Assessing long-term effectiveness and cost-effectiveness of statin therapy in the UK: a modelling study using individual participant data sets

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Scientific summary

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Scientific summary

Background

Despite substantial declines in cardiovascular disease (CVD) morbidity and mortality across high-income countries in recent decades, CVD remains a major disease burden. Across randomised trials, statin therapy has been reliably shown to reduce rates of CVD irrespective of age, sex, CVD risk and comorbidities, with more potent statin regimens achieving larger reductions in low-density lipoprotein cholesterol (LDL-C), demonstrating larger CVD risk reductions. While generally safe, statin therapy has been linked to small excesses in muscle events and incident diabetes.

Objectives

To develop a reliable evaluative framework, informed by large UK individual participant data (IPD), and to assess the long-term net health effects and cost-effectiveness of statin therapy across a wide range of UK population categories.

Methods

A CVD microsimulation policy model was developed using the Cholesterol Treatment Trialists' Collaboration (CTTC) data and the UK Biobank (UKB) cohort data. CTTC IPD and UKB IPD informed parametric proportional hazards risk equations for myocardial infarction (MI), stroke, coronary revascularisation, incident diabetes, incident cancer and vascular and nonvascular death using participant characteristics. UKB and linked UK primary and hospital care data and NHS reference costs informed healthcare costs related to participant characteristics and disease events (2020–1 Great British pounds); £1.10 standard and £1.68 higher-intensity generic statin treatment per 28 tablets. Health Survey for England data informed health-related quality of life (HRQoL) related to participant characteristics and disease events. CTTC IPD meta-analyses and further meta-analyses of trials and cohort studies informed the effects of statin therapies on cardiovascular events and the excess risks of myopathy, rhabdomyolysis and incident diabetes with statin therapy.

The net health effects and cost-effectiveness of lifetime standard statin (35–45% LDL-C reduction) and of higher-intensity (≥ 45% LDL-C reduction) statin therapy prescribed and monitored in the UK primary healthcare service were assessed. We report the quality-adjusted life-years (QALYs) gained and incremental cost per QALY gained with the two levels of intensity of statin regimens from the perspective of UK healthcare services across UKB and Whitehall II participants in categories by previous CVD status, sex, age (40–49; 50–59; 60–70, ≥ 70 years), 10-year CVD risk [QRISK®3 (%): < 5; 5–10, 10–15, 15–20, ≥ 20] and/or LDL-C level (< 3.4, 3.4–4.1, ≥ 4.1 mmol/l) at statin therapy initiation.

In the base-case analyses, the proportional effects of statin therapy on disease risks were assumed constant across categories of individuals and over time. Key parameters were varied in sensitivity and scenario analyses, including scenarios with hypothetical disutility of daily statin treatment, higher statin cost, and more limited reductions in cardiovascular events with statin therapy.

Results

A total of 117,896 participants in 16 statin versus control trials in the CTTC, 501,854 UKB participants and 6761 Whitehall II participants informed the analyses. Age, sex, socioeconomic deprivation, smoking,

hypertension, diabetes, MI and stroke events were key determinants of CVD risk. Model-predicted event rates corresponded well to observed rates across participant categories in UKB and Whitehall II studies. Modelled CVD and nonvascular disease events were associated with reductions in HRQoL and increases in hospital admission and primary care costs.

Across categories of participants 40–70 years old, there were estimated gains in undiscounted QALYs of 0.20–1.09 per person with lifetime use of standard statin therapy, and higher-intensity statin therapy added a further 0.03–0.20 QALYs per person. Among participants aged ≥ 70 years, lifetime use of standard statin increased quality of life-adjusted life expectancy by 0.24–0.70 QALYs and higher-intensity statin by further 0.04–0.13 QALYs per person. Health benefits with statin therapy were larger among participants at higher CVD risk and with higher LDL-C levels.

Standard-intensity statin therapy was cost-effective across all population categories 40–70 years old with an incremental cost per QALY gained ranging from £280 to £8530. Higher-intensity statin therapy was cost-effective at higher CVD risk and higher LDL-C levels. Both standard and higher-intensity statin therapies appeared to be cost-effective for people aged ≥ 70 years with an incremental cost per QALY gained below £3500 for standard statin versus no statin and below £11,780 for higher-intensity versus standard statin.

Statin therapy, either standard or higher intensity, was found certain to be cost effective at a willingness-to-pay threshold of £20,000 per QALY, with higher-intensity statin therapy preferred at higher CVD risk or higher LDL-C level. The probability of statin therapy being cost-effective remained above 80% across all participant categories at £10,000-per-QALY threshold, albeit with a shift towards a preference for standard statin therapy across some categories of people. Statin therapy remained cost-effective in sensitivity analyses.

Limitations

The randomised evidence for effects of statin therapy is for duration of statin treatment of about 5 years in trials. There is only limited randomised evidence for effects of statin therapy in older people without previous CVD. In the base-case analysis, it is assumed that statin therapy has a constant proportional effect on CVD risks over lifetime and across different categories of patients.

Conclusions

Based on current evidence of effects of statin therapy and modelled analyses of contemporary disease risks, low-cost statin therapy is likely to be highly cost-effective across categories of men and women aged ≥ 40 years in the UK, with higher-intensity regimens cost-effective at higher CVD risk or higher LDL-C levels.

Future work

The CTTC has an ongoing programme of work conducting comprehensive analyses of the effects of statin therapy, both adverse and beneficial, using IPD from randomised controlled trials. In addition, ongoing randomised controlled trials are currently studying the effects of statin therapy in people aged ≥ 70 years. Future economic assessments should integrate this new evidence for effects of statin therapy, both beneficial and adverse, in categories of individuals.

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