282:2340-6.
[6] Ebrahim S, Smith GD, McCabe C, Payne N, Pickin M, Sheldon TA, Lampe F, Sampson F, Ward S, Wannamethee G. What role for statins? A review and economic model. Health Technol Assess. 1999;3:i-iv, 1-91.
[7] http://www.ctsu.ox.ac.uk/projects/hps.shtml
[8] Scandinavian Simvastatin Survival Study Group. Baseline serum cholesterol and treatment effect in the Scandinavian Simvastatin Survival study (4S). Lancet 1995;345:1274-5.
[9] Sacks FM, Pfeffer MA, Moye LA, Roubleau JL, Rutherford JD, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. N Engl J Med 1996;335:1001-9.
[10] The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in ptients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998;339:1349-57.

- Use of 10-year age bands for cohorts aged 35-44 to 75-84 (previously 5-year age bands 35-30 to 80-84).

- Updated non-pharmaceutical Health Sector costs (HFA DRG prices 99/00), and updated clinical trial data (unpublished) on the effectiveness of statins at reducing such costs over time (previously had used attributable risk estimates to help derive costs offsets):

Health sector costs/patient (differences between simvastatin and placebo groups costed on basis of NZ DRG costings)

	Myocardial Infarction drg 121-123	Bypass drg 106,107	Revascularisation drg 112	Angina drg 124, 125, 140	Arrhythmias drg 138	Cerebrovascular drg 14	Cerebrovascular drg 15	Revascularisation drg131/132	Others	total
	MI	CABG	PTCA	angina	arrhythmias	CVA	TIA	vascular proc	other - not categorised by MSD	
unit cost	**$3.729**	**$12.093**	**$3.456**	**$1.614**	**$2.779**	**$14.581**	**$1.967**	**$5.939**	**$2.044**	
placebo										
Year 1	$238	$256	$12	$62	$16	$72	$3	$8	$19	$687
Year 2	$201	$354	$16	$57	$20	$85	$3	$13	$25	$774
Year 3	$208	$397	$20	$73	$19	$125	$2	$3	$25	$871
Year 4	$164	$462	$22	$62	$18	$105	$9	$8	$29	$878
Year 5	$176	$305	$17	$52	$24	$98	$4	$8	$29	$712
Year 5.4	$69	$92	$17	$22	$8	$39	$5	$3	$17	$272
Total	$1,057	$1,866	$104	$329	$104	$525	$25	$43	$143	$4,194
5 years	$979	$1,728	$96	$305	$96	$486	$23	$40	$132	$3,884
simvastatin										
Year 1	$170	$245	$19	$74	$23	$66	$2	$11	$10	$618
Year 2	$128	$261	$14	$47	$19	$92	$4	$8	$15	$587
Year 3	$101	$267	$20	$42	$33	$85	$4	$5	$20	$577
Year 4	$101	$152	$19	$39	$33	$53	$4	$5	$23	$428
Year 5	$112	$169	$19	$36	$35	$66	$4	$11	$16	$468
Year 5.4	$50	$76	$8	$15	$29	$33	$1	$8	$16	$235
Total	$662	$1,171	$98	$254	$170	$394	$18	$48	$99	$2,913
5 years	$613	$1,084	$91	$235	$158	$365	$16	$45	$92	$2,697

- Use only of potential (ideal) cost/QALYs based on intention-to-treat results from clinical trials (with relatively high patient continuation/adherence rates in a select population) (previously had used both potential and actual cost/QALYs, where actual cost/QALYs adjusted for likely continuation/adherence rates expected for all New Zealand users).

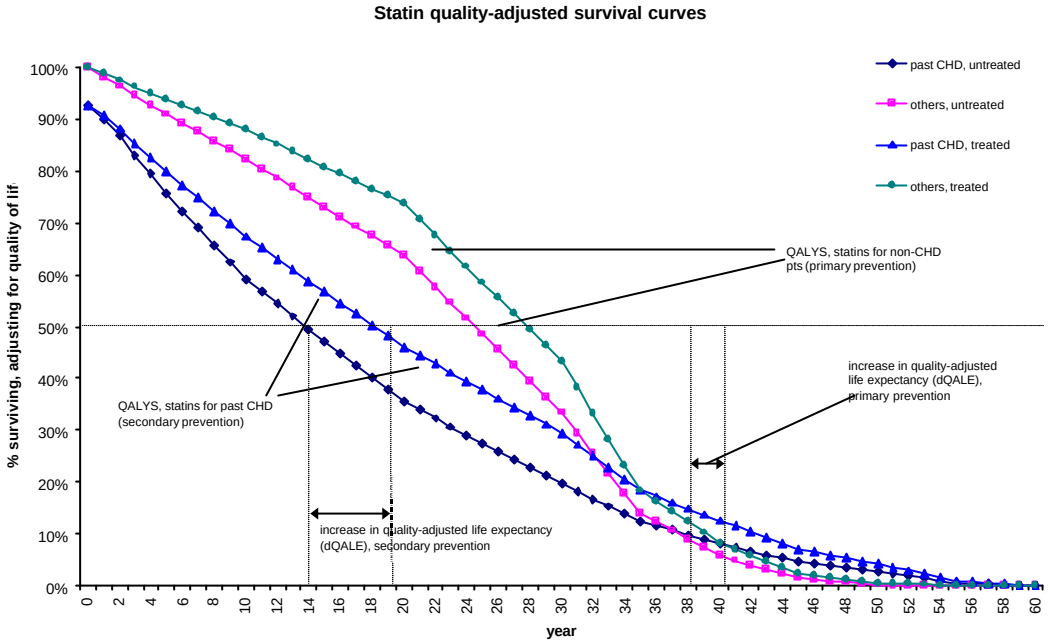
- 10% discount rate (PHARMAC's current rate for economic analyses) (previously 11.4%).

Although total cholesterol levels rather than the more predictive total:HDL ratios are used to define the cohorts used in the model, differences are likely to be minor.

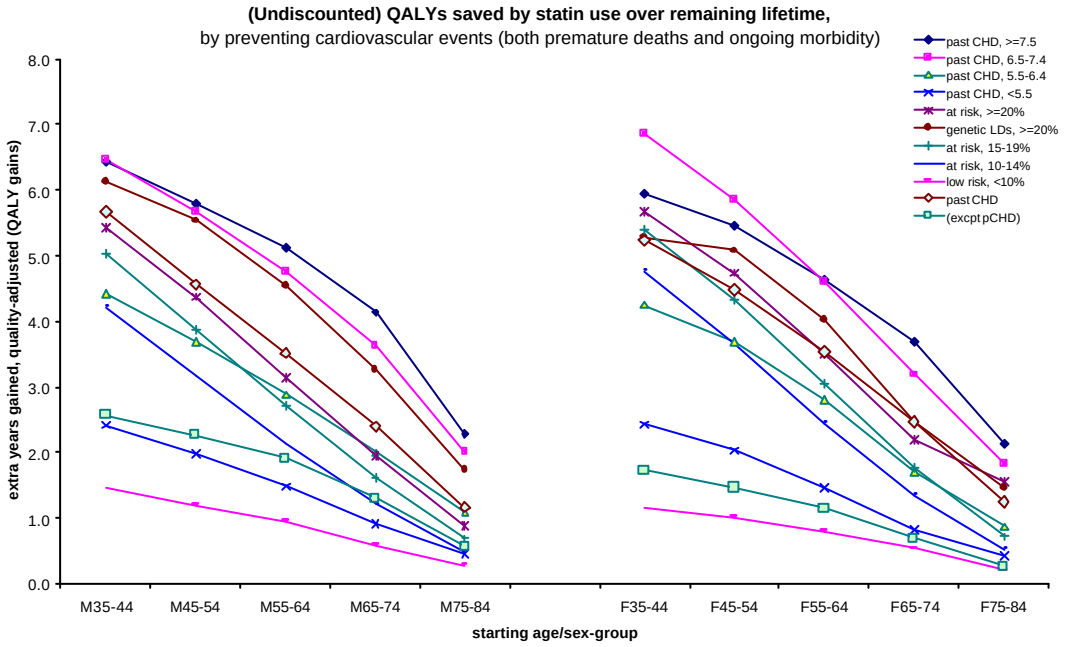
For patients without established CHD (i.e. primary prevention - NHF risk groups A2 and B-E above), the model assumes dyslipidaemia i.e. total cholesterol > 5.5 mmol/l.

The updated model has not formally included coronary artery bypass graft (CABG) and angioplasty patients, heart transplant patients, patients with proven ischaemic stroke or unequivocal history of transient ischaemic attack due to arteriosclerosis, patients with unequivocal history of intermittent claudication, or diabetes with established nephropathy (NHF groups A1:2, A1:3, A1:4 and A3). Results for these groups however are expected to be at least as beneficial and cost-effective as occur for those with > 20% 5-year cardiovascular disease risk (NHF group B).

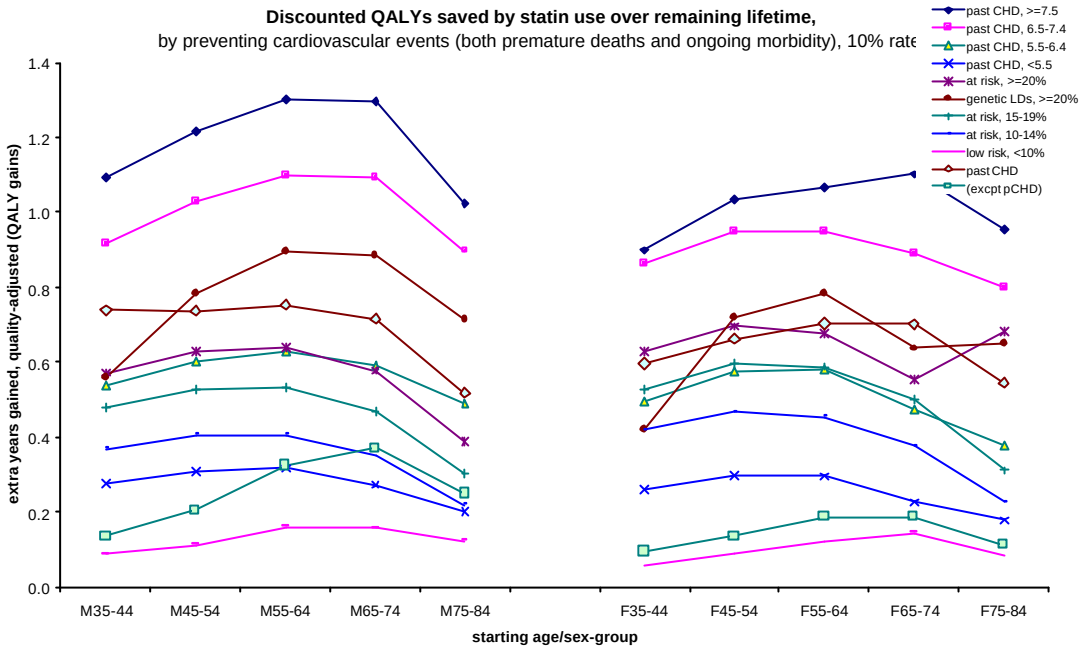
The modelling creates a series of quality-adjusted survival curves, showing the effects of statins on quality-adjusted life expectancy of untreated patients at various levels of risk. QALY gains are seen by the gap between untreated and treated cohorts, e.g.:



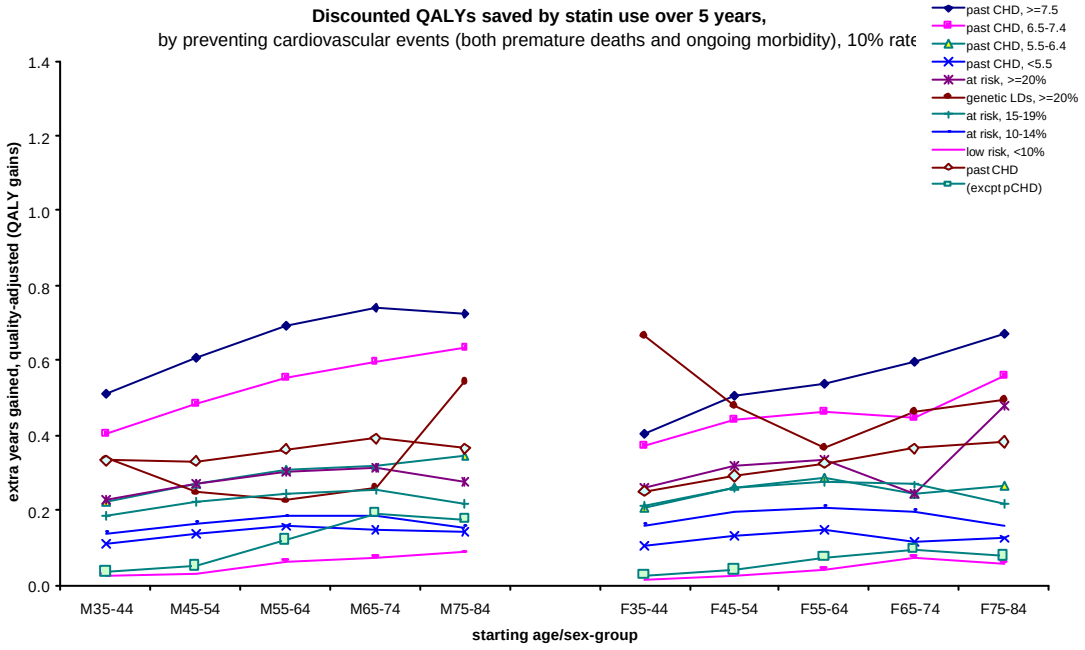
Before discounting, QALY gains increase with cardiovascular risk but are also highest for younger age groups:



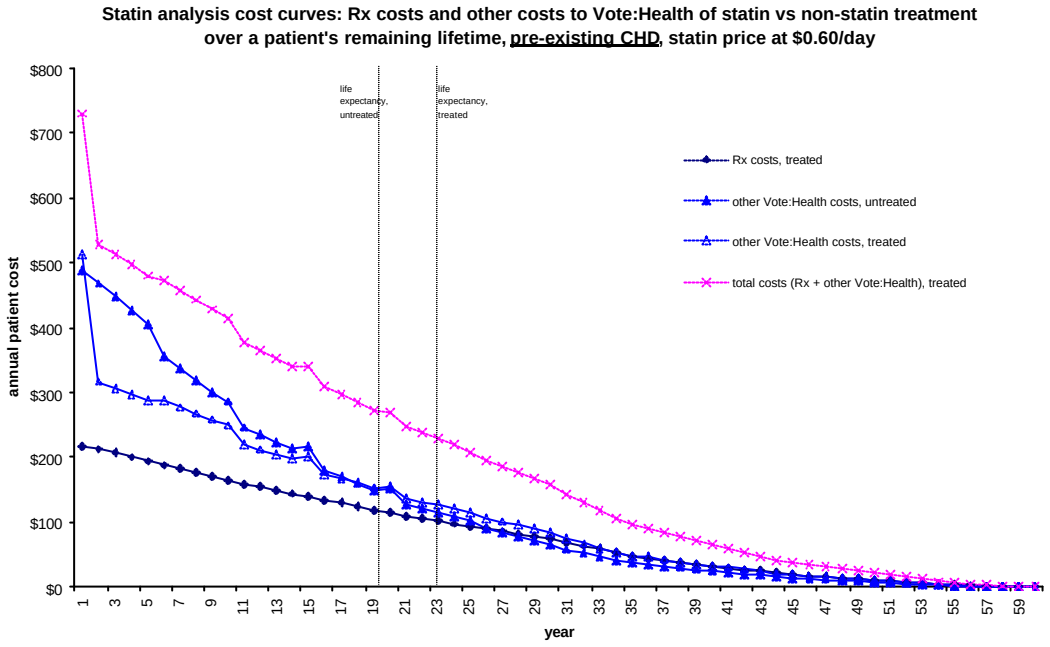
However, discounting blunts much of these age gradients, especially for those with established CHD (who have maximum QALY gains for men aged 55-74):



QALYs saved by 5 years' statin use are somewhat less than for the above remaining lifetime use:

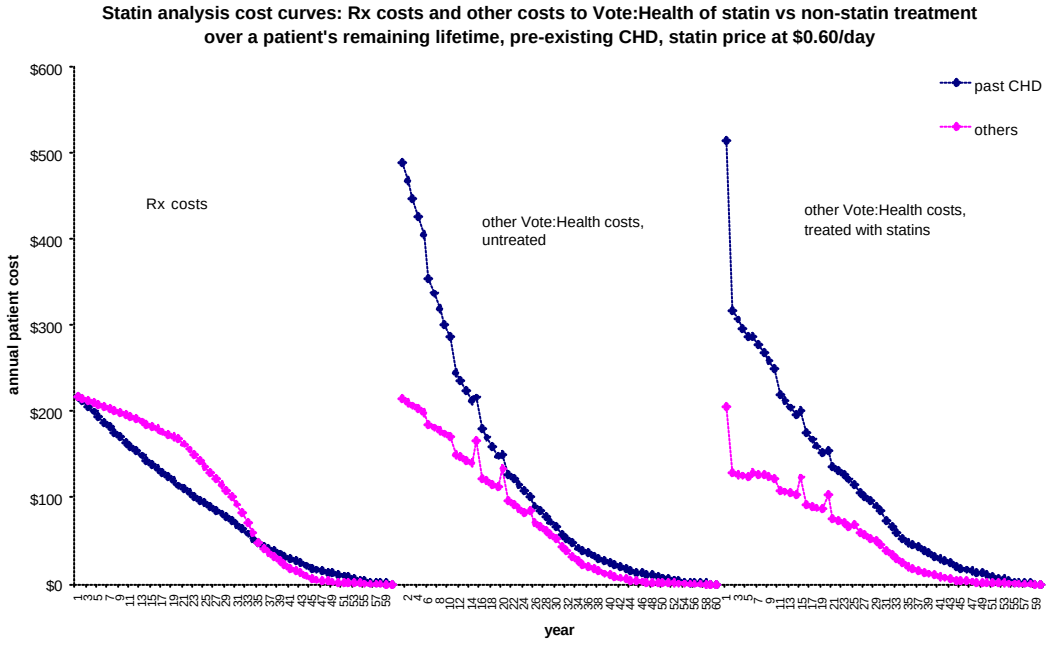


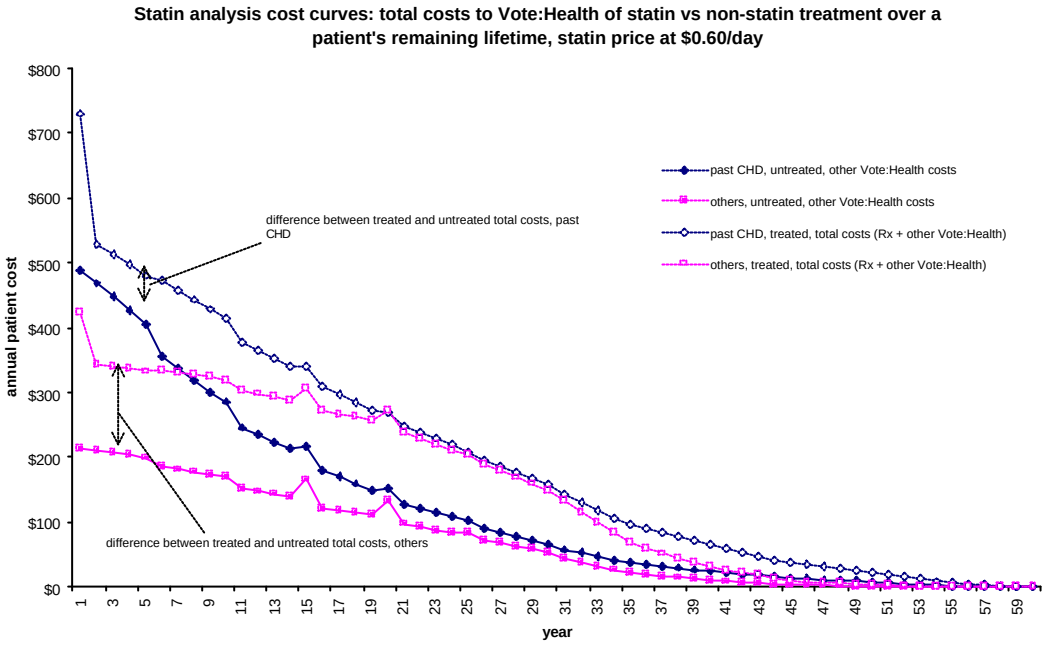
Likewise, the model shows patterns of pharmaceutical and non-pharmaceutical costs of treating or not treating various groups with statins. Patients with established CHD have lower non-statin Health Sector costs when treated with statins than those who are not treated. However, this pattern is reversed by the cost of statins causing total costs to be higher for treated groups:



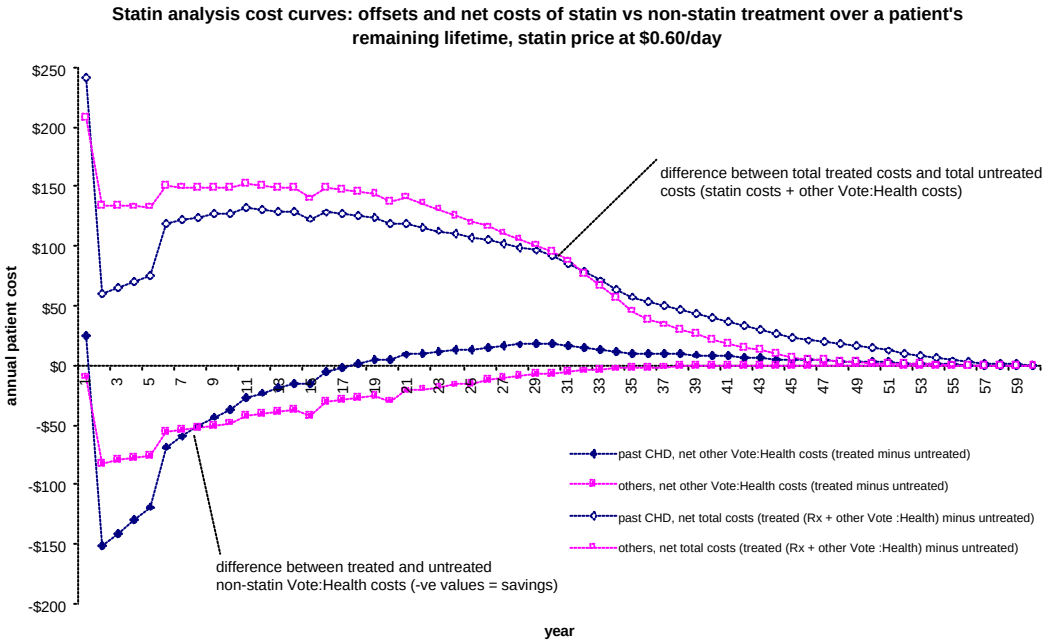
Note that the above and all following graphs relate to statins priced at $0.60 weighted average daily cost.

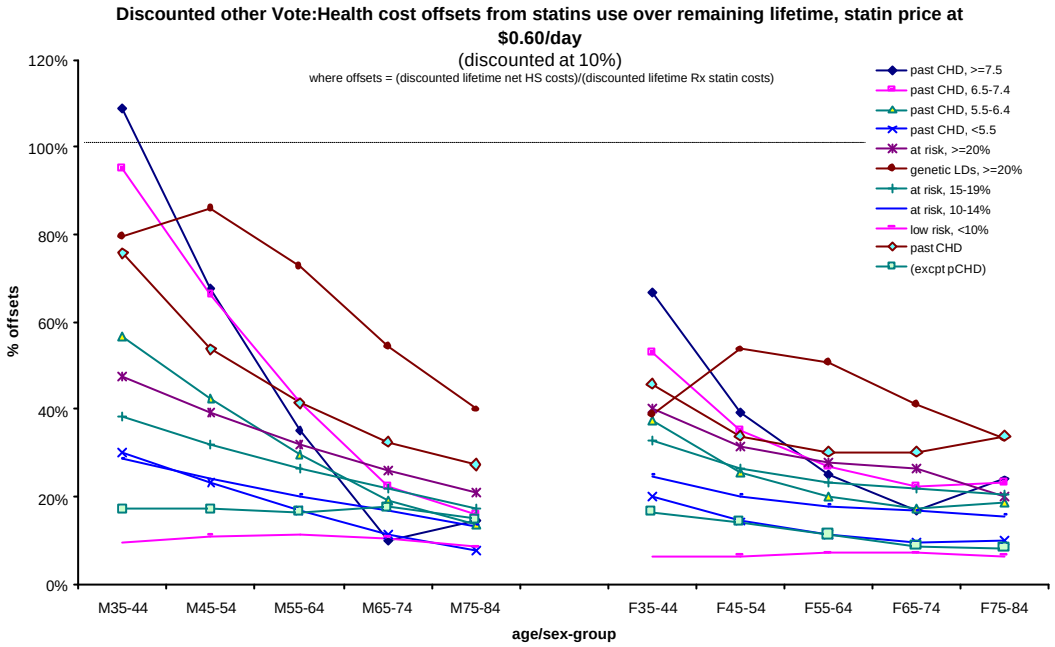
Non-statin Health Sector costs are lower and occur later for patients without established CHD, but patterns are otherwise similar to CHD for treated and untreated patients:



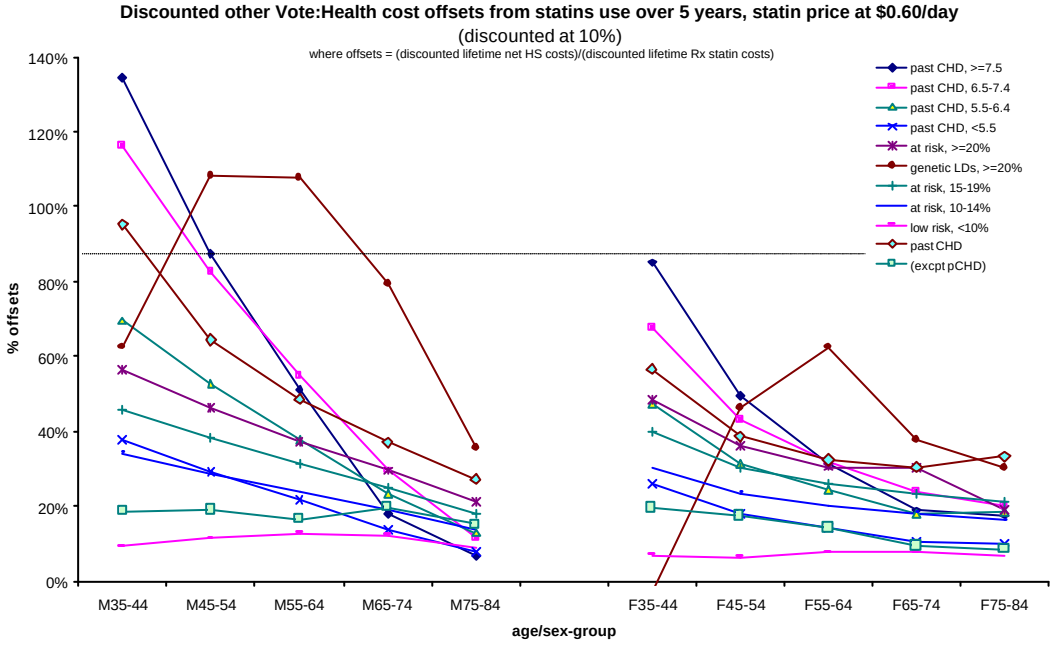


Savings from statin use occur early on, as non-statin Health Sector costs decrease alongside reduced cardiovascular events. This pattern reverses in later years as treated patients incur higher costs when surviving for longer:



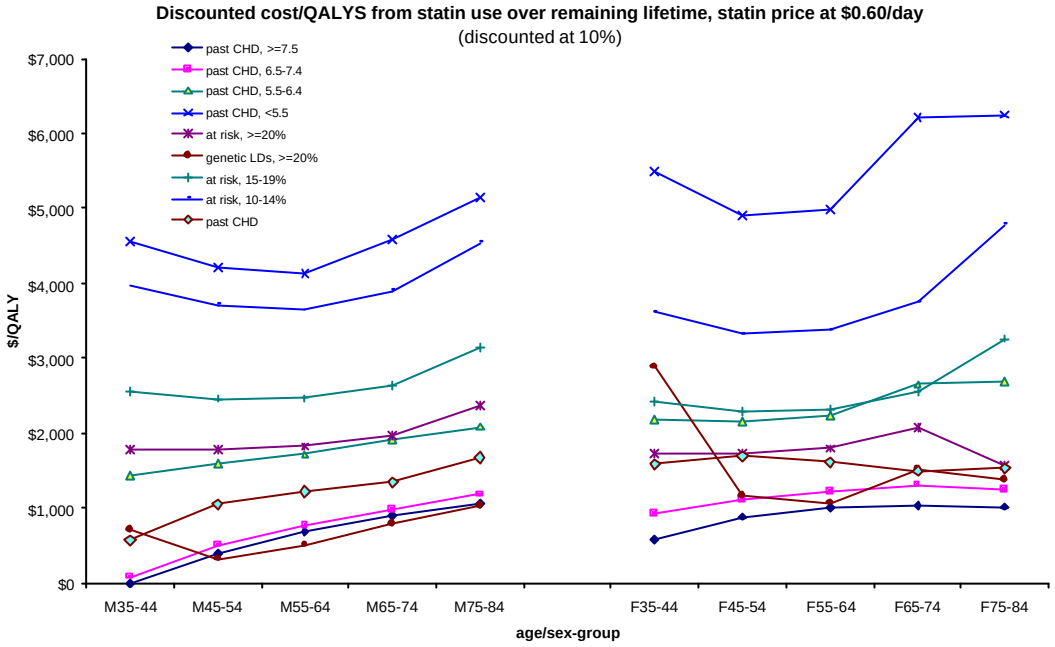


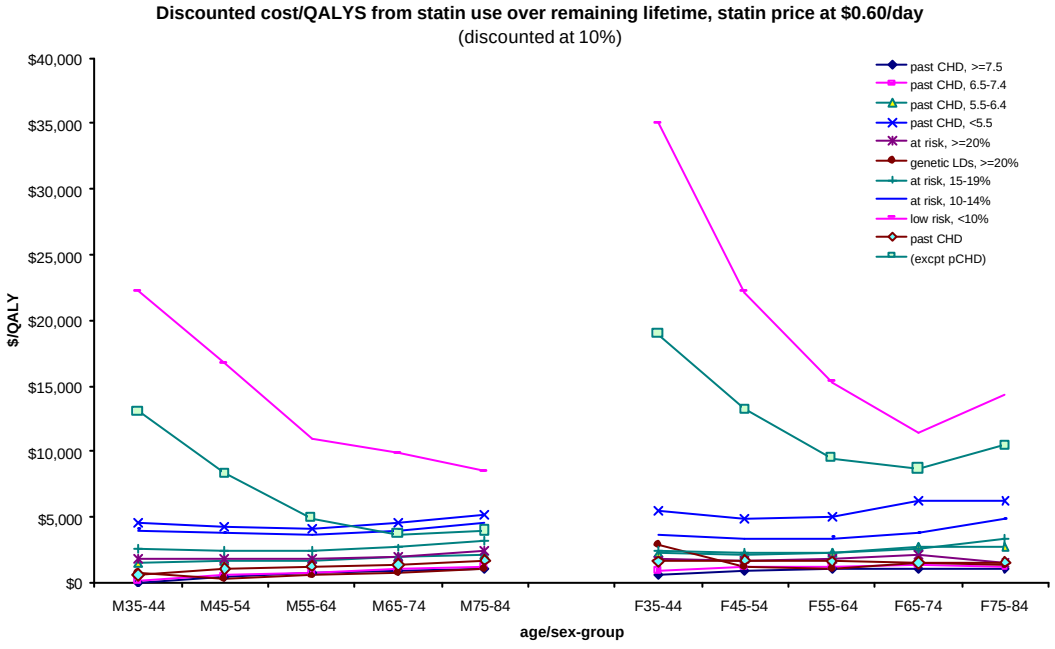
Patterns of net costs differ for 5-year statin use when compared with the above remaining lifetime use:



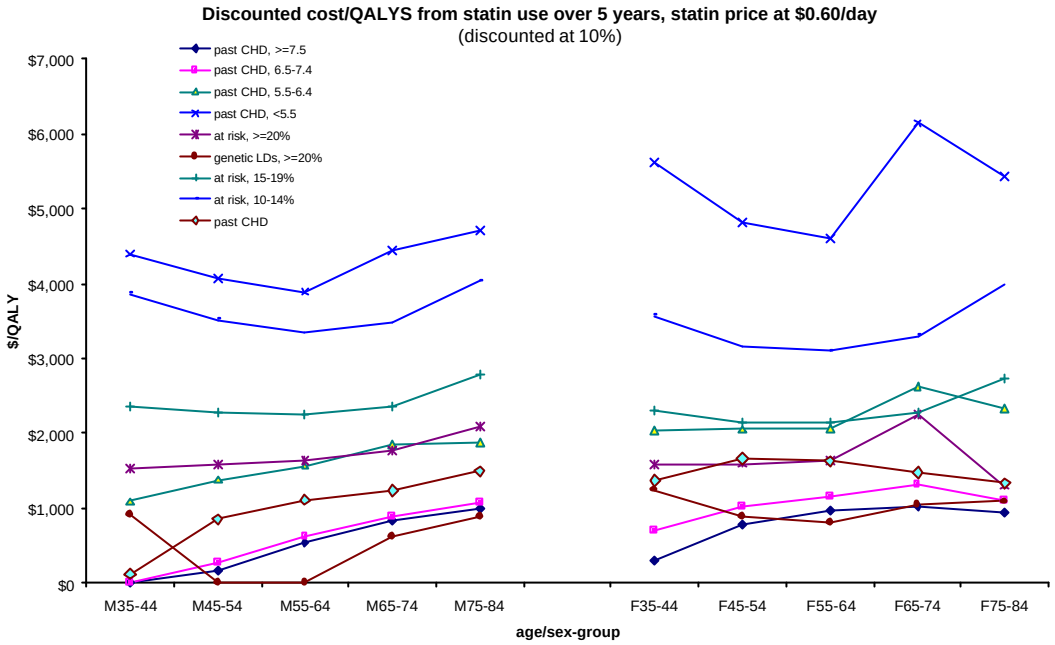
QALY gain and net cost patterns combine to form cost/QALY patterns. Cost/QALYs largely relate to overall cardiovascular risk. Best value-for-money (lowest cost/QALYS) occurs with those groups with highest absolute cardiovascular risk, i.e. patients with established CHD and total cholesterol >= 7.5 mmol/l. Value decreases (cost/QALYS increase) as absolute risk

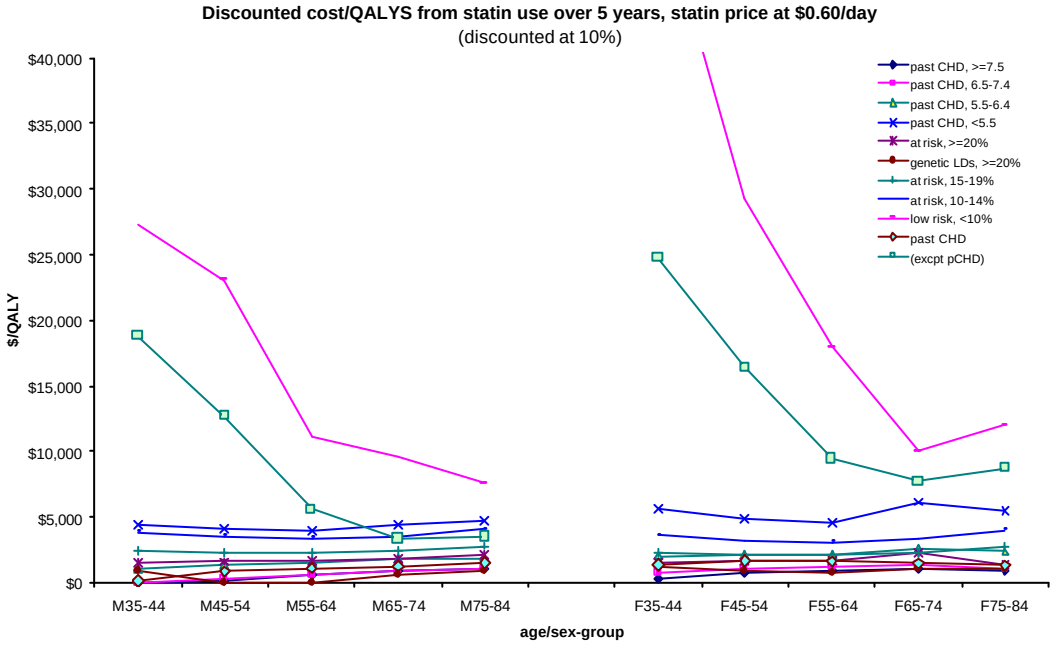
decreases. For most risk groups, especially very high risk, value is greatest at younger age-groups. However, for low risk patients (<10% 5-year risk) value is lowest at younger ages:





Patterns again differ for 5-year statin use when compared with the above remaining lifetime use:


Discounted cost/QALYS from statin use over 5 years, statin price at $0.60/day
(discounted at 10%)
past CHD, >=7.5
past CHD, 6.5-7.4
past CHD, 5.5-6.4
past CHD, <5.5
at risk, >=20%
genetic LDs, >=20%
at risk, 15-19%
at risk, 10-14%
past CHD
$/QALY
$7,000
$6,000
$5,000
$4,000
$3,000
$2,000
$1,000
$0
M35-44
M45-54
M55-64
M65-74
M75-84
F35-44
F45-54
F55-64
F65-74
F75-84
age/sex-group


Discounted cost/QALYS from statin use over 5 years, statin price at $0.60/day
(discounted at 10%)
past CHD, >=7.5
past CHD, 6.5-7.4
past CHD, 5.5-6.4
past CHD, <5.5
at risk, >=20%
genetic LDs, >=20%
at risk, 15-19%
at risk, 10-14%
low risk, <10%
past CHD
(excpt pCHD)
$/QALY
$40,000
$35,000
$30,000
$25,000
$20,000
$15,000
$10,000
$5,000
$0
M35-44
M45-54
M55-64
M65-74
M75-84
F35-44
F45-54
F55-64
F65-74
F75-84
age/sex-group