2018 surveillance – Cardiovascular disease: risk assessment and reduction, including lipid modification (2014) NICE guideline CG181

Appendix B: stakeholder consultation comments table

Consultation dates: 19 October to 03 November 2017

Do you agree with the proposal to partially update the guideline?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	Yes	No comments provided	Thank you.
Primary Care Diabetes Society	Yes	No comments provided	Thank you.
NHS Medway CCG	Yes	No comments provided	Thank you.
Wolfson Institute of Preventive Medicine	Not answered	The opportunity to comment on the guideline on cardiovascular disease is welcome.	Thank you.
Boston Scientific	Yes	No comments provided	Thank you.
Association of British Clinical Diabetologists (ABCD)	Yes	No comments provided	Thank you.
Royal College of Nursing	Yes	There is a strong indication that there is substantial evidence for the required update. The issues highlighted appear relevant.	Thank you.

Novo Nordisk	Yes	No comments provided	Thank you.
Public Health England	Not answered	No comments provided	Stakeholder provided no comment.
HEART UK- The Cholesterol Charity	Not answered	No comments provided	Stakeholder provided no comment.
Amgen Ltd	Yes	We feel that it is essential that the Guideline is reviewed and specifically the following key areas are covered in the Guideline update (see lines below): 1) Absolute clarity on the frequency of monitoring and follow up of both primary and secondary prevention patients to ensure that lipid levels are adequately controlled in a timely manner and that patients receive the appropriate advice, care and medication they need to modify their lipid levels and reduce their risk of cardiovascular events. We support expert feedback which highlighted that further guidance was considered necessary on the methods to use across the healthcare pathway to identify people with an estimated increased risk of CVD, how frequently this identification should be done and which healthcare professionals should carry it out. It is disappointing to note (page 5) that despite the fact new systematic review evidence indicates that more frequent monitoring strategies are cost effective, NICE seem to have taken the view that this partially supports the current recommendations (i.e. to use a systematic strategy to identify people who are likely to be at high risk) but that as CG181 does not stipulate monitoring frequencies new evidence is unlikely to change guideline recommendations. We feel that clinical guidelines should provide clear guidance to the NHS thereby avoiding inappropriate variation in patient treatment and ensuring patients at high risk are both identified and have their treatment optimised appropriately in an efficient and timely manner to prevent avoidable events. We therefore recommend that NICE clearly consider monitoring and follow up frequency of both primary and secondary prevention patients. Clinicians currently have a suite of lipid modifying therapies available to them which can be used to dramatically decrease the risk of cardiovascular events. However, without clear and effective monitoring to identify appropriate patients, initiate treatment and subsequently manage their lipids through to an optimal lipid lowering regime, patients are left at significant cardiovascular event risk. Cardiovascular events are life-changing and importantly avoidable, contributing to a considerable burden on the NHS and society. With regard to patient follow-up, we note the current guideline recommendation 1.3.28 (as detailed on page 30) indicates following up patients at 3 months of treatment. However,	Thank you for comments. 1) frequency of monitoring The surveillance review did not find evidence to impact on recommendations 1.3.28 and 1.3.29, relating to initial follow up at 3 months and thereafter annual medication reviews for people taking statins. Since the new evidence for annual monitoring was derived from computer models, there is unlikely to be an impact on the guideline until further validation studies become available to substantiate the findings. New research will be considered in this area at the next surveillance review. 2) Monoclonal antibodies The surveillance review acknowledged the potential value of PSCK9 inhibitors (monoclonal antibodies) in prevention of CVD, which is captured by the following technology appraisals: TA393 Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (June 2016) TA394 Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (June 2016) There is a potential need for CG181 to cross refer to these technology appraisals in the section on lipid

		assuming patients do not achieve recommended targets, we feel there is unclear guidance on how to proceed should statin treatment need to be modified or if the patient is already on maximally tolerated statin therapy, especially as this is followed by recommendation 1.3.29 suggesting provision of annual medication reviews for people taking statins. If treatment is modified we feel it should be explicitly stated that ongoing follow up at 3 month intervals is recommended to ensure that optimal lipid modifying treatment is achieved quickly. Once that has been achieved then annual monitoring is welcome, but not before. In addition, if maximally tolerated statin therapy has been achieved and target reductions not met then clear guidance on alternative treatment options or referrals should be made. 2) We note that the surveillance decision was made not to add the review question 'Monoclonal antibodies for the primary and secondary prevention of CVD' as it is felt that new evidence is unlikely to change guideline recommendations. It was noted however that the technology appraisals relating to evolocumab (TA394) and alirocumab (TA393) have already been included in the related NICE Pathway. We firmly believe that the intention of this clinical guideline should be to provide clear clinical guidance to the NHS on the risk assessment and reduction of cardiovascular disease, including lipid modification. As an innovative and important treatment option for the management of patients who remain at very high risk of cardiovascular events due to elevated LDL-C levels despite treatment with e.g. statins, we therefore feel it is imperative that the appropriate use of PCSK9 inhibitors is clearly described in the guideline in line with their current NICE guidance. As indicated in the review proposal, Topic experts noted widespread confusion over the separate technology appraisals, and as such this guideline offers the perfect opportunity for NICE to clearly guide the NHS on the most appropriate methods of lipid modification for patients at high risk of cardiovascular events. 3) We note that the current recommendation 1.3.28 (as detailed on page 30 of the review proposal) indicates that total cholesterol, HDL cholesterol and non-HDL cholesterol should be measured. Since the publication of CG181 the use of PSCK9 inhibitors has been approved by NICE (TA393 and TA394), however, qualification for treatment with a PCSK9 inhibitor is currently based on LDL-C thresholds. As PCSK9 inhibitors represent an innovative and important treatment option for the management of lipid levels we would strongly recommend that LDL-C levels are also routinely measured at treatment initiation and follow up, so that appropriate clinical decisions can be made in a timely and efficient manner to the benefit of patients. 4) We welcome (page 39) the statement that new evidence and expert feedback indicated that patients with statin intolerance are now recognised as a group at increased cardiovascular disease risk, and that there is a need to set out a clearer definition of statin intolerance. However, we would strongly challenge the findings that new evidence is unlikely to impact the	modification therapy for the primary and secondary prevention of CVD. This will be explored in the scoping process for the update. As noted, the technology appraisals are already included in the related NICE Pathway. 3) LDL-cholesterol measurement Recommendation 1.3.28 refers to follow up of people started on statin treatment, as distinct from people started on PCSK9 inhibitors. We did not identify evidence for measuring LDL-C routinely at follow up for people started on statin treatment. In formulating the recommendations for CG181, the guideline committee discussed that the Friedewald equation for calculation of LDL-cholesterol as commonly used for risk assessment requires a fasting sample and triglycerides below 4.5 mmol/litre. The committee were aware that a recent very large database analysis had revealed excess variance and bias in the calculation of LDL cholesterol such that a complicated table of correction factors would have to be applied by clinical laboratories. The formula was also limited in its utility at low LDL-cholesterol levels as seen with high-intensity statin treatment. The use of direct LDL-cholesterol measurement is limited by cost and availability in the NHS. Meta-analyses of CVD outcomes in relation to lipid fractions by the Emerging Risk Factors collaboration and others have consistently shown the superior predictive value of non-HDL cholesterol (that is, the difference between total and HDL cholesterol) on CVD events. Non-HDL cholesterol does not require a fasting blood sample. The committee decided that the use of non-HDL cholesterol was preferable to calculated or measured LDL

		current recommendations (to simply seek specialist advice about other possible treatment options as there were no alternatives to statins) as no alternative treatments were identified in the surveillance review. With reference to our comment above (2) current guidance for evolocumab recommends it as a treatment option for patients if LDL-C concentrations are persistently above defined thresholds despite maximal tolerated lipid lowering therapy (that is, either the maximum dose has been reached, or further titration is limited by intolerance). It is therefore surprising to us that 'no alternative treatments were identified in the surveillance review' when the use of evolocumab is currently recommended by NICE in statin intolerant patients and that there is clinical trial evidence for the use of evolocumab in statin intolerant patients (GAUSS-2, J Am Coll Cardiol 2014;63:2541-8; GAUSS-3, JAMA 2016;315:1580-90). We would recommend that this statement is reviewed and clear guidance given on approved treatment options. 5) We agree with topic experts who noted that a review of recommendation 1.3.28 for using high-intensity statins to achieve a percentage reduction, rather than an absolute lipid target level, should also be undertaken, especially as feedback has indicated that the recommended approach has not been adopted universally and many in both primary and secondary care are still treating to target in both primary and secondary prevention. The current recommended approach has particular issues for those patients who have extremely high lipid levels, whereby a proportional reduction, even if quite significant, may leave patients with high lipid levels and therefore they will remain at very high risk of cardiovascular events. We are concerned however that NICE believes this is not supported by any new evidence specifically for statin interventions. Given the suite of NICE approved lipid modifying therapies that are now available to clinicians and the growing body of evidence supporting a 'lower is better' approach to lipid management in order to reduce the risk of avoidable cardiovascular events (e.g. Giugliano, http://dx.doi.org/10.1016/S0140-6736(17)32290-0; Boekholdt, J Am Coll Cardiol 2014;64:485-94; Nicholls, JAMA 2016;316:2373-2384; Ference, Eur Heart J 2017;38:2459-2472; JBS3, Heart 2014;100:ii1–ii67) we feel it is essential that NICE reviews this recommendation to better manage residual risk in very high risk patients.	cholesterol given its greater practicality. No evidence was identified through surveillance to change this view. 4) Statin intolerance Recommendation 1.3.43 relating to statin intolerance advises that specialist advice is sought about options for treating people at high risk of CVD such as those with CKD, type 1 diabetes, type 2 diabetes or genetic dyslipidaemias, and those with CVD, who are intolerant to 3 different statins. Advice can be sought for example, by telephone, virtual clinic or referral. In the section of the surveillance review on lipid modification therapy for the primary and secondary prevention of CVD, it has been acknowledged that there is a potential need for CG181 to cross refer to the technology appraisals: TA385 Ezetimibe for treating primary heterozygous-familial and non-familial hypercholesterolaemia; TA393 Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (June 2016) TA394 Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (June 2016) This will be explored in the scoping process. 5) Percentage and absolute lipid level reduction Topic expert feedback indicated the need to review recommendation 1.3.28 for using high-intensity statins to achieve a percentage reduction rather than an absolute lipid target level. This was not supported by any new evidence in the surveillance review specifically for statin interventions. The initial

			conclusion from the surveillance review was therefore that there is a potential future impact on this recommendation if new evidence emerges that is directly relevant to statins. However, the studies by Boekholdt et al. (2014) and Ference et al. (2017) cited in the stakeholder consultation have a potential impact on recommendation 1.3.28, and will be considered in the update of this areas. The other evidence cited is either not specific to statin treatment or does not meet the study design eligibility criteria for the surveillance review. For any evidence relating to published or ongoing NICE technology appraisals, the guideline surveillance review deferred to the technology appraisal decision. This included evidence on alirocumab and evolocumab.
South Asian Health Foundation	Yes	No comments provided	Thank you.
British Cardiovascular Society	Yes	There have been important developments in CVD prevention in the last few years. Especially need to incorporate new trial data on Ezetemibe and PCSK9 inhibitors and seamlessly cross reference to relevant TAs Thank you for the opportunity to comment on the NICE Consultation on CG181 (cardiovascular disease: risk assessment and reduction, including lipid modification) on behalf of the British Cardiovascular Society. 1. Multiple risk factor measurement (QRISK) screening versus age-screening In selecting people for statin treatment age-screening has been inappropriately removed from consideration in the proposed review of the Guideline. This needs to be rectified. The following points are relevant to this: I. Statins are safe and highly effective, but under-used in the prevention of cardiovascular disease. Any new guideline should aim to simplify access to such treatment. The current guideline is too complicated, requiring two risk factor based assessments before a person can be considered for preventive treatment.	Thank you for your comments. 1) Age screening The guideline committee had requested information on age screening as part of the evidence review for CG181. They acknowledged that since age is the most important contributor to CVD risk, an age-alone strategy would identify most people at risk. The committee were concerned however that an age-alone strategy would not allow identification of people with increased risk at a younger age whose risk is increased by ethnicity, comorbidity or lifestyle factors. Younger people will also gain from treatment over a longer time period. The only evidence available for age was from a simulated cohort. The committee

		II. A simpler approach is to offer statins according to age-alone. The most recent JBS3 Guideline acknowledges that this is a reasonable approach given that age is the dominant risk factor determining a person's risk of CVD. Research has shown that other risk factors (eg. cholesterol, blood pressure etc) included in QRISK scores (the system currently recommended by NICE) add little discrimination, but add considerable complexity. QRISK also adds considerable cost, but NICE ignore this extra cost. This needs to be included in any comparison of screening strategies. III. NICE reject age-screening without giving a justification. This is wrong. IV. NICE plan to remove any mention of age-screening, even as a research plan, without giving a justification. V. NICE ignore research papers that directly compare age-screening and risk factor-based screening (eg. QRISK) both in terms of screening performance and cost. These papers (referenced below) should be included in the new NICE guideline review, as they provide the answer. VI. In the previous NICE guideline, an expert advocate of QRISK (Gary Collins) was invited to speak to the NICE Guideline Development Group more than once. Experts on age-screening were not invited, even once. This was wrong. There is an opportunity to rectify this in this Guideline update. VII. In the new Guideline review process, a fair balance should be reached between the two screening approaches. The researchers, Professor Joan Morris or Professor Sir Nicholas Wald, who are experts on age-screening for CVD should be invited to present the relevant research to group, so this is properly understood and included in the assessment. VIII. Senior NICE management (eg. Mark Baker) should consider the appropriateness of including on the NICE Guideline Development Group a member who may have an interest in risk factor measurement for the purposes of selecting who is offered a statin. For example, anyone who may have a professional or pecuniary interest in cholesterol measurement (eg. runs a lab that performs such measurements) has a clear conflict of interest in seeing cholesterol measurement remaining part of the selection process, even though cholesterol is known to be a poor screening test. Conclusion: Screening based on age-alone should be on the NICE agenda. 2. Blood pressure Reduction It is a mistake to consider cholesterol reduction in the prevention of CVD separately from blood pressure reduction. Both risk factors should be lowered in anyone who is considered to be at sufficient risk of a future CVD event. Both risk factors show the same log-linear relationship between risk factor and risk of CVD, without a threshold. Both lowering cholesterol and blood pressure have been shown to reduce risk of CVD in randomised trials. The JBS3 guidelines considered the two risk factors together and so too should NICE.	considered it worthwhile to develop a research recommendation to use a prospective cohort to compare age and other simplified methods of risk assessment with validated risk tools. The surveillance review proposal to withdraw this research recommendation will be reconsidered in the light of stakeholder feedback. It should be noted that QRISK 2 has an upper limit of 84 years. All people of 85 years and older are at high risk of CVD by virtue of age alone. The guideline committee stated that decisions about interventions should be made on a clinical basis according to proposed treatments and other factors such as comorbidities and patient choice. 2) Blood pressure measurement In developing CG181, the guideline committee emphasised that lipid modification should take place as part of a programme of risk reduction which also include attention to the management of all other known CVD risk factors. Recommendation 1.3.13 states that before starting statin treatment baseline blood tests and clinical assessment should be performed, and comorbidities and secondary causes of dyslipidaemia should be treated. All of the following are recommended for assessment: •smoking status •alcohol consumption •blood pressure (see hypertension [NICE guideline CG127])

		Conclusion: Blood pressure reduction should be considered as well as cholesterol reduction. 3. Precision of risk estimation versus estimation of health gain from preventive treatment NICE focus on the precision of risk estimation when what is important is the benefit gained from adopting a preventive intervention which is simply and accurately summarised with two numbers, (i) the proportion who will benefit from adopting the intervention (realise this gain the) and (ii) among these the average years of life gained without a heart attack or stroke. These two metrics are the most useful in enabling a provider to recommend a preventive treatment and helping an individual chose whether to use it (eg. statin). NICE should consider, introducing these two metrics in their guideline update. Conclusion What is important is the benefit rather than the precision of risk estimation prior to preventive treatment. Summary The previous iteration of the NICE Guideline sensibly reduced the risk threshold for statin treatment, but increased the complexity of assessments needed before a statin is offered by a GP. Recent evidence suggests that statins are only offered to 1/5th of those eligible for them. The NICE review should consider whether this complexity is obstructing prevention. NICE should consider focusing more on cardiovascular disease prevention and less on risk factor measurements. Simply refining what has been done in the past is not adequate in dealing with the public health problem. References to be considered in this Guideline review. 1. Wald NJ, Simmonds M, Morris JK (2011). Screening for future cardiovascular disease using age alone compared with multiple risk factors and age.PLoS One vol. 6, (5) This paper shows that screening performance is similar using age alone compared with multiple risk factors, but one is considerably more complex and costly than the other. 2. Simmonds MC, Wald NJ (2012) . Risk estimation versus screening performance: a comparison of six risk algorithms for cardiovascular disease. J Med Screen vol. 19, (4) 201-205. This paper shows that different risk algorithms (including QRISK2) have similar screening performances. The accuracy (calibration) of CVD risk estimation does not materially affect	•body mass index or other measure of obesity (see obesity [NICE guideline CG43]) •total cholesterol, non‑HDL cholesterol, HDL cholesterol and triglycerides •HbA1c •renal function and eGFR •transaminase level (alanine aminotransferase or aspartate aminotransferase) •thyroid‑stimulating hormone. [new 2014] The related NICE guideline on hypertension covers identifying and treating primary hypertension in people aged 18 and over. It aims to reduce the risk of CVD by helping healthcare professionals to diagnose hypertension accurately and treat it effectively. Both lipid lowering and blood pressure reduction are included in NICE's CVD prevention interactive flowchart. 3) Precision of risk estimation versus estimation of health gain from preventive treatment In developing the guideline, the committee concluded that primary prevention of CVD should make use of strategies to prioritise patients likely to be at highest risk and to invite patients in descending order of CVD risk estimated from available data in the GP database. Recommendation 1.1.1 advises the use of a systematic strategy to identify people who are likely to be at high risk. Recommendation 1.1.5 advises discussing the process of risk assessment with the person identified as being

		screening performance. In distinguishing who will and will not develop CVD it is screening performance that matters rather than the accuracy of the risk estimation. 3. Wald NJ, Morris JK (2014) . Quantifying the health benefits of chronic disease prevention: a fresh approach using cardiovascular disease as an example.European journal of epidemiology vol. 29, (9) 605-612. This paper shows that what is important in helping a person decide on preventive treatment is not the precision of risk estimation but the proportion of people who will benefit from a preventive treatment and the number of years they gain without a heart attack or stroke from this treatment. People see what they could potentially gain not just what their starting risk is.	at risk, including the option of declining any formal risk assessment. The surveillance review did not identify any new evidence to impact on these recommendations, or to support the replacement of risk estimation with the use of estimated health gain. The studies cited in the stakeholder consultation either preceded the surveillance literature search period, or did not meet the eligibility criteria. Further evidence in this area will be considered in future surveillance reviews.
Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Yes	Sanofi welcomes the proposal to partially update the guideline. Sanofi welcomes the recommendation of the topic experts that PCSK9 inhibitors are within the scope of NICE guideline CG181 and have advised that these should be incorporated into the guideline recommendations as part of an update.	Thank you for your comments.

Do you agree with the proposal to update the review question?

181-02 Which risk assessment tools are the most accurate for predicting the risk of CVD events in adults without established CVD (primary prevention)?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	Yes	Yes, include QRISK3 and what to do in high risk groups not covered by QRISK3.Eg. RA and SLE are covered but not psoriatic arthritis. Need to be clear on what to do in over 84s and people with FH.	Thank you for your comments. The surveillance review did not identify evidence for risk assessment beyond QRISK3 for people with psoriatic arthritis. QRISK3 has an upper limit of 84 years. All people of 85 years and older are at high risk of CVD by virtue of

			age alone. Decisions about interventions should be made on a clinical basis according to proposed treatments and other factors such as comorbidities and patient choice. Risk assessment of people with familial hypercholesterolaemia are covered by Familial hypercholesterolaemia (NICE NG71).
Primary Care Diabetes Society	Yes	No comments provided	Thank you.
NHS Medway CCG	Yes	The recommendations from the review should inform the CVD prevention rules which are currently being developed to support the 5YFV aspirations. Contact Dr Matt Kearney NHSE, Dr Judith Richardson NICE. Risk should be expressed as the risk amenable to an intervention, not just as absolute risk. This allows care to be focused on those individuals who will benefit most, it allows better resource allocation and will therefore will produce better outcomes, given limited resources. I can't change a person's age, sex, family history, ethnicity or pre-existing illnesses. Even though this combination of factors may contribute all or most of an individual's risk.	Thank you for your comments. The recommendations from the review will be circulated to relevant internal and external stakeholders. Regarding risk assessment, in developing the guideline, the committee concluded that primary prevention of CVD should make use of strategies to prioritise patients likely to be at highest risk and to invite patients in descending order of CVD risk estimated from available data in the GP database. Recommendation 1.1.1 advises the use of a systematic strategy to identify people who are likely to be at high risk. Recommendation 1.1.5 advises discussing the process of risk assessment with the person identified as being at risk, including the option of declining any formal risk assessment. The surveillance review did not identify any new evidence to impact on these recommendations, or to support the replacement of risk estimation with the use of estimated health gain. Further evidence in this area will be considered in future surveillance reviews.

Wolfson Institute of Preventive Medicine	Not answered	No comments provided	Stakeholder provided no comment.
Boston Scientific	Yes	We welcome the update of this Clinical Guideline and we would like to emphasize the importance of access to screening for higher risk patients at the primary care level. We think access to screening for this group of patients needs better sign posting to reduce future major complications such as myocardial infarction or ischaemic stroke from this higher risk group (e.g. Type 1 Diabetes and in particular female patients) (1.1.9).	Thank you for your comments. Screening is outside the remit of the guideline but risk assessment in primary care is covered by QRISK2, to be replaced by QRISK3 in 2018.
Association of British Clinical Diabetologists (ABCD)	Yes	No comments provided	Thank you.
Royal College of Nursing	Yes	This is a critical consideration in terms of the health promotion and will provide invaluable to the practitioner when review differing assessment tools.	Thank you for your comments.
Novo Nordisk	Yes	1.1.10. Use the QRISK2 risk assessment tool to assess CVD risk in people with type 2 diabetes. Although this tool in its current form allows for the additional risk of diabetes, clinicians need to be aware that there are a number of parameters which render the resulting risk less accurate and are likely to under-estimate the risk and these include people already taking medication for hypertension or for cholesterol1 As this includes the majority of those with type 2 diabetes universal use of this tool will result in widespread underestimation of risk and consequential effects on clinical management. Guiding clinicians to use a risk assessment tool is then confounded if they are expected to use their clinical judgement to interpret the CVD scores On page 11 it is stated that "**Topic expert feedback also highlighted that people with type 2 diabetes should not have cardiovascular risk assessment – they should be considered automatically at high risk, but no evidence was cited in support of this".** Evidence does exist to support this as demonstrated in a meta-analysis reviewing nearly 700 000 UK patient records from 102 prospective studies concluding that "diabetes confers with about a two-fold excess risk for a wide range of vascular diseases, independently from other conventional risk factors[2]." It has also been long accepted that diabetes is associated with an increased risk of MI whether or not the individual has had a prior MI.[3] A review to simplify this section of the guideline is necessary to fully explore the evidence to support the recommendation that patients with diabetes are already at risk and do not require a risk assessment. Indeed the recently updated SIGN guideline **SIGN 149 • Risk estimation and the prevention of cardiovascular disease** recognises the need to automatically assess people	Thank you for your comments, which we are in broad agreement with, as reflected by the proposal to update this review question and to consider the use of QRISK3 in place of QRISK2. The guideline advises that risk assessment tools provide only an approximate value of CVD risk, and that risk will be underestimated in people who are already taking antihypertensive or lipid modification therapy: • Recommendation 1.1.7: Be aware that all CVD risk assessment tools can provide only an approximate value for CVD risk. Interpretation of CVD risk scores should always reflect informed clinical judgement. • Recommendation 1.1.19: Recognise that CVD risk will be underestimated in people who are already taking antihypertensive or

		with diabetes over the age of 40 (or those under the age of 40 with >20 years duration of diabetes or microvascular complications) as being at high risk of cardiovascular events[4]. 1.Silvia Rabar, Martin Harker, Norma O'Flynn, Anthony S Wierzbicki (2014) Lipid modification and cardiovascular risk assessment for the primary and secondary prevention of cardiovascular disease: summary of updated NICE guidance 2.N.Sawar et al, Lancet 2010;Volume 375, No. 9733, p2215–2222, available at http://dx.doi.org/10.1016/S0140-6736(10)60484-9 3.Hafner SM. N Engl J Med 1998;339:229–342 4.SIGN 149 Risk estimation and prevention of cardiovascular disease; available at http://www.sign.ac.uk/assets/sign149.pdf	lipid modification therapy, or who have recently stopped smoking. Use clinical judgement to decide on further treatment of risk factors in people who are below the CVD risk threshold for treatment. [2008, amended 2014] The cited studies either precede the surveillance search period, or do not meet the study design eligibility criteria for the surveillance review. However, the points highlighted by the consultee specifically on type 2 diabetes will be passed to developers for consideration in the update.
Public Health England	Yes	This is an important question, particularly for those in groups where Cardiovascular Disease (CVD) risk may be higher at a younger age than those in the general population i.e. people with severe mental illness (SMI), such as psychosis, schizophrenia, bipolar disorder. We know that QRISK2 underestimates risk in young women, even where they have abnormal risk factor profiles. Since this guidance was published the Joint British Cardiovascular Society published their third set of guidelines recommending the use of lifetime rather than 10-year risk (http://heart.bmj.com/content/100/Suppl_2/ii1). Therefore, it would also be helpful to consider which is most accurate and the limitations of both CVD risk scores in predicting risk in different groups. The current guidance recognises that CVD risk scores will underestimate people who have additional risk and includes people with serious mental health problems (1.1.18). Therefore, It would be helpful to review available risk assessment tools, both developed and in use, and those reviewed in the literature, to determine whether any are fit for purpose to be recommended for people with SMI and younger women. QRISK3 has been updated recently and now includes SMI as an additional risk factor and consideration of this would be timely. The current guidance also mentions that risk assessment tools are not appropriate for people who have familial hypercholesterolemia (FH) (1.1.16). New NICE guidance is about to be published on FH and this should be referenced and any updates CG181 should be aligned, particularly 1.1.16 and 1.3.7 in the current version of CG181.	Thank you for your comments. • Severe mental illness (SMI) and smoking status SMI and smoking status are included as additional variables in the QRISK3 tool. Alternative tools and additional biomarkers are unlikely to impact on CG181 for people with additional risk, such as those with SMI, because QRISK3 has been validated in these groups in England and Wales, and there does not appear to be any evidence that any of the alternative tools or variables have been shown to improve on QRISK3. • Familial hypercholesterolemia (FH) The existing cross reference from the guideline to NICE's guideline on familial hypercholesterolemia from recommendation 1.1.16 does not require updating as the corresponding recommendation in the FH guideline were not updated and remain extant. The potential amendment to recommendation 1.3.7 to reflect the updated recommendation in the FH

		In considering this question it would be helpful to reflect on the feasibility/cost effectiveness of using the tools. Currently, QRISK2 is used for the NHS Health Check programme. While it is essential that the risk score is as accurate as possible, it would be beneficial to understand the cost effectiveness of tools that require additional information. We would recommend interventions to identify tobacco smokers are included in the review of tools for risk assessment. In particular, we would welcome a robust assessment of the Lester Tool and its effect on outcomes for smoking cessation and how it compares to other interventions such as Very Brief Advice.	guideline (NICE CG71) will be noted for consideration in the guideline update. • Cost effectiveness of risk tools Alternative risk tools are unlikely to impact on the guideline, since none have been shown to perform better than QRISK3, and no cost effectiveness evidence was identified to inform a health economic analysis of the different tools. • Lifetime risk New evidence supporting the use of lifetime risk calculation to more accurately assess patients for lifestyle changes and eventually lipid lowering drugs was not specific to the UK population. However, topic expert and stakeholder feedback indicating the need to review this area, combined with the fact that the surveillance literature search strategy did not extend to observational studies, raises a potential impact on recommendation 1.1.4 to consider lifetime risk as an alternative to 10-year risk. This may also have consequential impacts on recommendation 1.1.26 for communicating risk and on recommendations 1.3.18 and 1.3.26 for primary prevention of CVD.
HEART UK- The Cholesterol Charity	Yes	1.1.8 QRisk 3 should be recommended instead of QRisk 2	Thank you for your comment.
Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	Yes	Yes based on evidence that need to focus on most at high risk and need to review weighting of risk scores for South Asians	Thank you for your comment.

British Cardiovascular Society	Yes	Agree there has been sufficient new work in this area to warrant an update, especially using novel biomarkers, imaging and including patient groups with diabetes and renal disease in risk models	Thank you for your comment, which we are in broad agreement with, as reflected by the proposal to update this review question and to consider the use of QRISK3 in place of QRISK2. Alternative tools and additional biomarkers are unlikely to impact on CG181, because QRISK3 has been validated in England and Wales, and the surveillance review did not identify any evidence indicating that any alternative tools or biomarkers have been shown to improve on QRISK3
Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you agree with the proposal to update the review question?

181-11 What is the clinical and cost effectiveness of statin therapy for adults without established CVD (primary prevention) and with established CVD (secondary prevention)?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	Yes	No comments provided	Thank you.
Primary Care Diabetes Society	Yes	No comments provided	Thank you.

NHS Medway CCG	Yes	No comments provided	Thank you.
Wolfson Institute of Preventive Medicine	Not answered	No comments provided	Stakeholder provided no comment.
Boston Scientific	Yes	No comments provided	Thank you.
Association of British Clinical Diabetologists (ABCD)	Yes	No comments provided	Thank you.
Royal College of Nursing	Yes	This is an important consideration for the practitioner considering the correct use of limited resources. The review question provides extensive exploration of the relevant primary data. There is clear justification for the revision of established review question.	Thank you for your comment.
Novo Nordisk	Not answered	No comments provide	Stakeholder provided no comment.
Public Health England	Yes	It would be helpful for this to include cost-effectiveness for groups who have additional risk because of underlying medical conditions or treatments (outlined in 1.1.18). If cost-effectiveness is shown to be equal to or exceed that of estimates for the general adult population, it may help make the case for targeting and developing specific services (or pathways into services) to focus on these groups which may not always be well-served or prioritised by mainstream services.	Thank you for your comment. The surveillance review did not identify cost effectiveness evidence for the specific groups with additional risk. Evidence in this area will be monitored for consideration in the next surveillance review.
HEART UK- The Cholesterol Charity	Not answered	No comments provide	Stakeholder provided no comment.
Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	Yes	Comment as above	Thank you.

British Cardiovascular Society	Yes	Clinical effectiveness is well established, but patent expiry on high potency statins will change cost-effectiveness estimates	Thank you for your comment.
Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you agree with the proposal to remove the research recommendation?

RR–01 What is the effectiveness of age alone and other routinely available risk factors compared with the formal structured multifactorial risk assessment to identify people at high risk of developing CVD?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	No answer	No comments provided	Stakeholder provided no comment.
Primary Care Diabetes Society	Yes	No comments provided	Thank you.
NHS Medway CCG	Yes	No comments provided	Thank you.
Wolfson Institute of Preventive Medicine	Not answered	The focus continues to be on estimating cardiovascular risk but public health priority is administering effective and safe preventive medication to the population at risk determined as simply as possible which in primary prevention is age. The focus should be more on intervention combining blood pressure lowering with LDL cholesterol reduction.	Thank you for your comments. This research recommendation will be retained and if needed, a new

			research recommendation may be made as part of the update process.
Boston Scientific	Yes	No comments provided	Stakeholder provided no comment.
Association of British Clinical Diabetologists (ABCD)	No	Further research into uptake and effectiveness of statins in high risk ethnic groups such as South Asian and Black groups is needed.	Thank you for your comments. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.
Royal College of Nursing	Yes	This research recommendation does not now appear relevant in terms of the guidelines and therefore it is appropriate for its removal.	Thank you for your comment. Other feedback has indicated value in retaining the research recommendation. It will therefore be retained and if needed, a new research recommendation may be made as part of the update process.
Novo Nordisk	Not answered	No comments provide	Stakeholder provided no comment.
Public Health England	Not answered	No comments provide	Stakeholder provided no comment.
HEART UK- The Cholesterol Charity	Not answered	No comments provide	Stakeholder provided no comment.
Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	No	Still need for research into black and S Asian groups on statin uptake and even effect	Thank you for your comments. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.

British Cardiovascular Society	Yes	None	Thank you.
Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you agree with the proposal to remove the research recommendation?

RR–02 What is the improvement in the cost-effectiveness metrics for statin therapy in reducing CVD that can be obtained when using a complete individual patient-based outcomes meta-analysis data set compared with using published outcomes data?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	No answer	No comments provided	Stakeholder provided no comment.
Primary Care Diabetes Society	Yes	No comments provided	Thank you.
NHS Medway CCG	No answer	No comments provided	Stakeholder provided no comment.
Wolfson Institute of Preventive Medicine	Not answered	It is, in our view, a mistake to remove research recommendations from screening based on the use of age alone and hence remove discussion of this strategy. Publications have shown that in terms of risk prediction this is nearly as effective as more complex risk estimation using multiple	Thank you for your comments, which apply more directly to research recommendation RR-01. No new

		variables including blood pressure and cholesterol. There is an urgent need to simplify the screening process, avoid the process that creates patients as a result and a need to offer preventive medication more widely for a disease that remains a major burden of illness and mortality in Britain. We believe that NICE should examine approach more closely and take evidence from a wide circle of experts in this area. We did not understand the second bullet point regarding withdrawing research recommendation. However, the focus should not be simply on statin therapy, it should be statin therapy combined with blood pressure reduction. There is an increasing body of opinion that considers so-called “risk scores” as unnecessarily fussy in relation to public health intervention and wasteful of scarce medical resources. One of us (NW) recently met Dr Frieden, former head of CDC in the USA. Dr Frieden has the same view that what is urgent is global reduction of adult blood pressures and LDL cholesterol levels rather than trying to improve the precision of risk estimates. The general topic needs further discussion and consideration in NICE.	evidence relevant to the research recommendation RR-02 was found and no ongoing studies were identified in the surveillance review. Therefore the research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area. It will, however, remain in the full versions of the guideline. See NICE’s research recommendations process and methods guide 2015 for more information.
Boston Scientific	Yes	No comments provided	Thank you.
Association of British Clinical Diabetologists (ABCD)	Yes	No comments provided	Thank you.
Royal College of Nursing	Yes	Outdated findings and therefore less relevant in terms of the review.	Thank you for your comment.
Novo Nordisk	Not answered	No comments provide	Stakeholder provided no comment.
Public Health England	Not answered	No comments provide	Stakeholder provided no comment.
HEART UK- The Cholesterol Charity	Not answered	No comments provide	Stakeholder provided no comment.

Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	Yes	No comments provide	Thank you.
British Cardiovascular Society	Yes	None	Thank you.
Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you agree with the proposal to remove the research recommendation?

RR–03 What is the effectiveness of statin therapy in older people?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	No answer	No comments provided	Stakeholder provided no comment.
Primary Care Diabetes Society	No	No comments provided	Thank you. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.

NHS Medway CCG	No answer	No comments provided	Stakeholder provided no comment.
Wolfson Institute of Preventive Medicine	No answer	No comments provided	Stakeholder provided no comment.
Boston Scientific	Yes	No comments provided	Thank you.
Association of British Clinical Diabetologists (ABCD)	No	Research is needed on risk/benefits ratio of statins usage in CVD risk reduction and the use of statins on quality of life in elderly population.	Thank you for your comments. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.
Royal College of Nursing	Yes	The conceptual basis of statin therapy needs to be the central concern here rather than peripheral considerations	Thank you for your comments. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.
Novo Nordisk	Not answered	No comments provide	Stakeholder provided no comment.
Public Health England	Not answered	No comments provide	Stakeholder provided no comment.
HEART UK- The Cholesterol Charity	Not answered	No comments provide	Stakeholder provided no comment.
Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	No	There remains need for research in those over 80 on overall improvement of treatment on quality of life and research on informing patient choice and partnership.	Thank you for your comments. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.

British Cardiovascular Society	Yes	None	Thank you.
Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you agree with the proposal to remove the research recommendation?

RR–04 What is the effectiveness of statins and/or other LDL‑cholesterol‑lowering treatment in people with type 1 diabetes?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	No answer	No comments provided	Stakeholder provided no comment.
Primary Care Diabetes Society	No answer	No comments provided	Stakeholder provided no comment.
NHS Medway CCG	No answer	No comments provided	Stakeholder provided no comment.
Wolfson Institute of Preventive Medicine	No answer	No comments provided	Stakeholder provided no comment.
Boston Scientific	Yes	No comments provided	Thank you.

Association of British Clinical Diabetologists (ABCD)	No	The use of statins in various subgroups of Type 1 diabetes defined by age, duration of diabetes and other risk factors needs to be clarified.	Thank you for your comments. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.
Royal College of Nursing	Yes	Type I diabetes needs to be recommendation for therapy rather than a research debate correctly removed.	Thank you for your comment. Other feedback has indicated value in retaining the research recommendation. It will therefore be retained and if needed, a new research recommendation may be made as part of the update process.
Novo Nordisk	Not answered	No comments provide	Stakeholder provided no comment.
Public Health England	Not answered	No comments provide	Stakeholder provided no comment.
HEART UK- The Cholesterol Charity	Not answered	No comments provide	Stakeholder provided no comment.
Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	No	It remains unclear what age the statins should be started in type 1 and need to refine the risk in this group	Thank you for your comments. This research recommendation will be retained and if needed, a new research recommendation may be made as part of the update process.
British Cardiovascular Society	Yes	None	Thank you.

Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you agree with the proposal to remove the research recommendation?

RR–05 What is the clinical effectiveness and rate of adverse events of statin therapy using atorvastatin 20 mg per day compared with atorvastatin 40 mg per day and atorvastatin 80 mg per day in people without established CVD?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	No answer	No comments provided	Stakeholder provided no comment.
Primary Care Diabetes Society	No answer	No comments provided	Stakeholder provided no comment.
NHS Medway CCG	No answer	No comments provided	Stakeholder provided no comment.
Wolfson Institute of Preventive Medicine	No answer	No comments provided	Stakeholder provided no comment.
Boston Scientific	Yes	No comments provided	Thank you.
Association of British Clinical	Yes	As above	Thank you.

Diabetologists (ABCD)			
Royal College of Nursing	Yes	Relates to older research and therefore needs to be removed from consideration of these guidelines.	Thank you.
Novo Nordisk	Not answered	No comments provide	Stakeholder provided no comment.
Public Health England	Not answered	No comments provide	Stakeholder provided no comment.
HEART UK- The Cholesterol Charity	Not answered	No comments provide	Stakeholder provided no comment.
Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	Yes	Appears to have been answered	Thank you.
British Cardiovascular Society	Yes	None	Thank you.
Royal College pf Physicians and Surgeons of Glasgow	Yes	No comments provided	Thank you.
Merck Sharp & Dohme Limited	Yes	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you have any comments on areas excluded from the scope of the guideline?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	Yes	Will there be any recommendations for end of life care or a reference to 1.5.1 NG31?	Thank you for your comment. NG31 recommendation 1.5.1 is a generic recommendation and is not specific to end of life care in cardiovascular disease. The NICE pathway on Patient experience in adult NHS services, which refers to end of life care in addressing patient concerns, is linked to the NICE pathway on Cardiovascular disease prevention.
Primary Care Diabetes Society	Yes	1. It is well established that diabetes carries a significant cardiovascular risk as demonstrated with the Haffner (1) data. 2. It has become common practice to risk stratify people with diabetes at an earlier age with lifestyle modification and the addition of preventative agents. New therapies and studies have come to light suggesting reduced cardiovascular outcomes if some of the newer agents are introduced. The newer agents of note are Sodium-glucose transport inhibitors and GLP-1 agonists. The evidence has been compelling enough to change guidelines in other Western countries to promote the earlier introduction of these agents. Regulatory authorities in the US, Canada, Japan , Switzerland, Italy and France have already recognised this new evidence and their guidelines now support the use of SGLT2 inhibitors and the GLP-1 RA liraglutide at 1.8mg dose for cardioprotection in high risk individuals. NICE has not yet done so and indeed has stated that it will not consider the question of CV protection with these agents until all studies have reported i.e. after 2019/2020. 3. Cardiovascular safety trials ,to ensure no harm comes from taking these newer agents ,have demonstrated protection of significant level that we feel should not be overlooked when putting together cardiovascular protection guidelines that involve people with diabetes. 4. EMPA-REG (2) – study looked at patients with established cardiovascular disease and demonstrated a significant reduction in heart failure , MACE and mortality that appears more favourable than the use of statin therapy. This study has recently been supported with the CANVAS (3) study and the real world publication of CVD-REAL (4). 5. New studies have also demonstrated significant benefit in cardiovascular outcomes in people who have diabetes and treated with GLP1-RA . The two agents with current data are Liraglutide (5) (LEADER study) and the new once weekly Semaglutide (6) (SUSTAIN-6)	Thank you for your comments. The remit of CG181 covers lipid modification in the prevention of CVD and therefore other pharmacological treatments, including those specific to type 2 diabetes, are outside the remit. These treatments are covered by the following NICE guidelines: Type 2 diabetes management (NICE NG28) Canagliflozin in combination therapy for treating type 2 diabetes (NICE TA315) Dapagliflozin in combination therapy for treating type 2 diabetes (NICE TA288) Empagliflozin in combination therapy for treating type 2 diabetes (NICE TA336) Dapagliflozin in triple therapy for treating type 2 diabetes (TA418) Empagliflozin for reducing the risk of cardiovascular events in type 2 diabetes (in process)

		Many prescribers working within Primary Care are constrained in their prescribing by LHB and CCG medicine management formularies. These formularies will often not be changed unless there has been NICE approval or endorsement of a therapy. This will lead to many at risk patients not having access to therapies that are likely to lead to a significant reduction in morbidity and mortality. 1. Haffner SM. N Engl J Med. 1998 :339;229-234 2. Zinman B, Wanner C, Lachin J M et al. Empagliflozin, Cardiovascular Outcomes and Mortality in Type 2 Diabetes. N Engl J Med 2015;373:2117-28 3. Bruce N, Perkovik V, Mahaffey KW et al. Canagliflozin and Cardiovascular and renal events in type 2 Diabetes. N Engl J Med 2017;377:644-657 4. Kosiborod M., Cavander,M.A.,Fu,A.Z.,Wilding,J.P. et al. Lower risk of heart failure and death in patients initiated on SGLT-2 inhibitors versus other Glucose –lowering drugs: The CVD-REAL Study. Circulation 2017 5. 7 Marso, S.P., Daniels,G.H., Brown-Frandsen, K. et al. Liragluitide and Cardiovascular Outcomes in Type 2 Diabetes. (LEADER) N Engl J Med 2016 375; 4: 311-321 6. Marso SP, Bain SC, Consoli A et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes (SUSTAIN 6). N Engl J Med 2016 375;19:1834-44	The feedback and evidence will be noted for consideration in the next review of the clinical and technology appraisal guidance on Type 2 Diabetes.
NHS Medway CCG	No answer	No comments provided	Stakeholder provided no comment.
Wolfson Institute of Preventive Medicine	No answer	No comments provided	Stakeholder provided no comment.
Boston Scientific	No answer	No comments provided	Stakeholder provided no comment.
Association of British Clinical Diabetologists (ABCD)	Yes	Diabetes, especially T2 diabetes is a major risk factor for the development of cardiovascular disease (CVD) conferring approximately a two-fold increase in the risk of developing CVD including potentially fatal presentation of myocardial infarction (1,2). The 2016 Scottish Diabetes Survey noted that 9.7 % of patients with T2 Diabetes have had a myocardial infarction and survived, 7.5% cardiac revascularisation and 5.3% a stroke (3). Diabetes and impaired glucose tolerance are very common among people with CVD - seen in almost two-thirds of the patients at presentation with manifest coronary heart disease - and are associated with an approximately two-fold increase in mortality rate compared to those with normoglycaemia (2, 4). Aggressive management of multiple cardiovascular risk factors of hyperglycaemia, hypertension and hyperlipideamia have shown to improve CVD outcomes in people with type 2 diabetes (5,6). While improved management of these risk factors have improved CVD outcomes in recent	Thank you for your comments. The remit of CG181 covers lipid modification in the prevention of CVD and therefore other pharmacological treatments, including those specific to type 2 diabetes, are outside the remit. These treatments are covered by the following NICE guidelines: Type 2 diabetes management (NICE NG28)

		years, rising rates of diabetes and obesity are threatening to reverse the recent trends of improvement in CVD mortality seen over the last few decades (7). Urgent actions are therefore needed exploring various strategies to tackle this challenge. Over the last two years large, well-conducted trials have showed that glucose lowering agents SGLT2 inhibiotors (8,9,10) and GLP-1 analogues (11,12,13) offer substantial cardiovascular protection, bringing new hopes in improving CV outcomes in people with type 2 diabetes. Such cardiovascular benefits are of similar scale to that offered by statins and therefore needs to be passed on to diabetes patients without further delay. In the EMPA-REG trial involving about 7000 patients with type 2 diabetes and established CVD, compared with placebo, patients on SGLT2 inhibitor Empagliflozin significantly benefited from relative risk reduction in cardiovascular (CV) deaths, admission for heart failure and all-cause mortality by 38%, 35% and 32% respectively (8). The NNT to prevent one death with Empagliflozin in this trial was 39 over 3 years compared to 30 for statins. The benefit of this glucose lowering therapy was over and above that from blood pressure control and lipid lowering. About 80% and 77% of patients were treated with ACE inhibitors/Angiotensin receptor blockers and statins respectively in this trial (8). Similar findings of reductions in CV deaths, heart failure and all-cause mortality has been seen with another SGLT2 inhibitor Canagliflozin in the CANVAS randomised controlled trial (n=6000) (9). Furthermore in a real-world multinational observational study, CV protective effects were observed for all currently licensed SGLT2 inhibitors (10). Looking at the CV protection offered by the GLP-1 analogues, four large trials have been reported thus far of which two (11,12) have shown clear CV reduction in people with type 2 diabetes and in the third trial (13) a trend towards improved CV outcomes was observed. In the LEADER study, compared with placebo, Liraglutide 1.8mg once a day significantly reduced composite outcome of CV death, non-fatal MI and stroke in people with type 2 diabetes and established CVD or CV risk factors (11). The NNT to avoid the composite of major cardiovascular event with Liraglutide was 66 in this trial. Similar results were observed with once weekly Semaglutide in the SUSTAIN -6 trial (12). In the EXSCEL trial, the direction and scale of the CV benefits with weekly use of extended-release exenatide were in line with those seen in the LEADER and the SUSTAIN-6 trials but the findings did not reach a statistically significant level (13). In the ELIXA trial though, only non-inferiority of the less potent Lixisenatide versus placebo (i.e. demonstrate CV safety) but no evidence for cardioprotection was observed (14). The mechanisms behind these differences in achieved CV outcomes among various GLP-1 analogues are a matter of further research but likely to related to difference in their molecular structures and affinity towards receptors in the heart and other body tissues. Overall though, the evidence for use of Liraglutide and also Semaglutide for CV protection in patients with a high risk of cardiovascular disease is undisputable (11,12). Moreover there is now a drive worldwide to use SGLT2 inhibitors and GLP-1 analogues, especially Liraglutide 1.8mg, for CV risk reduction with national and international guidelines from the USA, Canada, Japan , Switzerland, Italy and France supporting their use in high risk individuals with type 2 diabetes. On this background, the decision by the NICE to not address the subject of CV benefits offered by these agents until all studies have been reported over next	Canagliflozin in combination therapy for treating type 2 diabetes (NICE TA315) Dapagliflozin in combination therapy for treating type 2 diabetes (NICE TA288) Empagliflozin in combination therapy for treating type 2 diabetes (NICE TA336) Dapagliflozin in triple therapy for treating type 2 diabetes (TA418) Empagliflozin for reducing the risk of cardiovascular events in type 2 diabetes (in process) The feedback and evidence will be noted for consideration in the next review of the clinical and technology appraisal guidance on Type 2 Diabetes.

		2-3 years is alarming, ignores high quality randomised controlled trials, places the NICE guidelines out of kilter with international guidelines and denotes them as being outdated from their launch. Furthermore this decision is not in our patient's best interest and the Scottish Data from 2016 highlights that these medications are highly appropriate for 10% of those with T2 diabetes (3). In view of a very strong current evidence favouring use of these agents to reduce CV events including deaths, any decision depriving high-risk individual of these potentially life-saving therapies raises serious concerns around neglecting our duty of care towards these patients. A timely approval of use of these agents from the NICE at this stage is also extremely important to avoid further procedural delays usually incurred during implementing the change in clinical practice at local level through CCG and medicines management. Delaying the use of these agents in CV protection also has implications on cost saving since substantial savings could be made from avoiding deaths and admissions with heart failure. For example, based on the findings of EMPA-REG trial, by treating the 525,000 patients with type 2 diabetes in the UK who are known to have cardiovascular disease, an estimated 4375 deaths per annum could be avoided. Furthermore, as highlighted by a recent audit (15), 6164 admissions from heart failure per year would be avoided potentially saving 73968 bed days (£26 million annually), thereby offsetting any increase in treatment costs associated with use of these agents. On the whole, the current evidence certainly makes a very strong clinical, economic and moral case for the NICE to recommend the use of GLP-1 analogues especially Liraglutide 1.8 mg in both those with established CVD or with CV risk factors and that of SGLT2 inhibitors in at least in those with established CVD. Any further delay in making such recommendations until all the evidence in this area becomes available is really unwarranted. Further studies and economic analysis however will be needed before the use of SGLT2 inhibitors could be broadened to also include those without established CVD but harbouring one or more CV risk factors. In summary, we believe, in accordance with other national and international guidelines that advice from NICE must include the currently available, well conducted and robust evidence of cardioprotective benefits of SGLT-2 inhibitors and the GLP-1 analogue Liraglutide in high risk patients with T2DM. We strongly request the NICE to incorporate recommendations on use of these agents in secondary prevention of CVD in patients with T2DM in their update of NICE CG181. This will empower clinicians within both primary and secondary care in the UK to appropriately use these agents in high-risk individuals with type 2 diabetes improving their mortality and morbidity from CVD. REFERENCES 1. The Emerging Risk Factors Collaboration. Diabetes mellitus, fasting blood glucose concentration, and risk of vascular disease: a collaborative meta-analysis of 102 prospective studies. Lancet 2010; 375: 2215-2222. 2. Rydén L, Grant PJ, Anker SD, Berne C, Cosentino F, et al. ESC Guidelines on diabetes, pre-diabetes, and cardiovascular diseases developed in collaboration with the EASD: the Task Force on diabetes, pre-diabetes, and cardiovascular diseases of the European Society	

		of Cardiology (ESC) and developed in collaboration with the European Association for the Study of Diabetes (EASD). Eur Heart J 2013;34:3035-3087 3. Scottish Diabetes Survey Monitoring Group. Scottish Diabetes Survey 2016. http://www.diabetesinscotland.org.uk/Publications/Scottish%20Diabetes%20Survey%202016.pdf 4. Gholap NN, Achana FA, Davies MJ, Ray KK, Gray L and Khunti K. Long-term mortality after acute myocardial infarction among individuals with and without diabetes: A systematic review and meta-analysis of studies in the post-reperfusion era. Diabetes Obes Metab. 2016 doi: 10.1111/dom.12827. 5. Gæde P, Lund-Andersen H, Parving H, Pedersen O. Effect of a multifactorial intervention on mortality in type 2 diabetes. N Engl J Med 2008;358:580-591. 6. Holman RR, Paul SK, Bethel MA, Matthews DR, Neil HAW. 10-year follow-up of intensive glucose control in type 2 diabetes. N Engl J Med 2008; 359:1577-1589. 7. Bottle A, Millett C, Khunti K & Majeed A.Trends in cardiovascular admissions and procedures for people with and without diabetes in England, 1996–2005. Diabetologia 2009; 52:74–80. 8. Zinman B, Wanner C, Lachin J M et al. Empagliflozin, Cardiovascular Outcomes and Mortality in Type 2 Diabetes. N Engl J Med 2015;373:2117-2 9. Bruce N, Perkovik V, Mahaffey KW et al. Canagliflozin and Cardiovascular and renal events in type 2 Diabetes. N Engl J Med 2017;377:644-657 10. Kosiborod M., Cavander,M.A.,Fu,A.Z.,Wilding,J.P. et al. Lower risk of heart failure and death in patients initiated on SGLT-2 inhibitors versus other Glucose –lowering drugs: The CVD-REAL Study. Circulation 2017 Https://doi.org/10.1161/CIRCULATIONAHA.117.029190 11. Marso, S.P., Daniels,G.H., Brown-Frandsen, K. et al. Liragluitide and Cardiovascular Outcomes in Type 2 Diabetes. (LEADER) N Engl J Med 2016 375; 4: 311-321 12. Marso SP, Bain SC, Consoli A et al. Semaglutide and Cardiovascular Outcomes in Patients with Type 2 Diabetes (SUSTAIN 6). N Engl J Med 2016 375;19:1834-44 13. Holman RR, Bethel MA, Mentz RJ et al. Effects of once –weekly Exenatide on Cardiovascular Outcomes in type 2 Diabetes. N Engl J Med 2017 ;377 :1228-39 14. Pfeffer MA, Clagget B, Diaz R et al. Lixisenatide in patients with type 2 Diabetes and acute coronary syndrome. N Engl J Med 2015;373:2247-57 15. https://www.ucl.ac.uk/nicor/audits/heartfailure/documents/annualreports/hfannual12-13.pdf	
Royal College of Nursing	No	No comments provided	Thank you.
Novo Nordisk	Yes	In relation to the scope of this guideline, drugs specifically for lipid management are no longer the only compounds with proven reduction in cardiovascular morbidity and mortality. In two large randomised controlled cardiovascular outcomes trials, empagliflozin and liraglutide have shown significant reductions (38%1 and 22%2 respectively) in cardiovascular death in patients with high CV risk and type 2 diabetes. The 2016 European Guidelines on Cardiovascular	Thank you for your comments. The remit of CG181 covers lipid modification in the prevention of CVD and therefore other pharmacological treatments, including those specific to type 2 diabetes, are outside the remit.

		Disease Prevention in Clinical Practice3 and the joint AHA/ADA4 have updated their guidelines to include this new data and provide specific recommendations for high risk patients with type 2 diabetes. Such an update should be considered within this guideline as it is currently not addressed in any other UK guideline. 1.Zinman B et al. N Engl J Med 2015;373:2117–2128 2.Marso SP et al. N Engl J Med 2016;375:311–322 3. Piepoli MF et al. Eur Heart J 2016;37:2315–2381 4.Fox CS et al. Diabetes Care 2015;38:1777–1803	These treatments are covered by the following NICE guidelines: Type 2 diabetes management (NICE NG28) Canagliflozin in combination therapy for treating type 2 diabetes (NICE TA315) Dapagliflozin in combination therapy for treating type 2 diabetes (NICE TA288) Empagliflozin in combination therapy for treating type 2 diabetes (NICE TA336) Dapagliflozin in triple therapy for treating type 2 diabetes (TA418) Empagliflozin for reducing the risk of cardiovascular events in type 2 diabetes (in process) The feedback and evidence will be noted for consideration in the next review of the clinical and technology appraisal guidance on Type 2 Diabetes.
Public Health England	Not answered	In addition to considering the risk calculators it would be helpful to consider how the information about CVD risk is communicated. There is some evidence that people do not understand their CVD risk score and therefore may not be likely to take their advice of their General Practitioner regarding lifestyle or clinical management. Understanding whether other methods of communication such as Heart Age have an impact on understanding and behaviour would be beneficial.	Thank you for your comments. NICE has produced guidance on Patient experience in adult NHS services. (NICE CG138) which includes recommendations on communication and information in section 1.5 Enabling patients to actively participate in their care. This guidance is listed as related guidance in CG181 for GPs and other health professionals to refer to.
HEART UK- The Cholesterol Charity	Not answered	1.2.1 advises mono and polyunsaturated fats as replacements for saturated fats and this is absolutely correct but 1.2.2 only talks about monounsaturated fats and gives rapeseed and olive oil as examples. We consider that this should be extended to include polyunsaturated fats and sunflower oil given as the example. Most spreads are sunflower based, although some spreads do contain olive oil it is usually only there as a percentage of the total fat. Research shows that replacing saturated fat with polyunsaturated fats has a bigger effect on cholesterol than replacing with monounsaturated fats, but both are needed as there are issues with too high a PUFA intake.	Thank you for your comments. Section 1.2 Lifestyle modifications for the primary and secondary prevention of CVD • Cardioprotective diet The collective new evidence and topic expert feedback in the surveillance review were consistent with recommendations in the section of the guideline on

		1.2.4 Advice to limit oily fish to 2 portions in pregnant women should be extended to all children and women of child bearing age. https://www.nhs.uk/Livewell/Goodfood/Pages/fish-shellfish.aspx 1.2.3 Could there be a reference to “sustainable fish” 1.2.3 Also could we have a reference to either eating more meat free meals please or alternatively less red and processed meat. See Eatwell Plate https://www.nhs.uk/Livewell/goodfood/Pages/the-eatwell-guide.aspx 1.2.13 Advice on alcohol needs updating as guidelines on units are now the same for both men and women. Also a reference to having alcohol free days please 1.2.17 There is a blanket reference to not recommending plant sterols and stanols which should also including consideration during pregnancy and breastfeeding. It also should be considered that foods fortified with plant sterols and stanols may be used on top of first line drug and more basic dietary measures to help manage lifetime risk from raised cholesterol in people with Familial Hypercholesterolaemia and other similar lipid conditions provided they are taken routinely and as part of a healthy diet and lifestyle. Advice on plant sterols and stanols for people with Familial Hypercholesterolaemia also should be consistent NICE guidelines on the management and treatment of FH This section should also highlight the concerns about coconut oil and its adverse effect on cholesterol, which is a growing problem seen in many lipid clinics. 1.3 There needs to be consistency with NICE technology appraisal guidance for alirocumab (TA393) and evolocumab (TA394) 1.3.23 says consider treating all T1DM with a statin. This is a superfluous statement as 1.3.24 then goes on to dictate which Type 1s should be offered statins 1.3.33 should consider adding: exclude effects of strenuous exercise on CK 1.3.46 Nicotinic acid no longer has a UK licence 1.3.7 Should be consistent with 2017 NICE guidelines on the management and treatment of FH, which states: Suspect familial hypercholesterolaemia (FH) as a possible diagnosis in adults with:a total cholesterol level greater than 7.5 mmol/l and/ora personal or family history of premature coronary heart disease (an event before 60 years in an index individual or first-degree relative).[2008, amended 2017]	cardioprotective diet, which cross refer to NHS choices advice on healthy eating and NICE guideline PH6 behaviour change: the principles for effective interventions. New evidence in the areas highlighted will be considered at the next surveillance review. • Alcohol consumption The feedback relating to advice on alcohol in recommendation 1.2.13 will be noted for amendment in the update of the guideline. • Alirocumab and evolocumab technology appraisals New evidence and topic expert feedback indicates the potential value of PSCK9 inhibitors (monoclonal antibodies) in prevention of CVD and is captured by the following technology appraisals: TA393 Alirocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (June 2016) TA394 Evolocumab for treating primary hypercholesterolaemia and mixed dyslipidaemia (June 2016) There is a potential need for CG181 to cross refer to these technology appraisals in the section on lipid modification therapy for the primary and secondary prevention of CVD. This will be explored as part of the guideline update. The technology appraisals are already included in the related NICE interactive flowchart. • Type 1 diabetes Recommendation 1.3.23 states that statin treatment for the primary prevention of CVD in all adults with type 1 diabetes should be considered. However,

		Systematically search primary care records for people: younger than 30 years, with a total cholesterol concentration greater than 7.5 mmol/l and30 years or older, with a total cholesterol concentration greater than 9.0 mmol/las these are the people who are at highest risk of FH. [2017] For people with a personal or family history of premature coronary heart disease (an event before 60 years in an index individual or first-degree relative), but whose total cholesterol is unknown, offer to measure their total cholesterol. [2017]	recommendation 1.3.24 is a stronger recommendation stating that statins should be offered to adults with type 1 diabetes and with additional risk factors. The guideline committee agreed using informal consensus that all adults with type 1 diabetes may benefit from treatment with a statin and that statin treatment should be considered. They agreed that statin treatment should be offered to adults with any additional risk factors to their type 1 diabetes and made a recommendation listing common factors such as age over 40 years, length of time people have had diabetes for, presence of additional CVD risk factors and evidence of abnormal renal function. • Nicotinic acid Although nicotinic acid is no longer licensed in the UK, it is widely available as a dietary supplement. It is therefore possible that a GP could prescribe or recommend it, and recommendation 1.3.46 advising against this is therefore still relevant. • Familial Hypercholestrolaemia The existing cross reference from the guideline to NICE's guideline on familial hypercholesterolemia from recommendation 1.1.16 does not require updating as the corresponding recommendation in the FH guideline were not updated and remain extant. The potential amendment to recommendation 1.3.7 to reflect the updated recommendation in the FH guideline (NICE CG71) will be noted for consideration in the guideline update.

Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	Yes	We believe this guideline needs to recognise that in addition to statins there are now SGLT1 inhibitors and GLP1 inhibitors that afford cardioprotection and that advice to use these agents for primary prevention in type 2 diabetes should be included. We believe there have recently been major breakthroughs in treatments which include SGLT-2 inhibitors and GLP-1 Receptor Agonists (GLP-1 RAs) that can provide significant cardioprotection for patients with diabetes with established cardiovascular disease. Large RCTs with SGLT-2 inhibitors (3, 4) suggest that in terms of cardiovascular (CV) mortality and CV events and protection from heart failure, this treatment approach appears almost as powerful as that seen with statin treatment and indeed complements and adds to this protection. THE NNT to prevent one death with an SGLT2 inhibitor was 39 over 3 years compared to 30 for statins (3).The convincing results of the EMPA-REG study of Empagliflozin in 7000 patients all of whom had established cardiovascular disease (3) have now been reinforced by the CANVAS study with Canagliflozin in 6000 with established cardiovascular disease (4) confirming the lowering of cardiovascular and heart failure events from this class.. These studies are complemented by the evidence from a large real-world CVD-REAL study (5) looking at all licensed drugs in the SGLT2 class and confirming almost exactly the same relative and absolute risk reduction for both CV mortality and events and hospitalisation for heart failure shown in EMPA-REG (3).In summary, this class of drugs reduced all-cause mortality by 32%, CV death by 30% and hospitalisations for heart failure (an increasing cost pressure to the NHS) by 35% (3,4,5). In addition, the subanalysis forest plots showed greater reductions for south Asians for the primary MACE outcomes compared to white populations. (3) Two large cardiovascular outcome RCTs (6,7) looking at the GLP1RAs liraglutide 1.8 mg(LEADER) and the once weekly Semaglutide (SUSTAIN) which is not yet licensed in the UK have shown significant reductions in cardiovascular deaths, all-cause mortality and cardiovascular events with NNT over 3 years of 66. Regulatory authorities in the US, Canada, Japan , Switzerland, Italy and France have already recognised this new evidence and their guidelines now support the use of SGLT2 inhibitors and the GLP-1 RA liraglutide at 1.8mg dose for cardioprotection in high risk individuals. NICE has not yet done so and indeed has stated that it will not consider the question of CV protection with these agents until all studies have reported i.e. after 2019/2020. We believe that this excessively cautious approach and delay is likely to harm many patients by failing to endorse proven life-saving treatments. Many GPs directed by their CCGs through their Medicine Management Teams will not change their management practice until approved by NICE, licences reflect new indications and there is endorsement from local formulary groups-all adding to further delays!. This will deprive potentially life-saving treatments for many of our most vulnerable South Asian patients with established cardiovascular disease. We believe that the	Thank you for your comments. The remit of CG181 covers lipid modification in the prevention of CVD and therefore other pharmacological treatments, including those specific to type 2 diabetes, are outside the remit. These treatments are covered by the following NICE guidelines: Type 2 diabetes management (NICE NG28) Canagliflozin in combination therapy for treating type 2 diabetes (NICE TA315) Dapagliflozin in combination therapy for treating type 2 diabetes (NICE TA288) Empagliflozin in combination therapy for treating type 2 diabetes (NICE TA336) Dapagliflozin in triple therapy for treating type 2 diabetes (TA418) Empagliflozin for reducing the risk of cardiovascular events in type 2 diabetes (in process) The feedback and evidence will be noted for consideration in the next review of the clinical and technology appraisal guidance on Type 2 Diabetes.

		evidence for using these agents for secondary prevention is overwhelming and that it would be a neglect of duty of care to further delay their endorsement. On the basis of the NNT of 39 over 3 years for people with cardiovascular disease (secondary prevention) with Empagliflozin, plus the reduction of hospitalisation for heart failure by 35% (3) CV events could be prevented and the lives of our patients prolonged. Substantial savings would also be made on avoidance of hospital treatment for heart failure. Based on the criteria used in these studies (3), if the 525,000 patients with Type 2DM in the UK who are known to have cardiovascular disease were treated, it is estimated that 4375 deaths per annum could be avoided. In addition, 6164 admissions from heart failure per year would be avoided saving 73968 bed days (£26 million annually). This is highlighted by a recent audit (8) which suggested that the savings would offset increased treatment costs. We believe that for patients with established cardiovascular disease, the moral and economic case for treatment is overwhelming and further delay unjustified. This is particularly the case in South Asians with their very great susceptibility to and high mortality from CVD. There is also an argument from the studies of SGLT-2 inhibitors that these agents should be recommended more widely to people with T2DM who have 1 or 2 cardiovascular risk factors (as described in the CANVAS Study (4). We accept that extending to this at risk group may require more studies and more health economic analysis before adoption as a NICE recommendation. The picture is somewhat more complex with GLP-1 RAs. Two studies, one with Liraglutide (LEADER) (6), and the other with Semaglutide (SUSTAIN 6) (7) demonstrated both non-inferiority (safety) and superiority for reduction of the composite primary endpoint of CV death and non-fatal MI and stroke versus placebo. LEADER also reported significant reduction in CV mortality. The two other long term cardiovascular safety studies with Lixisenatide (ELIXA) (9) and long acting once weekly Exanetide (EXSCEL) (10) studies showed non-inferiority versus placebo (ie demonstrate CV safety) but no evidence for cardioprotection. The explanation and mechanisms to explain these differences within class are not understood and require further research but the molecular structures of these GLP- 1 analogues and their ability to bind the receptors in the heart and in different body tissues appear to differ. The evidence from LEADER has, however, been thought sufficient by many national and international guideline bodies to recommend Liraglutide 1.8 mg as a treatment for patients with T2DM at high CV risk. We believe that a similar approach should be taken by NICE particularly in the context of our very high CV risk South Asian patients. In summary, we believe that there is sufficient evidence from well-conducted cardiovascular outcome studies, to recommend that both SGLT-2 inhibitors and/or the GLP-1 RA Liraglutide be considered as part of the management regime for secondary prevention in patients with T2DM and specifically in those at particularly high risk including the South Asian population. These issues MUST be considered by NICE in their update of NICE CG181. This will then guide UK healthcare professionals to introduce these treatments appropriately to help reduce cardiovascular events, mortality and heart failure in our most vulnerable patients. REFERENCES	

		1 Bellary S, O'Hare JP, Raymond NT et al. Premature cardiovascular events and mortality in South Asians with type 2 diabetes in the United Kingdom Asian Diabetes Study Current Medical Research and Opinion 2010 ;26 (8):1873-1879 2 Barnett A H, Dixon A N, Bellamy S et al. Type 2 Diabetes and cardiovascular risk in the UK South Asian community. Diabetologia 2006;49:2234-46 3 Zinman B, Wanner C, Lachin J M et al. Empagliflozin, Cardiovascular Outcomes and Mortality in Type 2 Diabetes. N Engl J Med 2015;373:2117-28 4 Bruce N, Perkovik V, Mahaffey KW et al. Canagliflozin and Cardiovascular and renal events in type 2 Diabetes. N Engl J Med 2017;377:644-657 5 Kosiborod M., Cavander,M.A.,Fu,A.Z.,Wilding,J.P. et al. Lower risk of heart failure and death in patients initiated on SGLT-2 inhibitors versus other Glucose –lowering drugs: The CVD-REAL Study. Circulation 2017 Https://doi.org/10.1161/CIRCULATIONAHA.117.029190	
British Cardiovascular Society	Yes: 181-04 Dietary advice, especially on saturated fats	There has been significant controversy about this in the wider media in the last few years, with an opposite view supported by some doctors. The high profile PURE study from Salim Yusuf (Dehghan M et al. Associations of fats and carbohydrate intake with cardiovascular disease and mortality in 18 countries from five continents (PURE): a prospective cohort study. Lancet. 2017 Aug 28. pii: S0140-6736(17)32252-3) has added to the debate. The committee may wish to update this section. Some acknowledgment of the issue should be made and countered with evidence to support NICE's position (which is shared by BHF, AHA etc).	Thank you for your comments. • Cardioprotective diet The collective new evidence and topic expert feedback in the surveillance review were consistent with recommendations in the section of the guideline on cardioprotective diet, which cross refer to NHS choices advice on healthy eating and NICE guideline PH6 behaviour change: the principles for effective interventions. New evidence in the areas highlighted will be considered at the next surveillance review.
Royal College of Physicians and Surgeons of Glasgow	Yes	While the issue of smoking and cessation is fully explored and dealt with by this and previous guidelines, there may be scope to add a Research Question on the usefulness of Vapourisers when trying to quit smoking. There is little guidance for clinicians on the benefits or harms of this practice on CV risk.	Thank you for your comments. The addition of this research recommendation on this topic will be considered during the update scoping process.
Merck Sharp & Dohme Limited	No	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Do you have any comments on equalities issues?

Stakeholder	Overall response	Comments	NICE response
Medicines and Technologies Programme	No	No comments provided	Thank you.
Primary Care Diabetes Society	Yes	Diabetes and ethnicity carry a higher risk of cardiovascular disease with poorer results. It does not appear to have been included within this document as a special consideration.	Thank you for your comments. The QRISK2 risk assessment tool, and its successor QRISK3, include ethnicity as a risk factor in calculating overall risk of CVD.
NHS Medway CCG	No answer	No comments provided	Stakeholder provided no comment.
Wolfson Institute of Preventive Medicine	No answer	No comments provided	Stakeholder provided no comment.
Boston Scientific	No answer	No comments provided	Stakeholder provided no comment.
Association of British Clinical Diabetologists (ABCD)	No	No comments provided	Thank you.
Royal College of Nursing	No	No comments provided	Thank you.
Novo Nordisk	No	No comments provided	Thank you.

Public Health England	No answer	No comments provided	Stakeholder provided no comment.
HEART UK- The Cholesterol Charity	No answer	No comments provided	Stakeholder provided no comment.
Amgen Ltd	Not answered	No comments provide	Stakeholder provided no comment.
South Asian Health Foundation	Yes	South Asians with type2 diabetes need to be treated with the newer flozins as primary protection and this could be as powerful an addition to preventing deaths and heart failure as the use of statins. Inclusion in this guideline will help to reverse the inequity in treatment this group suffers.	Thank you for your comments. Treatments for diabetes are not included in the remit of CG181, but are covered in NICE's guideline on type 2 diabetes management.
British Cardiovascular Society	No	No comments provided	Thank you.
Royal College pf Physicians and Surgeons of Glasgow	No	No comments provided	Thank you.
Merck Sharp & Dohme Limited	No	No comments provided	Thank you.
Sanofi	Not answered	No comments provide	Stakeholder provided no comment.

Comments:

RCN Unfortunately we have no comments to submit to inform on the above review proposal at this present time