# The assumption of no statin effect in 1991-1992

In 1991-92 statins were not widely used, and only reserved for individuals with very high cholesterol. This is supported from the Health Survey for England 1991-92 data; utilisation of any lipid lowering medications, including statins, was 0.5% (95% CI: 0.3% to 1.0%) and the mean total cholesterol of the participants, on this medication, was 6.46 mmol/L (95% CI: 6.04 to 6.87). Moreover, statins available at that time were less effective and generally were prescribed in smaller strengths than today. So the Ew for 1991-92 would be much lower than the Ew for 2001-12. Finally statins are the most effective medication in lowering total cholesterol on individuals.

Let us consider the following scenario. All the lipid lowering medication users in 1991-92 were on statins and statins effectiveness was as high as we observed in 2011-12 (Ew for 1991-92 equal to Ew for 2011-12). Even in this extreme and highly unlikely scenario, the mean total cholesterol of the population for 1991-92 with the effect of statin removed, would be 5.87 mmol/L (95% CI: 5.83 to 5.91). Not much different from the observed one of 5.86 mmol/L (95% CI: 5.82 to 5.90). Therefore, we consider the bias from our decision to ignore any possible statin effect in 1991-92 negligible.

Table 1. Final percentage reductions of each specific statin and strength that were used for the estimation of the weighted average $E\_{w}$

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| **Chemical name** | **Strength** | **Total cholesterol reduction** | **Weights** **(for the weighted mean** $E\_{w}$**)** |
| Atorvastatin | 10 | 27.3% (24.9-30.2%) | 0.1046 |
| Atorvastatin | 20 | 32.7% (30.1-35.7%) | 0.0361 |
| Atorvastatin | 30 | 35.8% (34.8-36.7%)\* | 0.0005 |
| Atorvastatin | 40 | 38.4% (34.6-42.3%) | 0.0350 |
| Atorvastatin | 60 | 41.0% (39.7-42.3%)\* | 0.0005 |
| Atorvastatin | 80 | 42.8% (37.4-48.0%) | 0.0118 |
| Fluvastatin Sodium | 20 | 16.4% (14.6-18.4%) | 0.0006 |
| Fluvastatin Sodium | 40 | 20.7% (19.0-22.5%) | 0.0173 |
| Fluvastatin Sodium | 80 | 23.3% (20.6-25.9%) | 0.0163 |
| Pravastatin Sodium | 5 | 10.4% (0.7-20.2%) | 0.0001 |
| Pravastatin Sodium | 10 | 14.5% (12.5-16.2%) | 0.0038 |
| Pravastatin Sodium | 20 | 17.7% (16.9-18.9%) | 0.0111 |
| Pravastatin Sodium | 40 | 22.0% (20.7-23.0%) | 0.0106 |
| Rosuvastatin Calcium | 5 | 25.9% (24.7-27.6%) | 0.0114 |
| Rosuvastatin Calcium | 10 | 29.0% (27.8-30.6%) | 0.0214 |
| Rosuvastatin Calcium | 20 | 32.1% (30.9-33.6%) | 0.0042 |
| Rosuvastatin Calcium | 40 | 35.2% (34.0-36.6%) | 0.0012 |
| Simvastatin | 10 | 20.1% (18.9-21.7%) | 0.0477 |
| Simvastatin | 20 | 23.5% (22.4-25.0%) | 0.4261 |
| Simvastatin | 25 | 24.6% (24.3-25.0%)\* | 0.0001 |
| Simvastatin | 40 | 27.0% (25.2-28.9%) | 0.2339 |
| Simvastatin | 80 | 30.4% (29.6-31.3%) | 0.0045 |
| Simvastatin & Ezetimibe | 20 | 23.5% (22.4-25.0%) | 0.0003 |
| Simvastatin & Ezetimibe | 40 | 27.0% (25.2-28.9%) | 0.0008 |
| Simvastatin & Ezetimibe | 80 | 30.4% (29.6-31.3%) | 0.0001 |
| \* Values derived from linear regression with total cholesterol reduction as the dependent variable and the natural logarithm of strength as the independent one. The model was weighted against the inverse variance of the cholesterol reduction (not presented in this table) |

Table 2. Predicted mean total cholesterol (mmol/L) overall, and by age group, sex and quintiles of index of multiple deprivation (QIMD) (1 = most affluent, 5 = most deprived) in England, 2011-12. Socioeconomic trends are also presented. Brackets contain 95% confidence intervals.

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| --- | --- | --- | --- | --- |
|  | **18-34 (years)** | **35-54** | **55+** | **Overall\*** |
| **QIMD** | **Men** | **Women** | **Men** | **Women** | **Men** | **Women** |
| 1 (most affluent) | 4.81 (4.61 to 5.01) | 4.76 (4.60-4.92) | 5.60 (5.49 to 5.70) | 5.27 (5.16 to 5.39) | 5.64 (5.52 to 5.75) | 6.07 (5.97 to 6.17) | 5.50 (5.40 to 5.61) |
| 2 | 4.71 (4.56 to 4.86) | 4.46 (4.31 to 4.61) | 5.55 (5.40 to 5.69) | 5.24 (5.12 to 5.36) | 5.60 (5.48 to 5.72) | 6.04 (5.94 to 6.15) | 5.44 (5.33 to 5.54) |
| 3 | 4.64 (4.41 to 4.86) | 4.71 (4.53 to 4.88) | 5.73 (5.58 to 5.89) | 5.28 (5.17 to 5.40) | 5.47 (5.34 to 5.59) | 6.13 (6.00 to 6.25) | 5.43 (5.31 to 5.54) |
| 4 | 4.84 (4.65 to 5.02) | 4.61 (4.46 to 4.77) | 5.60 (5.42 to 5.78) | 5.42 (5.26 to 5.58) | 5.57 (5.41 to 5.74) | 5.99 (5.84 to 6.14) | 5.40 (5.28 to 5.51) |
| 5 (most deprived) | 4.79 (4.57 to 5.01) | 4.61 (4.46 to 4.76) | 5.58 (5.42 to 5.74) | 5.45 (5.30 to 5.60) | 5.38 (5.19 to 5.57) | 5.87 (5.69 to 6.05) | 5.28 (5.17 to 5.39) |
| **All** | 4.75 (4.66 to 4.84) | 4.62 (4.55 to 4.69) | 5.61 (5.54 to 5.68) | 5.32 (5.26 to 5.38) | 5.55 (5.49 to 5.61) | 6.03 (5.98 to 6.09) |  |
| **Slope of the trend** | 0.02 (-0.05 to 0.08) | -0.01 (-0.06 to 0.04) | 0.00 (-0.04 to 0.04) | 0.05 (0.01 to 0.09) | -0.05 (-0.10 to-0.01) | -0.04 (-0.08 to0.01) | -0.01 (-0.03 to0.01)\* |
| ***p* for trend** | 0.63 | 0.76 | 0.90 | **0.01** | **0.03** | 0.09 | 0.45\* |
| \* Adjusted for age and sex |