

Appendix A

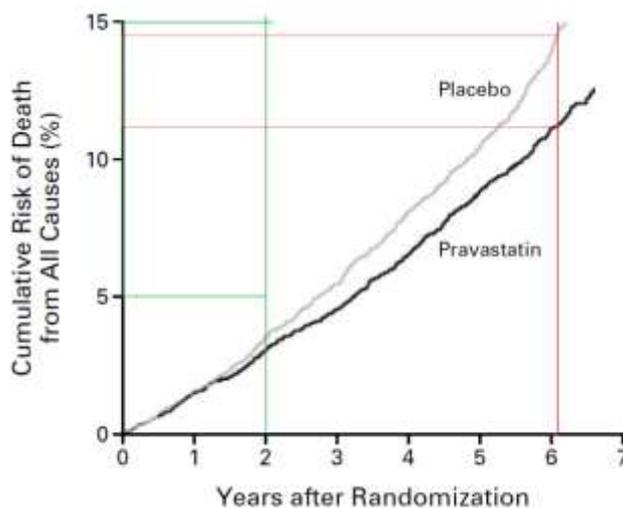
Statin trials excluded from the endpoint postponement analysis

Study	Reason for exclusion
Wanner C, Krane V, Marz W, et al. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. <i>N Engl J Med</i> 2005; 353: 238–48.	Kaplan-Meier plot on all-cause mortality was not published
Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. <i>JAMA</i> 1998; 279: 1615–22.	All-cause mortality was not analyzed
Holdaas H, Fellstrom B, Jardine AG, et al. Effect of fluvastatin on cardiac outcomes in renal transplant recipients: a multicentre, randomised, placebo-controlled trial. <i>Lancet</i> 2003; 361: 2024–31.	Kaplan-Meier plot on all-cause mortality was not published
Koren MJ, Hunninghake DB. Clinical outcomes in managed-care patients with coronary heart disease treated aggressively in lipidlowering disease management clinics: the alliance study. <i>J Am Coll Cardiol</i> 2004; 44: 1772–79	Kaplan-Meier plot on all-cause mortality was not published
Knopp RH, d’Emden M, Smilde JG, Pocock SJ. Efficacy and safety of atorvastatin in the prevention of cardiovascular end points in subjects with type 2 diabetes: the Atorvastatin Study for Prevention of Coronary Heart Disease Endpoints in non-insulin-dependent diabetes mellitus (ASPEN). <i>Diabetes Care</i> 2006; 29: 1478–85.	Kaplan-Meier plot on all-cause mortality was not published
de Lemos JA, Blazing MA, Wiviott SD, et al. Early intensive vs a delayed conservative simvastatin strategy in patients with acute coronary syndromes: phase Z of the A to Z trial. <i>JAMA</i> 2004; 292: 1307–16.	More versus less aggressive statin therapy
Fellstrom BC, Jardine AG, Schmieder RE, et al, for the AURORA Study Group. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. <i>N Engl J Med</i> 2009; 360: 1395–407.	Kaplan-Meier plot on all-cause mortality was not published
Sacks FM, Pfeffer MA, Moyé LA, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. Cholesterol and Recurrent Events Trial investigators. <i>N Engl J Med</i> 1996; 335: 1001–09.	Kaplan-Meier plot on all-cause mortality was not published
Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20 536 high-risk individuals: a randomised placebo-controlled trial. <i>Lancet</i> 2002; 360: 7–22.	Kaplan-Meier plot on all-cause mortality was not published
Pedersen TR, Faergeman O, Kastelein JJ, et al. High-dose atorvastatin vs usual-dose simvastatin for secondary prevention after myocardial infarction: the IDEAL study: a randomized controlled trial. <i>JAMA</i> 2005; 294: 2437–45.	More versus less aggressive statin therapy
Serruys PWJC, de Feyter P, Macaya C, et al, for the Lescol Intervention Study (LIPS) Investigators. Fluvastatin for prevention of cardiac events following successful first percutaneous coronary intervention. <i>JAMA</i> 2002; 287: 3215–22.	Kaplan-Meier plot on all-cause mortality was not published
The Post Coronary Artery Bypass Graft Trial Investigators. The effect of aggressive lowering of low-density lipoprotein cholesterol levels and low-dose anticoagulation on obstructive changes in saphenous-vein coronary-artery bypass grafts. <i>N Engl J Med</i> 1997; 336: 153–62.	More versus less aggressive statin therapy

<p>Shepherd J, Blauw GJ, Murphy MB, et al, on behalf of the PROSPER study group. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomised controlled trial. <i>Lancet</i> 2002; 360: 1623–30.</p>	<p>Kaplan-Meier plot on all-cause mortality was not published</p>
<p>Cannon CP, Braunwald E, McCabe CH, et al. Intensive versus moderate lipid lowering with statins after acute coronary syndromes. <i>N Engl J Med</i> 2004; 350: 1495–504.</p>	<p>More versus less aggressive statin therapy</p>
<p>Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine (SEARCH) Collaborative Group. Intensive lowering of LDL cholesterol with 80 mg versus 20 mg simvastatin daily in 12 064 survivors of myocardial infarction: a double-blind randomised trial. <i>Lancet</i> 2010; published online Nov 9. DOI:10.1016/S0140-6736(10)60310-8.</p>	<p>More versus less aggressive statin therapy</p>
<p>LaRosa JC, Grundy SM, Waters DD, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. <i>N Engl J Med</i> 2005; 352: 1425–35.</p>	<p>More versus less aggressive statin therapy</p>

## Appendix B

Example of calculation of endpoint postponement, LIPID study.



1. The graph is copied from the published article in PDF format to the program Paint (300% zoom) where it is saved in bitmap format. A reference area is drawn by straight lines, using the tick marks of the graph, here 0-2 years follow-up on the x-axis and 5-15% cumulative risk on the y-axis (green box). A vertical line to represent the right border of the area between curves is drawn at 6.1 years (red line).

2. The graph is imported into Adobe Photoshop Elements 10, and the area in the reference area and between survival curves is redrawn by using the polygonal lasso tool. The size of the areas can be read directly. In this example:

Size of reference area: 106220 pixels

Size of area between survival curves: 32118 pixels

3. The average postponement of delay is calculated as:

$\text{Pixel count (area between curves)} * \Delta y \text{ (reference area)} * \Delta x \text{ (reference area)} / \text{Pixel count (reference area)}$

In this example:

$$32118 * 0.10 * 2 \text{ years} / 106220 = 22.07 \text{ days}$$

All analyses were carried out by three observers and the results are expressed as the average of these three individual observations.