NICE National Institute for Health and Care Excellence

Appendix B1: Stakeholder consultation comments table

2019 surveillance of NG17 Type 1 diabetes in adults: diagnosis and management (2015)

Stakeholders were consulted on the surveillance proposal to update NICE guideline NG17 for 2 weeks. Consultation dates: 25 April 2019 to 8 May 2019

Themes from stakeholder comments

Overall, 32 stakeholders commented on the proposal to update the guideline. Several themes emerged from the comments received at consultation which are detailed below.

Diagnosis

Some stakeholders highlighted new evidence to suggest that misclassification of type 1 diabetes may be common in adults diagnosed after the age of 35 years. Further evidence was identified on the use of C-peptide to avoid misclassification of late-onset type 1 diabetes and added to Appendix A for consideration. They raised concerns that the guideline currently only recommends the use of C-peptide tests if there is clinical uncertainty about diagnosis, particularly as the evidence suggests this could be leading to missed diagnoses. The use of C-peptide tests was an area highlighted by the original guideline committee as needing further evidence, who at the time, made the recommendations based on a consensus agreement. In light of this feedback and the new evidence, we are proposing that this area is reviewed.

Blood glucose monitoring

Many stakeholders called for an update in the area of continuous glucose monitoring (CGM) due to newer trials showing the benefits of CGM since the guideline was last updated. We initially judged the new evidence to be broadly consistent with the guideline, which currently recommends considering CGM if people have problems with hypoglycaemia. However, after feedback from stakeholders and further consideration of the evidence, which shows a benefit for people with sub-optimal glucose control as well as people with hypoglycaemia, we are now proposing to review this area.

Diabetic eye screening

A number of stakeholders were concerned about the proposal to withdraw the recommendations on screening and referral for diabetic eye disease. After taking into account these comments and to emphasise the importance of regular screening, we will add in a cross referral to the screening programme so that this guidance can be more easily referred to.

Insulin therapy

Many concerns were raised about the proposal not to add recommendations on closed-loop pump therapies, given the emerging evidence base and other NICE guidance in this area. Further evidence was highlighted which was published after the search cut-off dates for this surveillance review and we have since included it in Appendix A for consideration. Two ongoing trials were also brought to our attention and have been added to our review. We initially judged the evidence to be insufficient to inform recommendations at this point, noting the lack of studies with long-term outcomes and in patients with sub-optimal diabetes control. The new evidence highlighted by stakeholders has a longer follow-up period and includes people with sub-optimal diabetes control. Following the strong steer from stakeholders and the emerging evidence, we are now proposing to review this area.

Psychological support

Concerns were raised about the recommendations relating to psychological support, with some calling for specific recommendations for people with diabetes (rather than a cross-referral to other related guidelines). Currently the guideline contains recommendations on recognition and referral for psychological support, with additional signposting to relevant NICE guidelines which offer more specific advice. We therefore judge this area to be sufficiently covered by existing NICE guidance. As we did not identify any new evidence in this area during the surveillance review, the recommendations will not be changed at this point.

Other areas

Other areas were highlighted for update by individual stakeholders; however, these were not considered to impact the guideline at this point either due to insufficient evidence or because the issue is covered by existing guidance. These areas included: management of newly diagnosed adults, discussion of diabetic eye screening results, digital photographic and optical coherence tomography surveillance, routine use of autoantibody tests, education, low GI diets, carbohydrate counting, very low calorie diets, blood ketone monitoring, person-centred care, bolus calculators, transition from child to adult services, management of renal complications, diabulimia, immunotherapy and language concerns. See the individual responses below for further details.

Stakeholder consultation comments table

Consultation dates: 25 April 2019 to 8 May 2019

Do you agree with the proposal to update the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Training, Research and Education for Nurses in Diabetes	Yes	No comments provided	Thank you.
Sheffield Teaching Hospital NHS Foundation Trust	Yes	No comments provided	Thank you.
Coeliac UK	Yes	No comments provided	Thank you.
South Sefton Clinical Commissioning Group	Yes	No comments provided	Thank you.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

British Dental Association	Yes	No comments provided	Thank you.
UK Clinical Pharmacy Association (UKCPA) Diabetes and Endocrinology Group	Yes	Adjuncts to insulin We identified several trials examining the effect of SGLT2 inhibitors as an adjunct to insulin therapy. It talks about reduction in HbA1c and weight loss should the benefits of cardiovascular outcomes be considered.	Thank you for your comment regarding adjuncts to insulin, which is an area planned for update. Many of the trials identified in this area were related to NICE technology appraisal guidelines in development, so were not considered in this surveillance review. The only evidence not related to a NICE technology appraisal was a trial that reported on HbA1c and weight loss outcomes (see Appendix A). Therefore, other outcomes were not mentioned in the evidence summary. However, we acknowledge that cardiovascular outcomes are important in diabetes. In line with the NICE guidelines manual, input on the main outcomes to be considered will be obtained through the scoping process and protocol development for the update. We will pass your comment regarding cardiovascular outcomes to the developers working on the update so this information can be considered during the scoping and protocol development phases.
Northumbria Healthcare NHS Foundation Trust – National DAFNE Executive Board	Yes	Flash glucose monitoring: there are as yet no clinical trials that demonstrate an HbA1c benefit of using Flash. It is difficult to justify its use until this evidence is available. Research should be encouraged to obtain this evidence. Practical guidance would be welcomed from NICE in particular to challenge the current restriction for access to flash monitoring only for people who are achieving high number of CBG tests.	Thank you for your comments, please see the separate responses below: 1. Flash glucose monitoring: Thank you for your comment. We plan to update this section of the guideline as evidence was identified through the surveillance review to support its use in people with well-controlled diabetes. The guideline committee will be considering the available evidence as a factor during the update process and take this into consideration when making recommendations.

		Adjuncts to insulin: we welcome the inclusion of a review of the SGLT2 class of drugs in type 1 diabetes We propose that management of the adult newly diagnosed with T1D is highlighted as an area for research. This is because current structured education programmes are not recommended until 6 months after diagnosis. This is a critical period during which insulin requirements vary widely. There is a wide range of different approaches to insulin initiation across the UK aiming to optimise glucose control and self management skills. There is a strong evidence base for well designed structured education in type 1 diabetes self management. The evidence base for digital support tools in type 1 diabetes self management is less strong. We welcome the review of evidence for telemedicine, smartphone applications and online platforms in supporting adults with T1D to improve glycaemic control. We believe these technologies can be valuable in supporting self-management but do not replace the need for high quality skills-based training currently known as structured education.	2. Adjuncts to insulin: thank you for your comment. 3. Management in newly diagnosed adults: Thank you for highlighting the need for further research in this area. As you mention, the guideline currently recommends offering structured education programmes 6-12 months after diagnosis (recommendation 1.3.1). During guideline development, the committee felt that the first few months post diagnosis are a period of considerable adjustment and that trying intensive education at this stage would be less worthwhile and even counter-productive. However they acknowledged the need for further guidance in this area and issued the following research recommendation which can be found in the full text of the guideline: "In adults with newly diagnosed type 1 diabetes, what is the optimal timing and method of delivering structured education in terms of clinical and cost-effectiveness?". 4. Digital support tools: Thank you for your support for this identified area for update. The recommendations on structured education still stand and are not an area identified for update. However, the committee will consider the evidence on digital support tools in the context of the other self-management interventions recommended in the guideline.
Digital Diabetes Media Ltd	Yes	No comments provided	Thank you.
Diabetes Research Unit Cymru (Wales) (DRUC)	Yes	No comments provided	Thank you.

JDRF, the type 1 diabetes research charity	Yes	We particularly strongly agree with the need to update the guideline with regards to flash glucose monitoring, long-acting insulin and biosimilar insulins.	Thank you for your comment.
Abbott Diabetes Care	Yes	No comments provided	Thank you.
Royal College of Ophthalmologists	Yes	New and emerging evidence on management of sight threatening complications would need to be included. ''The evidence supports the use of anti-VEGF treatment and intravitreous injection of aflibercept for diabetic retinopathy and laser therapy for diabetic macular oedema. Currently the guideline has recommendations on screening and referral, but no recommendations on specific treatments. However, there are many treatments covered in NICE technology appraisal guidance, suggesting that there may be a gap in the recommendations of NICE guideline NG17. Given the growing evidence base and the related NICE technology appraisal guidance, we propose that this area is reviewed. '' In response to this, we fully agree that the treatment options for diabetic retinopathy need reviewing/updating and these have not previously been specified in the NICE guidelines. They have previously been detailed in RCOphth guidelines which are due for an update in terms of evidence for treatment of diabetic macular oedema and proliferative diabetic retinopathy. This will need specialist	Thank you for your comments, please see the separate responses below: 1. Treatment for diabetic retinopathy: Thank you, we plan to update this section of the guideline. 2. Missing publications: Please see our response to the comment in question below. 3. Anti-VEGF treatments: Thank you for highlighting that intravitreal aflibercept is an anti-VEGF treatment. We have amended Appendix A accordingly. 4. Withdrawal of recommendations on diabetic eye screening: Thank you for your comment. As you acknowledge, recommendations on screening and referral for diabetic eye disease fall under the remit of the NHS Diabetic Eye Screening Programme so we plan to withdraw these recommendations. However, in light of your comments and to emphasise the importance of regular screening, we will add in a cross referral to the screening programme so that this guidance can be more easily referred to. 5. Discussion of diabetic eye screening results: Thank you for your comment and suggestion to add discussion of

		ophthalmic input, and there has been a considerable body of new evidence since the RCOphth last updated its guidelines. As per comments below, various highly relevant publications do not seem to be referenced int the document/table 7. It is also clear from that statement quoted above, as well as the statement on page 32 which says ' 'We identified new evidence on the treatment of proliferative diabetic retinopathy, supporting the use of anti-VEGF treatment and also intravitreous injection of aflibercept'' that there is some confusion about what aflibercept represents. In fact, intravitreal aflibercept IS an anti-VEGF treatment (and the anti-VEGF treatments are delivered by intravitreal injection), so the additional comment specifically about Aflibercept is not required in those paragraphs. The document also states: ''Topic experts also highlighted new evidence on the optimum frequency of diabetic eye screening. This area was not considered in the surveillance review because it falls under the remit of the NHS Diabetic Eye Screening Programme who cover screening and referral criteria for people with diabetes. However, to avoid an overlap in guidance we plan to withdraw the recommendations on screening and referral'' Whilst we agree that this work should not be repeated, it would seem sensible to both reference the NHS Diabetic Eye screening programme here as well as including a short summary of the referral guidelines/recommendations, to emphasise the importance of regular screening etc. As with the paediatric guidelines, it would be good to also stress the benefits of	retinopathy screening results to the regular diabetes review. Recommendation 1.2.5 already states "Set up an individual care plan jointly agreed with the adult with type 1 diabetes, review it annually and modify it taking into account changes in the person's wishes, circumstances and medical findings, and record the details" and identifies "complications monitoring and management" as one of the aspects of the plan to review. We consider regular discussion of diabetic eye disease management to be covered by this recommendation. 6. New evidence on fibrates: Thank you for highlighting the trials on the use of fibrates in addition to statins for diabetic retinopathy. Both the ACCORD study and the FIELD study focussed on people with type 2 diabetes and therefore are not in scope for NICE guideline NG17 and more relevant to the NICE guideline on type 2 diabetes in adults (NG28). However, as they were published before the search dates for the NG28 surveillance review, they are not eligible for inclusion. As you noted, we are monitoring the progress of the LENS study (which includes people with both type 1 and type 2 diabetes) and will review the impact when results are available. 7. Digital photographic and OCT surveillance: Thank you for this information, we did not identify any evidence in the surveillance in relation to digital photographic and OCT surveillance for this population to support the addition of recommendations in this area. As no evidence was identified through the stakeholder consultation, this is not an area proposed for update.

		discussing retinopathy screening results during the regular diabetes review appointments either by the GP/practice nurse or diabetologist. We would like request that data on the use of fibrates in addition to statin are reviewed in terms of the effects on diabetic retinopathy, based on evidence from Accord Eye study (and the FIELD study before that), where fibrates were shown to reduce the rates of progression of retinopathy. We are pleased to see that comment has been made about reviewing the results in due course from the Lowering Events in NPDR study (Scotland) which also concerns fibrate use. Data is also emerging about digital photographic and OCT surveillance for certain patients who had already been referred to the diabetic eye clinics ('virtual clinics') and that could be reviewed in the section about the treatment of diabetic retinopathy.	
Novo Nordisk	Yes	**Page 2 Blood glucose management: Smartphone applications and online platforms** Novo Nordisk would like NICE to consider the benefits of insulins that can be used with a digital connected pen, some of which link directly with CGM, and which can provide potential benefits to people living with type 1 diabetes. **Page 2 Insulin Therapy: Long-acting insulin**	Thank you for your comments, please see the separate responses below: 1. Digital connected pen: Thank you for your comment. Recommendation 1.8.1 in the guideline currently advises that "Adults with type 1 diabetes who inject insulin should have access to the insulin injection delivery device they find allows them optimal wellbeing, often using one or more types of insulin injection pen". We did not identify any new evidence on the use of digitally connected pens, therefore this recommendation is unlikely to be updated at this time.

		Novo Nordisk welcomes the recognition of the evidence supporting the use of ultra-long-lasting insulin degludec and agrees with the expert opinion to review the basal insulin section of this guideline. It is important to differentiate between the available basal insulins, helping healthcare professionals to make the best choice based on patient-focused considerations such as hypoglycaemia and flexibility. **1) <u>Hypoglycaemia</u>** There is evidence demonstrating a reduction in hypoglycaemia versus insulin glargine U100, in particular the SWITCH 1 trial which was conducted in patients at high risk of hypoglycaemia with hypoglycaemia as a primary endpoint. In this trial, insulin degludec compared with insulin glargine U100 resulted in a significantly lower rate of overall symptomatic, nocturnal and severe hypoglycaemic episodes[1] In addition, we would like to highlight real world evidence that supports the randomised controlled trial data demonstrating a reduction in hypoglycaemia versus insulin glargine U100 which is currently missing from the references[2] **2) <u>Flexibility</u>** We would also like to highlight the flexibility in dosing time with insulin degludec, having a minimum dosing time of 8 hours between doses, which can be advantageous to certain adult populations [3,4] With respect to the definition of 'ultra long', for the purpose of clarity, Novo Nordisk suggests adding the insulin duration of action to those insulins categorised as 'ultra long' within the guideline	2. Thank you for your comments on insulin therapy, please see our responses below: a. Hypoglycaemia SWITCH-1 trial: this trial was identified in the surveillance review (see Appendix A) and the results form the basis of our update proposal. EU-TREAT trial: This study was not identified in our searches and will not be added to Appendix A as it does not meet the inclusion criteria for this surveillance review. However, we will pass on this information to the developers for consideration in the update of the guideline. b. Flexibility: Thank you for your comment on insulin degludec, which is area planned for update. Thank you for highlighting evidence on insulin degludec. The study by Mathieu et al (2013) was considered during the development of the original guideline. However, we will pass on your comments regarding the need for a definition of 'ultra long' to developers for consideration in the update of the guideline. c. Safety and cost-effectiveness: Thank you for highlighting the studies by Lui et al (2018) and Evans et al (2018). Both of these studies were identified in the searches for this surveillance review, however they were excluded because there was inadequate data reported in the abstracts. However, we will pass on this information to the developers for consideration in the update of the guideline.

		Novo Nordisk believes that insulin degludec fulfils an important clinical need for people with type 1 diabetes where hypoglycaemia and the need for flexibility are clinical considerations and that this is therefore reflected in the updated guideline. **3) <u>Safety and cost effectiveness</u>** Not currently included in the references is the Liu et al meta-analysis demonstrating the efficacy and safety of Insulin degludec versus Insulin Glargine[5]. This is a systematic review and meta-analysis of 15 clinical trials and we would ask please that it is included to inform the next stage of guideline development. A cost effectiveness trial of insulin degludec versus insulin glargine U100 found that insulin degludec was highly cost-effective in type 1 diabetes compared with glargine U100[6] This reference is also currently missing from the searches. <u>References</u> 1. SWITCH-1 2. Siegmund T et al (2017) A European, multicentre, retrospective, non-interventional study (EU-TREAT) of the effectiveness of insulin degludec after switching basal insulin in a population with type 1 or type 2 diabetes. Diabetes, Obesity and Metabolism. 2017;1-9. 3. Mathieu C (2013) Efficacy and Safety of Insulin Degludec in a Flexible Dosing Regimen vs Insulin Glargine in Patients With Type 1 Diabetes (BEGIN: Flex T1): A 26-Week Randomized, Treat-	3. Biosimilar insulins: thank you for your comment and for highlighting the Diabetes UK position statement on their use. Considering the rise in evidence on biosimilar insulins since the guideline was published and the existing advice in the guideline to ensure acquisition cost is taken into account (see recommendation 1.7.5), we are proposing that this area is reviewed.

		to-Target Trial With a 26-Week Extension. J Clin Endocrinol Metab, March 2013, 98(3):1154–1162 4. SmPC Tresiba November 2018 5. Liu W et al (2018) Efficacy and Safety of Insulin Degludec versus Insulin Glargine: A Systematic Review and Meta-Analysis of Fifteen Clinical Trials. Internatioinal Journal of Endocrinology. 2018 Mar 12;2018:8726046. doi: 10.1155/2018/8726046 6. Evans M, Mehta R, Gundgaard J, Chubb B (2018) Cost-Effectiveness of Insulin Degludec vs. Insulin Glargine U100 in Type 1 and Type 2 Diabetes Mellitus in a UK Setting. Diabetes Therapy 9(5):1919–30 **<u>Page 3</u> Insulin Therapy: Biosimilar insulins** Evidence has been identified to suggest non-inferiority of biosimilar insulins. However, there is no evidence to suggest cost effectiveness of switching to a biosimilar basal or bolus insulin from an existing regimen. A Position Statement from Diabetes UK on the use of Biosimilar insulins states that any change of insulin needs to be a joint decision between the patient and the healthcare professional and that people who are already established on insulin and well controlled should continue with that treatment and not be made to change to a biosimilar[1] 1. Diabetes UK (2018) Diabetes UK position on the use of biosimilar insulin. July 2018.	

British Society of Periodontology	Yes	There is sufficient new evidence to justify this	Thank you for your comment.
AstraZeneca Ltd	Yes	AstraZeneca agrees with the proposal to update the guidelines. The current guidelines acknowledge that research into new interventions is urgently needed. Since the publication of these guidelines, there have been a number of trials looking at adjunct therapy in patients with Type 1 diabetes. These have led to recent indications being granted for both dapagliflozin and sotagliflozin as adjunct therapy to insulin, in patients with a BMI ≥ 27 kg/m^2, when insulin alone does not provide adequate glycaemic control despite optimal insulin therapy. Currently, there are no other adjunctive therapies licensed for treating Type 1 diabetes in the UK. Technology appraisals are currently in development for both these agents (ID1478 and ID1376, respectively). Given the majority of people with Type 1 diabetes are currently not achieving optimal glycaemic control with insulin alone, putting them at risk for diabetes-related complications and premature mortality, it will be important to cover adjunctive approaches in the updated guideline.	Thank you for your comments. As they relate to areas proposed for update, we will pass them on to developers for consideration.
UCL Eastman Dental Institute	Yes	A bulk of evidence suggests that oral health is closely linked to diabetes in a bidirectional manner.	Thank you for your comment. The aetiology of diabetes is not within scope for NICE guideline NG17, NG18 or NG28 however NICE guideline NG18 cross-refers to NICE guideline CG19 on dental recall. This highlights diabetes as a risk factor for developing dental disease and notes that 'People with diabetes (both type I and type II)

			are at increased risk of developing destructive periodontal disease … individuals with diabetes may need a more frequent recall. Inadequate plaque control and the presence of other risk factors will modify the recall interval further.' This issue will be put forward for consideration for scoping discussions for NICE guidelines NG17 and NG28 as expert input is required to determine an appropriate way of highlighting oral health in people with diabetes.
Children and Young People's Wales Diabetes Network	Yes	No comments provided	Thank you.
MedTech Europe	Yes	**Assess observational data/Real World Evidence (RWE)**: HTA bodies should not only focus on RCTs but draw on broader sources of evidence, especially observational data / RWE. This is to support early adoption and help managing uncertainty risks.	Thank you for your comment on the use of real world data. Please note that for the purposes of this surveillance review only Cochrane reviews and RCTs are included. Therefore, studies submitted within other study designs were not included and are stated as out of scope. This included real world data. NICE is considering how real world data may be further used to inform guideline development and a public consultation on this will be taking place in the Summer 2019.
Bayer plc	Yes	No comments provided	Thank you.
Association for Clinical Biochemistry and Laboratory Medicine	Yes	Timely given digital developments and newer agents	Thank you for your comment.

London Diabetes Clinical Network	Yes	No comments provided	Thank you.
South Asian Health Foundation	Yes	1. We would propose that the evidence to review SGLT 2 inhibitors and their use in Type 1 Diabetes Mellitus is not just limited to canagliflozin but also covers all SGLT 2 inhibitors. 2. We would also like to propose better quality evidence review for long term use of flash glucose monitoring and its impact on long term outcomes such as HbA1c	Thank you for your comments, please see the separate responses below: 1. SGLT-2 inhibitors: Thank you for supporting a review of the SGLT-2 class of drugs in type 1 diabetes. The surveillance proposal is to review all evidence on the use of SGLT-2 inhibitors as adjuncts to insulin in type 1 diabetes, not just canagliflozin. The evidence on the use of other SGLT-2 inhibitors in type 1 diabetes was not considered in this surveillance review because they are already the subject of various ongoing NICE technology appraisals. The outcome of the ongoing appraisals, as well as the additional evidence identified in this surveillance review, will be considered in the update process. 2. Long term outcomes of Flash glucose monitoring: Thank you for your comment. We plan to update this section of the guideline as evidence was identified through the surveillance review to support a decision to consider Flash glucose monitoring as a new intervention in the guideline. The guideline committee will be considering the available evidence, with a focus on the important outcomes they have prioritised, as a factor during the update process and take this into consideration when making recommendations.
Roche Diabetes Care, Ltd	Yes	Agree with the proposal to update the guideline and would ask NICE to consider the following general points: • The recently published evidence framework for digital health technologies should be consulted and	Thank you for your comments, please see the separate responses below: 1. Digital health technologies: Thank you for your comments in support of our proposal to update this section of the

		referenced to allow evidence beyond traditional RCTs to be considered, particularly when reviewing smartphone applications and telemedicine. • Where provision of support (e.g. structured education) has traditionally been via face-to-face methods, the wording of the guidelines should be reviewed to include clarity where digital alternatives may be appropriate. Specific areas of agreement with additional points to consider: **1.6 Blood glucose management**: Agree that this is a key area to update and request that significant consideration is taken to patient reported outcomes particularly around improvements in quality of life and mental health when reviewing evidence. Where guidelines for Flash glucose monitoring are reviewed; consider recommendations for suitable alternatives in the event of skin reactions to adhesives. **1.7 Insulin therapy**: For long acting insulin consider additional publications relating to higher concentration insulins. - Lamos et al 2016 Concentrated insulins: the new basal insulins Ther Clin Risk Manag. Mar 9;12:389-400; - Schloot et al 2019 Concentrated insulins in current clinical practice. Diabetes Res Clin Pract. Feb;148:93-101	guideline. Thank you for highlighting the evidence framework for digital health technologies, which outlines a framework for different tiers of evidence for certain health technologies. This framework may be used for guidelines that consider health technologies in the future. We also agree it is important to ensure that any new recommendations on digital support tools are clear about how they relate to existing guidance on face-to-face support and will pass on these concerns to the developers for consideration during the update process. 2. Blood glucose management: Thank you for your comments in support of our proposal to update this section of the guideline. The safety alert issued around the risk of skin reactions to the adhesive used in Flash glucose monitoring was considered as part of the surveillance review and informed the proposal to update the guideline. We will ensure the developers are aware of this safety alert during the update of the guideline. 3. Insulin therapy: Thank you for your comments. This section of the guideline is planned for update. We have considered the evidence highlighted in your comment but are unable to add the studies to Appendix A for the following reasons: a. Long acting insulins: The review by Lamos et al (2016) was identified in the search and the review by Schloot et al (2018) was published after the search cut-off dates. Both publications are narrative reviews and therefore do not meet the inclusion criteria for this surveillance review, which included only RCTs and Cochrane reviews.

		For adjuncts to insulin we propose the risk of euglycemic DKA and potential treatments are considered as well as evidence for dual SGLT1/2 inhibitors: - Garg et el 2018 Strategy for Mitigating DKA Risk in Patients with Type 1 Diabetes on Adjunctive Treatment with SGLT Inhibitors: A STICH Protocol. Diabetes Technol Ther. Sep;20(9):571-575; - Musso et al 2019 Efficacy and safety of dual SGLT 1/2 inhibitor sotagliflozin in type 1 diabetes: meta-analysis of randomised controlled trials. BMJ. Apr 9;365:l1328; - Danne et al 2019 Improved Time in Range and Glycemic Variability With Sotagliflozin in Combination With Insulin in Adults With Type 1 Diabetes: A Pooled Analysis of 24-Week Continuous Glucose Monitoring Data From the inTandem Program. Diabetes Care. May;42(5):919-930.	b. Adjuncts to insulins: The study by Garg et al (2018) was not identified in the search but will not be added to Appendix A because it is an editorial and therefore does not meet the inclusion criteria for this surveillance review or the original guideline. The studies by Musso et al (2019) and Danne et al (2019) were published after the search cut-off dates for this surveillance review. They will not be added to Appendix A because they relate to the SGLT-2 inhibitor sotagliflozin, which is the subject of an ongoing NICE technology appraisal (GID-TA10376). However, they will be passed on to the appraisals team for consideration.
Medtronic Ltd	Yes	No comments provided	Thank you.
Diabetes Technology Network	Yes	DTN agree with the areas identified for review in light of evidence available since NG17 was published. In particular from a technology perspective we are pleased to see Flash Glucose Monitoring (FGM) included as part of the proposed update and would ask NICE to consider commenting on FGM as a replacement for self-monitoring of blood glucose and the importance of Time in Range as a metric for glycaemic control which has more immediate relevance for the user than HbA1c.	Thank you for your comments in support of the planned area for update. We identified new evidence to support considering flash glucose monitoring as an option for people with well-controlled type 1 diabetes, in comparison to standard monitoring using capillary blood glucose. However, we did not identify any evidence to support flash glucose monitoring as a replacement for other monitoring options. In line with the NICE guidelines manual, the developers will identify if there is a suitable core outcome set that could be used for diabetes. Additional input on the main outcomes that should be

			considered would be obtained through the scoping process and protocol development for the update. We will pass your comment about the importance of 'time in range' outcomes to the developers working on the update so this information can be considered during the scoping and protocol development phases.
Dexcom Operating Ltd	Yes	No comments provided	Thank you.
Royal College of Nursing	Yes	No comments provided	Thank you.
University of Exeter	Yes	Our comments principally relate to diagnosis of type 1 diabetes: Section 1.1.3 *"Do not measure C-peptide and/or diabetes-specific autoantibody titres routinely to confirm type 1 diabetes in adults"* We agree that C-peptide should not be measured routinely at diagnosis. We suggest islet antibodies are measured routinely in those aged <30 at diagnosis for the purpose of detecting monogenic diabetes (Shepherd Diabetes Care 2016 PMID: 27271189, Shields Diabetes Care 2017 PMID: 28701371). We suggest C-peptide is measured in all those diagnosed as type 1 diabetes in adults after at least 3 years diabetes duration (to avoid the honeymoon period) for the following reasons: 1. Misclassification is common in adults (overall rates from testing whole clinics c10-15%), especially when diagnosed over age 30 (38% of Type 1 diabetes) References: Thomas Diabetologia 2019 pubmed ID (PMID):	Thank you for your comments on the diagnosis of type 1 diabetes. Please see the separate responses below: 1. **Routine measurement of islet antibodies for detection of monogenic diabetes:** Thank you for highlighting the study by Shields et al (2017), this paper was not identified in this surveillance review and has now been added to Appendix A. The study describes the outcome of a biomarker-based screening pathway for monogenic diabetes. The pathway included 3 stages: 1) Assessment of endogenous insulin secretion using urinary C-peptide/creatinine ratio (UCPCR); 2) if UCPCR was ≥0.2 nmol/mmol, measurement of GAD and IA2 islet autoantibodies; and 3) if negative for both autoantibodies, molecular genetic diagnostic testing for 35 monogenic diabetes subtypes. The results showed that an extra 17 cases of monogenic diabetes were confirmed in the study population using this pathway (total n = 1407). The positive and negative predictive values of the screening pathway were 20% and 99.9% respectively.

		30969375, Thomas Lancet Diabetes 2018, PMID: 29199115, Hope Diabetologia 2018 PMID: 28983693, Hope BJGP PMID: 27080317 2. Clinical criteria for identifying type 1 diabetes in adults work very poorly, for example the age of diagnosis <50 and BMI <25 criteria given in the previous guidance NG17 have a low predictive value: In insulin treated patients diagnosed after age 30 the sensitivity of these criteria is 81% and specificity only 41%. Positive predictive value of these criteria for type 1 diabetes in a population cohort including non-insulin treated patients would therefore be <10% (the vast majority of people meeting these criteria will have type 2 diabetes). References: Thomas Diabetologia 2019 PMID 30969375, Shields BMJ Open 2015 PMID: 26525723. 3. C-peptide testing is inexpensive (full cost £10.50 in routine NHS laboratories (eg Royal Devon and Exeter NHS trust) and in the context of classification and predicting hypoglycaemia and treatment response can be performed on a single non fasting random blood or urine sample after patient's own meals. References: Hope Diabetes Med 2016 PMID: 27100275, Berger 2000 Scand J Clin Lab Invest PMID: 11218151, Hope Diabetologia 2018 PMID: 28983693, Jones Diabetes Care 2016 PMID: 26242184, Jones Diabetic Medicine 2013 PMID: 21843301, Besser Diabetes Care 2011 PMID: 21285386 4. Differences in treatment guidelines for glycaemic management are almost entirely driven by differences in endogenous insulin secretion in longstanding disease. In	Currently, the guideline does not recommend routine use of C-peptide and/or diabetes-specific autoantibody titres assessments to confirm diagnosis of type 1 diabetes (recommendation 1.1.3). However, recommendation 1.1.4 does advise considering C peptide and/or diabetes-specific autoantibody titres if there are either atypical features in the presentation, clinical suspicion of monogenic diabetes, or classification is uncertain. The new evidence suggests that a 3-stage biomarker-based pathway may be beneficial in identifying people with monogenic diabetes, however the positive predictive value of the pathway is notably low. The negative predictive value is high (99.9%), however this is likely to be due to the low prevalence of monogenic diabetes in the population. The study findings are limited by the small numbers of people with monogenic diabetes which limits the ability to evaluate diagnostic sensitivity. Furthermore, evidence reviewed during guideline development suggests that the C-peptide test has better discriminative value the longer the test is done after diagnosis, whereas the antibody test may be more effective at the time of diagnosis. The new evidence recommends using the tests at the same point in time, which is not supported by the large body of evidence considered during guideline development. Given these limitations, the guideline recommendations are unlikely to be impacted by the results of this study. However, we will consider this area at the next surveillance point. **2. Routine measurement of C-peptide in all adults diagnosed as having type 1 diabetes after at least 3 years diabetes duration:**

		longstanding diabetes C-peptide measurement defines the treatment requirement and hypoglycaemia risk of type 1 or 2 diabetes, independent of the clinicians diagnosis: a. As shown in numerous studies (tabulated in Jones 2013 PMID: 23413806) patients with high post meal C-peptide (> 600pmol/l) are able to safely attempt insulin withdrawal, and can frequently replace insulin with oral therapies with improved or maintained glycaemic control. This will have major cost savings associated with reduced medication and monitoring costs, and is a preferred treatment modality to insulin for patients with diabetes. b. Patients with low C-peptide (regardless of clinical classification) have the high glucose variability and hypoglycaemia risk that is characteristic of Type 1 diabetes, and should therefore have access to the 'type 1 diabetes' treatments strategies needed to address this, including carbohydrate counting and where appropriate flash glucose monitoring or insulin pumps. References: Hope Diabetologia 2018 PMID: 28983693 and references within. c. Patients with preserved C-peptide (regardless of clinical classification) have the low glucose variability and hypoglycaemia risk characteristic of	Thank you for highlighting the studies by Thomas et al (2018; 2019). They were not identified in the surveillance review, and have now been added to Appendix A. Collectively, the findings suggest that individuals with late-onset type 1 diabetes show similar clinical characteristics as those with young-onset type 1 diabetes. With further results indicating that late-onset type 1 diabetes may be misclassified as type 2 diabetes which more commonly emerges after 30 years. Thank you for highlighting the paper by Hope et al (2016), this was not identified in the surveillance review searches and has now been added to Appendix A. The study (n = 601) examined the diagnostic accuracy of the criteria in the Royal College of General Practitioners' (RCGP) UK Practical Classification Guidelines for Diabetes compared to the reference standard defined as "continuous insulin treatment within 3 years of diagnosis and absolute insulin deficiency (Urinary C-peptide creatinine ratio <0.2 nmol/mmol ≥5 years post-diagnosis)". The RCGP guideline uses age at diagnosis (less than 35 years) and time to commencing insulin treatment from diagnosis (at diagnosis or within 6 months afterwards) as its diagnostic criteria for type 1 diabetes. Results indicated that the RCGP's criteria correctly classified 86% of participants, with 87 people being misclassified, when compared to the reference standard. Time to insulin treatment performed best in predicting long-term endogenous insulin production (ROC AUC = 0.904); followed by age at diagnosis (AUC = 0.871). Findings also indicate that BMI was a less strong predictor of diabetes type (AUC = 0.824).

		type 2 diabetes, and retain glucose lowering response to non-insulin/non SGLT2 co-therapies. References: Hope Diabetologia 2018 PMID: 28983693, Jones Diabetes Care 2016 PMID: 26242184, Jones 2013 PMID: 23413806 (review). d. In non obese younger patients (onset < age 30) the presence of retained C-peptide is strongly suggestive of monogenic diabetes. Reference: Shepherd Diabetes Care 2016 PMID: 27271189, Shields Diabetes Care 2017 PMID: 28701371 e. The experience of those who have introduced routine testing to clinical practice has been that numerous patients either being able to discontinue 'life long' insulin and/or diagnosed with monogenic forms of diabetes which have implications for both the patient and their extended family. This has been illustrated by the experience of the Western General Hospital diabetes team of offering testing to every patient with apparent type 1 diabetes C-peptide testing, recently presented at 2019 Diabetes UK meeting (Strachan et al, journal article not yet published). *1.1.4 Consider further investigation in adults that involves measurement of C-peptide and/or diabetes-specific*	Thank you for highlighting the paper by Shields et al 2015, this was identified in the surveillance searches but was excluded because it did not meet the inclusion criteria for this surveillance review. We have since added it to Appendix A, as it meets the inclusion criteria for the original guideline. This systematic review examined which clinical criteria could be used to discriminate type 1 and type 2 diabetes. Results indicated that age at diagnosis and time to insulin were the most discriminatory criteria. Furthermore, BMI was found to add little to these two criteria. As stated above, the guideline currently recommends considering C-peptide tests only if there is clinical uncertainty and to refer to the clinical characteristics outlined in recommendation 1.1.1 for a diagnosis decision. The new evidence suggests that people with late-onset type 1 diabetes may be at risk of misclassifications, and that clinical characteristics like age at diagnosis and BMI (mentioned in recommendation 1.1.1) may not be as accurate as C-peptide tests when distinguishing between diabetes types (in people aged over 35 years). During original guideline development, the committee noted that more evidence is required on the use and timing of urine C-peptide and urine C-peptide/creatine ratios before any further recommendations could be made on their use. As the new evidence sheds some light on the risk of misclassification of late-onset type 1 diabetes and highlights limits of the clinical criteria currently listed in recommendation 1.1.1, we propose that this area is

		autoantibody titres if: type 1 diabetes is suspected but the clinical presentation includes some atypical features (for example, age 50 years or above, BMI of 25 kg/m2 or above, slow evolution of hyperglycaemia or long prodrome) or type 1 diabetes has been diagnosed and treatment started but there is a clinical suspicion that the person may have a monogenic form of diabetes, and C-peptide and/ or autoantibody testing may guide the use of genetic testing or classification is uncertain, and confirming type 1 diabetes would have implications for availability of therapy (for example, continuous subcutaneous insulin infusion [CSII or 'insulin pump'] therapy). [new 2015] We suggest the following amendments to this section: - 'prolonged low glucose variability' is included in the list of clinical features that suggest a person with suspected type 1 diabetes has been misclassified. - Include reference to utility of confirmation of type 2 diabetes e.g. confirmation of type 2 diabetes may allow insulin withdrawal or use of adjuvant glucose lowering therapies. - Refer to the need to consider type 1 diabetes in all patients initially thought to have type 2 diabetes who require insulin within 3 years of diagnosis. (reference Thomas Diabetologia 2019 PMID 30969375). 1.1.5 *"When measuring C-peptide and/or diabetes-specific autoantibody titres, take into account that: autoantibody tests have their lowest false negative rate at the time of diagnosis, and that the false negative rate rises thereafter C-peptide has better discriminative value the longer the test is done after diagnosis with autoantibody testing, carrying out tests for 2 different diabetes-specific autoantibodies, with at least 1 being positive, reduces the false negative rate. [new 2015]"*	reviewed to consider the value of routine testing with C-peptides after at least 3 years of diabetes duration. Several of the studies you have suggested were not identified in the searches but cannot be considered in this surveillance review, please see the reasons for exclusion below: - Shepherd et al (2016): observational study describing the prevalence of monogenic diabetes in UK paediatric clinics and does not report on the diagnostic accuracy of biomarker tests or the prevalence of specific biomarkers for diagnostic purposes. - Jones et al (2013) is a narrative review and therefore does not meet the study type inclusion criteria for this surveillance review or the original guideline. - Hope et al (2016); Hope et al (2018); Berger et al (2000): Sample size is less than 50, which was the cut-off rule during this surveillance review and the original guideline. - Jones et al (2016): examines the use of C-peptide to detect risk of reduced glycaemic response to GLP-1RA therapy in people with type 2 diabetes, which is out of scope for this guideline. - Jones et al (2013): Published outside the search cut-offs for this surveillance review. - Besser et al (2011): Considered during the development of the original guideline. - Strachan et al (tbc): unpublished work. We will consider the results of this study when it is published should you wish to get in touch.

		We suggest the following revision to this text: When performing biochemical testing for diagnosis of diabetes type: - Measure islet autoantibodies (GAD and IA2 and ideally ZnT8, not ICA autoantibodies as commercially available rodent assays have poor diagnostic performance, in contrast to the human islets used research studies) as the initial investigation in short duration diabetes (<3 years) - Negative islet autoantibodies do not exclude Type 1 diabetes. Carrying out tests for 2 or more different diabetes-specific autoantibodies, with at least 1 being positive, reduces the false negative rate but will not eliminate it, - Measure C-peptide (non fasting, within 5 hours post meal) as the initial investigation of choice where diabetes duration is >3 years, and a patient is insulin treated. - A low C-peptide (<200pmol/L non fasting) in the absence of hypoglycaemia confirms severe insulin deficiency and requirement for management as type 1 diabetes, regardless of diabetes duration. This level also allows exclusion of MODY. - A high C-peptide (>600pmol/L non fasting) with diabetes duration over 3 years confirms lack of absolute insulin requirement and is associated with low hypoglycaemia risk and preserved response to non-insulin glucose lowering therapy. - Consider testing for MODY where islet autoantibodies are negative and C-peptide (non-fasting) is >200pmol/L.	

Association of British Clinical Diabetologists	Yes	*We wish to say that the 2019 surveillance of 4 diabetes guidelines is welcomed and that there has obviously been a lot of thought and work put in to identifying areas ripe for updating. We are supportive of all areas annotated in the document.*	Thank you for your comment.
NHS England	Yes	A National Project Board established by the Office of Chief Dental Officer, England had developed a Commissioning Standard – Dental Care for Patients with Diabetes (type 1 and type 2), which is now at the final stages of the Gateway process and will be published on NHS England and NHS Improvement website. Production of this standard involved key dental (British Society of Periodontology, European Federation of Periodontology) and medical stakeholders (National Clinical Directors for Diabetes and Obesity, Programme Director NHS Diabetes Programme). As stated in the commissioning standard and evidenced below, the effective management of periodontal disease by the dental team has a role in prevention and treatment of diabetes. (SJH)	Thank you for your comment. The aetiology of diabetes is not within scope for NICE guideline NG17, NG18 or NG28 however NICE guideline NG18 cross-refers to NICE guideline CG19 on dental recall. This highlights diabetes as a risk factor for developing dental disease and notes that 'People with diabetes (both type I and type II) are at increased risk of developing destructive periodontal disease … individuals with diabetes may need a more frequent recall. Inadequate plaque control and the presence of other risk factors will modify the recall interval further.' This issue will be put forward for consideration for scoping discussions for NICE guidelines NG17 and NG28 as expert input is required to determine an appropriate way of highlighting oral health in people with diabetes.

Royal College of Physicians		We would like to endorse the responses submitted by the Diabetes Technology Network (DTN) and the Association of British Clinical Diabetologists (ABCD).	Thank you for your comment.
Diabetes UK	Yes	Diabetes UK agrees with the proposal to update NG17, and supports the specific areas for review that have been identified (including telemedicine, Flash Glucose Monitoring and insulin therapy). However, we would strongly suggest that additional topics also need reviewing and updating.	Thank you for your comment. Regarding the additional areas for update, please see our response to the relevant comment below.

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

Stakeholder	Overall response	Comments	NICE response
Training, Research and Education for Nurses in Diabetes	No	No comments provided	Thank you.
Sheffield Teaching Hospital NHS Foundation Trust	Yes	Given the fact that data from GOLD and DIAMOND is more robust than that from Flash Glucose Monitoring, the role of CGM for poor control ought to be reviewed. The data for improvement in HbA1c is as good as for pump therapy, and due to the nature of the intervention is cheaper to utilise (less patient training, staff costs etc). Therefore the use of CGM ought to be widened beyond severe hypoglycaemia, as the fear of hypoglycaemia is	Thank you for your comments. Currently the guideline recommends use of CGM not just for people with severe hypoglycaemia, but also for people with extreme fear of hypoglycaemia (see recommendation 1.6.22). However, in light of stakeholder comments on the benefit of CGM in people with sub-optimal diabetes control, we have revisited the evidence and decided to review this area in the guideline update. We will pass on your comments to the developers for consideration in the update of the guideline.

		often the limiting factor in those with higher HbA1cs, which a real-time CGM with alarms can help overcome.	
Coeliac UK	Yes	Recommendation 1.12.1 states that adults who have a low BMI or unexplained weight loss should be tested for coeliac disease. We are reassured to see a reference to coeliac disease within the guideline, but feel that the recommendation could be better aligned with the NICE guideline for recognition, assessment and management of coeliac disease (NG20). NG20 recommends that people with type 1 diabetes are tested for coeliac disease at diagnosis and that for people with type 1 diabetes who have tested negative for coeliac disease, that: • coeliac disease may present with a wide range of symptoms **and** • they should consult their healthcare professional if any of the symptoms arise or persist. This recommendation should be included within NG17. In addition, NG17 only lists one symptom of coeliac disease (unexplained weight loss). Not all individuals with coeliac disease will experience weight loss and recommendation 1.12.1 within NG17 should be updated to cover additional symptoms that should prompt testing, including nutritional deficiencies, gastrointestinal symptoms, fatigue and severe or persistent mouth ulcers.	Thank you for your comments and for highlighting this discrepancy across NICE guidelines. We will address this issue with an editorial amendment to recommendation 1.12.1 to ensure that it is consistent with NICE guideline NG20.

South Sefton Clinical Commissioning Group	No	No comments provided	Thank you
British Dental Association	Yes	The BDA believes that this guideline needs to be updated to include discussion of oral health maintenance and complications, and to recommend the inclusion of dentists in the multi-disciplinary teams providing care to diabetes patients. In particular, periodontal disease has a bi-directional relationship with diabetes. https://www.nature.com/articles/sj.bdj.2017.544 https://www.nature.com/articles/sj.bdj.2014.907	Thank you for your comment. The aetiology of diabetes is not within scope for NICE guideline NG17, NG18 or NG28 however NICE guideline NG18 cross-refers to NICE guideline CG19 on dental recall. This highlights diabetes as a risk factor for developing dental disease and notes that 'People with diabetes (both type I and type II) are at increased risk of developing destructive periodontal disease … individuals with diabetes may need a more frequent recall. Inadequate plaque control and the presence of other risk factors will modify the recall interval further.' This issue will be put forward for consideration for scoping discussions for NICE guidelines NG17 and NG28 as expert input is required to determine an appropriate way of highlighting oral health in people with diabetes. We have checked the studies highlighted in your comment. Unfortunately, the studies will not be added to Appendix A because they do not meet the inclusion criteria for this surveillance review, which only considered RCTs and Cochrane reviews.
UK Clinical Pharmacy Association (UKCPA) Diabetes and Endocrinology Group	No	No comments provided	Thank you.
Northumbria Healthcare NHS	Yes	Given the fact that data from GOLD and DIAMOND is more robust than that from Flash Glucose Monitoring, the	Thank you for your comments, please see the separate responses below:

Foundation Trust – National DAFNE Executive Board		role of CGM in adults with sub-optimal glycaemic control ought to be reviewed. The data for improvement in HbA1c is as good as for pump therapy, and due to the nature of the intervention is cheaper to utilise alongside MDI therapy in comparison to switching to a pump (less patient training, staff costs etc). Fear of hypoglycaemia is often the limiting factor in those with higher HbA1cs, which a real-time CGM with alarms can help overcome. We wonder whether this more recent evidence might enable NICE to recommend CGM use more widely than in the current guidelines. We ask that the wording of 1.4.3 be reviewed. Whilst a diet restricted to low GI foods may not lead to improved glycaemic control, service users are concerned that the glycaemic index is being ignored. Perhaps an acknowledgement that understanding the glycaemic index is a key area in carbohydrate counting training and does impact on blood glucose values might be helpful. Currently blood ketone monitoring is only advised for "consideration" in adults whereas in pregnant women and children it is recommended. We contend that dual testing blood glucose and ketone meters are now widely available. DAFNE structured education includes "sick day rules" that are evidence-based in reducing DKA episodes and we propose that blood ketone testing equipment should be offered to all adults with T1D.	1. CGM: In light of new evidence and stakeholder comments, we have decided to review this area in the update of the guideline. We will pass on the information you have provided to the developers for consideration during the scoping phase of the update process. 2. Recommendation 1.4.3: The guideline currently states "do not advise adults with type 1 diabetes to follow a low glycaemic index diet for blood glucose control"; this is based on evidence which found no impact of a low GI diet on HbA1c or incidence of hypoglycaemia. However, the committee noted a lack of recently published evidence with long term follow-up times, therefore a research recommendation in this area was added to the guideline. We did not find any further evidence on low GI diets in this surveillance review and did not find any evidence of a benefit during carbohydrate counting. Therefore, until further evidence is available, the recommendation will not be updated. 3. Blood ketone monitoring: Recommendation 1.11.1 already mentions considering ketone monitoring "as part of 'sick-day rules' for adults with type 1 diabetes". During original guideline development, the committee noted that the quality of evidence regarding capillary blood ketone testing was low, and that there were no RCT data to support the use of capillary blood ketone strips in the emergency department setting. One study on blood ketone testing at home in young people was identified in the original review, however this was confounded (as described in section 12.3.2 for the full guideline). Given the substantially higher cost of blood ketone strips, the

			committee did not feel able to unequivocally recommend blood ketone monitoring as an option. As we did not identify any further evidence in this surveillance review, the recommendation will not be changed.
Digital Diabetes Media Ltd	Yes	Dietary management needs to be updated. The guidelines need a greater focus on 'person-centred care' and 'personalised-medicine' for lifestyle interventions. This is would support the clinical practice of balancing large scale trial evidence with the needs and specific requirements of an individual. There is a significant wide scale learning and change within the population of people with type 1 diabetes. This includes via online fora. Clinical guidelines would benefit from increased recognition of the change in how people with all forms of diabetes learn and improve their own care. This would likely improve the ability for clinicians to provide collaborative person-centred care (using safe personalised "quality improvement" style approaches). A paper published 7 May 2019 provides a useful summary of where the evidence is for low carbohydrate diets in type 1 diabetes. *Carbohydrate Restriction in Type 1 Diabetes: A Realistic Therapy for Improved Glycaemic Control and Athletic Performance?* *Nutrients* **2019**, *11*(5), 1022 https://www.mdpi.com/2072-6643/11/5/1022 Turton et al. published a systematic review in March 2018 *Low-carbohydrate diets for type 1 diabetes mellitus: A systematic review* https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0194987 In summary, due to these rapidly advancing changes in how education is accessed, and the improvements some people	Thank you for your comments, please see the separate responses below: 1. Person-centred care: Section 1.2 in the guideline gives advice on how to offer support and individualised care. The recommendations cover actions such as taking into account individual needs, regarding each person as an individual rather than as a member of any particular group, setting up individual care plans. This aspect is also reflected in other recommendations throughout the guideline. We agree that person-centred care is very important. NICE guideline NG17 will be amended with the following standard text placed at the beginning of the recommendations section: '*People have the right to be involved in discussions and make informed decisions about their care, as described in your care. Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations, and has information about prescribing medicines (including off label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.*' To take into account the changes occurring in the way people are accessing information and self-managing their condition, we have proposed that new evidence on digital health technologies is reviewed in the guideline update.

		with type 1 diabetes experience with a reduced carbohydrate diet, it would be useful for the guideline to acknowledge and reflect this. Without this there is a risk that person-centred care may be inadequate, with some clinician not personalising care for the individual, and the clinician-patient relationship harmed. Conversely recognising the importance of individual needs and circumstances will more likely achieve the best outcomes.	2. Low carbohydrate diets: Thank you for highlighting the paper by Scott et al (2019). This was not identified in this surveillance review because it was published after the search cut-off dates and it will not be added to Appendix A because it is a narrative review, which is an evidence type not considered in this surveillance review or in the original guideline. Thank you for highlighting the review by Turton et al (2018). This study was identified in the surveillance review however it was excluded because the results in the abstract do not distinguish between adults and children. Section 1.4 in the guideline currently recommends carbohydrate-counting as part of a self-management strategy and advises against low GI diets. We did not identify any evidence to indicate that these recommendations should be revised. Furthermore, topic experts did not highlight low carbohydrate diets as a priority area for update. Therefore, we will not be updating this section of the guideline at this point, however we will review again at the next surveillance point.
Diabetes Research Unit Cymru (Wales) (DRUC)	Yes	Flash glucose monitoring (P2, Surveillance proposal consultation document): DRUC welcomes a review of the use of Flash glucose monitoring, anticipating that the guideline will be based on more than simply the current cost of blood glucose testing strips (which appears to be the main determinant of the current eligibility criteria). Long-acting insulin (P2, Surveillance proposal consultation document): NG17 makes a forceful recommendation concerning the prescription of twice daily basal insulins, which is in	Thank you for your comments, please see the separate responses below: 1. Flash glucose monitoring: thank you for your comment. 2. Long-acting insulin: thank you for your comment, we are updating this section of the guideline. 3. Adjuncts to insulin: to clarify, the surveillance proposal is to review all evidence on the use of SGLT-2 inhibitors as adjuncts to insulin in type 1 diabetes, not just canagliflozin. The evidence on dapagliflozin was not considered in this

		conflict with the advice given for children and young adults (NG18) and for which the evidence base is weak. This whole area should be revisited. Adjuncts to insulin (P3, Surveillance proposal consultation document): It seems odd that the Surveillance proposal consultation document discusses the use of canagliflozin as an adjunct therapy for type 1 diabetes when there are no plans that DRUC is aware of for such a licence to be pursued. In contrast, adjunct therapy with dapagliflozin has already been launched in the UK. Eye disease (P3, Surveillance proposal consultation document): The current UK National Screening Committee (NSC) diabetic retinopathy recommendations for screening intervals (2016) need to consider differentiating between type 1 and type 2 diabetes. The current evidence (safety and health economic) is inadequate to extend the interval of screening beyond 1 year for persons with type 1 diabetes. In view of the continuing delay in implementing the recommended UK NSC diabetic retinopathy recommendations for screening intervals, NICE should retain their support for these recommendations and not withdraw as suggested.	surveillance review because it is already being considered in an ongoing NICE technology appraisal. The outcome of the ongoing appraisals, as well as the additional evidence identified in this surveillance review, will be considered in the update process. 4. Eye disease: as stated in the surveillance proposal, evidence on screening intervals for diabetic eye disease was not considered in the surveillance review because it falls under the remit of the NHS Diabetic Eye Screening Programme, who cover screening and referral criteria for people with diabetes. In light of stakeholder feedback, we will replace these recommendations with a link to guidance from the NHS Diabetic Eye Screening Programme.
JDRF, the type 1 diabetes research charity	Yes	1.6.16 – Empowering people to self-monitor blood glucose. JDRF would like to see the inclusion of Bolus calculator blood glucose meters in the guideline. This is because: • Type 1 patients using a bolus calculator blood glucose meter whilst performing advanced	Thank you for your comments, please see the separate responses below: 1. Bolus calculator: The evidence you have provided was identified in this surveillance review and was judged not to

		carbohydrate calculations spend more time within the target HbA1c range than when relying solely on advanced carbohydrate calculations. • Type 1 patients using a bolus calculator blood glucose meter as well as performing advanced carbohydrate calculations reported greater treatment satisfaction, contributing to the overall wellbeing of the patient.[1] 1.6.22 – Continuous glucose monitoring. Due to newer trials and evaluations showing the benefits of CGM since the guideline was last updated, we believe that the word "consider" should change to "offer" for those who meet the stated criteria. • Numerous studies have shown that, compared to self-monitoring of blood glucose (SMBG), continuous glucose monitoring (CGM) can significantly reduce and regulate HbA1c levels[2],[3], reducing the incidence and severity of long-term complications of type 1. • The GOLD trial also found that compared to SMBG, CGM has been shown to reduce the amount of time spent in hypoglycaemia by 42%.	impact on current recommendations. Please see Section 1.4 of Appendix A for further details. 2. Continuous glucose monitoring: In light of new evidence and stakeholder comments, we have decided to review this area in the update of the guideline. We will pass on the information you have provided to the developers for consideration during the scoping phase of the update process. The study by Van Beers et al (2016) was identified in this surveillance review but excluded because the sample size is less than 50. The study by Nathan et al (2014) was considered during the development of the original guideline. 3. Closed-loop systems: In light of stakeholder comments and the inclusion of new evidence published after the surveillance search ended, we are now proposing to review this area as part of the guideline update. Please see Appendix A for further details. Thank you for highlighting the new evidence. The study by Beato-Vibora et al (2018) was not identified in this surveillance review but will not be added to Appendix A because the results in the abstract do not differentiate

		This is associated with improved quality of life and a reduced risk of severe hypoglycaemia. • It also showed that CGM has further positive impacts on wellbeing, with hypoglycaemia fear being reduced and treatment satisfaction improving. • For those with impaired Hypoglycaemia awareness, CGM has been shown to reduce the number of episodes of severe hypoglycaemia by 59%, and the time spent in severe hypoglycaemia by 41%.[4] • A complication of tight glucose control is increased time in hypoglycaemia.[5] As the DIAMOND trial shows, using CGM can help to reduce time spent in hypoglycaemia. Closed-loop insulin delivery systems and sensor-augmented pump therapy in adults with type 1 diabetes – JDRF believes that there is evidence to support the addition of this technology to the guideline. • A study from November 2018 suggests that the MiniMed 640G reduces time in hypoglycaemia from 10% to 6% - in children and adults.[6] • A recent study from April 2019 suggests that predictive low glucose suspend can reduce the	between children and adults. The study by Thomakos et al (2019) was published after the search cut-off dates for this surveillance review. It will not be added to Appendix A because the sample size is less than 50 and therefore does not meet the inclusion criteria for this surveillance review.

		number of hypoglycaemia events from 3.6 to 1.9 events per week per person.[7] [1] Effects of advanced carbohydrate counting guided by an automated bolus calculator in Type 1 diabetes mellitus (StenoABC): a 12-month, randomized clinical trial; Hommel et al; Oct 2016 https://onlinelibrary.wiley.com/doi/abs/10.1111/dme.13275 [2] **Effect of Continuous Glucose Monitoring on Glycemic Control in Adults With Type 1 Diabetes Using Insulin Injections, The DIAMOND Randomized Clinical Trial; Beck et al; Jan 2017** **https://jamanetwork.com/journals/jama/fullarticle/2598770** [3] **Continuous Glucose Monitoring vs Conventional Therapy for Glycemic Control in Adults With Type 1 Diabetes Treated With Multiple Daily Insulin Injections, The GOLD Randomized Clinical Trial; Lind et al; Jan 2017**	

		https://jamanetwork.com/journals/jama/fullarticle/2598771 [4] Continuous glucose monitoring for patients with type 1 diabetes and impaired awareness of hypoglycaemia (IN CONTROL): a randomised, open-label, crossover trial; van Beers et al; Sept 2016 https://www.thelancet.com/journals/landia/article/PIIS2213-8587(16)30193-0/fulltext [5] **The Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study at 30 Years: Overview; David M. Nathan; Jan 2014** **http://care.diabetesjournals.org/content/37/1/9** [6] **Impact of Sensor-Augmented Pump Therapy with Predictive Low-Glucose Suspend Function on Glycemic Control and Patient Satisfaction in Adults and Children with Type 1 Diabetes; Beato-Vibora et al; Nov 2018** **https://www.ncbi.nlm.nih.gov/pubmed/30256132** [7] **The Predictive Low Glucose Management System in Prevention of Clinically Significant Hypoglycemia in Type 1 Diabetes. A Preliminary Study Identifying the Most Common Events Leading Up to Hypoglycemia During Insulin Pump Therapy; Thornakos et al; Apr 2019** **https://www.ncbi.nlm.nih.gov/pubmed/30986882**	
Abbott Diabetes Care	Yes	Prospective real-world studies are important data to show the generalisation of RCTs results in real world settings and	Thank you for your comment and for highlighting the studies by Hellmund et al (2018), Seibold et al (2018) and Dunn et al (2018).

		should therefore be considered. Some of the challenge to conducting medical device HTA may be overcome by applying pragmatic approaches to adjust assessment processes and drawing on broader sources of evidence; especially observational/real world evidence to support early adoption and help to manage the risks associated with uncertain evidence. Additionally, with the digitalisation of Health, observational data and real-world evidence is becoming increasingly significant. According to a recent analysis done by the EY (Healthcare data summit, Paris) a 44-fold increase in the volume of data created each year is expected worldwide by 2020, with 80 billion connected devices by 2020. To not consider real world evidence/observational studies would exclude an invaluable source of data that should be of value as it reflects how devices are used in real world settings. Below are the key additional data pieces, both clinical and cost effectiveness, Abbott would like to highlight for consideration. The Association of British Clinical Diabetologists (ABCD) FreeStyle Libre Nationwide Audit now has over 3500 patients with data entered, predominantly Type 1, currently in the region of 800 have follow up data collected. These patient numbers are constantly increasing as the uptake of FreeStyle Libre grows across the UK. ABCD will present results, on the patients with follow up data, at the American Diabetes Association (ADA) congress in June 2019, so will be available during the time frame of the NG17 update process, should this proceed. Outcomes	Please note that for the purposes of this surveillance review only Cochrane reviews and RCTs are included. Therefore, studies submitted within other study designs were not included and are stated as out of scope. This included real world data. NICE is considering how real world data may be further used to inform guideline development and a public consultation on this will be taking place in the Summer 2019.

		reported will include HbA1c, hypoglycaemia, Gold Score and hypoglycaemic awareness. Resource use data, such as hospitalisation, is also being collected in the coming months. Publications of the data are also planned once presented. CCG stakeholders request audit of local patient data and this database allows for a consistent approach/solution so is a valuable data source to assess the impact of FreeStyle Libre introduction in the UK. Seibold et al. poster, published at ADA June 2018 A meta-analysis on the impact of flash glucose monitoring on glycaemic control as measured by HbA1c https://ada.apprisor.org/index.cfm?k=b313xetsc2 A series of 17 studies were identified as reporting longitudinal HbA1c data in a total 1338 participants with type 1 (n=1112) or type 2 diabetes (n=226) using the FreeStyle Libre flash glucose monitoring system. Data included observations on children, adolescents and adults. Overall mean change in HbA1c was -0.56, 95% CI (-0.76, -0.36), with substantial heterogeneity between trials (I2=92.6%), mainly due to the different HbA1c levels at baseline. No significant differences were detected based on length of study, type of diabetes (T1DM v T2DM) or children versus adults. There has recently been an extended meta-analysis data set analysed and submitted for publication. Dunn et al publication: Real-world flash glucose monitoring patterns and associations between self- monitoring	

		frequency and glycaemic measures: A European analysis of over 60 million glucose tests: diabetes research and clinical practice 137 (2018) 37-46 This worldwide multinational database of over 50 000 users, 64.3 million glucose scan and 86.4 million hours of automatic glucose monitoring provides an unprecedented view into the usage of a new glucose monitoring technology. The data demonstrate high frequency of scanning, emphasising the ease by which glucose levels are checked. Moreover, this shows a strong correlation between the number of glucose scans and improvement in glycaemic markers including reduction in time spent in hypo and hyperglycaemia and increased time in euglycemia. This indicates that the FreeStyle Libre system, in real world settings, represents a powerful glucose monitoring strategy to improve glycaemia in patients with diabetes. This data set has since been updated and was presented at ATTD Berlin 2019 with nearly 500,000 patients data. Poster 0299: “Expanded real-world use confirms strong association between frequency of flash glucose monitoring and glucose control” The conclusion is the same: there is an association between increased glucose testing and lower mean glucose, less time spent in hypoglycaemia and hyperglycaemia, and greater time in range.	

		Although the sample is not described in these data the patient numbers are extremely high and so there is advantage to considering these results when assessing FreeStyle Libre flash glucose monitoring. R. Hellmund, R. Weitgasser, D. Blissett, Cost calculation for a flash glucose monitoring system for UK adults with type 1 diabetes mellitus receiving intensive insulin treatment, Diabetes Research and Clinical Practice (2018), doi: https://doi.org/10.1016/j.diabres.2018.01.028 There are further observational studies whose references we would be pleased to supply.	
Royal College of Ophthalmologists	Yes	As per comment above, the document states: ''Topic experts also highlighted new evidence on the optimum frequency of diabetic eye screening. This area was not considered in the surveillance review because it falls under the remit of the NHS Diabetic Eye Screening Programme who cover screening and referral criteria for people with diabetes. However, to avoid an overlap in guidance we plan to withdraw the recommendations on screening and referral'' Whilst we agree that this work should not be repeated, it would seem sensible to both reference the NHS Diabetic Eye screening programme here as well as including a short summary of the referral guidelines/recommendations, to emphasise the importance of regular screening etc.	Thank you for your comments, please see the separate responses below: 1. Withdrawal of recommendations on diabetic eye screening: Thank you for your comment. As you acknowledge, recommendations on screening and referral for diabetic eye disease fall under the remit of the NHS Diabetic Eye Screening Programme so we plan to withdraw these recommendations. However, in light of your comments and to emphasise the importance of regular screening, we will add in a cross referral to the screening programme so that this guidance can be more easily referred to. 2. Treatment for diabetic retinopathy: The surveillance team did not consider the evidence relating to NICE technology

		It is pertinent to include synopsis of screening programme, including screening intervals, referral pathways to keep the guidelines current and comprehensive. To include management of sight threatening complications – use of antiVEGF in established cases and the emerging evidence of disease modifying effect as well as earlier preventive treatment., On page 30 the document states '' We identified 2 Cochrane reviews and 3 RCTs on interventions to manage eye disease in type 1 diabetes (table 7). Two Cochrane reviews (55,56) and 5 RCTs (57–61) focussed on the use of anti-vascular endothelial growth factor (anti-VEGF) for diabetic macular oedema which relate to the NICE technology appraisal guidance on Ranibizumab for treating diabetic macular oedema (TA274). Therefore, these studies will not be considered in this surveillance review''. Table 7 is missing various key publications, such as a number of DRCR-net studies on the management of diabetic retinopathy (such as DRCR-net Protocol T, Protocol I). We think it would be desirable to include the evidence for the various treatments in one place, so it would seem unusual to exclude data assessed in TA 274, especially as the Aflibercept, Ozurdex and Iluvien data all needs to be considered as well as the data for Ranibizumab, to be taken in context. The studies generally to NOT only include patients with either Type 1 vs Type 2 diabetes, so the same data would be reviewed and would be relevant to both the guidelines. With respect to proliferative diabetic retinopathy, reference is made to the Clarity study but data from the DRCR-net Protocol S study should also be included and discussed.	appraisals; as such, the DRCR-net Protocol study was not included in the Appendix A. However, the information has been passed on to the appraisals team for consideration. Management of overlaps and linkages between the diabetes clinical guidelines and technology appraisal guidance on diabetic retinopathy will be considered as part of the update to NG17.

Novo Nordisk	Yes	See above	Thank you.
British Society of Periodontology	Yes	1. **Periodontal and dental diseases should be included within the assessment of diabetes-related complications and other comorbidities that affect people with diabetes.** • (Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes d2019 Diabetes Care 2019;42(Suppl. 1):S34–S45). • (Oral health: local authorities and partners Public health guideline Published: 22 October 2014 nice.org.uk/guidance/ph55) 2. **Evidence suggests that type 1 diabetes increases the risk of periodontal diseases** • (Does diabetes increase the risk of periodontitis? A systematic review and meta-regression analysis of longitudinal prospective studies. Nascimento GG, Leite FRM, Vestergaard P, Scheutz F, López R. Acta Diabetol. 2018 Jul;55(7):653-667). 3. **Patients with diabetes should be referred to a dentist for comprehensive dental and periodontal examination.** • (Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes d2019 Diabetes Care 2019;42(Suppl. 1):S34–S45). • (Scottish Dental Clinical Effectiveness Programme, 2014) • (Clinical Knowledge Summaries, Gingivitis and Periodontitis, https://cks.nice.org.uk/gingivitis-and-periodontitis#!scenario) • (Oral health: local authorities and partners Public health guideline Published: 22 October 2014 nice.org.uk/guidance/ph55)	Thank you for your comment. The aetiology of diabetes is not within scope for NICE guideline NG17, NG18 or NG28 however NICE guideline NG18 cross-refers to NICE guideline CG19 on dental recall. This highlights diabetes as a risk factor for developing dental disease and notes that 'People with diabetes (both type I and type II) are at increased risk of developing destructive periodontal disease … individuals with diabetes may need a more frequent recall. Inadequate plaque control and the presence of other risk factors will modify the recall interval further.' This issue will be put forward for consideration for scoping discussions for NICE guidelines NG17 and NG28 as expert input is required to determine an appropriate way of highlighting oral health in people with diabetes. Thank you highlighting the evidence in this area. We have checked the studies but will not add these to Appendix A for the following reasons: - Diabetes Care 2019, Scottish Dental Clinical Effectiveness Programme, Canada Clinical Practice Guidelines (2018), Swedish National Guidelines for Diabetes Care: The surveillance team at NICE do not consider guidelines from other organisations as an evidence type. - Leite et al (2018): Does not meet study type inclusion criteria as it is a systematic review. Due to the large volume

		• (2018 Clinical Practice Guidelines Introduction Diabetes Canada Clinical Practice Guidelines Expert Committee, Can J Diabetes 42 (2018) S1–S5) • (Swedish National Guidelines for Diabetes Care from the National Board of Health and Welfare – Support for governance and management. https://www.socialstyrelsen.se/publikationer2015/2015-4-12)	of evidence available for this topic, this surveillance review focussed specifically on RCTs and Cochrane reviews.
AstraZeneca Ltd	No	No comments provided	Thank you.
UCL Eastman Dental Institute	Yes	**1. Periodontal and dental diseases should be included within the assessment of diabetes-related complications and other comorbidities that affect people with diabetes.** • (Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes d2019 Diabetes Care 2019;42(Suppl. 1):S34–S45). • (Oral health: local authorities and partners Public health guideline Published: 22 October 2014 nice.org.uk/guidance/ph55) **2. Evidence suggests that type 1 diabetes increases the risk of periodontal diseases** • (Does diabetes increase the risk of periodontitis? A systematic review and meta-regression analysis of longitudinal prospective studies. Nascimento GG, Leite FRM, Vestergaard P, Scheutz F, López R. Acta Diabetol. 2018 Jul;55(7):653-667). **3. Patients with diabetes should be referred to a dentist for comprehensive dental and periodontal examination.** • (Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes d2019 Diabetes Care 2019;42(Suppl. 1):S34–S45).	Thank you for your comment. The aetiology of diabetes is not within scope for NICE guideline NG17, NG18 or NG28 however NICE guideline NG18 cross-refers to NICE guideline CG19 on dental recall. This highlights diabetes as a risk factor for developing dental disease and notes that 'People with diabetes (both type I and type II) are at increased risk of developing destructive periodontal disease … individuals with diabetes may need a more frequent recall. Inadequate plaque control and the presence of other risk factors will modify the recall interval further.' This issue will be put forward for consideration for scoping discussions for NICE guidelines NG17 and NG28 as expert input is required to determine an appropriate way of highlighting oral health in people with diabetes. Thank you highlighting the evidence in this area, we will not be adding these to Appendix A for the following reasons:

		• (Scottish Dental Clinical Effectiveness Programme, 2014) • (Clinical Knowledge Summaries, Gingivitis and Periodontitis, https://cks.nice.org.uk/gingivitis-and-periodontitis#!scenario) • (Oral health: local authorities and partners Public health guideline Published: 22 October 2014 nice.org.uk/guidance/ph55) • (2018 Clinical Practice Guidelines Introduction Diabetes Canada Clinical Practice Guidelines Expert Committee, Can J Diabetes 42 (2018) S1–S5) • (Swedish National Guidelines for Diabetes Care from the National Board of Health and Welfare – Support for governance and management. https://www.socialstyrelsen.se/publikationer2015/2015-4-12)	- Diabetes Care 2019, Scottish Dental Clinical Effectiveness Programme, Canada Clinical Practice Guidelines (2018), Swedish National Guidelines for Diabetes Care: The surveillance team at NICE do not consider guidelines from other organisations as an evidence type. - Leite et al (2018): Does not meet study type inclusion criteria as it is a systematic review. Due to the large volume of evidence available for this topic, this surveillance review focussed specifically on RCTs and Cochrane reviews.
Children and Young People's Wales Diabetes Network	Yes	There should be a review of the "transition" of young people from paediatric services to adult services. NG17 should mirror NG18 with regards to "transition" to ensure joined up working across the two services. NICE should consider the recommendations of the *All Wales Standard for People with Diabetes Moving from Paediatric to Adult Services in NHS Wales* (available from http://www.cypdiabetesnetwork.nhs.uk/index.php/download_file/3247/694/), particularly with regards to joint clinics between paediatric and adult services, the employment of youth workers across both paediatric and adult teams, ensuring diabetes education is tailored to young adults, continued provision of psychological support, uninterrupted continuation of technology (pump and CGM/flash to continue under care of adult team with no enforced changes or withdrawal of equipment)	Thank you for highlighting the 'All Wales Standard for People with Diabetes Moving from Paediatric to Adult Services in NHS Wales' and the work of the national Children and Young People's Wales Diabetes Network. Guidance from organisations that have been NICE accredited would be considered for cross-reference within guidance, however these organisations do not have NICE accreditation. Only Cochrane reviews and RCT evidence has been considered in the surveillance review. Recommendations 1.5.9-1.5.13 in NICE guideline NG18 cover transition from paediatric to adult care. We acknowledge the importance of providing joined-up care in this group and would like to highlight that these recommendations are linked to NICE guideline NG17 as well as the NICE guideline on Transition from

			children's to adults' services for young people using health or social care services in the diabetes interactive flowchart.
MedTech Europe	Yes	**Expand to surrogate endpoints**: With new technology, more data becomes available. We would suggest collecting and looking at data around surrogate endpoints (i.e. not only focusing on HbA1c but take into consideration Time In Range and other therapy relevant clinical endpoints).	Thank you for your comment. We are planning to update the area of digital health technologies. We agree with your comment around the importance of outcomes in guidance development. In line with the NICE guidelines manual, the developers will identify if there is a suitable core outcome set that could be used for diabetes. Additional input on the main outcomes that should be considered would be obtained through the scoping process and protocol development for the update. We will pass your comment about expanding to surrogate endpoints to the developers working on the update so this information can be considered during the scoping and protocol development phases.
Bayer plc	Not answered	No comments provided	Thank you.
Association for Clinical Biochemistry and Laboratory Medicine	No	No comments provided	Thank you.
London Diabetes Clinical Network	Yes	The new evidence for continuous glucose monitoring (CGM) for people with type 1 diabetes using a multiple dose insulin injection regimen (DIAMOND, GOLD, HypoDE) is important and may impact on the recommendations for use of CGM for people at highest risk of hypoglycaemia, especially in the light that the smaller evidence base for flash monitoring may be considered. The impact of adjunctive non-insulin therapies, including SGLT-1/2 inhibitors and GLP-1 receptor agonists in well	Thank you for your comments, please see the separate responses below: 1. CGM: In light of stakeholder comments on the benefit of CGM in people with sub-optimal diabetes control, we have revisited the evidence and decided to review this area in the guideline update. We will pass on the information you

		described populations of people with type 1 diabetes should be considered. The evidence for psychological support for people living with type 1 diabetes, and the potential to support effective self-management by addressing diabetes distress and hypoglycaemia fear should be considered. This may be especially relevant in people with recurrent DKA, those with type 1 diabetes and eating disorders and underlying psychiatric disorders. New evidence supporting stratified diagnostic approaches to type 1 diabetes may warrant review. New data for pancreatic auto-antibody testing, c-peptide assessment and the use of genetic risk scores is available and should be reviewed for use where diagnostic uncertainty would lead to a meaningful change in therapy.	have provided to the developers for consideration during the scoping phase of the update process. 2. Adjuncts to insulin: As stated in Appendix A, we plan to review the evidence on the use of SGLT-2 inhibitors in type 1 diabetes. We are not planning to review the evidence on GLP-1 receptor agonists as we only identified one trial in this area, which showed limited benefit. 3. Psychological support: We did not identify any evidence in this area that met the inclusion criteria for this surveillance review. Recommendations 1.15.41-1.15.42 in the guideline currently state that members of the diabetes professional team providing care should be alert to the symptoms of psychological problems (particularly if the person is having problems with self-management) and have the skills for basic management and referral if problems persist. This section of the guideline also includes cross referrals to other NICE guidelines on common mental health disorders, generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults and depression in adults with a chronic health problem. As this area is covered by existing guidance, we will not be making any changes to recommendations at this point. 4. Diagnostic approaches: In light of stakeholder comments, we have added new evidence to Appendix A on the use of C-peptide tests to prevent misdiagnosis in adults with late onset type 1 diabetes and are now proposing to review the evidence in this area during the guideline update process. We also considered new evidence on the use of autoantibody tests and genetic tests, however this was judged not to impact the guideline at this point.

South Asian Health Foundation	Yes	We would propose that evidence for the use of closed loop systems in Type 1 Diabetes should be looked at in more detail to enable consensus nationally about their use. An update on management of newly diagnosed patients with Type 1 Diabetes particularly with relevance to access to structured education early on in disease.	Thank you for your comment on closed-loop systems. In light of stakeholder comments and the inclusion of new evidence published after the surveillance search ended, we are now proposing to review this area as part of the guideline update. Please see Appendix A for further details.
Roche Diabetes Care, Ltd	Yes	**1.4 Dietary management**: Agree that the value of bolus advisors for some people is well-evidenced and the current guidelines allow provision where suitable. However, with increasing availability of bolus advisor functions via mobile applications we believe now is a good opportunity to review this area and provide clarity on these options, including guidance on regulatory requirements. **Closed-loop insulin delivery**: We believe there is sufficient evidence to review this section. <u>Evidence to support Automated Insulin Delivery (AID):</u> - Kropff et al 2015 AP@home consortium. 2 month evening and night closed-loop glucose control in patients with type 1 diabetes under free-living conditions: a randomised crossover trial. Lancet Diabetes Endocrinol. Dec;3(12):939-47. - Kovatchev et al 2017 Feasibility of Long-Term Closed-Loop Control: A Multicenter 6-Month Trial of 24/7 Automated Insulin Delivery. Diabetes Technol Ther. Jan;19(1):18-24.	Thank you for your comments, please see the separate responses below: 1. Bolus calculator functions via mobile phone applications: As stated in Appendix A, we plan to review the area of digital technology and we will pass on your comment to the developers for consideration during the guideline update. 2. Closed-loop insulin delivery: In light of stakeholder comments and the inclusion of new evidence published after the surveillance search ended, we are now proposing to review this area as part of the guideline update. Thank you for highlighting the further evidence, we identified each of these studies in the searches however they did not meet the inclusion criteria for this surveillance review for the reasons listed below. The new protocols developed for the guideline update will outline inclusion and exclusion criteria for the evidence base. If these studies meet the inclusion criteria stated in the revised protocol, they will be considered during the update process. :

		- Leelarathna et al 2014 AP@home consortium. Assessing the effectiveness of 3 months day and night home closed-loop insulin delivery in adults with suboptimally controlled type 1 diabetes: a randomised crossover study protocol. BMJ Open. Sep 3;4(9):e006075. - Anderson et al 2016 Control to Range Study Group. Multinational Home Use of Closed-Loop Control Is Safe and Effective. Diabetes Care. Jul;39(7):1143-50. - Bally et al 2017 Assessing the effectiveness of a 3-month day-and-night home closed-loop control combined with pump suspend feature compared with sensor-augmented pump therapy in youths and adults with suboptimally controlled type 1 diabetes: a randomized parallel study protocol. BMJ Open. Jul 13;7(7):e016738.	- Kroff et al (2015): inadequate data in the abstract - Kovatchev et al (2017): feasibility study. This surveillance review only considered RCTs and Cochrane reviews. Pilot and feasibility studies were excluded. - Anderson et al (2016): does not meet study type inclusion criteria (not an RCT or Cochrane review). The papers by Leearathna et al (2014) and Bally et al (2017) are study protocols and therefore cannot be considered in this surveillance review. However, we will monitor the ongoing trials and consider the results when they are published.
Medtronic Ltd	Yes	The proposal is not to include a new section closed-loop insulin delivery systems and sensor-augmented pump therapy. A 2019 review is planned for "DG21: Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system)". We suggest that a new section should be added to NG18 for "closed loop systems" and "sensor augmented pump therapy" to capture the recommendations from the review of DG21 and new evidence below. We would like to highlight the following studies that may not have been captured by the evidence review: A recently published RCT:	Thank you for your comment. We are aware of the planned review to NICE diagnostic guidance DG21 and have taken this into account in the surveillance review. Thank you for highlighting the study by Bosi et al (2019), this was published after the search cut-off dates for this review, however we have now added it to Appendix A for consideration. In light of stakeholder comments and the inclusion of new evidence published after the surveillance search ended, we are now proposing to review this area as part of the guideline update. Please see Appendix A for further details. Thank you for highlighting the further evidence by Agrawal et al (2015); Zhong et al (2016); and Battelino et al (2015). We did not identify these studies in the searches however they will not be

		Bosi, Choudhary et al. Efficacy and safety of suspend-before-low insulin pump technology in hypoglycaemia-prone adults with type 1 diabetes (SMILE): an open-label randomised controlled trial". Lancet Diabetes Endocrinol (online April 2019). The following real world, UK study has recently been accepted for publication by Diabetes Care: Chaudhary, de Portu et al. Use of sensor-integrated pump therapy to reduce hypoglycaemia in people with type 1 diabetes: a real-world study in the UK Additional relevant studies: Agrawal, Zhong et al. Retrospective Analysis of the Real-World Use of the Threshold Suspend Feature of Sensor-Augmented Insulin Pumps. Diabetes Technology & Therapeutics Volume 17, Number 5, 2015 Zhong, Choudhary et al. Effectiveness of Automated Insulin Management Features of the MiniMed 640G Sensor-Augmented Insulin Pump. Diabetes Technology & Therapeutics Volume 18, Number 10, 2016 Battelino, Liabat et al. Routine use of continuous glucose monitoring in 10 501 people with diabetes mellitus. Diabet. Med. 00, 000–000, 2015	added to Appendix A because they do not meet the study type inclusion criteria for this surveillance review.
Diabetes Technology Network	Yes	DTN would urge NICE to reconsider excluding closed-loop systems – we note only two studies have been included in the surveillance review and think this under-represents the available evidence base, although agree that to date studies demonstrating long-term evidence of effectiveness are lacking. However, since closed loop systems are an extension of the pump-continuous glucose monitoring (CGM) combination supported by NG17 in its recommendation about CGM we think it would be very helpful for NICE to include this in the review. There is a	Thank you for your comments, please see the separate responses below: 1. Closed-loop systems: In light of stakeholder comments and the inclusion of new evidence published after the surveillance search ended, we are now proposing to review this area as part of the guideline update. Please see Appendix A for further details.

		commercially available hybrid closed loop system, the Medtronic 670G, and the evidence base is likely to expand over the time NICE is carrying out the review so this is a pertinent aspect of care for NICE to make a recommendation about. DTN agree with the surveillance report that new evidence around CGM would not fundamentally alter the current NG17 recommendation. However, the new evidence does confirm the effectiveness of CGM when added to MDI and DTN would ask NICE to consider re-wording the current recommendation to emphasise that CGM is equally effective when added to MDI as when added to CSII. Further, with the cost of CGM having reduced (particularly the Dexcom G6 which has an extended 10 day life and does not require calibrating) DTN believe the current cost-effectiveness calculation for CGM should be updated. The surveillance report refers to evidence relating to the new rapid-acting insulin analogue FiAsp but argues that since NG17 did not specify a particular preferred rapid-acting analogue the recommendation relating to rapid-acting insulin did not need updating. However, the rapid-acting analogues considered in NG17 are all virtually the same, but FiAsp has a different pharmacokinetic profile which can potentially benefit certain people using an intensive insulin regimen and therefore we believe the recommendation does need updating to reflect these differences between FiAsp and the other rapid-acting analogues. The DTN committee has identified two areas not included in the surveillance report where we believe there is new evidence that the guideline review should consider: • Immunotherapy: there are several reported studies and ongoing trials considering interventions to prevent/reverse the development of type 1 diabetes.	2. CGM: In light of the new evidence and stakeholder comments, we have decided to review this area in the update of the guideline. We will pass on the information you have provided to the developers for consideration during the scoping phase of the update process. 3. Immunotherapy: We did not identify any evidence in this area that met the inclusion criteria for this surveillance review. Therefore, no changes will be made to the guideline. 4. C-peptide tests: In light of the new evidence and stakeholder comments, we have decided to review this area in the update of the guideline. We will pass on the information you have provided to the developers for consideration during the scoping phase of the update process. 5. Psychological therapy: We did not identify any evidence in this area that met the inclusion criteria for this surveillance review. Recommendations 1.15.41-1.15.42 in the guideline currently state that members of the diabetes professional team providing care should be alert to the symptoms of psychological problems (particularly if the person is having problems with self-management) and have the skills for basic management and referral if problems persist. This section of the guideline also includes cross referrals to other NICE guidelines on common mental health disorders, generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults and depression in adults with a chronic health problem. As this area is covered by existing guidance, we will not be making any changes to recommendations at this point.

		• In the section on diagnosis there are a number of publications relating to the use of C-peptide to correctly classify the diabetes type eg Shields BM et al Population-based assessment of a biomarker-based screening pathway to aid diagnosis of monogenic diabetes in young-onset patients Diabetes Care 2017;40:1017. The DTN committee believe that the current NG17 recommendation on psychological problems (1.15.41 and 1.15.42) would benefit from providing greater detail, given increasing evidence for the effectiveness of specific interventions as detailed in Schmidt CB et al. Systematic review and meta-analysis of psychological interventions in people with diabetes and elevated diabetes-distress. Diabet Med 2018 Jun 13. doi: 10.1111/dme.13709. [Epub ahead of print]	
Dexcom Operating Ltd	Yes	*RtCGM should be included in the scope of the NG17 guidelines update, resulting in a recommendation for rtCGM for patients with Type 1 Diabetes (T1D) and suboptimal glycaemic control, based on recent clinical data.* • There are 3 areas related to rt-CGM that should be considered in scope for this guideline update: HbA1c – sub optimal glycemic control • CGM digital platforms • CGM branding and terminology • HbA1c – sub-optimal glycemic control	Thank you for your comments, please see the separate responses below: 1) Interpretation of DIAMOND and GOLD trials: To clarify, both trials were correctly interpreted as including people taking multiple daily injections. They were not mistaken for people with problematic hypoglycaemia, as evidenced by the impact statement which considered all trials (DIAMOND, GOLD, HypoDE and HypoCOMPaSS) and read "We identified new evidence which supports the use of CGM in people having multiple daily injection therapy, *with and without impaired hypoglycaemia awareness or history of severe hypoglycaemia*." However, we have amended this statement for clarification purposes.

		At present, NG17 *does not recommend rtCGM to patients with T1D who have suboptimal glycaemic control* (evidenced by HbA1c >58 mmol/mol [>7.5%]) despite recent clinical studies demonstrating that rtCGM can significantly reduce mean glucose and HbA1c for uncontrolled T1D, this reduction is maintained for at least 2 years. The omission of rtCGM from the NG17 update is based on incorrect interpretation of two clinical trials: DIAMOND and GOLD. It seems the draft evidence review wrongly concluded that these trials only supported the use of rtCGM for patients with problematic hypoglycaemia. However, the DIAMOND and GOLD studies recruited patients with poorly-controlled T1D (HbA1c >69 mmol/mol [>8.5%]) on multiple daily insulin injections (MDI) and their primary objective was to determine changes in HbA1c after rtCGM use. As a secondary endpoint, DIAMOND and GOLD evaluated time spent in hypoglycaemia, By contrast, the HypoDE trial enrolled patients with well-controlled T1D (screening HbA1c ≤75.0 mmol/mol [≤9.0%]) and a history of severe hypoglycaemia or impaired hypoglycaemia awareness and its primary outcome was the baseline-adjusted number of hypoglycaemic events (defined as glucose ≤3·0 mmol/L for ≥20 min) during the 26-week follow-up phase. The evidence demonstrating the benefits of rt-CGM for adult T1 Diabetes patients has grown tremendously since the last guideline update. In particular, the following publications describe the clinically significant benefits of	However, we have carefully considered the responses from the many stakeholders who feel that the guideline update should consider the new evidence on rtCGM for people with sub-optimally controlled type 1 diabetes. Whilst the guideline advises that the principles of flexible insulin therapy with a multiple daily injection insulin regimen (or pump therapy) should be followed for people with CGM (recommendation 1.6.23), we acknowledge that currently rtCGM is only recommended in people with complete loss of hypoglycaemia awareness or history of severe hypocglycaemia (recommendation 1.6.22). Given the new evidence available for this population and the strong steer from stakeholders, we are now proposing that this area is reviewed as part of the guideline update. We will pass on your comments to the developers for consideration in the scoping phase of the guideline update. The following studies you have highlighted have already been included in this surveillance review: Beck et al (2017a; 2017b), Lind et al (2017). Some of the studies you have highlighted were identified in the surveillance review but were excluded because they did not meet the study type inclusion criteria for this review (were not a primary analysis of an RCT or a Cochrane review). These were: Billings et al (2018), Ruedy et al (2017), Ólafsdóttir et al (2018), Šoupal et al (2016; 2017), Mullinacci et al (2019). 2) rtCGM for people with hypoglycaemia: We agree that rtCGM should continue to be recommended in people with hypoglycaemic problems, having identified further evidence to support this recommendation. We identified

		rtCGM for individuals with suboptimal glycaemic control, and hence should be considered: • Beck et al., Effect of Continuous Glucose Monitoring on Glycaemic Control in Adults With Type 1 Diabetes Using Insulin Injections The DIAMOND Randomized Clinical Trial. JAMA. 2017;317(4):371-378 • Beck et al., Effect of initiating use of an insulin pump in adults with type 1 diabetes using multiple daily insulin injections and continuous glucose monitoring (DIAMOND): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol. 2017 Sep;5(9):700-708. • Billings et al., Baseline Glycated Hemoglobin Values Predict the Magnitude of Glycemic Improvement in Patients with Type 1 and Type 2 Diabetes: Subgroup Analyses from the DIAMOND Study Program. Diabetes Technol Ther, 2018. 20(8): p. 561-565 • Ruedy et al., Continuous glucose monitoring in older adults with type 1 and type 2 diabetes using multiple daily injections of insulin: Results from the DIAMOND trial. J Diabetes Sci Technol. 2017;11:1138-1146 • Lind et al., Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: The GOLD randomized clinical trial. JAMA 2017;317(4):379-387 • Ólafsdóttir et al., Randomized Clinical Trial of the Effect of Continuous Glucose Monitoring on Nocturnal Hypoglycemia, Daytime Hypoglycemia,	the study by Heinemann in this surveillance review and have included this in Appendix A. 3) rtCGM and digital platforms: We are planning to review the evidence on digital health technologies and will pass on your comment to the developers for consideration in the update of the guideline. 4) NHS long term plan: We have considered the NHS Long Term plan during this surveillance review and acknowledge the focus on digital technologies. 5) rtCGM and branding: Thank you for this information, we will pass on your comment to the developers for consideration in the update of the guideline. 6) Additional references: The following studies you have highlighted will not be added to the surveillance review because they do not meet this review's inclusion criteria for study type: Welsh et al (2019), Puhr et al (2019), Freckmann et al (2017), Diabetes Technology (2019). However we will pass on this information to the developers for consideration during the scoping phase of the guideline update.

		Glycemic Variability, and Hypoglycemia Confidence in Persons with Type 1 Diabetes Treated with Multiple Daily Insulin Injections (GOLD-3). Diabetes Technol Ther. 2018 Apr;20(4):274-284 • Šoupal et al., Comparison of different treatment modalities for type 1 diabetes, including sensor-augmented insulin regimens, in 52 weeks of follow-up: a COMISAIR study. Diabetes Technol Ther 2016; 18:532-38. • Šoupal et al., CGM combined with either MDI or CSII is superior to standalone MDI or CSII in type 1 diabetes: 2 years of follow-up in the COMISAIR study. Diabetologia. 2017;60(S1):S328-S329. • Mulinacci et al., Glycemic Outcomes with Early Initiation of Continuous Glucose Monitoring System in Recently Diagnosed Patients with Type 1 Diabetes. Diabetes Technol Ther. 2019;21(1):6-10. The DIAMOND trial, which randomized 158 participants with T1D and mean baseline HbA1c of 70 mmol/mol [8.6%, range 58 to 85 mmol/mol [7.5% to 9.9%] treated with MDI to rtCGM or usual care with SMBG, demonstrated that individuals in the rtCGM group exhibited a 1 percentage point reduction in HbA1c after 6 months while those in the SMBG group demonstrated only a 0.4 percentage point reduction in HbA1c, a significant between-groups difference (P < 0.001). Correspondingly, mean time in range (3.9 to 10.0 mmol/L) increased for those that initiated rtCGM use, from 660 minutes/day to 736 minutes/day after treatment, while it remained steady at 650 minutes/day throughout the trial for those in the	

		SMBG group. A second, 28-week phase of the DIAMOND trial assessed the value of keeping patients on rtCGM while changing their insulin delivery from injections to insulin pumps. The results demonstrated that initiation of insulin pump use improved time in range from 708 minutes/day to 791 minutes/day, while continued MDI therapy did not (between-groups difference P=0.01). This phase of the DIAMOND trial confirmed that rtCGM use alone (without the additional use of an insulin pump) is sufficient to improve glycaemic control. Adherence to rtCGM use was high throughout the trial, with more than 91% of participants using rtCGM ≥6 days a week throughout the trial. Billings et al. (2018) conducted a post-hoc analysis of the DIAMOND trial and investigated whether the previously demonstrated HbA1c reduction was still evident when participants were first stratified by baseline HbA1c. This analysis included 158 people with T1D and a mean baseline HbA1c of 70 mmol/mol [8.6%]. The analysis found that the change in HbA1c was significantly greater among participants in the rtCGM group compared to SMBG group at all predefined HbA1c thresholds at 12 and 24 weeks. Reductions in HbA1c ranged in magnitude from 1.0% to 1.4% and were greatest for participants with the highest baseline HbA1c ≥75 mmol/mol [≥9.0%]. Thus, rtCGM therapy improves glycemia for participants with the worst control. Importantly, the improvements seen in patients with high baseline HbA1c levels were achieved without the need for additional medications and their associated costs.	

		Ruedy et al. (2017) conducted a separate analysis of adults ≥60 years of age who completed the DIAMOND trial and found that HbA1c reductions were greater in the group assigned to CGM than in the control group. They additionally reported that CGM usage was high, and concluded that CGM should be considered for older adults with diabetes using MDI. The results from the first phase of the DIAMOND trial were consistent with those of the GOLD randomized controlled clinical trial (Lind et al., 2017), which used a crossover design to determine the difference in HbA1c between rtCGM and SMBG treatment for 161 MDI users with T1D. In this trial, mean baseline HbA1C was also 70 mmol/mol [8.60%]; mean HbA1c was 63 mmol/mol [7.92%] during rtCGM use and 67 mmol/mol [8.35%] during conventional treatment (mean difference, −0.43%; P <0.001). Results from the crossover design of the GOLD trial highlighted that continued access to CGM is necessary to obtain continued benefit. A secondary analysis of data from the GOLD study (Ólafsdóttir et al., 2018) showed the beneficial effects of CGM with respect to glycemic metrics other than HbA1c, as well as improvements in patient-reported outcomes including hypoglycemia confidence. Next, the nonrandomised, prospective, **real-life study** by Šoupal et al. (2016) was designed to compare the long-term efficacy of four, patient-selected, treatment modalities	

		including sensor-augmented insulin regimens (SAIRs), i.e. sensor-augmented pump (SAP) therapy or rtCGM+MDI, insulin pump therapy alone, or MDI therapy alone in 65 patients with T1D. This study provides data from the longest-term evaluation of the efficacy of rtCGM use. At baseline, the mean HbA1c was 67 mmol/mol [8.3%]. After 52 weeks, the SAIR group had significantly lower HbA1c than baseline (54 vs 67 mmol/mol [7.1% vs 8.3%], P<0.0001). This improvement in HbA1c from study baseline was observed both in the SAP therapy subgroup (54 vs 66 mmol/mol [7.1% vs 8.2%], P=0.0025) and the MDI + rtCGM group (55 vs 69 mmol/mol [7.2% vs 8.5%], P=0.0034) and was superior to the reduction observed with insulin pump therapy alone (63 vs 68 mmol/mol [7.9% vs 8.4%], P<0.05). The reduction in HbA1C was sustained for at least 2 years: after 2 years, mean HbA1c for those in the SAIR group was 54 mmol/mol [7.1%] and was still superior to HbA1c reduction observed during insulin pump use alone (64 mmol/mol [8.0%]). Further, after two years, 54% of those in the SAIR group achieved an HbA1c of <53 mmol/mol [<7%], while only 15% of those using insulin pump therapy alone achieved an HbA1c of <53 mmol/mol [<7%]. Data from the third year of follow-up may be published in 2019. Recently, Mulinacci et at (2019) performed a retrospective analysis of 396 patients with newly-diagnosed T1D and clearly demonstrated that initiating patients on CGM within a year of diagnosis, with or without insulin pump therapy, provided superior and sustained HbA1c benefit compared to insulin pump or MDI therapy alone. At baseline, mean	

		HbA1c did not vary significantly between groups and was ~ 102 mmol/mol [~11.5%]. For 2.5 years of follow-up, the MDI+CGM group had 16.4 mmol/mol [1.5%] lower HbA1c than the MDI-only group (61 vs 77 mmol/mol [7.7% vs. 9.2%,] [P < 0.0001]). The number of diabetes-related emergency department visits was also significantly lower among early CGM users compared with non-CGM users (P = 0.003). Because studies have shown that glycaemic control may settle into long-term patterns within the first 5 years after diagnosis, this study supports the notion that early initiation of CGM within 1 year of diagnosis may help to improve long-term control and reduce long-term complications. Based on the established evidence regarding HbA1c reduction (which was not available at the publication of the current NG17 guideline), *rtCGM should be reviewed in the proposed update.* Importantly, rtCGM should continue to be recommended for patients with T1D and a history of severe of hypoglycaemia or impaired hypoglycaemia awareness based on data recently published from the HypoDE trial. This 26-week trial of 149 participants with T1D and a history of severe of hypoglycaemia or impaired hypoglycaemia awareness who were randomized to rtCGM or SMBG demonstrated a 72% reduction in hypoglycaemia events during rtCGM use compared to usual care with SMBG. • Heinemann et al., Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe	

		hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial. Lancet. 2018;391(10128):1367-1377. • CGM digital platforms Rt- CGM should also be considered in scope for the sections of this guideline related to digital platforms. Rt-CGM systems such as the Dexcom G6® provide app-based technology where data can be uploaded and distributed to five people (followers) in real time with the share function. Connected individuals using the follow app can monitor glucose data in real time and be alerted to abnormal values in the person wearing the sensor and transmitter. A recent study analyzed the use of the CGM share and follow digital functionality and its impact on improved patient outcomes. The study concluded, "Real-time sharing and following of CGM data are associated with improved device utilization and glycemic parameters. The observed association suggests either more timely interventions or higher levels of engagement among the caregivers or the youth with diabetes."[1] Another study analyzed the digitally displayed predictive low glucose alert for rt-CGM. This alert was associated with significantly reduced hypoglycemia and over 93% of rt-CGM users enabled this digital functionality on their devices. [2] The NHS England long term plan communicates that the health care service will strive to offer a digital first option for most people. This document recognises that the potential benefits of the wider utilisation of technology will empower patients to better manage their condition. To	

		support the objectives set out in the long term plan NICE should include rt-CGM in the scope of NG17 "*When ill, people will be increasingly cared for in their own home, with the option for their physiology to be effortlessly monitored by wearable devices. People will be helped to stay well, to recognise important symptoms early, and to manage their own health, guided by digital tools."* (NHS England 2019, p92)[5] Rt-CGM branding and terminology The proposed scope includes the term "FLASH" glucose monitoring as a product class. This class includes only one individual product Freestyle Libre. Other diabetes guidelines have used the term "intermittently scanned" glucose monitoring (ISCGM or iscCGM) for this class.[3,4,] This is appropriate since Freestyle Libre requires users to "scan" in order to get information about current glucose, the direction and velocity of glucose change. This requires the user *to be able* to scan the reader over the sensor. Only when the patient decides to perform this activity are glucose values visible. As such the term "FLASH" should be changed to iscCGM or ISCGM. References 1) Welsh, J. B., Derdzinski, M., Parker, A. S., Puhr, S., Jimenez, A., & Walker, T. (2019). Real-Time Sharing and Following of	

		Continuous Glucose Monitoring Data in Youth. Diabetes Therapy.doi:10.1007/s13300-019-0571-0 2) Puhr, S., Derdzinski, M., Parker, A. S., Welsh, J. B., & Price, D. A. (2019). Real-World Hypoglycemia Avoidance With a Predictive Low Glucose Alert Does Not Depend on Frequent Screen Views. Journal of Diabetes Science and Technology, 193229681984069. doi:10.1177/1932296819840691 3) Freckmann, Guido & Schlter, S & Heinemann, Lutz. (2017). Statement of the AGDT on the replacement of blood glucose measurements by measurements with systems for real-time continuous glucose monitoring (rtCGM) or CGM with intermittent scanning (iscCGM). Diabetes, Stoffwechsel und Herz. 26. 43-46. 4) 7.Diabetes Technology: Standards of Medical Care in Diabetes-2019." Diabetes Care **42**(Suppl 1): S71-S80, doi.org/10.2337/dc19-S007 5) The Long Term Plan, NHS England, 2019 (accessed on 02.05.2019 https://www.longtermplan.nhs.uk/wp-content/uploads/2019/01/nhs-long-term-plan.pdf)	

Royal College of Nursing	Yes	Some direction and narrative about the use (or not) of SGLT2 inhibitors in patients with Type 1 Diabetes The inclusion of Flash glucose monitoring DVLA recommendations update on flash glucose monitoring	Thank you for your comments, please see the separate responses below: 1) SGLT-2 inhibitors: This is a proposed area for update and we will pass on your comment to the developers for consideration. 2) Flash glucose monitoring: This is a proposed area for update and we will pass on your comment to the developers for consideration. 3) DVLA recommendations: Thank you for highlighting that the DVLA have released new guidance on use of Flash whilst driving. As we are proposing to update the guideline around Flash glucose monitoring, we will pass on your information about the DVLA guidance to the developers for consideration in including as part of the guideline update.
University of Exeter	No	No comments provided	Thank you.
Association of British Clinical Diabetologists	Yes	*There are however some areas where ABCD believes there is evidence to warrant updating, expanding or which have been over looked, namely;* o *Ultrafast acting insulins* o *Management of renal complications in light of CREDENCE trial data* o *Low/ v low calorie diets*	Thank you for your comments, please see the separate responses below: 1) Ultrafast acting insulins: Thank you for your comments in support of this proposed area for update. 2) Management of renal complications: The CREDENCE trial was published after the search cut-off dates however it will not be included in Appendix A because it only includes people with type 2 diabetes and therefore is out of scope for NG17. The CREDENCE trial was also identified in the surveillance review of NG28. However, it will not be

		○ *Potential risks of SLG2 inhibitors: Fournier's gangrene, diabetic ketoacidosis & increased risk of lower limb amputation*	considered in the update the NICE guideline on type 2 diabetes in adults because it relates to a technology appraisal "TA390 Canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes" (May 2016). This information will be passed to the NICE technology appraisal team for consideration in reviewing this guidance. 3) Low/ very low calorie diets: We did not identify any new evidence on low calorie diets for people with type 1 diabetes. Therefore, we are not proposing to update this area. 4) Risks of SLT2 inhibitors: Thank you for your comments on the potential risks of SGLT-2 inhibitors, which is a proposed area for update. We are aware of the MHRA drug safety update which highlights the potential association between the use of SGLT-2 inhibitors and Fournier's gangrene in people with type 2 diabetes and have since added this to Appendix A. We will ensure that any adverse effects of treatment will be considered as part of the update process.
NHS England	Yes	**1 Periodontal and dental diseases should be included within the assessment of diabetes-related complications and other comorbidities that affect people with diabetes.** • (Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes d2019 Diabetes Care 2019;42(Suppl. 1):S34–S45).	Thank you for your comment. The aetiology of diabetes is not within scope for NICE guideline NG17, NG18 or NG28 however NICE guideline NG18 cross-refers to NICE guideline CG19 on dental recall. This highlights diabetes as a risk factor for developing dental disease and notes that 'People with diabetes (both type I and type II) are at increased risk of developing destructive periodontal disease … individuals with diabetes may need a more frequent recall.

		(Oral health: local authorities and partners Public health guideline Published: 22 October 2014 nice.org.uk/guidance/ph55) **2 Evidence suggests that type 1 diabetes increases the risk of periodontal diseases** (Does diabetes increase the risk of periodontitis? A systematic review and meta-regression analysis of longitudinal prospective studies. Nascimento GG, Leite FRM, Vestergaard P, Scheutz F, López R. Acta Diabetol. 2018 Jul;55(7):653-667). **3 Patients with diabetes should be referred to a dentist for comprehensive dental and periodontal examination.** • (Comprehensive Medical Evaluation and Assessment of Comorbidities: Standards of Medical Care in Diabetes d2019 Diabetes Care 2019;42(Suppl. 1):S34–S45). • (Scottish Dental Clinical Effectiveness Programme, 2014) • (Clinical Knowledge Summaries, Gingivitis and Periodontitis, https://cks.nice.org.uk/gingivitis-and-periodontitis#!scenario) • (Oral health: local authorities and partners Public health guideline Published: 22 October 2014 nice.org.uk/guidance/ph55) • (2018 Clinical Practice Guidelines Introduction Diabetes Canada Clinical Practice Guidelines Expert Committee, Can J Diabetes 42 (2018) S1–S5) 4. (Swedish National Guidelines for Diabetes Care from the National Board of Health and Welfare – Support for governance and management.	Inadequate plaque control and the presence of other risk factors will modify the recall interval further.' This issue will be put forward for consideration for scoping discussions for NICE guidelines NG17 and NG28 as expert input is required to determine an appropriate way of highlighting oral health in people with diabetes. The evidence you have highlighted will not be added to Appendix A because it does not meet the inclusion criteria for study type. This surveillance review considered only RCTs and Cochrane reviews.

		https://www.socialstyrelsen.se/publikationer2015/2015-4-12) (SJH) This is not a specific area of clinical expertise for the CAHPO team, however we would encourage engagement with the College of Podiatry, The British Dietetic Association, The British and Irish Orthoptics Society and The British Association of Prosthetists and Orthotists if this has not already been considered, for further comment. (SC)	
Royal College of Physicians		We would like to endorse the responses submitted by the Diabetes Technology Network (DTN) and the Association of British Clinical Diabetologists (ABCD).	Thank you. Please see our response to their comments.
Diabetes UK	Yes	**SGLT2s for treating Type 1 diabetes** We are pleased that NICE proposes to look at the growing evidence surrounding the use of sodium-glucose co-transporter 2 (SGLT2) inhibitors, in combination with insulin, in people with Type 1 diabetes. Trials so far have shown reductions in HbA1c, body weight and insulin need in people with Type 1 diabetes. A review of this evidence and any updates made to the guidelines in this area should also cover strategies to reduce the chance of potential adverse effects such as Diabetic Ketoacidosis.	Thank you for your comments, please see the separate responses below: 1. SGLT-2 inhibitors: Thank you for your comment on this proposed area for update. As noted in Appendix A, the indication of SGLT-2 inhibitors will be carefully considered when reviewing this evidence, as studies have shown effects on weight loss and insulin requirements as well as glycaemic control. We will also consider any adverse effects of treatment and will pass on these concerns to the developers for consideration during the scoping phase. The narrative review by Fattah et al (2018) was identified in the surveillance review but was excluded because it did not meet the study type inclusion criteria. The ABCD position statement you have highlighted is also an evidence type we

		Fattah, H and Vallon, V (2018)The Potential Role of SGLT2 Inhibitors in the Treatment of Type 1 Diabetes Mellitus. *Drugs* (78:7) pp. 717 - 726 **Association of British Clinical Diabetologists (ABCD) position statement on the use of SGLT2s in type 1 diabetes: https://bjd-abcd.com/index.php/bjd/article/view/335/518** **Optimising uptake of new treatments and technologies** New treatments and technologies for the management of Type 1 diabetes are regularly being developed and for those living with diabetes many of these developments have the potential to significantly improve their quality of life and health outcomes. We believe uptake of these new treatments and technologies should be optimised where appropriate. We suggest that NICE reviews its own approach to this and provides advice on how to effectively respond to new treatments and technologies in this guidance. **Use of diabetes technology** While we welcome the decision to review the evidence surrounding Flash Glucose Monitoring specifically, we strongly suggest that a much more comprehensive review of the guidelines surrounding insulin pumps, continuous glucose monitoring and flash glucose monitoring is required. We consider the existing guidance on these	did not consider in this surveillance review or the original guideline. 2. Optimising uptake of new treatments and technologies: NICE have a dedicated adoption team who are responsible for identifying ways to overcome potential barriers to the implementation of NICE guidance. They do this by working closely with health and social care organisations that are commissioning, implementing or using a product that has been recommended by a technology appraisal, or medical technologies or diagnostics guidance. See the website for our adoption and support resources. NICE is also a member of the Accelerated Access Collaborative. Their aim is to drive the uptake and adoption of innovation within the health and care system by identifying and supporting the best new innovations that will be most promising for patients. 3. Blood glucose monitoring technology: After considering new evidence published after the surveillance searches ended as well as the views of stakeholders, we have decided to add CGM and closed-loop systems (alongside Flash monitoring) to the review proposal. The scope will outline the proposed areas that the update will cover. Your comments will be passed on for consideration during this scoping phase. 4. Education and information: The new evidence identified in this surveillance review was found to be consistent with the guideline, however we are monitoring an ongoing trial on improving structured education and will assess the impact of the results when they are published. Therefore,

		technologies insufficient and recommend that NICE uses our technology pathway as a means to review the existing guidance and to bring it up-to-date. Diabetes UK consensus guideline on Type 1 diabetes technology and technology pathway: https://onlinelibrary.wiley.com/doi/pdf/10.1111/dme.13933 American Diabetes Association (ADA) (2019) *Diabetes Technology: Standards of Medical Care in Diabetes:* http://care.diabetesjournals.org/content/42/Supplement_1/S71 **Education and information (1.3)** While we welcome a commitment to reviewing the evidence surrounding education in online and smart-phone settings, we suggest that guidance surrounding structured education in a face-to-face setting should be reviewed too. For large numbers of people living with diabetes online-based structured education programmes are not accessible and research surrounding why this might be the case and how the situation can be improved should be reviewed and the guidance updated accordingly. We suggest a review of evidence which focuses on the uptake of structured education by people who have not recently been diagnosed with diabetes would be beneficial too. **Diabulimia (1.15.43)** While NG17 does mention bulimia nervosa, there is currently no specific mention of insulin omission for weight loss (diabulimia). Risk factors and signs that may indicate diabulimia should be reviewed, along with the potential	until further evidence is available, this area in the guideline is unlikely to be updated. 5. Diabulimia: We did not identify any new evidence in this area during this surveillance review. NICE guideline NG17 does contain a cross referral to NICE guideline NG69, which has a section specifically focusing on recommendations for people with diabetes. Recommendation 1.8.5 states "Address insulin misuse as part of any psychological treatment for eating disorders in people with diabetes." And recommendation 1.8.6 offers further advice for people with an eating disorder who are misusing insulin. 6. Psychological problems: We did not identify any new evidence in this area that met the inclusion criteria for this surveillance review. Recommendations 1.15.41-1.15.42 in the guideline currently state that members of the diabetes professional team providing care should be alert to the symptoms of psychological problems (particularly if the person is having problems with self-management) and have the skills for basic management and referral if problems persist. This section of the guideline also includes cross referrals to other NICE guidelines on common mental health disorders, generalised anxiety disorder and panic disorder (with or without agoraphobia) in adults and depression in adults with a chronic health problem. As this area is covered by existing guidance, we have not prioritised this section for update at present time. 7. Dietary management: We did not identify any new evidence on very low carbohydrate diets that met the inclusion criteria for this surveillance review. Thank you for

		short- and long-term complications resulting from the condition. This guideline should include clear recommendations on this condition. It is not sufficient to refer to NG69: Eating Disorders, as the relevant information is not included and the recommendations are not diabetes-specific. Diabetes UK (2018) Position Statement on Diabulimia https://www.diabetes.org.uk/resources-s3/2018-10/Diabulimia%20Position%20Statement%202018.pdf?_ga=2.152365177.1302772124.1540908607-1362513958.1522313951&_gac=1.161746510.1537347373.CjwKCAjw54fdBRBbEiwAW28S9sPmrJFbmQVXImzZKihBxKU_NWOOnhvD2WWULL6G1Ur-O45HVfYZqBoCv3IQAvD_BwE **Psychological problems** We would suggest that this part of the guidance needs reviewing and updating in light of insight work we conducted which found that the majority of people living with diabetes have not been able to access the *specialist* mental health support they felt they needed. Diabetes UK Report (2019), *'Diabetes and emotional health – a practical guide for healthcare professionals supporting adults with Type 1 and Type 2 diabetes'*: https://www.diabetes.org.uk/professionals/resources/shared-practice/psychological-care/emotional-health-professionals-guide This insight work further suggests that the other NICE guidance cross-referenced in this part of NG17 *is not specific enough to diabetes* and does not currently provide	highlighting a relevant study in this area. We checked this study but unfortunately, the paper you have highlighted by Turton et al (2018) does not meet the inclusion criteria for the surveillance review because it is not an RCT or Cochrane review, therefore it will not be added to Appendix A. This area was not highlighted by topic experts as being in need of update. Although we have received some feedback through this stakeholder consultation indicating this is an important area, we feel that the evidence base has not moved on sufficiently since 2015 to warrant an update at this time. We will consider this area again at the next surveillance review of the guideline.

		sufficient support or advice in cases where psychological problems are specifically related to diabetes. Diabetes UK Report (2019), '*Too often missing. Making emotional and psychological support routine in diabetes care*': www.diabetes.org.uk/emotional-wellbeing **Dietary management (1.4)** This part of the guideline has not been reviewed since 2015, despite there being new evidence surrounding dietary management and control of cardiovascular risk. We suggest that this part of the guideline needs to be updated, not least because we know that while many people living with Type 1 diabetes are adopting very low carbohydrate ketogenic diets in order to improve glycaemic control, for example, there is no clear guidance for them or healthcare professionals supporting them surrounding the appropriateness of such diets being used as a diabetes management strategy. Turton, J. L., Raab, R., & Rooney, K. B. (2018). Low-carbohydrate diets for type 1 diabetes mellitus: A systematic review. *PloS one*, *13*(3), e0194987. doi:10.1371/journal.pone.0194987	

Do you have any comments on equalities issues?			
Stakeholder	**Overall response**	**Comments**	**NICE response**

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees

Training, Research and Education for Nurses in Diabetes	No	No comments provided	Thank you.
Sheffield Teaching Hospital NHS Foundation Trust	No	No comments provided	Thank you.
Coeliac UK	No	No comments provided	Thank you.
South Sefton Clinical Commissioning Group	No	No comments provided	Thank you.
British Dental Association	No	No comments provided	Thank you.
UK Clinical Pharmacy Association (UKCPA) Diabetes and Endocrinology Group	No	No comments provided	Thank you.
Northumbria Healthcare NHS Foundation Trust – National DAFNE Executive Board	Yes	For those who struggle with health literacy, digital solutions may present challenges to learning self management skills; whereas face to face interventions, especially in groups, include the added value of peer support. Digital solutions must be well designed to minimise the impact of isolation and health literacy on the learning of self management skills. Recommendations to include digital options could lead to CCGs removing evidence-based structured group education in favour of "cheaper" digital options. Any new guidance needs to be very carefully worded so that this is not tacitly encouraged as an equivalent alternative option.	Thank you for your comments on the potential equality issues relating to digital tools and flash glucose monitoring. These issues will be covered during the scoping phase in the guideline update process. The scope will consider and assess any equality issues to establish: • whether there is any risk of unlawful discrimination arising from the guideline

		We have concern that the current NHS restriction of access to flash monitoring in adults based on the number of blood glucose tests a day represents indirect discrimination against people who have previously been told only to test 4 times a day. Published observational data suggests that glycaemic control may also be significantly improved in addition to quality of life, through access to flash. This links with our first comment in the scoping section.	• whether the guideline offers any opportunities for advancing equality • whether there might need to be reasonable adjustments to a recommendation to avoid putting any group of people covered by the scope at a substantial disadvantage • whether, and to what extent, particular equality issues should be included in the scope. These considerations are then reflected in the equality impact assessment, which is available during the consultation of the draft scope. For further details, please see the scope development chapter in the NICE guidelines manual.
Digital Diabetes Media Ltd	No	No comments provided	Thank you.
Diabetes Research Unit Cymru (Wales) (DRUC)	No	No comments provided	Thank you.
JDRF, the type 1 diabetes research charity	No	No comments provide	Thank you.
Abbott Diabetes Care	No	No comments provided	Thank you.
Royal College of Ophthalmologists	No	No comments provided	Thank you.
Novo Nordisk	No	No comments provided	Thank you.

British Society of Periodontology	No	No comments provided	Thank you.
AstraZeneca Ltd	No	No comments provided	Thank you.
UCL Eastman Dental Institute	No	No comments provided	Thank you.
Children and Young People's Wales Diabetes Network	No	No comments provided	Thank you.
MedTech Europe	No	No comments provided	Thank you.
Bayer plc		We agree that recommendations regarding the treatment of diabetic eye disease should be updated. As part of this update we agree that the recommendations from NICE technology appraisal 346, Aflibercept for treating diabetic macular oedema, should be incorporated into the guideline in accordance with the procedure outlined in the guidelines manual.	Thank you for your comment in support of our proposal to update the recommendations on management of eye disease. Management of overlaps and linkages between the diabetes clinical guidelines and technology appraisal guidance will be considered as part of the update to NG17.
Association for Clinical Biochemistry and Laboratory Medicine	No	No comments provided	Thank you.

London Diabetes Clinical Network	No	No comments provided	Thank you.
South Asian Health Foundation	No	No comments provided	Thank you.
Roche Diabetes Care, Ltd	No	No comments provided	Thank you.
Medtronic Ltd	No	No comments provided	Thank you.
Diabetes Technology Network	No	No comments provided	Thank you.
Dexcom Operating Ltd	Yes	The proposed scope has the potential to create an inequality for people with suboptimal HbA1c and those vulnerable patients in greatest need of a customised therapeutic intervention. To remove any inequality, rt-CGM should be added to the scope for people with suboptimal HbA1c so that these patients, too, are able to access the appropriate technology.	Thank you for your comment. In light of the new evidence and stakeholder comments, we have decided to review the evidence on CGM (including its use in people with sub-optimal glucose control) in the update of the guideline.
Royal College of Nursing	No	No comments provided	Thank you.
University of Exeter	No	No comments provided	Thank you.

Association of British Clinical Diabetologists	No	No comments provided	Thank you.
NHS England	No	No comments provided	Thank you.
Royal College of Physicians		We would like to endorse the responses submitted by the Diabetes Technology Network (DTN) and the Association of British Clinical Diabetologists (ABCD).	Thank you for your comment.
Diabetes UK	Yes	Language throughout the whole of NG17 should be amended to reflect the NHS England position statement 'Language Matters'. This should help to ensure that all people living with Type 2 diabetes are able to access the best possible care available regardless of their age, sex, gender, disability, religion, race, ethnicity or socio-economic status. NHS England (2018) https://www.england.nhs.uk/publication/language-matters-language-and-diabetes/	Thank you for your comment about the language used within NICE guideline NG18. All NICE guidelines and related products are developed with editors to ensure they are written and presented in a way that is clear and accessible to a range of different audiences. Further details can be found on the Language page of the NICE website.

Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees