What are the benefits of intensification of statins when used for primary prevention of cardiovascular disease?

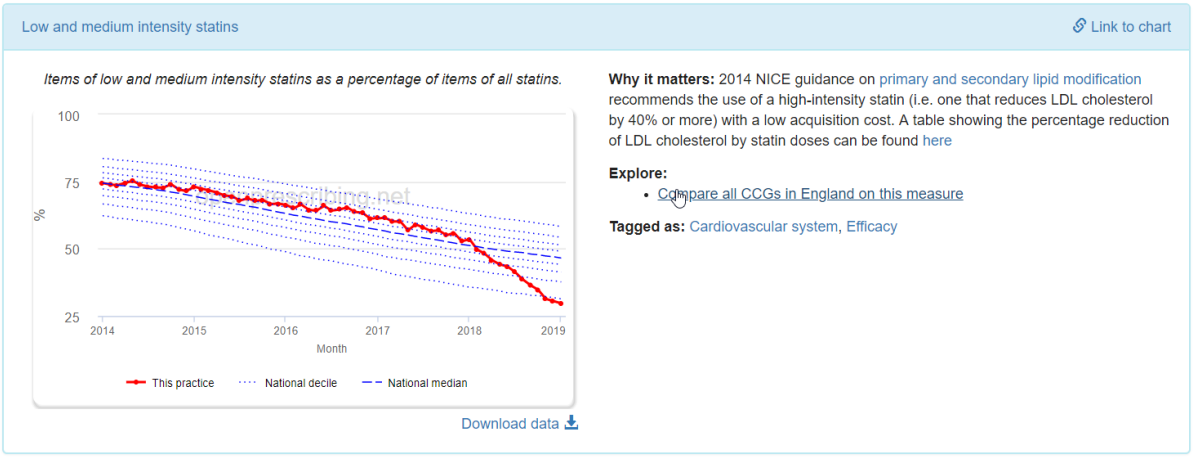
Bottom line (5th December 2018):

The group was surprised at the limited evidence, and, among the evidence available, the quality and generalisability (to the primary care population) of the available evidence examined and contained within the NICE guidelines for primary prevention of cardiovascular disease was low.

The group recognised their practice was not entirely aligned with the chronic kidney disease recommendations in NICE guidelines. However, this population is often excluded from primary evidence, therefore a further evidence review would be required before they had confidence that it would result in significant population-level overall clinical benefit.

Context:

The group reviewed practice level prescribing data for statins on openprescribing (https://openprescribing.net/), a source of freely available, practice-level prescribing data. This depicts high intensity statin prescribing in each practices population, highlighting high intensity statin use as positive clinical behaviour.



The group looked at the NICE Cardiovascular disease: risk assessment and reduction, including lipid modification CG181 https://www.nice.org.uk/guidance/cg181 - in particular

> 1.3.28 Measure total cholesterol, HDL cholesterol and non-HDL cholesterol in all people who have been started on high-intensity statin treatment (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) at 3 months of treatment and aim for a greater than 40% reduction in non-HDL cholesterol. If a greater than 40% reduction in non-HDL cholesterol is not achieved:
>
> - discuss adherence and timing of dose
> - optimise adherence to diet and lifestyle measures
> - consider increasing the dose if started on less than atorvastatin 80 mg and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement. **[new 2014]**

focussing on the following recommendation:

The group shared uncertainties about how best to implement these – for example:

- Whether this applies to people already on low intensity or 20mg atorvastatin but not new starters?
- How do you define those who are at higher risk because of risk score – which risk score and when?

The group noted that all patients with eGFR 30-59 should be given 20mg atorvastatin (see Section 4 https://www.nice.org.uk/guidance/cg181/evidence/lipid-modification-update-full-guideline-pdf-243786637).

> 63. Offer atorvastatin 20 mg for the primary or secondary prevention of CVD to people with CKD.
>
> - Increase the dose if a greater than 40% reduction in non-HDL cholesterol is not achieved (see recommendation 64) and eGFR is 30 ml/min/1.73 m2 or more.
> - Agree the use of higher doses with a renal specialist if eGFR is less than 30 ml/min/1.73 m2 . [new 2014]
>
> 64. Measure total cholesterol, HDL cholesterol and non HDL cholesterol in all people who have been started on high-intensity statin treatment (both primary and secondary prevention, including atorvastatin 20 mg for primary prevention) at 3 months of treatment and aim for a greater than 40% reduction in non HDL cholesterol. If a greater than 40% reduction in non HDL cholesterol is not achieved:
>
> - discuss adherence and timing of dose
> - optimise adherence to diet and lifestyle measures
> - consider increasing the dose if started on less than atorvastatin 80 mg and the person is judged to be at higher risk because of comorbidities, risk score or using clinical judgement. [new 2014] [This recommendation updates and replaces recommendation 1.10.2.7 from Type 1 diabetes (NICE clinical guideline 15).]

Most of the group recognised that their practice did not align exactly with management of people with CKD. Further, it was not clear as to the benefit of this practice.

PICO:

Not relevant – wanted to look at the basis of the recommendation

Evidence sources:

Looking at the background evidence in the NICE guideline CG181 – the recommendation came from 3 studies comparing 80mg atorvastatin with 20mg simvastatin and 10mg simvastatin – the results suggest non-statistically significant reductions in deaths and non-fatal MI. However, the NICE group classified the evidence as LOW (Table 48 in NICE guideline https://www.nice.org.uk/guidance/cg181/evidence/lipid-modification-update-full-guideline-pdf-243786637)

The group looked at 11.7 Evidence Statements in https://www.nice.org.uk/guidance/cg181/evidence/lipid-modification-update-full-guideline-pdf-243786637 and discussed the limited evidence supporting the use of statins.

Primary literature examined:

- Naci H et al. Comparative benefits of statins in the primary and secondary prevention of major coronary events and all-cause mortality: a network meta-analysis of placebo-controlled and active-comparator trials. European J of Preventative Cardiology. 2013;20(4):641-57.
- Ramos R et al. Statins for primary prevention of cardiovascular events and mortality in old and very old adults with and without type 2 diabetes: retrospective cohort study. BMJ. 2018;362:k3359

Impact:

I have stopped using a huge amount of resource to change things at a system level and, instead, will rely on ad-hoc medication reviews (GP Partner)