Indicator development programme Consultation report

Indicator area: Lipid modification

Consultation period: 04 October 2022 – 18 October 2022

Date of Indicator Advisory Committee meeting: 07 November 2022

Executive summary

Overview

This paper presents a proposal for an indicator on lipid modification (secondary prevention) potentially suitable for use in the QOF:

- IND2022-133: The percentage of patients with CVD in whom the last recorded non-HDL cholesterol (measured in the preceding 12 months) is less than 3.3 mmol/L.

The indicator aims to drive population level improvements in secondary prevention of cardiovascular disease. After committee consideration the indicator, or a revised version of it may progress to publication on the NICE indicator menu or work on this indicator may pause until a NICE guideline is available.

Development

The indicator was a referral from NHS England mid-2022. The development of a secondary prevention indicator that uses an absolute value was initially discussed by the IAC in mid-2021. Using a non-HDL value of 3.3 mmol/L was discussed and agreed between a subset of the IAC alongside members of the guideline development group working on the update to the NICE lipid modification guideline. The non-HDL treatment figure of 3.3 mmol/L is not based on NICE guidance or other published guidance.

Context

NICE's guideline on cardiovascular disease recommends lifestyle modification and lipid lowering therapies for secondary prevention of cardiovascular disease but does not include an absolute target for non-HDL cholesterol levels. NICE have heard that the current national data extraction system for QOF (GPES) cannot calculate patient level percentage reductions in non-HDL.

Existing NICE indicators relating to lipid modification in patients with cardiovascular disease are included in Appendix A.

Potential benefits

There are currently no QOF or NICE indicators on non-HDL cholesterol levels for secondary prevention of cardiovascular disease. NICE menu indicators focus on the prescription of lipid lowering therapies, the new indicator on secondary prevention (NICE IND230) approved by the IAC in June 2022 and available for contract negotiators for the 2023/2024 QOF

Feedback from stakeholders indicates that an absolute value non-HDL level for monitoring population level lipid management would be useful.

Validity concerns

A non-HDL cholesterol level of less than 3.3 mmol/l has been chosen as a starting point for incremental improvements at population level, drawing on current practice data from CVDPREVENT and guidance from NICE's technology appraisal programme. It is higher than some treatment goals included in the European Society of Cardiology (ESC), Joint British Societies lipid management guidelines (JBS) and the NICE-endorsed NHS England/Academic Health Science Networks (AHSN) / Accelerated Access Collaborative (AAC) lipid management pathway.

Stakeholders were concerned about the methodology used to develop the indicator and questioned the suggested evidence base.

Stakeholders report concern that the indicator may be interpreted as a patient level treatment target for lipid management rather than its intent as a population marker of lipid management. This may cause confusion, reduce escalation of treatment for people at high-risk of a cardiovascular event and make it difficult to amend the indicator in the future.

Consultation highlighted polarised views, whilst there was near universal agreement that the non-HDL figure of 3.3 mmol/L was not appropriate suggestions for alternatives ranged from an LDL-C of <1.4mmol/L to non-HDL of 4.0 mmol/L.

Alignment with future NICE guidelines

The next update to NICE's guideline on lipid modification (CG181) is expected to publish in May 2023, this will not cover secondary prevention. A future iteration of CG181 that will cover secondary prevention is now expected to publish in September 2023, with draft guidance expected in June 2023

If final NICE guidance on secondary prevention is available in September 2023 any indicator that is negotiated into the QOF going live in April 2023 will likely be misaligned with the latest NICE guidance after only 6 months. It will be misaligned with draft guidance after only 3 months.

A consistent message from consultation was unease at any QOF indicator that misaligns with existing guidance. Any QOF indicator NICE produce ahead of our own clinical guideline will be misaligned with our own guidance potentially resulting in confusion in the system.

Committee decision

The committee is asked to consider the consultation comments alongside the supporting slides. The broad options available to the NICE committee are to progress an indicator or pause the work and align with NICE guidance when available.

IND2022-133: Lipid modification: secondary prevention

The percentage of patients with CVD in whom the last recorded non-HDL cholesterol (measured in the preceding 12 months) is less than 3.3 mmol/L.

Rationale

Non-HDL cholesterol concentrations in blood are strongly associated with long-term risk of atherosclerotic cardiovascular disease (Brunner et al. 2019).

This indicator aims to drive population level improvements in secondary prevention of cardiovascular disease. It uses a non-HDL cholesterol level of 3.3 mmol/L as a population level marker of lipid management for people with cardiovascular disease.

Specification

Numerator: the number in the denominator in whom the last recorded non-HDL cholesterol (measured in the preceding 12 months) is less than 3.3 mmol/L.

Denominator: the number of patients with CVD.

Definition: CVD is defined as angina, previous myocardial infarction, revascularisations, ischaemic stroke or TIA or symptomatic peripheral arterial disease. Existing QOF registers could be used for coronary heart disease (CHD001), stroke or TIA (STIA001 excluding haemorrhagic stroke) and symptomatic peripheral arterial disease (PAD001).

Exclusions: Patients with a diagnosis of familial hypercholesterolaemia.

Personalised care adjustments should be considered to account for situations where the patient declines, does not respond to invite or if lipid management is not appropriate for the individual.

Summary of consultation comments

Stakeholders agree that this is an important indicator and that an absolute target level is key. This provides a simple message that is easy to implement. They note the lack of current QOF indicators for secondary prevention.

Stakeholders highlighted the need for a consistent approach to lipid management to aid implementation and improve clinical practice but were concerned that the proposed indicator would be regarded as a treatment target despite the intention to be a population level marker of lipid management.

Stakeholders felt it would need to be incentivised using a high number of QOF points and that a number of additional exclusions should be added.

Stakeholders noted that some laboratories do not report non-HDL using SNOMED codes, it may be reported as free text within the pathology report. GP practices will not have the capacity to calculate non-HDL.

Barriers to implantation were highlighted as:

- Burden of work for general practice.
- Previous promotion of 'fire and forget' approaches to lipid management still hold traction.
- Patient aversion to statins.

Potential unintended consequences were highlighted as:

- An increase in avoidable cardiovascular events and undermining NICE recommendations and the NHS England/AHSN/AAC initiatives. It may delay titration of high intensity statins and escalation using newer therapies.
- Increased GP appointments regarding statins and side effects.

Potential differential impacts were highlighted as:

- Practices and PCNs lacking capacity and workforce are in more deprived areas. This could potentially increase health inequality.

- Disproportionately affecting older patients with aches and pains that could be falsely attributed to statin use and those with a burden of multiple medications.

- Some practices may serve seldom heard communities, rural populations, deprived populations or have many people in institutional care. These have higher levels of CVD but patients are less able to interact with general practice.

Specific questions included at consultation

We welcome comments on the proposed non-HDL level of less than 3.3 mmol/L across a general practice population. Do you agree with using this to drive population level improvements in cholesterol management? If not, what level should be used and why?

Nearly all stakeholders disagreed with the proposed value though there were some stakeholders who did agree with the proposal.

Stakeholders consistently suggested a target non-HDL level of 2.5 mmol/L. They note that this aligns with current practice, clinical evidence and international target levels. Stakeholders suggested that this level is achievable using appropriate combination of NICE recommended treatments.

Stakeholders note existing guidance from the ESC that support the use of lower values, such as LDL cholesterol less than 1.4 mmol/L or 1.0 mmol/L.

A small number of key stakeholders suggested a level of 4.0 mmol/L. They felt that the NICE proposed level of 3.3 mmol/L is aspirational and insufficiently evidenced. They note that non-HDL <4.0 mmol/L is currently often used in primary care as a treatment target.

Stakeholders note that NICE's guideline on cardiovascular disease is currently undergoing an update and suggest it would be advisable to wait and introduce an indicator once the evidence has been reviewed and recommendations made.

Stakeholders noted a study ([McKay et al. 2022](#)) using Clinical Practice Research Database (CPRD) data that shows the median non-HDL for patients on statins is 3.4 mmol/L. They highlighted that the study shows people with a non-HDL cholesterol of 3.3 mmol/L have a 10-year risk of CV event of 29%.

Stakeholders suggested that the indicator could be constructed to address concerns about achievability, such as adjusting payment thresholds during QOF negotiations between NHS England and the BMA's GPC.

Should the indicator include an LDL component alongside non-HDL? For example: 'The percentage of patients with CVD in whom the last recorded non-HDL cholesterol (measured in the preceding 12 months) is less than 3.3 mmol/L, or where this is missing a recording of LDL cholesterol in the preceding 12 months that is less than 2.6 mmol/L'.

Most stakeholders agreed with including an LDL component:

- More labs will begin to report this measure.
- LDL is calculated from non-HDL using Friedewalde and therefore will always be available.
- Several newer therapies use LDL cholesterol in key trials testing their efficacy. Recent NICE technologies appraisals use LDL-C (TA733)
- This would align with JBS lipid management guidance.
- It would make sense to include as either/or options due to coding anomalies and inconsistencies in measuring cholesterol.

Stakeholders suggested starting using non-HDL and introducing LDL as the target is refined in later years.

Should patients with a diagnosis of familial hypercholesterolaemia be excluded?

Most stakeholders agreed that patients with familial hypercholesterolaemia (FH) should be excluded because many are often supported in secondary care and should have more aggressive targets.

Stakeholders noted that patients with FH have a higher risk of CVD and some proposed that for this reason they should be included, but others suggested a separate indicator and target level for patients with FH. Stakeholders highlighted the significantly raised baseline levels and therefore the challenge of reaching cholesterol targets.

Would a similar indicator focussed on people with chronic kidney disease be useful and should it use the same level of non-HDL cholesterol?

Most stakeholders agreed that an indicator would be useful, but some felt that this should only be considered once the proposed indicator has sufficient time for implementation and evaluation.

Stakeholders suggested the non-HDL value should be less than 2.5 mmol/L.

Stakeholders noted that the definition of CKD is too wide for this indicator to be applied to everyone.

Considerations for the advisory committee

The committee is asked to consider:

- What is the most appropriate non-HDL level for people with CVD? The majority of stakeholders suggest the current value of less than 3.3 mmol/L is not appropriate due to misalignment with evidence, existing guidance, current practice and potential unintended consequences.
- Is there potential for development of a set of indicators with different non-HDL target levels and potentially different payment thresholds?
- Should the indicator include an LDL cholesterol component?
- Stakeholders noted potential for increasing health inequalities if this indicator is implemented, due to capacity in general practice.
- Should patients with FH remain excluded from the indicator?
- Should the NICE indicator programme explore development of a similar indicator for patients with CKD?

Appendix A: NICE menu indicators

Indicators on the NICE menu that are suitable for inclusion in QOF are listed below.

ID	Indicator wording	QOF status
IND228	The percentage of patients with a CVD risk assessment score of 10% or more identified in the preceding 12 months who are offered advice and support for smoking cessation, safe alcohol consumption, healthy diet and exercise within 3 months of the score being recorded.	Not in QOF – Only published in August 2022. Available to negotiators for 23/24 QOF
IND229	The percentage of patients with a CVD risk assessment score of 10% or more who are currently treated with a lipid lowering therapy.	Not in QOF – Only published in August 2022. Available to negotiators for 23/24 QOF
IND230	The percentage of patients with CVD who are currently treated with a lipid lowering therapy.	Not in QOF – Only published in August 2022. Available to negotiators for 23/24 QOF
IND231	The percentage of patients with CKD, on the register, who are currently treated with a lipid lowering therapy.	Not in QOF – Only published in August 2022. Available to negotiators for 23/24 QOF

Appendix B: Consultation comments

ID	Question	Stakeholder	Comment	
1	General	Academic Health Science Network	**Adoption of an absolute target** In order to enable good clinical care, experience from the implementation of our National Programme since 2019 has shown that simplicity of message is key. Clinical colleagues in senior leadership roles, the majority of whom are still in clinical practice, have spoken with a single voice about the need to set an absolute target level. This is about enabling good clinical care through providing a simple message to busy clinicians in contrast to the existing NICE guideline which is more difficult to implement and monitor in every day clinical settings. By making medicine as easy to deliver as possible we will support better patient care for a larger number of patients. Setting a target level is a key means to achieve this. **Target level** We have heard in our programme strong consensus that the target level should be set at 2.5 mmol/L for non-HDL cholesterol (and 1.8 mmol/L for LDL-c) and not 3.3 mmol/L. This would bring us in line with best practice and the target levels that are being adopted internationally. We recognise that it has been important to take a pragmatic approach to the suggested target level. However, previous experience on blood pressure has shown us that reducing the clinical target, in order to make it achievable, is not the right approach. This type of approach endorses an acceptance of sub-optimal clinical care in minds of clinicians which it is then difficult to move away from. We would urge you to adopt the 2.5 mmol/L target for non-HDL-c and the concerns about achievability can be managed through	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.

ID	Question	Stakeholder	Comment	
			how the metric is constructed, i.e., adjusting payment triggers based on the number of patients that meet the target. This means that whilst we might adjust the payment thresholds between years, the clinical target remains consistent and becomes embedded. We strongly believe this is a key principle that needs to be adopted. Consistency Our experience of implementating programmes at scale in the NHS confirms that a key requirement is to ensure consistency to promote improved clinical practice. This is both in relation to aligning across the work and positions of key organisations that influence the clinical community but also in relation to consistency across NICE. We understand and support the need for pragmatism, but we would also urge NICE to move as quickly as possible to align the position within a potential indicator with what is contained in NICE guidelines (with the latter currently referencing a percentage reduction of non-HDL-c and the various NICE technology appraisals stating eligibility criteria for LDL-c). This lack of consistency if it continues for a significant period will be unhelpful.	
2	General	British Medical Association	Respondents consistently expressed concern about the amount and complexity of work associated with this proposed indicator, and that it needs to be tagged with a high number of QOF points to work as an effective incentive.	Thank you for your comment. NICE does not decide on QOF point allocation.
3	General	British Medical Association	Respondents consistently disagreed with NICE's assertion that a non-HDL cholesterol level of 3.3mmol/L is 'pragmatic'. This was widely perceived as an aspirational target that is insufficiently evidenced as necessary. There was a strong view that this should be revised to 4.0mmol/L.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022.

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				The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
4	General	British Medical Association	One respondent suggested that the exemption needs to include maximum tolerated therapy and frailty.	Thank you for your comment. Personalised care adjustments could be used to exclude patients from indicator denominators dependent on individual circumstances. Examples of these are included in the indicator specification and have been amended following consultation.
5	General	Daiichi Sankyo UK Ltd	Daiichi Sankyo UK Ltd welcomes the inclusion of a QOF indicator for lipid modification for secondary prevention. This is a critical addition to the QOF that will support the delivery of important national clinical policy objectives outlined in the NHS Long Term Plan. However, Daiichi Sankyo	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an

ID	Question	Stakeholder	Comment	
			disagrees with the proposed wording. We encourage NICE to consider the following revisions: - The proposed non-HDL-C target of <3.3mmol/L for secondary prevention is not aggressive enough to reduce the risk of CVD. These patients are at a very high risk of further cardiac events and need the most intensive reduction of LDL-C. While we understand this is an indicator target for QOF and it does not update or replace current NICE guidance, every opportunity should be capitalised to reduce cholesterol levels in line with the European Society of Cardiology (ESC), and European Atherosclerosis Society (EAS) guideline recommended targets for very high-risk patients at an LDL-C of <1.4mmol/L. In those patients with recurrent events, a target of <1.0mmol/L for LDL-C should be considered.[1] - Mendelian randomization studies and RCTs have consistently demonstrated a log-linear relationship between the absolute changes in plasma LDL-C and the risk of ASCVD and these studies provide compelling evidence that LDL-C is causally associated with the risk of ASCVD, and that lowering LDL-C reduces the risk of ASCVD proportionally to the absolute achieved reduction in LDL-C.[1] - Imaging studies have shown that in secondary prevention patients who achieve low and sustained LDL-C reduction through	indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. The construction now searches for LDL first, and if not found, non-HDL.

ID	Question	Stakeholder	Comment	
			combination therapies, there is an increase in plaque stabilization and regression.[2,3] - The proposed indicator target does not align with the JBS3 guidance, which recommends that patients with established CVD achieve at least <2.5mmol/L for non-HDL-C.[4] These targets are also cited in the Accelerated Access Collaborative guidelines (AAC) National Guidance for Lipid Management for Primary and Secondary Prevention of CVD.[5] Daiichi Sankyo asks NICE to consider aligning the QOF indicator target to ESC/EAS recommended LDL-C targets to drive the correct knowledge of guideline-recommended targets and improve quality and consistency in care. - Please consider the primary prevention population who have raised LDL-C levels and are at risk of CVD. Additionally, primary prevention patients at very high risk but without FH should receive the most intensive reduction of LDL-C targets of <1.4mmol/L.[1] - To achieve intensive management of lipid-lowering, we suggest the QOF indicator allows a combination therapy approach to support LDL-C reduction.[6,7] - Currently, NICE CG181 recommends measuring a reduction in non-HDL-C. However, we would ask NICE to align with the ESC/EAS guidelines and use tangible targets instead. The	

ID	Question	Stakeholder	Comment	
			relationship between non-HDL-C and CV risk is at least as strong as the relationship with LDL-C and thus LDL-C is a better indicator of CV risk.[8] While cholesterol management is part of the NHS Long Term Plan for CVD prevention, a considerable amount of work is needed to reduce population cholesterol levels. We should take every opportunity to intensively manage cholesterol levels to reduce inequality and variation in care. References 1. Mach et al. European Heart Journal, Volume 41, Issue 1, 1 January 2020, Pages 111–188, https://doi.org/10.1093/eurheartj/ehz455 2. Raber L, et al JAMA. 2022;327 (18): 1771-178 3. Nicholls SJ, et al. JACC Cardiovasc Imaging. 2022; 15(7):1308-1321 4. JBS3 Risk Calculator. Last accessed October 2022 5. Summary-of-national-guidance-for-lipid-management-for-primary-and-secondary-prevention-of-cardiovascular-disea.pdf (england.nhs.uk) Last accessed October 2022 6. Ray et al., 2021. Combination lipid-lowering therapy as a first-line strategy in very high-risk patients. European Heart Journal; 7. Masana et al, 2020. Reasons Why Combination Therapy Should Be the New Standard of Care to Achieve the LDL-Cholesterol	

ID	Question	Stakeholder	Comment	
			Targets: Lipid-lowering combination therapy. Curr Cardiol Rep, 22(8):66 8. Visseren et al. European Heart Journal, Volume 42, Issue 34, 7 September 2021, Pages 3227–3337	
6	General	East Midlands Academic Health Science Network	Currently no indicator for cholesterol in QoF in either secondary prevention of CHD disease, peripheral artery disease (PAD) or stroke (STIA) domains so agree, and welcome the rationale to introduce an indicator to drive populational level improvements and standardisation. However there is no link to the NICE approved NHSE/AAC lipid management pathway. Both GP IT systems I am aware of (TPP SystmOne and EMIS) are likely to have baseline or a tool to calculate a 40% reduction. This is an opportunity to really drive improvements in lipid management rather than measure a number that GPES can extract.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
7	General	East Midlands Academic Health Science Network	Using a non -HDL level of 3.3 is not evidence based and potentially harmful as will be regarded by many as a treatment target or threshold, despite the intention, and if then amended in subsequent iterations will delay appropriate readily available effective therapeutic interventions.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an

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			If only 23.7% of patients with CVD have achieved the target and we have an approved published relatively simple stepwise pathway, and- any delay in focussing on this area may cause harm to patients and increase costs of the NHS.	indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
8	General	East Midlands Academic Health Science Network	There are already a number of search tools within TPP SystmOne and EMIS that provide primary care with the data on lipid levels, as well as the NHS Digital lipid tool, as well other risk stratification tools such as UCLP Partners Proactive Care Frameworks, FAMCAT2, Innovation Agency, CDRC and Ardens templates – most are based on the NHSE/AAC guidelines. If GPES cannot extract the calculate the percentage reductions that does not seem to be a sensible rationale to use different lipid levels to those in the published guidelines.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be

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				consistent with the updated guideline.
9	General	East Midlands Academic Health Science Network	I would suggest in order to promote and enable a population health management approach and to ensure a consistent approach that indicators should be proposed around use of an appropriate risk stratification tool for patients so practices and PCN's can focus on smaller numbers of higher risk patients rather than a non-HDL cholesterol number (some labs do not report this, and many practices will not have the capacity to calculate the number.)

This would ensure a holistic approach as well as focussing efforts with limited capacity in primary care and providing practical resources rather than a target or threshold with overwhelming numbers of patients. The unintended consequences would be that practices or PCN's with capacity would start to address the clinical issues around secondary prevention, but many will not and this could potentially increase health inequality. These practices and PCN's in my experience that are lacking in capacity and workforce are in more deprived areas. | Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. The construction now searches for LDL first, and if not found, non-HDL. |
| 10 | General | East Midlands Academic Health Science Network | Other potential indicators should, in my view, be focussed on using the secondary prevention lipid management pathway such as percentage prescribing a high intensity statin (HIST), or maximally tolerated statin, atorvastatin 20mg (if also a patient with CKD 3-5), and ezetimibe prescribing for those patients not achieving the published target or statin intolerant. These should be easier to extract via GPES and encourage achievable changes in practice to a national standard far more quickly. | Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be |

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				consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. The current NICE menu indicator IND230 (general practice level indicator) measures the percentage of patients with cardiovascular disease who are currently treated with a lipid lowering therapy. We will continue to explore potential new indicators relevant to other aspects of the lipid management pathway.
11	General	Heart UK – The Cholesterol Charity	We would very much welcome the re-introduction of an absolute non-HDL-C threshold number as a population level marker of lipid management for people with cardiovascular disease. However, we strongly disagree with the suggested <3.3 mmol/L being used as the cut off as this appears to accept or even endorse less intensive lipid lowering therapy in the patients at highest risk. In doing so, it potentially puts at unnecessary risk many secondary prevention patients who would otherwise be more optimally treated, particularly higher risk patients	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-

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			including young people and those having recurrent events. Although the consultation text states that the 'Non-HDL-C level of <3.3 mmo/L should not be considered as a treatment target for individual patients' the perception will be that in practice it will be treated as such. It could even mean some patients who have appropriate levels have some treatment withdrawn which is likely to lead to significant unintended consequences. We also believe the suggested <3.3 mmol/L risks causing massive confusion when compared with the non-HDL-C target of 2.5 mmol/L that has been used by JBS3 and in the NICE endorsed National Lipid Management Pathway.

We would strongly suggest that the established Non-HDL-C target of 2.5 mmol/L should be used for QOF and the thresholds of %population achieving this should be negotiated instead. | based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. |
| 12 | General | Heart UK – The Cholesterol Charity | We would highly recommend when measuring the non-HDL-C that triglycerides must also be routinely measured, whether fasting or non-fasting. Fasting should not be a pre-requisite for triglyceride measurement – indeed non-fasting TG is a better predictor of CV risk and other adverse outcomes. High triglycerides are an adverse prognostic factor in CVD and may be associated with unrecognised secondary factors including diabetes, renal impairment and alcohol overuse. A repeat fasting test is advisable if non-fasting TG exceeds 4.5 mmol/L. Cholesterol in chylomicron accumulation not only creates a problem in interpreting non HDL-C levels, but it may indicate incipient risk of pancreatitis. Measuring both at the same time will identify patients with hypertriglyceridemia with a high CVD risk.

An example from a recent patient was: TC 10.5, Non HDL-C 9.0, TG 35.0 mmol/L. Although the non-HDL-C in this patient would probably be managed with statins/ezetimibe, without very high triglycerides treatment | Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be |

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			failure is likely and the patient is still at high risk from unaddressed chylomicronaemia.	consistent with the updated guideline.
13	General	Heart UK – The Cholesterol Charity	Apolipoprotein B is an alternative, non-fasting treatment indicator to non-fasting non-HDL-C, which have several important advantages, but the major disadvantage is the additional cost and current lack of widespread availability in primary care.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
14	General	IND1	I think this is an important indicator. I would personally like to see the target set to <2.5 for Non-hdl-C in line with the Joint British Societies but can appreciate this might be difficult to obtain for all patients in one year. The only problem with having a higher target is, it might lead to confusion over what the target actually is. If you were to survey primary care clinicians, I suspect many wouldn't be aware of these non-hdl-C targets in secondary prevention patients. Having a QOF target would actually support clinicians in highlighting this.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on

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			The other more pressing issue, is that not all trusts actually report the non-hdl level as a readcode/snomed-ct code when primary care request lipids.cholesterol tests through ICE. In some area's the non-hdl gets reports as written text within the pathology report. They usually only report a total cholesterol and hdl cholesterol (which are appropriately readcoded) and a triglyceride level (if fasting has been selected). This obviously varies depending on the trust. Its definitely something that will need consideration, and may require some preparation to ensure all trusts report it and that its linked to an appropriate readcode.	lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. The construction now searches for LDL first, and if not found, non-HDL.
15	General	IND3	I think it will be a serious and potentially high impact error if 3.3 is chosen as the metric. It will be assumed across general practice to be an evidence based NICE target, with no need to lower non-HDLc below that. Choosing 3.3 would repeat the error made in setting BP 150 systolic as the QOF target – this was widely seen in general practice as a reasonable clinical target because it was in QOF. It took many years of discussion before this could be corrected. Setting 3.3 now will establish a NICE standard in practitioners' eyes and attempting to reduce later will generate a lot of resistance and may take years to achieve. If the purpose of setting a higher level (3.3) is to make it easier to achieve and so not add unreasonably to GP workload, the same could be achieved by setting initial achievement thresholds lower (ie % achievement). This will achieve the same but without the risk of establishing an unintentional new standard that will undermine quality of care and outcomes for years to come.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.

ID	Question	Stakeholder	Comment	
16	General	IND4	I welcome a renewed focus on lipid management by NICE and the new lipid lowering indicators overall. I believe the introduction on the non HDL 3.3 mmol/l target is not evidence based and appears arbitrary in its design. It risks confusion across the prescribing community when we already have other accepted international targets of non HDL 2.5 mmol/l and creates an impression NICE is out of touch. It is of upmost importance in my view the regulators across the board work collaboratively to provide clear and consistent advice to general practice and others and I would strongly advise NICE to align with the emerging clinical consensus of the non HDL 2.5mmol target which will lead to an amplified impact in terms of GP behaviour in response to the indicator. I am also in favour of an equivalent LDL target being provided as increasingly I believe more labs will begin to report this measure.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. The construction now searches for LDL first, and if not found, non-HDL.
17	General	IND6	This topic has been at the forefront of any Primary Care guidance for over twenty years. Local guidance is now orientating what Statin to use with the view of reducing lipids figures. Is this what the evidence is suggesting(end point)?	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE

ID	Question	Stakeholder	Comment	
				guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
18	General	Innovation Agency	Overview It is reassuring to see consideration being given to how we can promote better lipid management. We are all aligned on the importance of CVD prevention and that we need to improve the support we provide to patients. We are also agreed on the need to focus on all of the modifiable risk factors in a holistic approach to achieve this goal.	Thank you for your comment.
19	General	Innovation Agency	Adoption of an absolute target Clinical colleagues in senior leadership roles, the majority of whom are still in clinical practice, have spoken with a single voice about the need to set an absolute target level. This is about enabling good clinical care through providing a simple message to busy clinicians in contrast to the existing NICE guideline which is more difficult to implement and monitor in every day clinical settings. By making medicine as easy to deliver as possible we will support better patient care for a larger number of patients. Setting a target level is a key means to achieve this. We welcome the consensus between us in this regard and believe the move to an absolute target is an important first step.	Thank you for your comment.
20	General	Innovation Agency	Consistency As outlined, one key requirement is to ensure consistency to promote improved clinical practice. This is both in relation to aligning across the work and positions of key organisations that influence the clinical community but also in relation to consistency across NICE. I understood	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022.

ID	Question	Stakeholder	Comment	
			from the discussion that the adoption of a non-HDL-c target indicator for 2023/24 was a pragmatic decision and would hopefully come in before a change to guidelines. We all understand and support the need for pragmatism, but we would also urge NICE to move as quickly as possible to align the position within a potential indicator with what is contained in NICE guidelines (with the latter currently referencing a percentage reduction of non-HDL-c and the various NICE technology appraisals stating eligibility criteria for LDL-c). This lack of consistency if it continues for a significant period will be unhelpful.	The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
21	General	IND5	We do not agree with the proposal to introduce a Non HDL C target of < 3.3 mmol/L for Secondary prevention at this will lead to under and overtreatment. People will see this value as a target and they will think everyone should be reduced below that value and that control has been achieved when people get below that value.

The current NICE CG 181 recommendation is to aim for a 40% reduction in Non-HDL from baseline. This is complicated by the fact that the guideline also recommends very high intensity statins which you would normally hope would lead to a greater than 40% reduction. We have used and recorded the target non-HDL cholesterol for a number of years. The prevalence of ASCVD in our practice is 6.2%, with (348) 92% of those patients on some form of lipid lowering. Excluding the 3 patients with FH, 287/345 (83.2%) patients have a non-HDL-C target (based on a 40% reduction of non-HDL-C). The distribution of those targets is set out below. | Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be |

ID	Question	Stakeholder	Comment	
			Frequency 67 patients have a target which is equal to or greater than 3.3. Of these 55 patients are achieving that target. Following the NICE guidance some of these patients will be eligible for treatment intensification with inclisiran or PCSK9i, based on their LDL-C levels. In our practice, only 5 out of these 55 patients would be potentially eligible. So there are 50/287 (17.4%) patients with appropriate lipid lowering who would be classed as 'not achieving' the indicator. On the flip side, there are large numbers of people who have a target much lower than 3.3. For example 39/287 patients have a target of 2.3 or lower. By setting the 'achievement level' at 3.3 many practitioners are not going to appropriately intensify these patient's treatment.	consistent with the updated guideline. The construction now searches for LDL first, and if not found, non-HDL.

ID	Question	Stakeholder	Comment	
			Our experience is that having a target non-HDL value is a very good tool to help work out with patients how intense their lipid lowering therapy needs to be. This is important as there are many frail and multimorbid patients where very intense lipid lowering is unlikely to be in their best interests. This approach prevents over and under treatment.	
			My recommendation would be to have a standard that a certain proportion of patients with ASCVD have a target non-HDL value set and then measure performance against this. I.e. target set and last non-HDL-C is less than target. This also offers the potential for patient involvement in setting their own target.	
			To include the inclisiran data you could also include a criteria that the LDL-C should also be <2.6	
22	General	NHS England (Primary Care Team)	Agree with the indicator and also the Non-HDL cholesterol target of 3.3mmol/L.	Thank you for your comment.
23	General	North East and North Cumbria Lipid Specialists Advisory Group	We do not agree with the proposal to introduce a Non HDL target of < 3.3 mmol/L for Secondary prevention as this is too high. The current NICE CG 181 recommendation to aim for a 40% reduction in Non-HDL from baseline is not practical and unhelpful. A set Non-HDL target is preferable. For this reason we adopted the JBS-3 recommendation of a target Non-HDL of < 2.5 mmol/L for our regional NEELI Lipid guideline. This is a conservative target when compared to those adopted by the ESC and AHA. There is clear clinical evidence demonstrating benefits from lower Non-HDL / LDL levels. Adopting a Non-HDL target < 3.3 / LDL < 2.6 would discourage use of high intensity statins and ezetimibe in patients with Non-HDL / LDL levels of 2.5 – 3.3 / 1.8 – 2.6 to achieve lower levels which are desirable to prevent further CVD events. Implementation of the Non-HDL / LDL target of < 3.3 / 2.6 may inappropriately signal that lipid optimisation is only necessary if patients	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published

ID	Question	Stakeholder	Comment	
			are eligible for newer injectable PCSK9 inhibiting therapies. This could actually lead to a delay in these therapies being commenced as local experience from a variety of lipid optimisation projects has been that patients identified as eligible for newer injectable therapies often require optimisation of statin therapy before they can be started on these medications and in many instances, patients are no longer eligible once they have been commenced on optimal high intensity statin therapy with or without Ezetimibe. Adopting a lower Non-HDL / LDL target would encourage optimisation of "standard therapy" and facilitate earlier use of newer agents in patients who are eligible. We would recommend a Non-HDL target of < 2.5 mmol/L. We have successfully implemented this locally	December 2023; the indicator has been updated to be consistent with the updated guideline.
24	General	Primary Care Cardiovascular Society	We can see no rationale for using the proposed target of a non- HDLC of less than 3.3 mmol/l and do not support this target. Current national AAC/Lipid pathway uses a non -HDL target of 2.5 mmol/l (equivalent to an LDL-cholesterol target of less than 1.8mmol/l). In comparison to other guidelines (e.g. ESC guidelines on dyslipidaemia) which recommend lower targets for those patients who are at the highest CVD risk even the LDL-C of 1.8 mmol/l / non HDL-C of 2.5mmol would be considered a high 'target'. Introducing the proposed (non-HDL-C 3.3 mmol/l) higher target, would not only support inadequate titration/escalation of patient treatment (which ultimately may affect patient outcomes such as additional cardiovascular mortality and cardiovascular events) but run the risk of causing confusion in primary care with differences in the ambitions.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be

ID	Question	Stakeholder	Comment	
			Effectively this is akin to paying for a QOF that people are already achieving. i.e., using CPRD data the median on statin non-HDL-C is 3.4 and results in a 10-year event rate of 29%. We need to learn from our previous expericine where QoF targets are higher than clinical evidence-based guidelines (hypertension 150/90 c.f. 140/90 which confused primary care and had a legacy of years where HCPs adopted the higher target with the obvious CVD morbidity and mortality as a consequence). Furthermore, although this is an indicator for secondary prevention it is worth noting that there is currently similar confusion around the use of QRISK 20% as an indicator where all the national guidance has adopted 10%. HCPs in Primary Care have clearly told us this is confusing and actually suggest that the target should be universally 10%. Guidelines and indicators standards need consistency.	consistent with the updated guideline.
25	General	Royal College of General Practitioners	Other points for consideration: While this is a worthy indicator, it must be placed in the context of the current primary care environment. GPs are still performing catch up blood tests which were put on hold due to the pandemic and should be given the time to review all their patients who require one before a new requirement is placed on them. Additionally, many people in the denominator for this indicator already have co-existing diabetes and bringing the HbA1C within target ranges also affects lipids levels. It is difficult to reach those in this group who may be in institutional care or rely on delivered meals and are less able to leave their homes. There is a risk that this indictor could negatively impact those practices signed up to QOF who serve more deprived populations	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator

ID	Question	Stakeholder	Comment	
			or have many in institutional care as they may have a higher incidence of CVD but less able to get a blood test or interact with their GP.	has been updated to be consistent with the updated guideline.
26	General	University Hospital of Derby and Burton	Given that the UK guideline for lipids in secondary prevention is to have LDL < 1.8mmol/L, which is said to be equivalent to a non-HDL cholesterol of <2.5 mmol/L (https://www.england.nhs.uk/aac/wp-content/uploads/sites/50/2020/04/Summary-of-national-guidance-for-lipid-management-for-primary-and-secondary-prevention-of-cardiovascular-disea.pdf) and the European guideline is 1.4mmol/L, (https://www.eas-society.org/page/dyslipidaemia_guidelines_2019_comment), setting a target for non-HDL cholesterol of 3.3 mmol/L seems to be designed as a lax target that lets people off for persistent failure to achieve the targets that have already clearly published and promoted for a very significant amount of time. Whilst it is clearly difficult to get patients with FH down to this level, non-FH patients should all be capable of having levels below 3.3. Therefore, if such a lax target is set, It would be appropriate that the target should be that 95% of secondary prevention patients should achieve the 3.3 mmol target with perhaps at least 70% achieving the 2.5mmol/L non-HDL target, with the proviso that proven FH patients be excluded from the patients under consideration for the standard. A separate target for secondary prevention FH patients should be included such that if they have not achieved the 3.3mmol non-HDL target	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. A separate indicator for people with FH is currently being explored.

ID	Question	Stakeholder	Comment	
			they should be at the very least treated with a PCSK-9 inhibitor [with or without a statin], again with a 95% target.	
27	General	West Midlands Academic Health Science Network, CVD Prevention & Management Team	the proposed indicators will lead to improvements in care and outcomes for patients? No – please see below	Thank you for your comment.
28	General	West Midlands Academic Health Science Network, CVD Prevention & Management Team	The non-HDL cholesterol threshold of 3.3mmol/L is not supported by an established evidence based. While CVDPrevent is a rich resource – it is limited by duration and is an observational platform from which clinically meaningful recommendations regarding clinical practice cannot be drawn. This is not an evidence-based approach to managing a modifiable risk factor. NICE have previously recommended a nonHDLC threshold of 2.5mmol/L – equating to an LDLC of 1.8mmol/L This is included in the NICE endorsed pathway for lipid management that all AHSNs (15 in total) across England have been promoting as part of the National Lipid Management & Familial Hypercholesterolaemia programme. There is a robust body of evidence to suggest the lower the LDLC the better the outcomes for a patient.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.

ID	Question	Stakeholder	Comment	
			We also know that coronary artery plaque regression occurs at LDLC thresholds ☐ 1.8mmol/L.	
			ESC and EAS recommend lower LDLC thresholds of 1.4 and 1.0mmolL for index and current events respectively.	
			Suggesting an incremental incentivised approach is not in line with the NHS LTP nor key clinical messages regarding the importance of improved cholesterol management to reduce recurrent cardiovascular events. Such a strategy will create more work – and avoidable CV events in the longer term.	
			It does not make any sense from a clinical effectiveness or cost-effectiveness perspective – and to continue with this recommendation will undermine NICE CG 181 recommendations.	
			Data from the APOLLO and GRACE registries have demonstrated that 1 in 5 people will go on to have a recurrent cardiovascular event within a year of their index presentation. This is due to sub-optimal pharmacological management. Introducing non-HDLC thresholds that are not evidence based nor even close to secondary prevention targets will further exacerbate this very problem.	

Question 1: Do you think there are any barriers to implementing the care described by these indicators?

ID	Question	Stakeholder	Comment	
29	1	British Cardiovascular Society (response endorsed by Royal College of Physicians)	Yes, difficulty of getting lipid checks done yearly	Thank you for your comment. The indicator uses a time frame to allow measurement of performance. The 12-month time frame is consistent with other indicators in QOF.

30	1	British Medical Association	With respect to barriers, respondents raised concerns about the strength of patient aversion to statins. There is a widespread belief that they 'do more harm than good', and that they 'always cause muscle aches', which this could turn patients away from this service.	Thank you for your comment. The indicator guidance highlights that personalised care adjustments should be considered when a patient declines treatment. As part of the update to NICE guideline CG181, tools and resources to support implementation and patient choice are being considered.
31	1	CaReMe-UK	Yes. Previous promotion of the 'fire and forget' approach to lipid management still holds traction and sometimes extends into the secondary prevention arena. Support and education will be required to facilitate obtaining annual lipid profiles for people with CVD.	Thank you for your comment.
32	1	Leeds Teaching Hospitals NHS Trust	Yes: we need to support annual lipid checks and ensure no "fire and forget approach"	Thank you for your comment.
33	1	CVD Prevention & Management Team West Midlands Academic Health Science Network	Yes, clinical inertia due to secondary prevention never being incentivised and previous threshold of TC = 5 was clinically inappropriate.	Thank you for your comment..

Question 2 : Do you think there are potential unintended consequences to implementing/using any of these indicators?

34	2	British Cardiovascular Society	No	Thank you for your comment.

		(response endorsed by Royal College of Physicians)		
35	2	British Medical Association	With respect to unintended consequences, respondents raised concerns that medication (e.g. statins) required could increase overall general practice appointments with patients concerned about side effects. Patients mistakenly identifying muscle aches as a symptom of the statin may discontinue treatment. Deprescribing is being strongly encouraged which is appropriate but can pose risks of medications being stopped too prematurely which could cause worsening of a lipid profile.	Thank you for your comment. The indicator guidance highlights that personalised care adjustments should be considered when a patient declines treatment. As part of the update to NICE guideline CG181, tools and resources to support implementation and patients choice are being considered.
36	2	CaReMe-UK	No.	Thank you for your comment.
37	2	Leeds Teaching Hospitals NHS Trust	No.	Thank you for your comment.
38	2	West Midlands Academic Health Science Network, CVD Prevention & Management Team	Yes, increase incidence of avoidable CV events in addition to undermining NICE CG181 recommendations and the AHSN Network, NHS England and Accelerated Access Collaborative initiatives to improving cholesterol management	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The

				guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.

Question 3: Do you think there is potential for differential impact (in respect of age, disability, gender and gender reassignment, pregnancy and maternity, race, religion or belief, and sexual orientation)? If so, please state whether this is adverse or positive and for which group.

39	3	British Cardiovascular Society (response endorsed by Royal College of Physicians)	No	Thank you for your comment.
40	3	British Medical Association	With respect to differential impact, respondents consistently argued this will disproportionately affect older patients, who are by default more likely to seek help for muscle aches and pains and may falsely attribute these to statins. Respondents were concerned that this indicator could worsen the existing struggle between meeting QOF thresholds whilst avoiding the burden of multiple medication for elderly patients.	Thank you for your comment. Personalised care adjustments could be used could be used to exclude patients from indicator denominators dependent on circumstances. Examples of these are included in the indicator specification and have been amended following consultation
41	3	CaReMe-UK	No.	Thank you for your comment.
42	3	Leeds Teaching Hospitals NHS Trust	No.	Thank you for your comment.

| 43 | 3 | West Midlands Academic Health Science Network, CVD Prevention & Management Team | Yes, seldom heard communities and those in rural populations will be further disadvantaged by this indicator. | Thank you for your comment. |

Question 4: If you think any of these indicators may have an adverse impact in different groups in the community, can you suggest how the indicator might be delivered differently to different groups to reduce health inequalities?

44	4	British Cardiovascular Society (response endorsed by Royal College of Physicians)	No.	Thank you for your comment.
45	4	CaReMe-UK	Not applicable.	Thank you for your comment.
46	4	Leeds Teaching Hospitals NHS Trust	No.	Thank you for your comment.

Question: We welcome comments on the proposed non-HDL level of less than 3.3 mmol/L across a general practice population. Do you agree with using this to drive population level improvements in cholesterol management? If not, what level should be used and why?

| 47 | General | British Cardiovascular Society (response endorsed by Royal College of Physicians) | No

BCS is surprised that it is not easy for QoF to use the 40% reduction cutoff. It would not seem that a complex software fix would be required to use this. | Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be |

				BCS has concerns that the widely recognised target for non-HDL level of <2.5 is not at the core of the proposed QOF target. We note, based on data from the SMART risk score using UK primary care data, that median non-HDL cholesterol is around 3.4mmol/l. (European Journal of Preventive Cardiology (2021) 00, 1–10 doi:10.1093/eurjpc/zwab093) This means that a QOF that uses this level will mean no additional lipid lowering is offered for half of CVD patients. Accepting a threshold of 3.3 as opposed to 2.5 would expose those patients to a substantially elevated risk of CVD events over the next ten years (about a 25% relative risk increase). A 3.3 threshold would only be useful if a very high proportion of CVD patients were expected to reach this threshold to qualify for the QOF target. At a median level of 3.4 already, status quo would be for 50% of patients to meet the threshold without any action. A substantially higher target percentage would need to be set for the threshold to have any significant impact. BCS would argue for as high a percentage target as realistically possible to be set. BCS would recommend that, for the sake of simplicity, a single target of <2.5 be used, in line with other guidance. However, if this is not felt achievable in the short term, BCS propose that, for patients already at the 3.3 non-HDL level, the target of <2.5 be used. We feel that hitting the <2.5 threshold is eminently possible if there is a big increase in combination therapies for lipid lowering (such as a High intensity statin with ezetimibe). Such treatment is likely to be practical and cost effective given that these therapies are now available as generics and are well tolerated. The QOF could accommodate a more aggressive lipid lowering approach by having a binary target:	consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.

			QOF target = x% of CVD patients have non-HDL <2.5 and y% have a non-HDL <3.3, (where x is significantly greater than 25% and y is significantly higher than 50%) Over time, BCS would expect that the 3.3 threshold would be gradually lowered, with the ultimate aim of the great majority of CVD patients hitting the 2.5 threshold, using combination therapies.	
48	General	CaReMe-UK	No. We strongly disagree with the proposed non-HDL level of 3.3mmol/L. The median non-HDL cholesterol concentration in the UK population in 3.4mmol/L so the proposed level of 3.3mmol/L will not add significant discrimination nor value (McKay AJ, et al. Eur J Prev Cardiol. 2022 Mar 30;29(4):654-663. doi: 10.1093/eurjpc/zwab093). It would provide no incentive to substantially improve lipid management in patients will CVD at a population level and allow delivery of the objectives of the NHS 10-year plan. People with non-HDL cholesterol concentration of 3.3mmol/L have a 10-year risk of cardiovascular events which is unacceptably hight at around of 29% (McKay AJ, et al. Eur J Prev Cardiol. 2022 Mar 30;29(4):654-663. doi: 10.1093/eurjpc/zwab093). We advocate using a non-HDL indicator level of less than 2.5 mmol/L (equivalent to LDL-cholesterol 1.8mmol) in keeping with other guidance. We also ask NICE to consider the importance of multiple risk factor intervention in high-risk individuals, particularly those with CVD in combination with diabetes and/or chronic kidney disease. In future, combining indices taking into account multiple risk factors may be advantageous. Finally, we suggest NICE considers the emerging emphasis on lifetime risk captured in the Joint British Societies JBS3 guidance.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.

49	General	IND2	Completely understand the rationale for picking non-HDL 3.3. I know it is not meant to infer that is the treatment target but I am worried that that is what will be inferred (therefore would prefer a lower target but understand that therefore it is unlikely that it will be met with success	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
50	General	Innovation Agency	Target level There was a strong consensus from those submitting on behalf of, that the target level should be set at 2.5 mmol/L for non-HDL cholesterol (and 1.8 mmol/L for LDL-c) and not 3.3 mmol/L. Witnessed in the meeting held on Tuesday 27 September between individuals listed in this response and NICE colleagues; Mark Minchin, Kay Nolan, and Catrina Charlton. This target level would bring us in line with best practice and the target levels that are being adopted internationally. We recognise that it has been important to take a pragmatic approach to the suggested target level. However, previous experience on blood pressure has shown us that reducing the clinical target, in order to make it achievable, is not the right approach. This type of approach endorses an acceptance of sub-optimal clinical care in minds of clinicians which it is then difficult to move away from. We would urge you to adopt the 2.5 mmol/L target for non-HDL-c	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published

			and the concerns about achievability can be managed through how the metric is constructed, i.e., adjusting payment triggers based on the number of patients that meet the target. This means that whilst we might adjust the payment thresholds between years, the clinical target remains consistent and becomes embedded. We strongly believe this is a key principle that needs to be adopted	December 2023; the indicator has been updated to be consistent with the updated guideline.
51	General	Leeds Teaching Hospitals NHS Trust	No. We strongly disagree with the proposed non-HDL level of 3.3mmol/L. The median non-HDL cholesterol concentration in the UK population in 3.4mmol/L so the proposed level of 3.3mmol/L will not add significant discrimination nor value (McKay AJ, et al. Eur J Prev Cardiol. 2022 Mar 30;29(4):654-663. doi: 10.1093/eurjpc/zwab093). It would provide no incentive to substantially improve lipid management in patients will CVD at a population level and allow delivery of the objectives of the NHS 10-year plan. People with non-HDL cholesterol concentration of 3.3mmol/L have a 10-year risk of cardiovascular events which is unacceptably hight at around of 29% (McKay AJ, et al. Eur J Prev Cardiol. 2022 Mar 30;29(4):654-663. doi: 10.1093/eurjpc/zwab093). We advocate using a non-HDL indicator level of less than 2.5 mmol/L (equivalent to LDL-cholesterol 1.8mmol) in keeping with other guidance. We also ask NICE to consider the importance of multiple risk factor intervention in high-risk individuals, particularly those with CVD in combination with diabetes and/or chronic kidney disease. In future, combining indices taking into account multiple risk factors may be advantageous. Finally, we suggest NICE considers the emerging emphasis on lifetime risk captured in the Joint British Societies JBS3 guidance.	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline.
52		Royal College of General Practitioners	The NICE guideline for Cardiovascular disease: risk assessment and reduction, including lipid modification (CG181) is currently undergoing a review and update which is due to publish in May 2023. We do not believe that a number should be chosen in advance of this formal review without full evidence of effect, long term benefit, understanding of	Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022.

			treatment burden and cost effectiveness. There are significant risks to choosing a random number based on "best guess" for this indicator. This will undermine the work of NICE's evidence-based approach, its rigour and as an unintended consequence, even its reputation as being robust and independent. We would therefore strongly advise against this as is likely to change within 12 months when the updated CG181 is published and could cause significant unintended consequences. It can take time for standard clinical practice to change, for codes and templates on computers to be updated with educational resources required to disseminate best practice. Whilst a fixed target is assumed to be the best approach, a moving fixed target will not help a workforce who have to make significant changes to their approach to care each time the cut off changes. Therefore, if is essential for an absolute figure is to be included in this indicator, then we propose it would be better to use already established markers within primary care as a starting point, whilst waiting for NICE to determine the evidence and cost-effective level to aim for. A value for non-HDL of <4 has long been used in primary care, and so we would support this aim as an interim figure as a college.	The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator has been updated to be consistent with the updated guideline. The current NICE menu indicator NM212 (general practice level indicator) measures the percentage of patients with cardiovascular disease who are currently treated with a lipid lowering therapies therapy (including statins). We will continue to explore potential new indicators relevant to other aspects of the lipid management pathway.
			Some comments from our clinical advisers below:	
			Non-HDL cholesterol is not necessarily the best predictor of CVD and hence aiming to reduce it may not produce improvements in all-cause mortality. There have been trials which have shown that using interventions to lower the serum cholesterol levels does not translate directly to a lower risk of death[1] and therefore this indicator may not have the impact intended and ultimately just increase workloads for general practice.	
			There is also research that shows that patients who have suffered an acute myocardial infarction have lower than normal LDL-C levels; that the degree of coronary artery calcification is not associated with LDL-C; and that 27 follow-up studies have shown that people with high total	

| | | | | cholesterol or LDL-C live just as long or longer than people with low cholesterol. The lack of exposure-response in the statin trials should also be considered as several of these trials have been unable to lower CVD or total mortality and no statin trial has succeeded with lowering mortality in women, elderly people, or diabetics[2].

Additionally, the research and evidence is not certain on how non-HDL levels create risk for men and women differently, particularly for older women. In a study looking at women aged 68 to 81 years, at baseline neither higher HDL nor lower LDL levels predicted survival to age 90, but higher LDL predicted healthy survival. These findings suggest the need for re-evaluation of healthy LDL levels in older women[3].

There is some evidence to show that an increased triglyceride/high-density lipoprotein cholesterol ratio (where TG are high and HDL-C are low) is a far better predictor of coronary atherosclerotic disease than identifying those with a non-HDL level over >3.3mmol/L if looking at CAC scores[4].

There needs to be the IT infrastructure to support any new lipid target. The system should be able to automatically identify when a patient's blood work has come back with a value higher than the one selected for the indicator and create a flag so that the acting physician knows that they should be offering lifestyle support and secondary interventions if necessary.

While having a specific target is simpler than calculating a percentage and more easily captured in the system, any particular value chosen in arbitrary. It would be simpler to make the indicator about prescribing atorvastatin 80mg (as per NICE guidance). This provides extra risk reduction and would be much easier for practices to simply do bulk switches of dose (if they chose to). Therefore, it is more likely to reach more patients with interventions rather than have everyone fiddling around with multiple repeat blood tests which will not be a priority in the current climate. | |

			1. Ramsden, C.E., et al., Re-evaluation of the traditional diet-heart hypothesis: analysis of recovered data from Minnesota Coronary Experiment (1968-73). BMJ, 2016. 353: p. i1246. 2. Ravnskov, U., et al., The new European guidelines for prevention of cardiovascular disease are misleading. Expert Rev Clin Pharmacol, 2021: p. 1-6. 3. Maihofer, A.X., et al., Associations between Serum Levels of Cholesterol and Survival to Age 90 in Postmenopausal Women. J Am Geriatr Soc, 2020. 68(2): p. 288-296. *4. Caselli, C., et al., Triglycerides and low HDL cholesterol predict coronary heart disease risk in patients with stable angina. Scientific Reports, 2021. 11(1): p. 20714.*	

Question: Should the indicator include an LDL component alongside non-HDL? For example:
'The percentage of patients with CVD in whom the last recorded non-HDL cholesterol (measured in the preceding 12 months) is less than 3.3 mmol/L, or where this is missing a recording of LDL cholesterol in the preceding 12 months that is less than 2.6 mmol/L'

53	General	British Cardiovascular Society (response endorsed by Royal College of Physicians)	Yes (but). There are definite advantages to having LDL-C alongside non-HDL, as several newer therapies use LDL-C thresholds in the key trials testing their efficacy. However, it clearly makes lipid monitoring more complex, and may not be widely available. It requires a fasting sample, so less convenient for patients and so may be more difficult to obtain for all patients. There may therefore be an argument for keeping the threshold simple to start with using non-HDL only, and introducing LDL as the target is refined in later years.	Thank you for your comment. The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and includes an LDL and non-HDL level.
54	General	British Medical Association	With respect to the question 'Should the indicator include an LDL component alongside non-HDL?', respondents said this should be	Thank you for your comment.

			deferred until existing and proposed QOF indicators have had sufficient time for implementation and evaluation.	The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and includes an LDL and non-HDL level.
55	General	CaReMe-UK	Yes. We strongly encourage an LDL-cholesterol indicator to be introduced alongside non-HDL. With the exception of statins, all of the lipid management treatments approved by NICE (bempedoic acid, PCSK9 inhibitors, inclisiran, icosapent ethyl) include LDL-cholesterol thresholds for initiation. It is counter-intuitive for this indicator to be presented solely as non-HDL cholesterol, when LDL-cholesterol concentrations are mandatory for prescribing decisions in lipid optimisation. For consistency across NICE technology appraisals, NICE guidance and QOF indicators, routine measurement and utilisation of LDL-cholesterol concentrations should be advocated.	Thank you for your comment. The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and includes an LDL and non-HDL level.
56	General	Heart UK – The Cholesterol Charity	LDL-C is calculated FROM non-HDL-C (by Friedewald, as commonly used LDL-C = non-HDL-C –(fTG/2.2). Therefore even if only LDL- C is reported, there will always be the non HDL-C used to derive LDL-C, although it may not be reported by some laboratories. LDL-C should ONLY be reported if the sample has been collected in the overnight fasting condition (10-14 hours). Samples and requests should therefore be clearly labelled as fasting or non-fasting, which aids the interpretation of triglyceride results.	Thank you for your comment. The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and includes an LDL and non-HDL level.
57	General	IND2	I think LDL should definitely be included as the treatment pathways for additional drugs are based on LDLs so everyone should have access. One thing to consider should LDL be the lead and non-HDL an additional?	Thank you for your comment. The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and

					includes an LDL and non-HDL level.
58	General	Leeds Teaching Hospitals NHS Trusts	Yes. Most NICE approved treatments include or specifically include an LDL-C threshold for initiation and are essential in prescribing decision making. In order to ensure consistency across NICE TAs/ guidelines and QOF indicators then LDL-C needs to be included. We understand that getting fasting samples can be challenging, however we strongly advocate measurements and performance indicators based on LDL-C.		Thank you for your comment. The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and includes an LDL and non-HDL level.
59	General	North East and North Cumbria Lipid Specialists Advisory Group	The indicator should have an LDL component alongside Non-HDL. For a Non-HDL target of <2.5 mmol/L the corresponding LDL target would be < 1.8 mmol/L		Thank you for your comment. The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and includes an LDL and non-HDL level.
60	General	Royal College of General Practitioners	Currently many CVD prevention guidelines include both a non-HDL and an LDL value. While this may not be absolutely necessary, it may make it easier for practices to adhere to this indicator and still keep track of patients who may require lipid lowering interventions.		Thank you for your comment. The guideline was updated and published December 2023; the indicator has been updated to be consistent with the updated guideline and includes an LDL and non-HDL level.

Question: Should patients with a diagnosis of familial hypercholesterolaemia be excluded?

61	General	British Cardiovascular Society (response endorsed by Royal College of Physicians)	Yes - they should be managed with individualised care plan. Target levels for nonHDL will likely be different for this group.	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator.
62	General	British Medical Association	With respect to the question 'Should patients with a diagnosis of familial hypercholesterolaemia be excluded?', respondents said yes. One respondent explained this was because these patients often receive care in secondary care settings, and are far more challenging to engage.	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator.
63	General	CaReMe-UK	Yes – people with FH should be excluded from the general secondary prevention population and should have a distinct and more stringent indicator.	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator.
64	General	Heart UK – The Cholesterol Charity	Familial hypercholesterolaemia patients should absolutely be included within this population. These patients need and deserve the same, indeed possibly lower since these individuals maybe younger or having recurrent events.	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator given consideration of comments and exclusion from the evidence review for the supporting recommendations. A separate indicator for people with FH is currently being explored.

65	General	IND2	I think FH patients should be included as this is secondary prevention so we need at least an LDL <2.6 due to the fact the main risk in these patients is the LDL so we should be particularly aggressive (but admit may have less success due to elevated baseline).	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator given consideration of comments and exclusion from the evidence review for the supporting recommendations. A separate indicator for people with FH is currently being explored.
66	General	Leeds Teaching Hospitals NHS Trusts	Yes. People with FH should have a separate measures and targets.	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator.
67	General	North East and North Cumbria Lipid Specialists Advisory Group	Patient with Familial Hypercholesterolaemia should not be excluded. These patients are at higher risk of CVD and if they develop CVD it is important that lipid profiles are managed aggressively to achieve low Non-HDL / LDL to prevent further CVD events. Use of combination therapy (high intensity statins / ezetimibe / PCSK9i) can help achieve lower NonHDL / LDL targets in the majority of FH patients with CVD,	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator given consideration of comments and exclusion from the evidence review for the supporting recommendations. A separate indicator for people with FH is currently being explored.

68	General	Primary Care Cardiovascular Society	In terms of secondary prevention patients with a diagnosis of familial hypercholesterolaemia should be included. These patients may be eligible for injectable lipid lowering medicines with CVD outcome data (PCSK9 inhibitors). However, as baseline levels are significantly raised in FH patients getting to this target for patients with FH is very challenging. Higher achievement of the targets would be possible if the NICE criteria for PCSK9 inhibitor were to be reviewed with a lower LDL-C threshold for treatment. The focus of treatment of FH should be on early identification and treatment to prevent the years of LDL-C burden and consequent early cardiovascular disease.	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator given consideration of comments and exclusion from the evidence review for the supporting recommendations. A separate indicator for people with FH is currently being explored.
69	General	Royal College of General Practitioners	We don't see any reason why patients with familial hypercholesterolaemia should be excluded from this indicator. However, there are some patients who we feel should be excluded from this indicator such as those who are pregnant, breast feeding, of reproductive age not using contraception and those taking other drugs which interact with statins such as amiodarone	Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator given consideration of comments and exclusion from the evidence review for the supporting recommendations. A separate indicator for people with FH is currently being explored. The indicator guidance highlights that personalised care adjustments should be considered when lipid lowering therapy is not appropriate for the individual.

Question: Would a similar indicator focussed on people with chronic kidney disease be useful and should it use the same level of non-HDL cholesterol?

70	General	British Cardiovascular Society (response endorsed by Royal College of Physicians)	Yes. Yes.	Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.
71	General	British Medical Association	With respect to the question 'Would a similar indicator focussed on people with chronic kidney disease be useful and should it use the same level of non-HDL cholesterol?', respondents had mixed views. There was a sense that this may have clinical merit, but that this should be considered at a later point once existing and proposed QOF indicators have had sufficient time for implementation and evaluation.	Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.
72	General	CaReMe-UK	Yes. We advocate using a similar indicator in people with chronic kidney disease. We advocate using a non-HDL indicator level of less than 2.5 mmol/L (equivalent to LDL-cholesterol 1.8mmol).	Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without

					cardiovascular disease will not be included in the denominator.
73	General	Heart UK – The Cholesterol Charity	The non-HDL-C indicator is appropriate in CKD, however the importance of simultaneous measurement of triglycerides is even more important in this population.		Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.
74	General	IND2	I think we do need to include CKD but I agree this is trickier. As the pts are eligible for injectables would it be simplest to use the same target?		Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.
75	General	IND5	I would recommend the same approach for primary prevention and CKD as above but not including the inclisiran addition. This targeted approach is even more important in primary prevention because initial therapy will almost always be of lower intensity statin than used for ASCVD so far fewer patients will achieve 40% reduction, so having a target becomes more important.		Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular

					disease. Those without cardiovascular disease will not be included in the denominator.
76	General	Leeds Teaching Hospitals NHS Trusts	Yes. We would support a non-HDL indicator level of less than 2.5mmol/L (equivalent to LDL-cholesterol 1.8mmol).		Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.
77	General	North East and North Cumbria Lipid Specialists Advisory Group	A similar indicator focused on patients with CKD (eGFR < 60) would be useful and should use the same Non-HDL / LDL targets. Again the targets should be Non-HDL < 2.5 / LDL < 1.8. CKD does not significantly restrict the therapeutic options available in terms of lipid lowering agents and these patients are at high risk of further CVD so a more ambitious target is preferable.		Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.
78	General	Primary Care Cardiovascular Society	A similar indictor for people with CKD for secondary prevention would be useful and the same targets should be used		Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they

				have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.
79	General	Royal College of General Practitioners	We don't believe that an indicator similar to this one should be developed for people with CKD, especially not with the target being HDL-C. Definitions for CKD are too wide for this type of indicator to be applied to everyone.	Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator.

Appendix C: Consultation comments from respondents with links to the tobacco industry

Novartis Pharmaceuticals UK Ltd declared that:

- Since April 2005 Novartis has exclusively licensed glycopyrronium bromide and certain intellectual property relating to its use and formulation from Vectura and its co-development partner, Sosei Heptares.
- The following inhaled medications are comprised of, or contain glycopyrronium bromide:
  - Seebri® Breezhaler® (glycopyrronium bromide) (used as a maintenance treatment for Chronic Obstructive Pulmonary Disease (COPD))
  - Ultibro® Breezhaler® (indacaterol/glycopyrronium bromide) is used as a maintenance treatment for COPD
  - Enerzair® Breezhaler® (indacaterol/glycopyrronium bromide/mometasone furoate) is used as a maintenance treatment for asthma uncontrolled with LABA/ICS.
- Phillip Morris International (a tobacco company) has acquired Vectura Group Limited (formerly Vectura Group plc).

ID	Question	Stakeholder	Comment	
1	General	Novartis Pharmaceuticals UK Ltd.	We welcome the proposed move towards absolute target for cholesterol levels within the QOF. The current iteration of NICE guidance for lipid management CG181 recommends a 40% non-HDL-C reduction target which has several limitations recognised in the consultation. This approach has conflicted with more recent Joint British Society (JBS) lipid management guidance, which specifies absolute threshold targets of non-HDL <2.5mmol/L (equivalent to LDL-C <1.8mmol/L) and European Society of Cardiology	Thank you for your comment.

I D	Question	Stakeholder	Comment	
			(ESC) guidance with an LDL-C target of 1.4mmol/L in secondary prevention patients (and even 1.0mmol/L in some cases). Use of an absolute cholesterol measure, as opposed to a percentage reduction from baseline, is an evidence-based practice that has been adopted by international guidelines to reduce associated risks of CV events in secondary prevention population. Aligning UK practice with international guidelines using an absolute measure for cholesterol will bring much needed clarity and simplicity for healthcare practitioners, allowing them to follow one consistent indicator across the nation to deliver optimal care for the whole population, thus reducing the associated risks of cardiovascular events. .	

Question: We welcome comments on the proposed non-HDL level of less than 3.3 mmol/L across a general practice population. Do you agree with using this to drive population level improvements in cholesterol management? If not, what level should be used and why?

| 2 | IND2022-133 | Novartis Pharmaceuticals UK Ltd. | We welcome comments on the proposed non-HDL level of less than 3.3 mmol/L across a general practice population. Do you agree with using this to drive population level improvements in cholesterol management? If not, what level should be used and why?

No - we believe the proposed non-HDL indicator of 3.3 mmol/L is neither sufficiently ambitious nor evidence based to drive improvements in patient care with CV risk, in line with the NHS Long Term Plan.

The NHS Long Term Plan sets out an ambition to prevent up to 150,000 cardiovascular events in 10 years and whilst the addition of an absolute indicator is welcomed as an important step forward to drive prioritisation of cholesterol management in general practice, using a threshold of non-HDL-C of less than 3.3mmol/L poses significant clinical risks and will not | Thank you for your comment. Development of this indicator was paused following the Indicator Advisory Committee meeting in November 2022. The committee agreed that an indicator should reflect and be consistent with evidence-based recommendations on lipid management in the NICE guideline for cardiovascular disease (CG181). The guideline was subsequently updated and published December 2023; the indicator |

| | | | help drive the aforementioned NHS ambition. The secondary prevention population to which this QOF indicator applies currently has an average non-HDL-C of 3.4mmol/L 1, as such a new target of 3.3 mmol/L will add system costs without bringing any significant clinical improvement at population level versus what is already being achieved and may therefore drive inaction. A non-HDL-C of 3.3 mmol/L is associated with a 10 CV-year risk of 29%1. Evidence from meta-analysis has demonstrated that every 1 mmol reduction in LDL-C reduces CV risk by 21%2.

We believe the indicator should align with the most recent Joint British Society (JBS) lipid management guidance, referenced in the nationally recognised AAC/NHS lipid guidance pathway, which specifies a non-HDL-C target of <2.5mmol/L (equivalent to LDL-C <1.8mmol/L). It is important that the NICE indicator reflects both national and international best practice, since setting an indicator any higher risks encouraging sub-optimal management of hypercholesterolaemia within general practice.

The inclusion of an additional threshold number for non-HDL cholesterol attainment risks creating further confusion for a primary care workforce who are not currently working to a hard target. It could have the unintended consequence of decreased prioritisation of patients who achieve non-HDL-C of 3.3mmol/L QOF threshold, but crucially may remain above the clinical treatment targets and so at increased risk of further cardiovascular events. Within the consultation document, NICE refer to the baseline CVDPrevent data which assessed, and will continue to assess, the English population against hard targets of non-HDL-C<2.5mmol/L or LDL-C<1.8mmol/L. Having two conflicting sets of standards for lipid management would be likely to cause significant confusion within primary care. Alignment with CVDPrevent and guidelines is of important educational value to drive excellence in care, assisting with local pathway implementation and supporting both | has been updated to be consistent with the updated guideline. |

| | | | | clinicians and patients in better management of their cholesterol to agreed clinical target levels.

The current CVDPrevent analysis showing 23.7% of patients currently achieving a target of 2.5 mmol/L reflects generalised monotherapy lipid management, with very little use of ezetimibe, bempedoic acid / ezetimibe combinations or inclisiran. However, we believe optimised lipid management, including appropriate combination use of NICE recommended treatments, can make a target of 2.5 mmol/L achievable. For example, approximately 70% of patients achieved an LDL-C of 1.8 in the pivotal trials for inclisiran (equivalent to non-HDL-C of 2.5 mmol/L). Optimised lipid management has the potential to positively impact CV risk at a population level.

Whilst we recognise that achieving non-HDL-C levels of <2.5mmol/L for all patients could initially be challenging for many practices, we suggest a more appropriate way of tackling this issue, would be by amending the threshold patient percentages that trigger payments over time, rather than amending the non-HDL-C value itself. We consider that embedding an aspirational non-HDL-C target which remains constant over the long-term, will drive longer-lasting improvements in care and more meaningful reductions in CV risk for individual patients.

We note that ambitious QOF targets have been set in other clinical domains, and hence query why an alternative approach is proposed for hypercholesterolaemia. Furthermore, learning from the experience with blood pressure, where it has been acknowledged that reducing clinical targets to those that are more feasible, has not been the best approach. | |

| | | | In line with the above, we suggest NICE re-consider the non-HDL-C threshold level of 3.3 mmol/L to align with other national and international evidence-based guidance. We propose a non-HDL cholesterol level of 2.5 mmol/L (with equivalent LDL-C 1.8 mmol/L) would be a more appropriate indicator, signalling the ambition that will be necessary to drive improvements in patient care.

Reference 1: McKay, Ailsa J., et al. "Is the SMART risk prediction model ready for real-world implementation? A validation study in a routine care setting of approximately 380 000 individuals." European Journal of Preventive Cardiology 29.4 (2022): 654-663)

Reference 2: Efficacy and Safety of Further Lowering of Low-Density Lipoprotein Cholesterol in Patients Starting With Very Low Levels - PMC (nih.gov) | |

Question: Should the indicator include an LDL component alongside non-HDL? For example:
'The percentage of patients with CVD in whom the last recorded non-HDL cholesterol (measured in the preceding 12 months) is less than 3.3 mmol/L, or where this is missing a recording of LDL cholesterol in the preceding 12 months that is less than 2.6 mmol/L'

| 3 | IND2022-133 | Novartis Pharmaceuticals UK Ltd. | Should the indicator include an LDL component alongside non-HDL?

Yes – we consider it would be appropriate to include both LDL-C and non-HDL-C components.

Aligned to both CVDPrevent and Joint British Society (JBS) lipid management guidance, which specify target values for both LDL-C and non-HDL-C, we believe it would be appropriate to include both components within the NICE indicator. As outlined above, we believe the appropriate levels are those aligned to both national and international | Thank you for your comment. |

| | | | best practice guidelines i.e. non-HDL-C<2.5mmol/L and LDL-C <1.8mmol/L.

Given the various geographical coding anomalies and inconsistencies in ways of measuring cholesterol, we believe it would make sense to include both non-HDL-C and LDL-C as "either /or" options within the indicator. We cannot foresee any disadvantages associated with inclusion of LDL-C alongside non-HDL-C.

Furthermore, adding an LDL-C metric would aid alignment with NICE technology appraisal guidance for individual therapies, which commonly stipulate threshold criteria in terms of LDL-C, rather than non-HDL-C. | |

Question: Should patients with a diagnosis of familial hypercholesterolaemia be excluded?

| 4 | IND2022-133 | Novartis Pharmaceuticals UK Ltd. | Should patients with a diagnosis of familial hypercholesterolaemia be excluded?

Yes. We believe including familial hypercholesterolaemia patients would risk sub-optimal cholesterol management within this high-risk group, who should be managed to more aggressive targets aligned with international guidelines. | Thank you for your comment. People with familial hypercholesterolemia have been excluded in the specification for the published indicator given consideration of comments. A separate indicator for people with FH is currently being explored. |

Question: Would a similar indicator focussed on people with chronic kidney disease be useful and should it use the same level of non-HDL cholesterol?

| 5 | IND2022-133 | Novartis Pharmaceuticals UK Ltd. | Would a similar indicator focussed on people with chronic kidney disease be useful and should it use the same level of non-HDL cholesterol?

Yes. We believe a similar indicator focused on people with chronic kidney disease (CKD) would be useful. CKD patients have high rates of cardiovascular disease, including CV-related mortality, and yet more | Thank you for your comment. In line with the updated guideline on lipid modification (CG181), people with chronic kidney disease will be included in the indicator if they have |

| | | | intensive lipid-lowering therapy options are not recommended in this group (see CG181), with the result that many CKD patients remain at above target cholesterol levels. Any efforts that support better management of these patients are to be welcomed. We recognise there are substantial clinical unmet needs in both primary and secondary prevention CKD patients, so would urge consideration of both these populations within an indicator. We believe that renal disease experts are best placed to advise on the selection of appropriate levels for non-HDL-C and LDL-C in both primary and secondary prevention CKD patients. | existing cardiovascular disease. Those without cardiovascular disease will not be included in the denominator. |