Type 2 Diabetes scope SH subgroup discussions Group 4 Date: 6 September 2022	
Population Adults (aged 18 years and older) with T2D. Specific consideration to: People w/ moderate or severe frailty. People with early onset T2D People w/ long term conditions People at high risk of developing CV disease People with obesity People with specific ethnic groups Not be covered: Children and young people with T1 or T2D. Pregnant people. Covered: All settings where NHS funded care is provided.	Are there any specific subgroups that have not been mentioned? Can any of the subgroups be de-prioritised? • People with cognitive impairment/ dementia was suggested. Some therapies with dementia can impact T2D. The side effects of the drugs must be considered. (This might be under the umbrella of frailty/ older age) • People with metabolic syndrome/ non-alcoholic fatty liver disease was suggested. There is little guidance around NAFLD (a guideline for NAFLD is available but should perhaps be cross-referenced). This was identified as an unmet need. A metabolic syndrome group should be considered. • People with hypogonadism was suggested (where testosterone replacement therapy has been identified to improve glycaemic control.) • People with a genetic background/ family history of T2D. It might be worth making the distinction of monogenetic diabetes (a single gene defect). It's worth looking, but outside the scope of this document. Pre-diabetes falls outside this scope as well. • For people with long-term conditions, it should capture people who have a long-term condition when they develop T2D or people who develop a long-term condition later after a T2D diagnosis.

	• Do the age cut-offs seem reasonable? Yes, due to varying treatments when developing T2D • Regarding ethnic groups. SE Asians and Afro-Caribbean groups at higher risk. Would the treatment be different or is it broadly similar? Treatment options are the same, but awareness of high-risk groups needs improvement. In some cases, the treatment may need to be different for individualisation (but this is not available yet). BMI is the main measurement for this. • Monogenetic diabetes should be included under the "Not covered" section. • People with learning difficulties/ mental health illnesses. Does this need to be included? Symptoms could be missed due to the level of illness. Also, it is important to keep in mind how someone with learning difficulties can manage their own treatment (even if it means one that is not as clinically effective). People with severe/ enduring mental illness may struggle with managing the disease. Should people with alcoholic liver disease need to be examined differently.
Key issues and draft questions	Any comments on these questions? Can any drugs/classes be omitted? We do not propose updating insulin-based treatments compared to one another, do you have any comments on this?

	• The standard therapy list isn't one that practicing physicians would recognise as standard. Standard care now has moved away from metformin as the default first-line therapy (consider other things first). Sulfonylureas would not be the second-line therapy. Use newer therapies that offer more cardiac and renal benefits. Need to consider additional benefits that are not just about glucose lowering (this can pay off clinically and financially in the long-term). Moving more towards the European and North American guideline recommendations. • GLP-1 receptor agonist does not appear to be widely used in NICE like in other guidelines (this was possibly due to not being cost-effective or borderline cost-effective). In diabetes drugs are considered in classes, not as individual drugs (despite some not having CV benefits in trials). There is a rumour that the GLP-1s cost-effectiveness were miscalculated by NICE. Did this happen? At consultation, stakeholders raised concerns about the model. Even after re-running the analysis, the treatment was still not cost-effective. If there were errors in the model, they were picked up at consultation. There is a concern that there were benefits that weren't picked up. In that one only CV was examined. • There is no proposed update for insulin treatments. The proposed treatment is prior to insulin therapy (third line). Sometimes insulin is a first-line treatment in certain populations (depending on high BMI or older age patients). There is a value in having insulin earlier in the treatment pathway. • Polypharmacy should be noted for clinical implications (and cost-effectiveness) as well. We should also consider the cost impact of switching therapy. Deprescribing is a big research area in pharmacy regarding older populations. Consider different drugs starting and

	stopping rules (ie GLP-1s). If you stop GLP1, you replace it with insulin which can result in weight gain and limited diabetic control. • Some classes of medicines have not been reviewed for quite some time, we don't know for sure if they are cost-effective or not. As newer treatments come online, we will be able to have a comprehensive economic model, to allow it to stay up to date more efficiently (allow for a more robust guideline).
Critical issues	Are there any critical issues relating to medicines for T2D that aren't included in the scope? Any safety issues? Areas with the greatest potential for improved patient outcomes? Areas with potential for NHS resource savings?
Outcomes Main outcomes: All cause mortality CV mortality, serious CV events, changes in HBA1C, changes in weight/ BMI, changes in lipid levels, changes in BP, HRQoL, frequency/ timing/ severity of hypoglycaemic episodes, and SAE.	Any comments on the outcomes? • Regarding the CVOT drug trials, CV outcomes were not the main outcomes. There are now well-established CV outcomes in trials, but the method to complete the analysis needs to be noted. It might not be possible to analyse all the data. • The outcomes are very focused on the macrovascular events. There isn't enough emphasis on the day-to-day events. It's worth considering other complications, such as neuropathy, visual impairments, cognitive complications, erectile dysfunction, amputation, etc. Infections is an important one, but difficult to identify (particularly in older patients). • Remission should be included (people might have to stop taking some drugs).

Health economics model Assess the CE of different treatment options by calculating expected cost to the NHS and personal social services, expected QALYs and cost per QALY gained. Estimate the mean number of events that will occur over the lifetime of a cohort of patients receiving standard care. Apply treatment effects and re-calculate the number of events and other treatments Attribute NHS costs and QALY losses to each event (acute and chronic) Calculate the total cost for each treatment option. Existing guideline model: Main model population = Adults with T2D. Different risk subgroups= People with a BMI of greater than or equal to 30kg/m2, people with a high risk of a CV event who have not had a prior event, people who have had a prior CV event, people Model interventions= Standard care vs CVOT drugs. Model events/ outcomes for CVOT drugs= Heart attack, stroke, ischaemic heart disease, heart failure, hypoglycaemia. Model events/ outcomes (same incidence rate in each model arm)= blindness, renal failure, ulcer, amputation). Model structure: Standard care arms = metformin for the initial therapy. THIN data analysis was used for the baseline characteristics/ risk factors and 20,000 populations. Applied treatment effects (HBA1C and weight) for the standard care therapy. UK DPS equations were used to model changes over 40 years for each of the 20,000 patients.	Any comments on HE modelling for this guideline?

Time-dependent probabilities were calculated for movement between about 700 different health states. For the new guideline: How to adapt and expand the model with additions/ changes to drugs evaluated, outcomes modelled, population strata (risk subgroup sand lines of treatment). Will also include updated prices/ costs and QoL scores. The treatment effects will be based upon the results of the new guideline's systematic review, which needs to include outcomes that are most important to patients and clinicians.	
GC membership At present, 2 vacant posts (1 lay member and 1 diabetologist)	Any comments on the committee membership composition? • Most of the roles are already filled. • An endocrinologist with regards to hypogonadism • Specialist dietician (a dietician is currently included) • Cardiologist- already included • Clinician with a health economic understanding • More patient input (lay members are currently involved, but we will consider including more)

Group 1 discussions regarding specific subgroups (women of childbearing age). Comparing insulins. Outcomes fairly comprehensive as is (should include weight gain). The order of the outcome list is not meant to be read as prioritisation. HE modelling should include triple treatment GC membership largely happy with the composition.
Group 2- Special consideration to learning disabilities/ cognitive disabilities. Some medication is out of use now. Symptoms like weight gain should be noted. The release of new medications should also be considered. GC membership should include someone who looks at liver levels (lipids and enzymes) as well as a dietician.
Group 3- Learning disabilities/ cognitive disabilities. People with multiple morbidities are not largely covered by the scope. Second generation-based insulins was determined to be relevant. It was noted that because a lot of the outcomes are CV, where do the drugs stand regarding other CV treatments (ie statins), should they be included/ cross-referenced. We do not seem to be covering lifestyle intervention. The outcomes listed was sufficient, but the ordering did not

seem right. Remission was noted to be missing from the list. Standard care as described was not reflective of current practice. We should also make sure we are using contemporary data for background risks.
Group 4- Cognitive impairments/ mental illnesses and metabolic syndrome (NAFLD) should be included. Standard care does not reflect practice. In terms of outcomes, it should include more day-to-day outcomes and hospital admissions and infections. GC membership should include endocrinologist, dietician and clinician with health economic understanding.