NICE National Institute for Health and Care Excellence

Appendix B3: Stakeholder consultation comments table

2019 surveillance of NG18 Diabetes (type 1 and type 2) in children and young people: diagnosis and management (2015)

Stakeholders were consulted on the surveillance proposal to update NICE guideline NG18 for 2 weeks. Consultation dates: 25 April 2019 to 8 May 2019

Themes from stakeholder comments

Overall, 27 stakeholders commented. All stakeholders agreed with the decision to update the guideline, however several proposed that additional areas should be updated.

Diagnosis

A stakeholder raised concerns that the recommendations on diagnosis do not include the use of islet autoantibody testing to distinguish type 1 diabetes from monogenic diabetes. During the development of NICE guideline NG18 evidence on diagnosis, including the use of islet autoantibody testing was reviewed. Recommendations concerning antibody screening were not made because most of the included studies incorporated an antibody test as part of the gold standard and were not designed as

diagnostic test accuracy studies (instead they were prevalence studies). Antibody testing was also described as expensive and not considered cost effective. The guideline development group noted that current practice at the time was to use C-peptide and antibody tests as part of the work-up for diagnosis. However, the evidence included in the guideline review suggested that 'such tests are of no benefit in distinguishing between different types of diabetes and so use of the tests should be discontinued'. The stakeholder provided evidence, but none of the studies were diagnostic accuracy or cost-effectiveness studies, as such this is not currently being considered as an area for update.

The stakeholder also raised concerns that some of the content of recommendation 1.1.6 was incorrect. Specifically, they requested that the recommendation to consider types of diabetes other than types 1 or 2 (such as other insulin resistance syndromes, or monogenic or mitochondrial diabetes) in children and young people with suspected diabetes who have diabetes in the first year of life be changed to 'diabetes in the first 9 months of life'; however the current recommendation does not seem at odds with guidance highlighted by the stakeholder from the International society for pediatric and adolescent diabetes. The stakeholder also noted that the criterion of rarely or never developing ketone bodies in the blood (ketonaemia) during episodes of hyperglycaemia for considering other types of diabetes than type 1 or type 2 diabetes is incorrect. While rarely or never developing ketonaemia during episodes of hyperglycaemia is rare in people with monogenic or mitochondrial diabetes, this is also the case for children with type 2 diabetes (except in ketosis-prone subtype), we will therefore request that the guideline committee updating NICE guideline NG18 considers how this can be clarified.

Another stakeholder also requested that 'visual disturbance' is added to recommendation 1.1.1 as a characteristic of type 1 diabetes in children and young people. As the evidence referenced is not currently published, we were not able to determine the impact of the study's findings, which has been added as ongoing research to consider once published (see appendix A3).

Insulin therapy for children and young people with type 1 diabetes

Several stakeholders requested that sensor-augmented pump therapy and closed-loop therapy be included as areas for update, however none of the highlighted evidence met the surveillance review inclusion criteria. During the surveillance review only 1 relevant RCT was identified, as such, the evidence base remains limited and further evidence from larger RCTs would be required in order to consider whether this should be an area for update.

Blood glucose monitoring

Seven stakeholders responded that NICE guideline NG18 should be updated in relation to the use of flash glucose monitoring in children with type 1 diabetes. No RCT evidence was provided, but stakeholders reported that it is already being prescribed to some children and young people on the NHS and some guidance indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met). We have therefore decided that NICE should consider the use of this technology in children with type 1 diabetes.

Several stakeholders also responded that real time continuous glucose monitoring should be considered as an area for update, alongside the use of technology such as mobile Apps; however the evidence provided by stakeholders had either already been

considered within the surveillance review, or did not meet inclusion criteria. The evidence identified in the surveillance review in relation to continuous glucose monitoring, including the use of Apps and consideration of the psychological benefits of continuous glucose monitoring, supports the content of the current recommendations 1.2.58-1.2.64 and will therefore not be considered as an area for update. Two pieces of relevant ongoing research that were identified by stakeholders will be considered when the results of the studies are published.

One stakeholder also reported that there are issues with the interpretation of 'high levels of physical activity' in recommendation 1.2.63 by clinical commissioning groups determining whether ongoing real-time continuous glucose monitoring should be funded or not. This implementation issue will be address by requesting that the guideline committee updating NICE guideline NG18 considers how the recommendation could be amended to provide other examples of 'high levels of physical activity'.

Medications for children with type 2 diabetes

Two stakeholders requested that the update of NICE guideline NG18 looks at the use of insulin in children with type 2 diabetes and the use of glucagon-like peptide-1 receptor agonist liraglutide. Due to the lack of RCT-level evidence exploring the effectiveness of insulin in children with type 2 diabetes, this is not being considered as an area for update at this time. Liraglutide is not currently licenced for use in children, so evidence on this medication is not being considered. If liraglutide is approved for use in children with diabetes, we will look at published RCT evidence of effectiveness in this population at the next surveillance review.

Psychological and social issues in children and young people with type 1 or type 2 diabetes

Several stakeholders raised concerns that some psychological conditions were being prioritised over others, that physical health was prioritised over mental health and that person-centred care needed more emphasis. NICE guideline NG18 covers issues on a wide range of psychological conditions, cross-refers to relevant existing NICE guidelines and highlights the importance of emotional well-being and coping in the recommendations sections on 'Psychological and social issues in children and young people with type 1 diabetes' and 'Psychological and social issues in children and young people with type 2 diabetes'. We agree that person-centred care is very important and NICE guideline NG18 will be amended with standard text placed at the beginning of the recommendations section which highlights that 'People have the right to be involved in discussions and make informed decisions about their care, as described in your care.'

Several stakeholders also highlighted that patient-related characteristics and fluctuations in glycaemic control may cause cognitive impairment in children and young people with type 1 diabetes. This is already acknowledged in NICE guideline NG18. Recommendation 1.2.86 highlights that diabetes teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age.

Monitoring for complications and associated conditions of type 2 diabetes

One stakeholder requested that non-alcoholic fatty liver disease (NAFLD) is added as a complication to recommendations 1.3.43-1.3.45 on 'Monitoring for complications and associated conditions of type 2 diabetes'. As NICE has existing guidance (NICE

guideline NG49) on NAFLD which recommends that children and young people with type 2 diabetes are offered a liver ultrasound, we will request an editorial amendment to cross-refer to NICE guideline NG49.

Insulin therapy for type 1 diabetes

Several stakeholders commented that NICE diagnostics guidance 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) (DG21) is out of date. This guidance is due to be reviewed in 2019 and is not part of the current diabetes NICE guidelines surveillance review. All information provided by stakeholders will be shared with the NICE Diagnostics Assessment Programme.

Real-world data

Several stakeholders requested that observational and real-world data should be used in guideline development and considered as evidence within surveillance reviews. For the purposes of this surveillance review, due to the volume of published evidence on diabetes, only Cochrane review and RCT level evidence was included. NICE is however considering how real-world data could be used, and there will be a public consultation on this, alongside other data analytic considerations, in the Summer of 2019.

Other responses

Comments were also received from single stakeholders in relation to the frequency of eye screening, the definition of hypoglycaemia, the frequency of capillary blood glucose tests per day, treatment of hypoglycemia using fast-acting and long-acting carbohydrates, treating complications of type 1 diabetes, providing more in-depth recommendations on metabolic surgery and on

other NICE guidelines. These comments have not resulted in any changes to the surveillance decision due to lack of supporting evidence that meets the inclusion criteria for this surveillance review or applicability to NICE guideline NG18.

Stakeholder consultation comments table

Do you agree with the proposal to update the guideline?			
Stakeholder	**Overall response**	**Comments**	**NICE response**
Sheffield Teaching Hospital NHS Foundation Trust	Yes	No comments provided	Thank you for your response.
Association of Children's Diabetes Clinicians	Yes	• We agree that investigating the effectiveness of incorporating behaviour change techniques and psychological interventions for children with diabetes is an area for review to improve screening for diabetes retinopathy • We agree that Fluid and insulin therapy for management of moderate to severe DKA should be reviewed	Thank you for your comments and for agreeing with the update proposal.
Optical Confederation	Yes	We welcome the opportunity to review these guidelines to be more specific on advice, access and referrals in relation to eye health care. We also now have considerable	Thank you for your comments on the proposed update decisions for NICE guidelines NG17 and NG28. Please see Appendix B1 and B2

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		experience of working with these guidelines, expanding roles in primary eye care to meet need and working with diabetic eye screening services. We therefore welcome the opportunity to review the guidelines to reflect changing practice especially on pathways, access and referrals in relation to diabetic eye disease and eye health services Page 3 Managing complications, Eye Disease: We are pleased to see a review around appropriate treatments for diabetic eye disease. There is potential to use newer treatments for diabetic eye disease to improve patient outcomes. Page 7 Managing complications, Eye disease: We are pleased to see a review around appropriate treatments for diabetic eye disease. There is potential to use newer treatments for diabetic eye disease to improve patient outcomes.	for responses concerning treatment for diabetic eye disease, which is an area recommended for update in both guidelines.
Institute of Child Health	Yes	We agree that diabetic eye screening amongst children and young people is sub-optimal and NICE should make recommendations on how to increase attendance. However, it is important to note that the existing evidence relating to improving attendance at screening and for behaviour change techniques is almost entirely for adults, as evidenced by the recent NIHR funded WIDeR-EyeS systematic reviews. There is a need for considerable primary research addressing the barriers and enablers of screening uptake by those under 18 years. Additionally, as evidence is emerging that screening uptake is not homogenous within this paediatric population,1 some	Thank you for your comments and for agreeing with the update proposal on measures to encourage screening for diabetic retinopathy. Thank you for highlighting research that is about to publish, we will share the reference with developers of the guideline update.

		groups may need specific interventions to improve their uptake of eye screening.	
Coeliac UK	Yes	No comments provide	Thank you for your response.
British Dental Association	Yes	No comments provided	Thank you for your response.
Digital Diabetes Media Ltd	Yes	No comments provided	Thank you for your response.
JDRF, the type 1 diabetes research charity	Yes	No comments provided	Thank you for your response.
Abbott Diabetes Care	Yes	No comments provided	Thank you for your response.
Royal Devon and Exeter NHS Foundation Trust	Yes	Sections relating to diagnosis 1.1.4-1.1.9 need review **The information currently provided about islet autoantibodies is incorrect and should be changed.** There is new evidence which shows comprehensive antibody (GAD, IA2 and ZnT8) testing has a key role in identifying children and young people who do not have Type 1 diabetes (Pihoker 2013, Fendler 2012, Shepherd 2016, Irgens 2013,McDonald 2011).	Thank you for your comments and references regarding the recommendations on diagnosis of monogenic diabetes. Please note that during the surveillance review process substantial changes to the content of a recommendation are not made. The purpose of surveillance is to identify relevant evidence and determine whether it has an impact on existing recommendations. If evidence is found that indicates recommendations should be updated, this is then reviewed by a committee following the process for guideline development. Please see Developing NICE guidelines: the manual for further details. In relation to the use of islet autoantibody testing, during the development of NICE guideline NG18 the guideline development group (GDG) reviewed the evidence related to diagnosis, and

		1 in 4 children negative to all these 3 antibodies have monogenic diabetes (Shepherd 2016) Use of comprehensive antibodies are recommended by ISPAD to identify non Type 1 diabetes(Rubio-Cabezas 2014) **Section 1.1.4** In light of the above evidence this section should read ' Assume type 1 diabetes unless negative to GAD, IA2 and ZnT8 antibodies' **Section 1.1.6** This section is incorrect (diagnosis in the 1st year of life is incorrect, ketones are also not an appropriate criteria, the other associated features point to rarer forms of monogenic diabetes). This section should be changed to read: Think about the possibility of monogenic diabetes in all patients who are negative to GAD, IA2 and ZnT8. Those diagnosed within the first 9 months should have genetic testing for neonatal diabetes. Those with a parent with diabetes and persistent c-peptide outside the honeymoon period should be referred for genetic testing. **Section 1.1.7** Should be changed to read: Measuring GAD, IA2 and ZnT8 antibodies is recommended as this represents the easiest way of identifying non Type 1 diabetes. Testing all three antibodies is important. Use of ICA is not recommended. We would not advise measuring c-peptide at diagnosis **Section 1.1.8** is OK **Section 1.1.9** should be changed to read: 'Genetic testing should be performed in individuals negative to GAD, IA2	specifically evidence for distinguishing between type 1 and type 2 diabetes, as the diagnosis and management of children and young people with other forms of diabetes mellitus such as monogenic diabetes and cystic fibrosis-related diabetes was out of scope. The specific review question was 'What is the effectiveness of C-peptide and antibody tests to distinguish type 1 and type 2 diabetes?' and evidence searches were performed which included publications up to 26th August 2014 of studies that showed the presence of diagnostic markers (C-peptide and/or antibodies including GAD, IA2 and ZnT8) in young people with different types of diabetes (type 1 diabetes, type 2 diabetes, latent autoimmune diabetes of adulthood (LADA) and maturity onset diabetes of the young (MODY), with the aim of seeing which markers could be used to distinguish between the diabetes types and thus aid diagnosis. Twenty two observational studies were included (for further details please see section 4.3 of the full guideline). As such the references you have provided from Pihoker C, et al. 2013, Fendler W, et al. 2012, Irgens et al. 2013 and McDonald TJ et al. 2011 would have been considered, if relevant, during guideline development. The references by Pihoker and the 2014 International society for pediatric and adolescent diabetes (ISPAD) guideline (Rubio-Cabezas O et al. 2014) were also specifically highlighted by stakeholders during the draft NICE guideline NG18 stakeholder consultation and the guideline committee considered views and evidence concerning the diagnosis of monogenic diabetes at that time. Studies identified in the evidence review reported on the prevalence of antibodies in young people with type 1 diabetes but no studies assessing the antibodies GAD, IA2 or ZnT8 were found that reported data in young people with type 2 diabetes, LADA or MODY. Thank you for highlighting the Shepherd M et al, 2016 observational study which reported that

		and ZnT8 who score more than 30% on the MODY probability calculator (www.diabetesgenes.org/mody-probability-calculator/) We therefore recommend the guidelines are changed to advise: • Comprehensive (GAD, IA2 and ZnT8) antibody screening in all children and young people at diagnosis of diabetes in order to identify those with non Type 1 diabetes **References** • Pihoker C, Gilliam LK, Ellard S et al. and for the SEARCH for Diabetes in Youth Study Group. Prevalence, characteristics and clinical diagnosis of maturity onset diabetes of the young due to mutations in HNF1A, HNF4A and glucokinase: results from the SEARCH for diabetes in youth. J Clin Endocrinol Metab. 2013; 98 (10); 4055-4062 • Fendler W, Borowiec M, Baranowska-Jazwiecka A et al. Prevalence of monogenic diabetes amongst Polish children after a nationwide genetic screening campaign. Diabetologia. 2012. 55: 2631-2635 • Irgens HU, Molnes J, Johansson BB et al. Prevalence of monogenic diabetes in the population based Norwegian childhood diabetes registry. Diabetologia. 2013; 56: 1512-1519 • Shepherd M et al, Systematic population screening using biomarkers and genetic testing identifies 2.5% of the UK paediatric diabetes	2.5% of 808 patients with diabetes aged under 20 years of age attending 6 UK paediatric had monogenic diabetes (95% CI of 1.6-3.9%); and highlighted that measuring C-peptide, followed by islet autoantibody (GAD and IA2) testing in those who are C-peptide-positive, then followed by genetic testing in patients who were autoantibody negative, identified patients with monogenic diabetes. The current recommendation 1.1.8 does highlight measuring C-peptide after initial presentation if there is difficulty distinguishing type 1 diabetes from other types of diabetes. Recommendations concerning antibody screening were not made because most of the included studies incorporated an antibody test as part of the gold standard and most of the studies were not designed as diagnostic test accuracy studies (instead they were prevalence studies). In the absence of diagnostic test accuracy studies that provide measures such as sensitivity and specificity, this is not an area that can be considered for update. The guideline committee also noted that antibody testing is expensive and would not be considered cost effective. They recognised that genetic testing is the gold standard for identifying monogenic forms of diabetes and is the only method that can confirm a suspicion of monogenic diabetes (hence the content of recommendation 1.1.9). The group noted that current practice at the time was to use C-peptide and antibody tests as part of the work-up for diagnosis. However, the evidence included in the guideline review suggested that 'such tests are of no benefit in distinguishing between different types of diabetes and so use of the tests should be discontinued'. In the absence of further evidence on the diagnostic accuracy and cost effectiveness of antibody testing this will not be considered as an area for update. In response to your concerns that some of the information in recommendation 1.1.6 on criteria that may indicate diabetes other

		population with monogenic diabetes. Diabetes Care. 2016. 39, 1-10 • Rubio-Cabezas O, Hattersley AT, Njølstad PR et al. The diagnosis and management of monogenic diabetes in children and adolescents. Pediatric Diabetes. 2014. 15 (Suppl. 20): 47-64 • McDonald TJ, Colclough K, Brown R et al. Islet autoantibodies can discriminate maturity-onset diabetes of the young (MODY) from Type 1 diabetes. Diabet Med. 2011 Sep;28(9):1028-33	than types 1 or 2 in children and young people with suspected diabetes, the latest 2018 guidance from ISPAD on The diagnosis and management of monogenic diabetes in children and adolescents states that 'All patients diagnosed with diabetes in the first 6 months of life should have immediate molecular genetic testing to define their subtype of monogenic neonatal diabetes mellitus (NDM), as type 1 diabetes is extremely rare in this subgroup (B). In patients diagnosed between 6 and 12 months of age, testing for NDM should be limited to those without islet antibodies as the majority of patients in this age group have type 1 diabetes (B).' The recommendation to consider other types of diabetes in children presenting with diabetes in the first year of life of 1 year is therefore not incorrect, but ensures that consideration is rightly given to other types of diabetes for children diagnosed with diabetes in the first year of life. The rationale for changing this to 9 months of age is not clear. In relation to the criteria of rarely or never developing ketone bodies in the blood (ketonaemia) during episodes of hyperglycaemia, ketonaemia is rare in people with MODY, but we can see that, based on the wording at the beginning of the recommendation, it could be interpreted that children with type 2 diabetes would be expected to develop ketonaemia during episodes of hyperglycaemia, which is rare except in ketosis-prone subtype. We will request that the guideline committee updating NICE guideline NG18 considers how this can be clarified. The 2018 ISPAD guidance will be added to the intelligence section of the evidence summary for this surveillance review and we will consider the issue of autoantibody testing at the next surveillance review.

Novo Nordisk	Yes	We would like to bring to your attention the published study demonstrating the safety and efficacy of liraglutide in children and adolescents[1]. This was submitted to the EMA and approval is expected in the coming months. Reference 1. W. Tamporlane et al (2019) Liraglutide in children and adolescents with type 2 diabetes. New England Journal of Medicine 28th April 2019. DOI: 10.1056/NEJMoa1903822 Whilst we are aware that NICE is not currently planning to update the insulin section of this guidelines, we would like to make you aware of the recently presented trial of Fast-acting insulin aspart. This randomised control trial in children and adolescents with type 1 diabetes (age >1 to <18), n= 927, demonstrated efficacy and safety of Fast-acting insulin aspart in comparison with Insulin aspart. The results were presented at the ISPAD 2018 conference and are expected to be published in 2019. These results are expected to update the label for Fiasp and we therefore request NICE to include this data in the review process. Reference Bode B et al (2018) 44th International Society for Pediatric and Adolescent Diabetes, Poster 110LB	Thank you for this information, however evidence on medications that are not currently licenced for use in children with diabetes are not included in the surveillance review. If liraglutide is approved for use in children with diabetes, we will look at published RCT evidence of effectiveness in this population at the next surveillance review. Thank you for highlighting the RCT work undertaken assessing the safety and efficacy of Fast-acting insulin aspart compared to Insulin aspart in children with type 1 diabetes. As the publication has now published, we have included this data in the surveillance review alongside the other RCT evidence in relation to insulin therapy for children and young people with type 1 diabetes. As the evidence overall still indicates that no particular type of fast- or long-acting insulin has greater clinical effectiveness than any other, this remains an area that will not be updated at this time.
The Royal College of Ophthalmologists	Yes	The Royal College of Ophthalmologists supports the comments made in the consultation response from Dr Maria Ibanez Bruron and Professor Jugnoo Rahi academic group based at UCL GOS Institute of Child Health	Thank you for your comment. Please see responses to the Institute of Child Health for further information.

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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 out of scope for NICE guideline NG18. The issue of the importance of oral health is covered by recommendation 1.2.4 for children with type 1 diabetes and recommendation 1.3.3 for type 2 diabetes which highlights the importance of having regular dental examinations and cross-references the NICE guideline on dental recall.
Children and Young People's Wales Diabetes Network	Yes	No comments provided	Thank you for your response.
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. For the purpose of this surveillance review only Cochrane reviews and RCTs have been included. Please note that NICE is considering how real world data may be used to inform guideline development and a public consultation on this will be taking place in the Summer.
Royal College of Psychiatrists	Yes	1.2.99 highlighting the two disorders depression and conduct disorder (probably because there are specific NICE guidelines on these) is misleading and as suggestive that conduct disorders are seen in excess in diabetes (which is not the case, there is a risk that this is used to describe adherence challenges) 1.2.100 *Diabetes teams* need to work closely with / have access also to **psychiatric** professionals to address the challenges of managing diabetes in the presence of	Thank you for your comments. Please note that the purpose of surveillance is to identify relevant evidence and determine whether it has an impact on existing recommendations. Please see Developing NICE guidelines: the manual chapter 13 Ensuring that published guidelines are current and accurate for further details. If evidence is found that indicates recommendations should be updated, this is then reviewed by a committee following the process for guideline development. In relation to concerns that the guideline is misleading by highlighting depression and conduct disorder, the section on

		comorbid mental disorder including suicidality and psychosis. 1.2.106 Refer children and young people with type 1 diabetes and suspected **excessive and impairing anxiety and/or** depression promptly to child mental health professionals. 1.2.108 guidance needs to be clear about diabetes specific eating disordered behaviours, specifically, omitting insulin in order to manage weight. Sub diagnostic threshold eating disorder behaviours in diabetes can have significant impact on physical health and therefore even greater need for early intervention. 1.2.109 Evidence that people with ED and diabetes are more likely to disengage from ED services and have poorer outcomes therefore essential that services work together. 1.3.34 The ISPAD guidelines suggest that young people with Type2 have increased risk of mental health difficulties and eating disorder behaviour prior to diagnosis and therefore we should be screening for these difficulties at diagnosis. This is different from Type 1. 1.3.15 very vague, What would this support look like? No mention of specific behaviour change techniques?	'Psychological and social issues in children and young people with type 1 diabetes' (recommendations 1.2.94-1.2.109) covers a broad range of both psychological and social issues, acknowledging more than conduct disorders. NICE guideline NG18 also notes that children and young people with type 1 diabetes 'may experience psychological problems (such as anxiety, depression, behavioural and conduct disorders and family conflict) or psychosocial difficulties that can impact on the management of diabetes and wellbeing'. The purpose of recommendation 1.2.99 is to highlight existing NICE guidance that may be of use if treatment of depression, antisocial behaviour or conduct disorders is needed. All mentions of teams that provide psychological support would include psychiatrists, we do not list all relevant professionals in recommendations. In the absence of references to published evidence or a clear rationale for changes to recommendations, the proposed changes cannot be considered as areas for update. Information on support highlighted in recommendation 1.3.15 can be found by looking at recommendation 1.3.14 which cross-references NICE guidelines on maintaining a healthy weight and managing obesity.
Association for Clinical Biochemistry and Laboratory Medicine	Yes	No comments provided	Thank you for your response.

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Imperial College Health Care NHS Trust – St Mary's Hospital	Yes	No comments provided	Thank you for your response.
Perspectum Diagnostics	Yes	No comments provided	Thank you for your response.
Medtronic Ltd	Yes	No comments provided	Thank you for your response.
Dexcom Operating Ltd	Yes	No comments provided	Thank you for your response.
Royal College of Nursing		This is just to let you know that the feedback I have received from nurses caring from people with diabetes suggests that there is no additional comments to submit to inform on the consultation of the above draft guidelines.	Thank you for your response.
Royal College of Paediatrics and Child Health	To some extent Yes it is agreed that there needs to be a consultation to review DKA and retinopathy as suggested	Evidence is required for fluid resuscitation changes in DKA Some early evidence was identified to support the use of Flash glucose monitoring in children is emerging. Currently the guideline does not contain any recommendations on Flash glucose monitoring Current NICE diagnostics guidance DG21 relating to sensor augmented pump therapy (SAPT) and when it should be considered is now very out of date. DG21 suggested that "MiniMed Paradigm Veo system is recommended as an option for managing blood glucose levels in people with	Thank you for your comment agreeing with the update proposal to review evidence on measures to encourage screening for diabetic retinopathy and fluid and insulin therapy for diabetic ketoacidosis. Thank you for your comment on the use of flash glucose monitoring in children and young people with type 1 diabetes. We will include this as an area for update within NICE guideline NG18. Please note that while there are currently no recommendations specifically on the use of a Flash glucose monitor in NICE guideline NG18, it does recommend offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60), which could therefore include

		type 1 diabetes only if they have disabling hypoglycaemia" "The Vibe and G4 PLATINUM CGM system shows promise but there is currently insufficient evidence to support its routine adoption in the NHS for managing blood glucose levels in people with type 1 diabetes" It is now important to note that more advanced sensor augmented systems are available and any reference to specific companies should be removed Suggest review management of hypoglycaemia and should incorporate use of CGM metrics and technology in light of technology being used It's important that the need to include Flash blood glucose monitoring in the Children's review (and not just adult Type 1, as proposed) is emphasised, as well as the review of sensor-augmented pump therapy.	flash glucose monitoring; in addition, the NICE medtech innovation briefing on Freestyle Libre for glucose monitoring (MIB110) which describes this technology is available in the NICE Diabetes in Children and Young people interactive flowchart. Evidence was identified in the surveillance review which is relevant to flash blood glucose monitoring in adults with type 1 diabetes, but not for children with type 1 diabetes. While there remains a lack of evidence on the effectiveness of a Flash glucose monitor in children and young people with type 1 diabetes under the age of 18 years old, given that stakeholders have stated that it is being prescribed to some children and young people on the NHS and some guidance indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met), we have concluded that NICE should consider making a recommendation on the use of this technology in children with type 1 diabetes. Thank you for your comment on NICE diagnostics guidance DG21. This guidance is due to be reviewed this year by the NICE Diagnostics Assessment Programme; and we will share your comments with this team. NICE guideline NG18 does not make any recommendations on this device, but it is in the Diabetes in Children and Young people NICE pathway. If further evidence is identified in future then the impact of this guideline on NG18 will be considered. Please note that NICE diagnostics guidance DG21 is not part of the current diabetes NICE guidelines surveillance review. The use of sensor-augmented pump therapy will not be proposed as an area for update in NICE guideline NG18 due to a lack of evidence. During the surveillance review we identified only 1 relevant RCT, which indicated that hybrid closed-loop therapy may be superior to sensor-augmented pump therapy in controlling glucose and reducing the risk of hypoglycaemia in people with T1D

			of all ages, including children with sub-optimally controlled T1D. As the evidence base for this new technology is still emerging, this will not currently be considered as an area for update. New evidence that was identified in the surveillance review on blood glucose targets and monitoring is consistent with existing recommendations and therefore has no impact on NICE guideline NG18.
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 comments and for agreeing with the update proposal.
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 responses to comments made by the Diabetes Technology Network and the Association of British Clinical Diabetologists for further information.
Children and Young People's NE and N Cumbria Diabetes Network	Yes	We agree that the fluid and insulin therapy for DKA should be reviewed in line with recent international evidence. Agree that evidence should be looked at to increase the uptake of retinal screening. Include the definition of a high HbA1c as >69mmol/l.	Thank you for your comments and for agreeing with the update proposal. In relation to the definition of high HBA1c levels we assume that you mean high HbA1c is >69 mmol/mol rather than >69mmol/l. NICE guideline NG18 recommendation 1.2.103 already states high HbA1c levels are HbA1c above 69 mmol/mol [8.5%]. In the absence of references to evidence on regular downloading, inpatient admission, use of technology, additional MDT contacts/clinic reviews, these areas cannot be considered for

		Additional evidence of the benefit of different intervention techniques in managing high HbA1c's such as regular downloading, inpatient admission, use of technology, additional MDT contacts/clinic reviews.	update. The surveillance review included Cochrane reviews and RCTs, none were identified on regular downloading, inpatient admission, additional MDT contacts/clinic reviews. A small amount of evidence on the use of digital technologies which identified that a blood glucose meter that integrates blood glucose testing with a smartphone App does not lead to additional improvements in blood glucose monitoring in comparison to using a traditional glucose meter in young people with type 1 diabetes. As such, there is currently insufficient evidence to propose this as an area for update.
Diabetes UK	Yes	Diabetes UK agrees with the proposal to update NG18, and supports the specific areas that have been identified (diabetic retinopathy in children and young people with Type 1 or Type 2 diabetes, fluid and insulin therapy for diabetic ketoacidosis). However, we would strongly suggest that additional topics also need reviewing and updating.	Thank you for your comments and for agreeing with the update proposal. Responses to your comments on other areas for update are provided in the relevant sections below.

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

Stakeholder	Overall response	Comments	NICE response
Sheffield Teaching Hospital NHS Foundation Trust	Yes	The role of glucose measurement via CGM and flash glucose monitoring ought to be included	Thank you for your comment on the use of flash glucose monitoring in children and young people with type 1 diabetes. We will include this as an area for update within NICE guideline NG18. Please note that while there are currently no recommendations specifically on the use of a Flash glucose monitor in NICE guideline NG18, it does recommend offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60), which could therefore include

			flash glucose monitoring; in addition, the NICE medtech innovation briefing on Freestyle Libre for glucose monitoring (MIB110) which describes this technology is available in the NICE Diabetes in Children and Young people interactive flowchart. While there remains a lack of evidence on the effectiveness of a Flash glucose monitor in children and young people with type 1 diabetes under the age of 18 years old, given that stakeholders have stated that it is being prescribed to some children and young people on the NHS and some guidance indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met), we have concluded that NICE should consider making a recommendation on the use of this technology in children with type 1 diabetes. The sections on 'Insulin therapy for children and young people with type 1 diabetes' and 'Blood glucose targets and monitoring' in the surveillance review Appendix A3 describes the evidence that we identified in relation to continuous glucose monitoring. As this supports the content of the current recommendations, and in the absence of further new evidence, continuous glucose monitoring will not be considered as an area for update.
Association of Children's Diabetes Clinicians	Yes	• We believe that evidence was identified to support the use of **Flash glucose monitoring** and CGM in children is emerging. Topic experts also highlighted this as an area in need of review. Currently the guideline does not contain any recommendations on **Flash glucose monitoring** however some of the evidence identified has already been considered in the NICE medtech innovation.	Thank you for your comment on the use of flash glucose monitoring in children and young people with type 1 diabetes. We will include this as an area for update within NICE guideline NG18. Please note that while there are currently no recommendations specifically on the use of a Flash glucose monitor in NICE guideline NG18, it does recommend offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60), which could therefore include flash glucose monitoring; in addition, the NICE medtech innovation

		• Importantly, the current NICE diagnostics guidance DG21 relating to sensor augmented pump therapy (SAPT) and when it should be considered is **now very out of date.** DG21 suggested that "MiniMed Paradigm Veo system is recommended as an option for managing blood glucose levels in people with type 1 diabetes only if they have disabling hypoglycaemia" "The Vibe and G4 PLATINUM CGM system shows promise but there is currently insufficient evidence to support its routine adoption in the NHS for managing blood glucose levels in people with type 1 diabetes" "MiniMedTM 640G system has not been assessed in the guidance, and the recommendations, therefore, do not relate to its routine use in the NHS. • **It is now important to note that more advanced sensor augmented systems are available and any reference to specific companies should be removed** • Definition of hypoglycaemie and review management should incorporate use of CGM metrics and technology in light of technology being used with Libre and CGM widely as at present no definitions of hypoglycaemia are specified in the guideline recommendations 1.2.76 to 1.2.86 but reference is made to mild, moderate and severe hypoglycaemia. • the new evidence on smartphone applications and the importance of digital platforms emphasised in the NHS Long-Term Plan, it is proposed that this area is reviewed in the population of children and	briefing on Freestyle Libre for glucose monitoring (MIB110) which describes this technology is available in the NICE Diabetes in Children and Young people interactive flowchart. While there remains a lack of evidence on the effectiveness of a Flash glucose monitor in children and young people with type 1 diabetes under the age of 18 years old, given that stakeholders have stated that it is being prescribed to some children and young people on the NHS and some guidance indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met), we have concluded that NICE should consider making a recommendation on the use of this technology in children with type 1 diabetes. Thank you for your comment on NICE diagnostics guidance DG21. This guidance is due to be reviewed this year by the NICE Diagnostics Assessment Programme; and we will share your comments with this team. NICE guideline NG18 does not make any recommendations on this device, but it is in the Diabetes in Children and Young people NICE pathway. If further evidence is identified in the future, then the impact of this guideline on NG18 will be considered. Please note that NICE diagnostics guidance DG21 is not part of the current diabetes NICE guidelines review. In relation to the definition of hypoglycaemia, the full guideline reports that 'there is no consistent or agreed definition of hypoglycaemia. In theory, hypoglycaemia is the level of blood glucose at which physiological neurological dysfunction begins. In practice, neurological dysfunction can be symptomatic or asymptomatic, and the level at which it occurs varies between individuals, may vary with time and circumstance, and is affected by antecedent hypoglycaemia or hyperglycaemia. Symptoms usually occur in most people when the blood glucose level is less than 3.0

		young people as they are high users of apps and social media	mmol/l, although for some it may be as low as 2.0 mmol/l or as high as 3.5 mmol/l.' The use of digital technologies was included in the surveillance review, however very little evidence was identified on the effectiveness of smartphone applications or digital platforms with children and young people with diabetes; and the evidence that was identified from 1 RCT indicates that a blood glucose meter that integrates blood glucose testing with a smartphone App does not lead to additional improvements in blood glucose monitoring in comparison to using a traditional glucose meter in young people with T1D. As such, there is currently insufficient evidence to propose this as an area for update. Evidence on digital technologies will be included in the next surveillance review.
Optical Confederation	Yes	We are pleased to see the avoidance of duplication in guidance between this and that provided by the NHS Diabetic Eye Screening Programme. However, it is important to ensure that if items are now under that remit that the consultation process is equally as robust.	Thank you for your comment. Please note that the NHS diabetic eye screening (DES) programme is not part of NICE and as such we cannot comment on their consultation processes.
Institute of Child Health	Yes	We suggest NICE reviews its previous recommendation of eye examination by an optician every 2 years for children and young people living with type 1 or 2 diabetes. Regular optician exams has been considered by the National Screening Committee and is not recommended for children from general population. NSC recommends only that children aged 4 to 5 years undergo vision screening in an orthoptic-led (not optician-delivered) service. So we are unclear about the evidence-base for NICE's recommendation for biennial optician exams for children	Thank you for your comment concerning recommendations 1.2.4 and 1.3.3 which advise having an eye examination by an optician every 2 years. This is in line with the NHS Diabetic Eye Screening Programme which states that people with diabetes should also see their optician every two years for a regular eye test. We have not been able to find the National screening committee information that you have mentioned. NHS information on eye tests does specify ages at which children should have an eye test, including at around 1 years old, or between 2 and 2-and-a-half years old and then at around 4 or 5 years old. The issue of when eye tests should be

		and young people living with diabetes. Furthermore, there is potential that this might undermine the national diabetic eye screening programme as children/young people and their parents might think that a regular eye exam by an optician comprises eye screening – which it does not unless it is the formal exam (retinal examination after dilation of pupils) as part of a local eye screening programme – in which case it would be administered annually from the age of 12 years. We suggest that NICE reviews the evidence base for this recommendation and any risks associated with it. If NICE decides to maintain this recommendation, we suggest it specifies the purpose of this clinical surveillance and the age at which it should start and what the 'eye exam' by an optician should comprise. We suggest adding visual disturbance, e.g. rapid visual loss, as an additional **characteristic of type 1 diabetes in children and young people**. Acute-onset cataract occurs around diabetes diagnosis and visual loss might be the first symptom of the diabetes.2- We suggest specifying that the recommendation to **offer surgery to children and young people with type 1 diabetes only in centres that have dedicated paediatric facilities for caring for children and young people with diabetes** is also relevant for children and young people requiring surgery for diabetes related eye disease (e.g. cataract surgery) Regarding the recommendation of **monitoring diabetic retinopathy in children and young people with diabetes**,	performed was raised during the stakeholder consultation on the draft NICE guideline NG18 and it was decided that this recommendation should remain. The rationale for this recommendation given in the full guideline is that 'the guideline development group agreed that the consensus recommendation in the 2004 guideline advising children and young people with type 1 diabetes to have an eye examination by an optician every 2 years was still considered good practice and they found that there was no evidence to direct a change from the previous recommendation.' There is no evidence to indicate that recommendation 1.2.4 undermines the information in the separate recommendations on annual retinopathy screening from the age of 12 years old. As the proposed update of NICE guideline NG18 will be considering ways to improve attendance at retinopathy screening, if there is evidence to indicate that there is a conflict in how these recommendations are being interpreted, this would be considered during the development of the update. Thank you for your suggestion concerning adding visual disturbance as a characteristic of type 1 diabetes in children and young people. We assume that this is in relation to recommendation 1.1.1 on diagnosis. As the reference you have provided is not currently published, we are not able to determine the impact of results on the current recommendation. We will consider the paper when it is published as juvenile cataracts have been highlighted in the recommendations (1.2.113), but as a rare complication/associated condition in type 1 diabetes. Recommendations 1.2.91-1.2.93 on Surgery for children and young people with type 1 diabetes would include surgery for eye disease. As such, we do not think any update is required.

		we suggest that emerging evidence supports that the guideline should specify that screening results should be discussed with children and young people during their general diabetes care consultations at paediatric diabetes units, as to reinforce the positive effect of maintaining or improving blood glucose control. This would require better information flows and coordination between diabetic eye screening programmes and paediatric diabetes units than currently exist.5,6 The findings from our national surveillance study of sight-threatening diabetic eye disease in children and young people conducted between 2015-2017 (in press) support the statement that **diabetic retinopathy that needs treatment is extremely rare in children and young people under 12 year** as no cases of diabetic retinopathy that requiring referral to Hospital Eye Services were reported in children younger than 12 years old.2	We agree that all screening and other test results should be discussed with patients and this is highlighted within all NICE guidance as part of our commitment to person-centred care. NICE guideline NG18 will be updated 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.' Thank you for highlighting the work that you have done which confirms the information in recommendation 1.2.115 that diabetic retinopathy that needs treatment is extremely rare in children and young people under 12 year. Please note that for a study to be included as evidence in the surveillance review of NICE guideline NG18 it must have been published after August 2014, be a Cochrane review, or an RCT with the following information in the abstract: a sample size greater or equal to 40 and clearly stating that the population includes children with diabetes aged under 18 years old. We have checked the evidence you provided on monitoring diabetic retinopathy but as one reports on a conference proceeding and the other has no abstract available, these are not being included in the surveillance review.
Coeliac UK	Yes	We are reassured to see that recommendation 1.2.111 refers to the NICE guideline on recognition, assessment and management of coeliac disease (NG20).	Thank you for your comments. As the recommendation on monitoring for coeliac disease in children and young people with type 1 diabetes is in the section on

		We feel that it would be useful to also include a statement around the fact that people with type 1 diabetes, are at a higher risk than the general population of having coeliac disease. This would provide the rationale behind the need for monitoring for coeliac disease in children and young people with type 1 diabetes.	monitoring for complications and associated conditions of type 1 diabetes, it should be clear that this is a complication associated with type 1 diabetes. In general, recommendations do not provide a rationale, this information is available in the full guideline.
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 issue of the importance of oral health is covered by recommendation 1.2.4 for children with type 1 diabetes and recommendation 1.3.3 for type 2 diabetes which highlights the importance of having regular dental examinations and cross-references the NICE guideline on dental recall. Please note that the aetiology of diabetes is out of scope for NICE guideline NG18 and as such, the references you have highlighted will not be included as evidence for the surveillance review.
Digital Diabetes Media Ltd	Yes	The key areas of lifestyle and psychology/support would benefit from greater emphasis within the guideline. Person-centred and personalised-medicine is essential for the best individual outcomes. The guideline placing a greater emphasis on these topics would like drive better care in practice. The limitations of management approaches such as DAFNE should be recognised (with respect to "Normal Eating", which needs to better recognise the homogenous population standard dietary recommendations may not suit many individuals). Equally a greater recognition of the role hope plays in the management of diabetes is important for individuals to feel fully empowered best manage their condition in their circumstances.	We agree that person-centred care is very important. NICE guideline NG18 will be updated 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.' Thank you for highlighting publications on very low calorie diets and the role of hope and optimism. For the purposes of this surveillance review only Cochrane reviews and RCTs are included. As these papers report on the findings of an online survey and longitudinal study respectively, they will not be included as evidence.

		Recent publications which should be taken in to account for an updated guideline: *Management of Type 1 Diabetes With a Very Low–Carbohydrate Diet. Lennerz et al.* *Pediatrics - June 2018, VOLUME 141 / ISSUE 6* *https://pediatrics.aappublications.org/content/141/6/e20173349* *A Longitudinal Examination of Hope and Optimism and Their Role in Type 1 Diabetes in Youths. Van Allen et al.* *J Pediatr Psychol. 2016 Aug;41(7):741-9* *https://www.ncbi.nlm.nih.gov/pubmed/26628250*	
JDRF, the type 1 diabetes research charity	Yes	1.2.60 – Blood glucose monitoring. 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 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	Thank you for your comments. Please note that for a study to be included as evidence in the surveillance review of NICE guideline NG18 it must have been published after August 2014, be a Cochrane review, or an RCT with the following information in the abstract: a sample size greater or equal to 40 and clearly stating that the population includes children aged under 18 years old. **Blood glucose monitoring** Thank you for highlighting the RCT on the 'Effects of advanced carbohydrate counting guided by an automated bolus calculator in Type 1 diabetes mellitus', however as this study is in an adult population, it does not meet the inclusion criteria for the surveillance review of NICE guideline NG18; and the current recommendations 1.2.58-1.2.64 in 'Blood glucose monitoring' do not preclude the use of bolus calculator. This RCT was however considered in the surveillance review for Type 1 diabetes in adults: diagnosis and management (NICE guideline NG17) and it was decided that the findings of this research are in line with

		treatment satisfaction, contributing to the overall wellbeing of the patient.[1] Flash glucose monitoring – JDRF believes that flash glucose monitoring should be reviewed in NG18, for the same reasons that it is being reviewed in NG17. There does not appear to be a reason to review it for one and not the other guideline. Sensor augmented pump with predictive low glucose suspend - JDRF believes that there is evidence to support the addition of this technology to the guideline. • Research from October 2018, conducted in adults and children, suggests that the MiniMed 640G reduced the proportion of time with glucose levels below 3.9 mmol/L from 10% to 6%, compared to whatever their previous treatment regime was (some were injecting, others had pump+CGM but no predictive low glucose suspend).2 Psychological and social issues in children and young people with type 1 diabetes – Whilst we agree that new evidence is unlikely to change guideline recommendations, it should be noted that health related quality of life is in	recommendations 1.4.1 and 1.4.2 which advise carbohydrate counting training for adults with type 1 diabetes as part of structured education programmes (which may or may not cover the use of a bolus calculator). Therefore, no impact on NICE guideline NG17 is expected. **Flash glucose monitoring** Thank you for your comment on the use of flash glucose monitoring in children and young people with type 1 diabetes. We will include this as an area for update within NICE guideline NG18. Please note that while there are currently no recommendations specifically on the use of a Flash glucose monitor in NICE guideline NG18, it does recommend offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60), which could therefore include flash glucose monitoring; in addition, the NICE medtech innovation briefing on Freestyle Libre for glucose monitoring (MIB110) which describes this technology is available in the NICE Diabetes in Children and Young people interactive flowchart. Evidence was identified in the surveillance review which is relevant to flash blood glucose monitoring in adults with type 1 diabetes, but not for children with type 1 diabetes. While there remains a lack of evidence on the effectiveness of a Flash glucose monitor in children and young people with type 1 diabetes under the age of 18 years

		itself a positive outcome that people with type 1 diabetes want to see. Transition from paediatric to adult care – Whilst we agree that new evidence is unlikely to change guideline recommendations, transition from paediatric to adult care is an important stage for people with type 1 diabetes, so guidance should stress the importance of a well-planned transition in care planning.	old, given that stakeholders have stated that it is being prescribed to some children and young people on the NHS and some guidance indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met), we have concluded that NICE should consider making a recommendation on the use of this technology in children with type 1 diabetes. **Sensor augmented pump** Thank you for highlighting the research on MiniMed 640G®. As this research is not an RCT, it will not be included in the surveillance review. The use of sensor-augmented pump therapy will not be proposed as an area for update in NICE guideline NG18 due to a lack of evidence. NICE has published the MiniMed 640G system with SmartGuard for managing blood glucose levels in people with type 1 diabetes (February 2016) MIB51 which indicated that the evidence was still in proof of concept phase. We will share the information you have provided with the NICE Medical Technologies Evaluation Programme (MTEP) team for consideration if they do any future work in this area. Thank you for your comments concerning the importance of health-related quality of life and transition from paediatric to adult care. Recommendations 1.5.9-1.5.13 in NICE guideline NG18 cover transition from paediatric to adult care and cover the issues raised in the stakeholder consultation.
Abbott Diabetes Care	Yes	Prospective real-world studies are important data to show the generalisation of RCTs results in real world settings and should therefore be considered. Some of the challenge to conducting medical device HTA may be overcome by applying pragmatic approaches to adjust assessment	Thank you for your comment on the use of real-world data. For the purpose of this surveillance review only Cochrane reviews and RCTs have been included. Please note that 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.

		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 Abbott would like to highlight for consideration. Campbell et al, publication: Outcomes of using flash glucose monitoring technology by children and young people with type 1 diabetes in a single arm study, Pediatric Diabetes, First published: 28 July 2018, https://onlinelibrary.wiley.com/doi/10.1111/pedi.12735 Results: A total of 76 children and teenagers (46.1% male; age 10.3 _ 4.0 years, type 1 diabetes duration 5.4 _ 3.7 years; mean _ SD) from 10 sites participated. TIR improved significantly by 0.9 _ 2.8 h/d (P = 0.005) vs SMBG baseline. Time in hyperglycaemia (>180 mg/dL) reduced by −1.2 _ 3.3 h/d (P = 0.004). HbA1c reduced by −0.4% (−4.4 mmol/mol), from 7.9 _ 1.0% (62.9 _ 11.2 mmol/mol) baseline to 7.5 _ 0.9% (58.5 _ 9.8 mmol/mol) study end (P <	Thank you for your comment on the use of flash glucose monitoring in children and young people with type 1 diabetes. We will include this as an area for update within NICE guideline NG18. Please note that while there are currently no recommendations specifically on the use of a Flash glucose monitor in NICE guideline NG18, it does recommend offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60), which could therefore include flash glucose monitoring; in addition, the NICE medtech innovation briefing on Freestyle Libre for glucose monitoring (MIB110) which describes this technology is available in the NICE Diabetes in Children and Young people interactive flowchart. While there remains a lack of evidence on the effectiveness of a Flash glucose monitor in children and young people with type 1 diabetes under the age of 18 years old, given that stakeholders have stated that it is being prescribed to some children and young people on the NHS and some guidance indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met), we have concluded that NICE should consider making a recommendation on the use of this technology in children with type 1 diabetes.

		0.0001) with reductions across all age-subgroups (4-6, 7-12 and 13-17 years). Time in hypoglycaemia (<70 mg/dL) was unaffected. Diabetes Treatment Satisfaction Questionnaire "Total Treatment Satisfaction" score improved for parents (P < 0.0001) and teenagers (P < 0.0001). Conclusions: Children with diabetes improved glycaemic control safely and effectively with short-term flash glucose monitoring compared to use of SMBG in a single arm study. The Association of British Clinical Diabetologists (ABCD) FreeStyle Libre Nationwide Audit now has over 3500 patients with data entered, approximately 900 of which are paediatrics. These patient numbers are constantly increasing as the uptake of FreeStyle Libre grows across the UK. The paediatric data set will be analysed and available later this year. 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,	

		there were 7 studies included with 346 paediatric subjects. 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. There are further observational studies whose references we would be pleased to supply.	
Royal Devon and Exeter NHS Foundation Trust	No	No comments provided	Thank you for your response.
Novo Nordisk	Yes	See above	Thank you, please see response above.
The Royal College of Ophthalmologists	Yes	A clear pathway for children with diabetes to diabetic eye screening needs to be recommended and that this should be via an annual visit to the local diabetic eye screening programme (DESP) and not via a hospital paediatric ophthalmology service as we frequently get requests from GP’s to see patients rather than patients and families being informed that they should attend their DESP. Clearly	Thank you for your comment. Diabetic eye screening is not within the remit of NICE guidance as it is under the remit of the NHS Diabetic Eye Screening Programme. We will pass this information on to the NICE Field team.

		current information is confusing to referrers, diabetic specialist nurses and diabetes clinicians.	
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 in children/young people.** • (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). • (Periodontal changes in children and adolescents with diabetes: a case-control study. Lalla E, Cheng B, Lal S, Tucker S, Greenberg E, Goland R, Lamster IB. Diabetes Care. 2006 Feb;29(2):295-9). 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)	Thank you for your comments. Please note that the aetiology of diabetes is out of scope for NICE guideline NG18. The issue of the importance of oral health is covered by recommendation 1.2.4 for children with type 1 diabetes and recommendation 1.3.3 for type 2 diabetes which highlights the importance of having regular dental examinations and cross-references the NICE guideline on dental recall (NICE guideline NG19). This guideline highlights diabetes as a risk factor for developing dental disease. It also notes that 'People with diabetes (both type I and type II) are at increased risk of developing destructive periodontal disease. This may be due to an altered periodontal tissue response to plaque. Therefore, 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.' As the issues you highlighted are covered by existing NICE guideline, which is cross-referred to in NICE guideline NG18, this will not be an area proposed for update.

		• (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)	
Children and Young People's Wales Diabetes Network	Yes	The CYPWDN suggest the following are reviewed: - CYP with Type 1 Diabetes need expert advice about exercise - Local data gathered in Wales supports the view of NICE that guidance around fluid volumes in the treatment of DKA should be reviewed - All references to transition services in the CYP guidance need to be mirrored in the adult guidance, 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,	Thank you for your comments and for supporting the decision to update NICE guideline NG18 in the area of fluid and insulin therapy for diabetic ketoacidosis. As NICE guideline NG18 already covers the need for children and young people with diabetes to receive advice on exercise in recommendations 1.2.1, 1.2.47-1.2.53, 1.3.1 and 1.3.14 and no evidence was identified that indicates this is an area requiring update, this will not be an area proposed for update. 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 NICE guidance, however these organisations do not have

		ensuring diabetes education is tailored to young adults - Review diagnostic testing – all inappropriate testing should be reported as a clinical incident - There is a sub-group in the national Children and Young People's Wales Diabetes Network (covering all paediatric teams in England & Wales) reviewing care of Type 2 diabetes in children and young people. The recommendations of this group should be considered for inclusion in the guidance.	accreditation. Only Cochrane reviews and RCT evidence has been considered in the surveillance review. The evidence that was identified that relates to the recommendations on service provision supports existing recommendations that include the need for a multidisciplinary team to provide care (recommendation 1.5.1) and the provision of 24-hour telephone access (telemedicine; recommendation 1.5.4). While the evidence was mixed concerning the effectiveness of interventions on improving the transition from paediatric to adult care, the quality of the evidence was rated as low in the Cochrane review and there is overall only a small number of trials in this area. The evidence does not indicate that the principles in recommendations 1.5.9-1.5.13 on transition from paediatric to adult care do not hold. As such these areas will not be updated. Please note that there is also existing NICE guidance on Transition from children's to adults' services for young people using health or social care services (NICE guideline NG43) which covers the period before, during and after a young person moves from children's to adults' health and/or social care services. It aims to help young people and their carers have a better experience of transition by improving the way it's planned and carried out. Please note that it is beyond the remit of the guideline to make recommendations concerning inappropriate diagnostic testing being considered as a clinical incident.
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 comments, these will be passed on to the developers of the update to consider when thinking about relevant outcomes.

Royal College of Psychiatrists (RCPsych)	Yes	1. Assessment and management of **Neuropsychological deficits** and **cognitive impairment** in young people with Type 1 Diabetes need to be included References: • Gaudieri PA, Chen R, Greer TF, Holmes CS. Cognitive function in children with type 1 diabetes: a meta-analysis. Diabetes Care. 2008 Sep;31(9):1892-7. doi: 10.2337/dc07-2132. PubMed PMID: 18753668; PubMed Central PMCID: PMC2518367. • Naguib JM, Kulinskaya E, Lomax CL, Garralda ME (2008) Neuro-cognitive performance in children with type 1 diabetes – a meta analysis. Journal of Pediatric Psychology, 2009, 34, 271-282 - doi:10.1093/jpepsy/jsn074 • Cato A, Hershey T. Cognition and Type 1 Diabetes in Children and Adolescents. Diabetes Spectr. 2016;29(4):197–202. doi:10.2337/ds16-0036 **2. Safeguarding framework** 3. **Capacity / Gillick competence and Parental consent** is not explained (who assess this and how and how is it documented....) 4. **Family and psychosocial factors** in type 1 Diabetes • "Young people with T1D have a persistent, nearly threefold higher risk of mortality before age 30 years compared with the general population, with the 15 to 30-year-old age group at greatest risk. Before age 30, we found no deaths due to diabetic nephropathy and little evidence of microvascular disease contributing to death. The continuing predominance of mortality due to ketoacidosis, especially in patients who developed diabetes in later childhood, suggests the need to target behavioural factors including during and after the transition to adult	Thank you for your comments and for the references you have provided. Please note that only Cochrane reviews and RCT evidence is included in the surveillance review of NICE guideline NG18, and as such, the references you have provided will not be included as evidence in the surveillance review. The guideline development committee for NICE guideline NG18 recognised that patient-related characteristics and fluctuations in glycaemic control may cause cognitive impairment in children and young people with type 1 diabetes (see section 10.5 cognitive disorders in the full guideline for further details) and recommendation 1.2.86 highlights that diabetes teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age. NICE guideline NG18 will be updated 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.' In relation to the issues you raise concerning family and psychosocial factors, these are addressed in recommendations on psychological and social issues in children and young people with type 1 diabetes (recommendations 1.2.94- 1.2.109) and with type 2 diabetes (recommendations 1.3.33- 1.3.42), including assessing the emotional and psychological wellbeing of young people with type 1

		clinics. Psychological input is required for some patients. Consideration of who might be at risk of suicide is important. " **Refernce:** Wasag DR, Gregory JW, Dayan C on behalf of the Brecon Group, et al (2018) Excess all-cause mortality before age 30 in childhood onset type 1 diabetes: data from the Brecon Group Cohort in Wales Archives of Disease in Childhood 103:44-48. • "Drawing on the views of ≥650 children, parents and clinicians, this qualitative literature synthesis found that children and young people of all ages value positive, relationship-based approaches that engage with their social, as well as physical, health. Children, young people and parents valued care that was as sensitive to the wider context of their lives as to their bodies." **Reference** Curtis-Tyler K, Arai L, Stephenson T, et al. (2015) Arch Dis Child 100:826–833. • "The results revealed two main conclusions: (i) diabetes-specific family conflict is associated with the occurrence of psychological distress in both parents and children and adolescents and (ii) the level of glycaemic control relates to the level of diabetes-specific family conflict." **Refernce:** Williams, L. B., Laffel, L. M. and Hood, K. K. (2009), Diabetes-specific family conflict and psychological distress in paediatric Type 1 diabetes. Diabetic Medicine, 26: 908-914. doi:10.1111/j.1464-5491.2009.02794.x • "Multimorbidity is persistent in children newly diagnosed with physical illnesses, regardless of the mental comorbidity experienced. **Integrating family-centred**	diabetes who present with frequent episodes of diabetic ketoacidosis (1.2.96), considering the needs of families and carers, and relationship-based approaches (e.g. recommendation 1.2.98). As such, this will not be an area proposed for update.

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		mental health services soon after the diagnosis of a physical illness should be prioritized in pediatric settings." **Reference** Reaume, SV, Ferro, MA. (2019) Chronicity of Mental Comorbidity in Children with New-onset Physical Illness. Child Care Health Dev. https://doi.org/10.1111/cch.12667 •. "The diagnosis of Type I Diabetes in a child was traumatic for mothers. Stress and PTSS in mothers adversely affected children's health. Management of stress symptoms in mothers may lead to improved behavioral and metabolic outcomes in children." **Refernce** Rechenberg K, Grey M, Sadler L. (2017) Stress and Posttraumatic Stress in Mothers of Children With Type 1 Diabetes. J Fam Nurs 23:201-225 **Refernce**: • "The mothers' psychological distress was associated with children's behaviour problems rather than their diabetes." Hannonen R, Eklund K, Tolvanen A, Komulainen J, Riikonen R, Delamater AM, Ahonen T (2015), Psychological distress of children with early-onset type 1 diabetes and their mothers' well-being. Acta Paediatrica 104: 1144–1149.	
Association for Clinical Biochemistry and Laboratory Medicine	No	No comments provided	Thank you for your response.
Imperial College Health Care NHS Trust – St Mary's Hospital	Yes	CGM and its role in the good management Flash glucose monitors The use of close loop system	Thank you for your comments. The sections on 'Blood glucose targets and monitoring' in the surveillance review Appendix A3 describes the evidence that we identified in relation to continuous glucose monitoring (CGM), including the use of Apps and considering the psychological benefits

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			of CGM, findings of which support the content of the current recommendations and will therefore not be considered as an area for update. Thank you for your comment on the use of flash glucose monitoring in children and young people with type 1 diabetes. We will include this as an area for update within NICE guideline NG18. Please note that while there are currently no recommendations specifically on the use of a Flash glucose monitor in NICE guideline NG18, it does recommend offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60), which could therefore include flash glucose monitoring; in addition, the NICE medtech innovation briefing on Freestyle Libre for glucose monitoring (MIB110) which describes this technology is available in the NICE Diabetes in Children and Young people interactive flowchart. While there remains a lack of evidence on the effectiveness of a Flash glucose monitor in children and young people with type 1 diabetes under the age of 18 years old, given that stakeholders have stated that it is being prescribed to some children and young people on the NHS and some guidance indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met), we have concluded that NICE should consider making a recommendation on the use of this technology in children with type 1 diabetes. In relation to closed-loop therapy, during the surveillance review only 1 RCT was identified. While the study reported that the hybrid closed-loop therapy led to significant improvements in glucose control and reduced the risk of hypoglycaemia compared to sensor-augmented pump therapy in children with sub-optimally controlled type 1 diabetes, the evidence base remains limited and further

			evidence from larger RCTs would be required in order to consider whether this should be an area for update.
Perspectum Diagnostics	Yes	In the NICE guideline on diabetes (type 1 and type 2) in children and young people (NG18) published in August 2015, section 17 Monitoring for associated conditions and complications of type 2 diabetes lists four complications associated with type 2 diabetes. It is proposed that **non-alcoholic fatty liver disease (NAFLD)** is added to the list of conditions within this section. It also recommended that this disease is appropriately aligned and linked to the NICE guidance on non-alcoholic fatty liver disease: assessment and management (NG49) to ensure the cross referral is current. As recommended in NICE's guidance on non-alcoholic fatty liver disease: assessment and management, recommendation 1.1.1 states that non-alcoholic fatty liver disease (NAFLD) is more common in people who have: type 2 diabetes or metabolic syndrome (T2DM). Recommendation 1.1.4 advises to offer a liver ultrasound to test children and young people for NAFLD if they: have type 2 diabetes or metabolic syndrome and do not misuse alcohol. In line with these recommendations we are recommending that investigations for the assessment of NAFLD should be considered in children and young people with type-2 diabetes and indication of abnormal liver blood tests or	Thank you for your comments concerning non-alcoholic fatty liver disease (NAFLD). We assume that this is in relation to recommendations 1.3.43-1.3.45 on monitoring for complications and associated conditions of type 2 diabetes. As NICE has existing guidance (NICE guideline NG49) on NAFLD which recommends that children and young people with type 2 diabetes are offered a liver ultrasound, we will request an editorial amendment to the recommendations to add 'for guidance on managing non-alcoholic fatty liver disease in children and young people with type 2 diabetes, see the NICE guideline on Non-alcoholic fatty liver disease (NAFLD).'

		ultrasound examination results. NAFLD is prevalent in 59.67% of T2DM patients and increases the burden of secondary complications and adverse outcomes including mortality[2]. An increase in microvascular defects such as retinopathy and chronic kidney disease and a 1.87-fold increase in cardiovascular adverse events associated with NAFLD in the scope of pre-existing type-2 diabetes has been reported[1,3]. Furthermore, a 1.5-fold increase in coronary microvascular dysfunction has been reported in NAFLD patients that strongly predicted future major cardiac adverse events[7].Ectopic accumulation of hepatic lipids is strongly associated to the development of type-2 diabetes, hepatic insulin resistance and eventual progressive hepatic fibrosis resulting in higher rates of mortality due to cirrhosis[2]. Adult and paediatric symptomatic NAFLD may include complaints of abdominal pain (45%), vomiting (13.8%) and general fatigue[4] although >80% of patients may still present with normal liver blood tests (https://www.nice.org.uk/guidance/NG49)[8]. There is a requirement to screen children and young people at high risk of NAFLD via non-invasive methods and allocate interventional strategies accordingly. Treatments that target metabolic defects in T2DM, such as weight loss and improved glycaemic control, are also advantageous in NAFLD management and therefore transferable[4,5]. Furthermore, the American Diabetes Association (ADA) 2019 guidelines already recommend that 'Patients with	

		type 2 diabetes or prediabetes and elevated liver enzymes (alanine aminotransferase) or fatty liver on ultrasound should be evaluated for presence of non-alcoholic steatohepatitis and liver fibrosis'[6]. References 1. Dharmalingam, M. and Yamasandhi, P.G., 2018. Nonalcoholic fatty liver disease and Type 2 diabetes mellitus. *Indian journal of endocrinology and metabolism*, *22*(3), p.421. 2. Anstee, Q.M., McPherson, S. and Day, C.P., 2011. How big a problem is non-alcoholic fatty liver disease?. *Bmj*, *343*, p.d3897. 3. Targher, G., Lonardo, A. and Byrne, C.D., 2018. Nonalcoholic fatty liver disease and chronic vascular complications of diabetes mellitus. *Nature Reviews Endocrinology*, *14*(2), p.99. 4. American Gastroenterological Association. American Gastroenterological Association medical position statement: nonalcoholic fatty liver disease. Gastroenterology 2002; 123:1702 – 1704. 5. Cusi K, Orsak B, Bril F, et al. Long-term pioglitazone treatment for patients with non-alcoholic steatohepatitis and prediabetes or type 2 diabetes mellitus: a randomized trial. Ann Intern Med 2016; 165:305–315. 6. Care, D., 2019. Standards of Medical Care in Diabetes 2019. *Diabetes Care*, *42*, p.S81. 7. Vita, T., Murphy, D.J., Osborne, M.T., Bajaj, N.S., Keraliya, A., Jacob, S., Diaz Martinez, A.J., Nodoushani, A., Bravo, P., Hainer, J. and Bibbo, C.F., 2019. Association	

		between nonalcoholic fatty liver disease at CT and coronary microvascular dysfunction at myocardial perfusion PET/CT. *Radiology*, p.181793. 8. https://www.nice.org.uk/guidance/NG49, published July 2016 In addition, Recommendation 1.3.1 of the diabetes (type 1 and type 2) in children and young people: diagnosis and management NICE guideline states that children and young people with type 2 diabetes and their family members or carers (as appropriate) are offered a continuing programme of education from diagnosis and to ensure that the programme includes the following care topics…the complications of type 2 diabetes and how to prevent them (new 2015). By including NAFLD to the list of complications associated with type 2 diabetes, type 2 diabetic children and young people, including their family members or carers, will be more aware of the increased prevalence of developing NAFLD.	
Medtronic Ltd	Yes	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.	Thank you for your comment on NICE diagnostics guidance DG21. As noted, this guidance is due to be reviewed this year by the NICE Diagnostics Assessment Programme; and we will share your comments with this team. NICE guideline NG18 does not make any recommendations on this device, but it is in the Diabetes in Children and Young people NICE pathway. If further evidence is identified in the future, then the impact of this guideline on NG18 will be considered. NICE diagnostics guidance DG21 is not part of the current diabetes NICE guidelines review.

		We would like to highlight the following studies that may not have been captured by the evidence review: A recently published RCT: *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*	With regard to the references you have highlighted, the RCT by Bosi et al. 2019 is within an adult population and therefore would not meet the inclusion criteria for the surveillance review of NICE guideline NG18. For a study to be included it must be a Cochrane review, or an RCT with a sample size greater or equal to 40 and must clearly identify in the abstract that the population includes children with diabetes aged under 18 years old. The other publications do not meet the inclusion criteria for the surveillance review. We also do not include studies that look at the effectiveness of features of a system, as in the study by Zhang et al. 2016. In relation to your request to update NICE guideline NG18 on closed-loop systems and sensor-augmented pump therapy, during the surveillance review only 1 relevant RCT was identified. While the study reported that the hybrid closed-loop therapy led to significant improvements in glucose control and reduced the risk of hypoglycaemia compared to sensor-augmented pump therapy in children with sub-optimally controlled type 1 diabetes, the evidence base remains limited and further evidence from larger RCTs with populations aged under 18 years old would be required in order to consider whether this should be an area for update.

Dexcom Operating Ltd	Yes	Rt-CGM has been omitted from the scope of NG18. Recent clinical evidence provides a compelling case for the inclusion of rt-CGM in the proposed scope of NG18, and the recommendation that rt-CGM should be offered to all diabetic children with suboptimal glycaemic control. The evidence gaps identified which should lead to the inclusion of rt-CGM in the scope are presented in order of importance: 1. HbA1c – sub optimal glycemic control 2. Rt-CGM digital platforms HbA1c – sub optimal glycemic control *Mulinacci et al, 2019*[1]' and two forthcoming publications, provide the evidence for rt-CGM to be included in the proposed scope. This allows NICE the opportunity to change the current guidance from '**consider'** to '**offer**' rt-CGM to help improve blood glucose control in children and young people who continue to have hyperglycaemia despite insulin adjustment and additional support" Recently Mulinacci et al (2019)[1] performed a retrospective analysis of 396 patients with newly-diagnosed T1D. 94% (372) of the study subjects were under the age of 18. This data 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 11.6% (103 mmol/mol). For 2.5 years of follow-up, the MDI+CGM group had 1.5% (16 mmol/mol)	Thank you for your comments. Please note that real time continuous glucose monitoring is not out of scope for NICE guideline NG18. The scope includes 'glucose monitoring strategies in children and young people with type 1 diabetes, including: continuous glucose monitoring with retrospective (intermittent) versus real-time (long-term) adjustment of treatment' and there is a specific review question asking 'What is the effectiveness of continuous glucose monitoring performed intermittently compared with continuous glucose monitoring performed in real-time in children and young people with type 1 diabetes?' NICE guideline NG18 recommends offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60). It also recommends offering ongoing real-time continuous glucose monitoring with alarms to children and young people with T1D who have frequent severe hypoglycaemia, or impaired awareness of hypoglycaemia associated with adverse or an inability to recognise, or communicate about, symptoms of hypoglycaemia (recommendation 1.2.62); and recommends considering ongoing real-time continuous glucose monitoring for neonates, infants and pre-school children, children and young people who undertake high levels of physical activity, children and young people who have comorbidities or are receiving treatments that can make blood glucose control difficult (recommendation 1.2.63). Making decisions using NICE guidelines explains how NICE uses words to show the strength (or certainty) of recommendations. The recommendations do say 'offer' rt-CGM under some circumstances, 'consider' was due to lack of evidence in under 5s, which led to the

		lower HbA1c than the MDI-only group (7.7% vs. 9.2% (61 vs 77 mmol/mol), [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). Studies have shown that glycaemic control may settle into long-term patterns within the first 5 years after diagnosis and 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. The benefits of using rt-CGM to reduce HbA1c levels in young people can be seen in children as young as three and a half years old (Dovc et al (2019)[4]). In addition to this, it has been shown that in the first year of diagnosis insulin pumps provide limited clinical and quality of life benefit to person with diabetes compared to multiple daily injections. There is an increase the cost of treatment due to the provision a pump[9]. It has been shown that in this first year a rt-CGM could and potentially should be provided due to both clinical and quality of life benefits[1,8]. Rt-CGM digital platforms 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 NG18	research recommendation 'What is the clinical and cost effectiveness of real-time continuous glucose monitoring systems compared to 5 or more capillary blood glucose tests per day in children aged 5 years or younger with type 1 diabetes who use insulin pump therapy?'. There remains a lack of research in this age group. For a study to be included as evidence in the surveillance review of NICE guideline NG18 it must be a Cochrane review, or an RCT with the following information in the abstract: a sample size greater or equal to 40 and clearly stating that the population includes children aged under 18 years old. The references you have provided do not meet these criteria, except for Blair, et al. 2019, however the data in this study has already been included in the surveillance review via the publication Blair, J., et al., *Continuous subcutaneous insulin infusion versus multiple daily injections in children and young people at diagnosis of type 1 diabetes: the SCIPI RCT.* Health Technology Assessment (Winchester, England), 2018. **22**(42): p. 1-112. We will add the 2 pieces of on-going research that you have highlighted (https://clinicaltrials.gov/ct2/show/NCT03263494 and https://clinicaltrials.gov/ct2/show/NCT02912728) as on-going research to be considered once published. The sections on 'Insulin therapy for children and young people with type 1 diabetes' and 'Blood glucose targets and monitoring' in the surveillance review Appendix A3 describes the evidence that we identified in relation to continuous glucose monitoring, including the use of Apps and considering the psychological benefits of CGM, findings of which support the content of the current recommendations and will therefore not be considered as an area for update.

		"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 systems such as the Dexcom G6® provide app-based technology where data can be uploaded and distributed to five people (the 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. The use of the real-time data and data sharing is associated with fewer low glucose episodes, suggesting that the shared glucose information prompted interventions by parents or caregivers which helped the children avoid severe or prolonged hypoglycaemia (Parker et al, 2017, Puhr et al, 2019, Welsh, 2019, Burckhardt, 2018)[2,6,7,8] In the younger population the value of rt-CGM should not solely focus on the child / young adult. It has been shown that rt-CGM plays an important role in decreasing the stress and worry that parents and caregivers feel when supporting a child / young adult with diabetes, Erie et al (2017)[3]. Rt-CGM offers digital platforms that enable the person with diabetes to share their data in real time with their support network through these platforms.	

		Forthcoming publications 1) CGM Intervention in Teens and Young Adults With Type 1 Diabetes (Available at https://clinicaltrials.gov/ct2/show/NCT03263494) Summary Adolescents and young adults with T1D and poor glycemic control (age 14-< 25 years, T1D duration >12 months, HbA1c 7.5-<11.0%, using an insulin pump or MDI)) will be randomly assigned to either CGM or BGM. Sample size will be 150. The primary outcome assessment will be HbA1c after 6 months. Secondary outcomes will include HbA1c, CGM metrics (control group will wear blinded CGM at 13 and 24 weeks) and quality of life measures. The randomized trial will be followed by a 6-month extension study during which the RCT control group will initiate CGM and the RCT CGM group will continue CGM. 2) Strategies to Enhance New CGM Use in Early Childhood (available at https://clinicaltrials.gov/ct2/show/NCT02912728) Summary The primary objective of this study is to compare the efficacy and safety of CGM alone and CGM combined with a family behavioural intervention with a control group using home blood glucose monitoring (BGM) alone. References 1. Mulinacci G, Alonso T, Snell-Bergeon JK, Shah VN. Glycemic Outcomes with Early Initiation of	

		Continuous Glucose Monitoring System in Recently Diagnosed Patients with Type 1 Diabetes, 2019 DOI: 10.1089/dia.2018.0257 2. Parker A, Welsh J, Jimenez A, Graham C. Effects of sharing continuous glucose monitoring (CGM) data from young children with diabetes on CGM usage and hypoglycemic exposure. Pediatr Diabetes. 2017;18(S25):76-77. 3. Erie, C., Van Name, M. A., Weyman, K., Weinzimer, S. A., Finnegan, J., Sikes, K., … Sherr, J. L. (2017). Schooling diabetes: Use of continuous glucose monitoring and remote monitors in the home and school settings. Pediatric Diabetes, 19(1), 92–97. doi:10.1111/pedi.12518 4. Dovc, K., Cargnelutti, K., Sturm, A., Selb, J., Bratina, N., & Battelino, T. (2018). Continuous Glucose Monitoring Use and Glucose Variability in Pre-school Children with Type 1 Diabetes. Diabetes Research and Clinical Practice. doi:10.1016/j.diabres.2018.10.005 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) 6. 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	

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		7. 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 8. Burckhardt, M.-A., Roberts, A., Smith, G. J., Abraham, M. B., Davis, E. A., & Jones, T. W. (2018). The Use of Continuous Glucose Monitoring With Remote Monitoring Improves Psychosocial Measures in Parents of Children With Type 1 Diabetes: A Randomized Crossover Trial. Diabetes Care, dc180938. doi:10.2337/dc18-0938 9. Blair, J. C., McKay, A., Ridyard, C., Thornborough, K., Bedson, E., Peak, M., … Gamble, C. (2019). Continuous subcutaneous insulin infusion versus multiple daily injection regimens in children and young people at diagnosis of type 1 diabetes: pragmatic randomised controlled trial and economic evaluation. BMJ, l1226.doi:10.1136/bmj.l1226	
Royal College of Nursing	Not answered	No comments provided	Thank you.
Royal College of Paediatrics and Child Health	No	No comments provided	Thank you for your response.

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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; ○ *Ultrafast acting insulins* ○ *Management of renal complications in light of CREDENCE trial data* ○ *Low/ v low calorie diets* ○ *Potential risks of SLG2 inhibitors: Fournier's gangrene, diabetic ketoacidosis & increased risk of lower limb amputation*	Thank you for your comments. Please note that 'ultrafast acting insulins' which are licenced for use in children have not been overlooked in the surveillance review. New evidence was identified which supports both the use of the long-acting insulin degludec in children with T1D, which can be delivered as a once-daily injection, or alternatively the use of detemir injected once- or twice-daily; however the evidence base remains limited, with only 2 published RCTs investigating long-acting insulin use in children and young people with T1D, as such it is proposed that this is not currently an area for update. As SLG2 inhibitors (Dapagliflozin, Canagliflozin and Empagliflozin) are not licenced for use with children, these medications would not be considered for review in the NICE guideline NG18 update. The CREDENCE trial looks at the effectiveness of Canagliflozin for end stage renal disease and cardiovascular events in patients diagnosed with Type 2 diabetes and chronic kidney disease. As this drug is an SLG2 inhibitor which is not licenced for children it would not be considered for recommendations in NICE guideline NG18, which already covers monitoring of kidney disease (recommendations 1.3.43 and 1.3.45) and there is a section on diabetic kidney disease in children and young people with type 2 diabetes (recommendations 1.3.54-1.3.57). No evidence was identified on the use of low versus very low-calorie diets in children or young 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. Please see responses to DTN and ABCD for information.

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Children and Young People's NE and N Cumbria Diabetes Network	No	No comments provided	Thank you for your response.
Diabetes UK	Yes	**Blood glucose monitoring (Type 1 diabetes) (1.2.58)** The guideline surrounding frequency of finger prick blood glucose checking should be reviewed in light of the International Society for Paediatric and Adolescent Diabetes (ISPAD) recommendation of at least 6-10 times a day with regular and frequent review of results, published in 2018. ISPAD Consensus Guidelines (2018) https://cdn.ymaws.com/www.ispad.org/resource/resmgr/consensus_guidelines_2018_/8.glycemic_control_targets_a.pdf **Use of continuous glucose monitoring (CGM) (1.2.63)** Recommendation 1.2.63 should be reviewed and amended. A review of the qualification of "for example sport of a regional, national or international level" in particular should be included in the scope of this guideline. We suggest this qualification is a barrier to provision of CGM as commissioning bodies often refuse CGM for children who undertake high levels of exercise but are not yet competing at these high levels. Lack of a CGM could risk impairing	Thank you for your detailed comments. Please be aware that for a study to be included as evidence in the surveillance review of NICE guideline NG18 it must have been published after August 2014, be a Cochrane review, or an RCT with the following information in the abstract: a sample size greater or equal to 40 and clearly stating that the population includes children with type 1 and/or type 2 diabetes aged under 18 years old. **Blood glucose monitoring** Thank you for your comment on the frequency of finger prick blood glucose checking. The recommendation from ISPAD is that 'When fingerstick BGs are used, testing may need to be performed 6 to 10 times per day to optimize intensive control. Regular review of these BG values should be performed with adjustments to medication/nutritional therapies to optimize control (B).' This is based on 2 pieces of evidence: Ziegler R, et al. Frequency of SMBG correlates with HbA1c and acute complications in children and adolescents with type 1 diabetes. Pediatr Diabetes. 2011;12(1):11-17 and Chiang JL, et al. Type 1 diabetes through the life span: a position statement of the American Diabetes Association. Diabetes Care. 2014;37(7):2034-2054. As these studies do not meet the inclusion criteria for the surveillance review, and the ISPAD guideline states that finger prick checks 6-10 times per day, 'may'

		their diabetes management meaning that they are never able to achieve such a level of sport. Type 1 diabetes technology: a consensus guideline, Diabetes UK, June 2018 https://www.diabetes.org.uk/resources-s3/2018-06/Diabetes%20UK%20consensus%20guideline%20for%20Type%201%20diabetes%20technology.pdf **Use of Freestyle Libre (Type 1 diabetes)** There is no mention of Flash glucose monitoring in the existing guideline and there is extensive new evidence surrounding its use. It should be noted that Flash glucose monitoring is currently being prescribed to some children and young people on the NHS and many prescribers may benefit from NICE guidance surrounding its use. NG18 should be updated to reflect current evidence surrounding the use of Flash glucose monitoring, with recommendations on its prescription and use. Diabetes UK Position Statement on Type 1 technology. https://www.diabetes.org.uk/position-statements-reports/specialist-care-for-children-and-adults-and-complications/type-1-technology-guidelines. Ayman A Al Hayek, Asirvatham A Robert, Mohamed A Al Dawish (2007) Evaluation of FreeStyle Libre Flash Glucose Monitoring System on Glycemic Control, Health-Related Quality of Life, and Fear of Hypoglycemia in Patients with Type 1 Diabetes https://journals.sagepub.com/doi/full/10.1177/1179551417746957.	rather than 'should' or 'must' be performed, recommendation 1.2.58 which recommends to 'Advise children and young people with type 1 diabetes and their family members or carers (as appropriate) to routinely perform at least 5 capillary blood glucose tests per day' will not be considered as an area for update. **Use of continuous glucose monitoring (CGM) (1.2.63)** Thank you for your comment on recommendation 1.2.63 which recommends considering 'ongoing real-time continuous glucose monitoring for children and young people who undertake high levels of physical activity (for example, sport at a regional, national or international level)'. Sport at a regional, national or international level has clearly been given as an example of a 'high level' of physical activity, rather than as a definition. Thank you for highlighting that CGMs are often refusing continuous glucose monitoring for children who undertake high levels of exercise. We will request that the guideline committee who develop the update of NICE guideline NG18 consider how this recommendation could be amended to provide other examples of high levels of physical activity. **Use of Freestyle Libre (Type 1 diabetes)** Thank you for your comment on the use of flash glucose monitoring in children and young people with type 1 diabetes. We will include this as an area for update within NICE guideline NG18. Please note that while there are currently no recommendations specifically on the use of a Flash glucose monitor in NICE guideline NG18, it does recommend offering a choice of equipment in order to optimise blood glucose control in response to adjustment of insulin, diet and exercise (recommendation 1.2.60), which could therefore include flash glucose monitoring; in addition, the NICE medtech innovation

		Giani, E et.al (2018) Performance of the Flash Glucose Monitoring System during exercise in youth with Type 1 diabetes. Diabetes Research and Clinical Practice, Vol.146, pp.321-329 https://www-sciencedirect-com.knowledge.idm.oclc.org/science/article/pii/S016882271830593X. **Treatment of hypoglycaemia (1.2.78)** NG18 currently includes no recommendations about the amount of fast-acting carbohydrate needed for treating hypoglycaemia. However, there is evidence to support the development of recommendations for this and the guidance should be reviewed and updated to reflect the ISPAD guidelines on treatment of hypoglycaemia. McTavish L, Wiltshire E. 2011. Effective treatment of hypoglycemia in children with type 1 diabetes: a randomized controlled clinical trial. Paediatric Diabetes. 12:381-387 Existing recommendations on treatment for hypoglycaemia in NG18 (1.2.80) advise that long-acting carbohydrate should always be taken as symptoms improve. However, long-acting carbohydrate is not always required, especially if the child uses and insulin pump. ISPAD consensus guidelines reflect this approach and we suggest that NG18 should be updated accordingly. ISPAD Consensus Guideline (2018) https://cdn.ymaws.com/www.ispad.org/resource/resmgr/consensus_guidelines_2018_/12.assessment_and_management.pdf **Monitoring of complications (1.2.110)**	briefing on Freestyle Libre for glucose monitoring (MIB110) which describes this technology is available in the NICE Diabetes in Children and Young people interactive flowchart. While there remains a lack of evidence on the effectiveness of a Flash glucose monitor in children and young people with type 1 diabetes under the age of 18 years old, given the information you have provided stating that it is being prescribed to some children and young people on the NHS, and the guidance from the Type 1 diabetes technology: a consensus guideline, Diabetes UK, June 2018 which indicates that children aged 4 years and older may receive a flash glucose monitor (if other conditions are met), we have concluded that NICE should consider making a recommendation on the use of this technology in children with type 1 diabetes. **Treatment of hypoglycaemia (1.2.78 and 1.2.80)** Thank you for your comment on recommendations concerning the amount of fast-acting carbohydrate needed for treating hypoglycaemia. NICE guideline NG18 recommends that children and young people with type 1 diabetes are offered level 3 carbohydrate counting education which would address the amount of fast-acting carbohydrate needed for treating hypoglycaemia (recommendation 1.2.37) and there are a set of recommendations concerning carbohydrate intake for treating hypoglycaemia (recommendations 1.2.51-1.2.53). Recommendation 1.2.80 also recommends that fast-acting glucose (for example, 10–20 g) is immediately given by mouth to treat mild to moderate hypoglycaemia in children and young people with type 1 diabetes, which is in line with current ISPAD guidelines. Please note that as the reference provided was published prior to August 2014 it does not meet the inclusion criteria to be considered as evidence in this surveillance review.

		NG18 currently recommends annual review of potential complications from age 12. This should be reviewed in the light of ISPAD Consensus Guidelines and American Diabetes Association (ADA) Standards of Medical Care which both make evidence-based recommendations for earlier screening. ISPAD Consensus Guidelines (2018) https://cdn.ymaws.com/www.ispad.org/resource/resmgr/consensus_guidelines_2018_/18.microvascular_and_macrova.pdf American Diabetes Association (2018) Children and Adolescents: Standards of medical care in diabetes http://care.diabetesjournals.org/content/41/Supplement_1/S126 This section (1.2.110) should also include recommendations for the treatment of complications. This is frequently highlighted by paediatric diabetes teams as an area they need guidance on. Recommendations for the treatment of dyslipidaemia, hypertension, albuminuria, and retinopathy should be developed and included this this guideline. **Coeliac disease (1.2.111)** NG18 refers to NG20 for recommendations for screening for coeliac disease. The evidence for this is not up-to-date and NG18 should therefore be reviewed and amended to be in line with ISPAD and ADA guidelines which are widely accepted internationally.	In relation to recommendation 1.2.80 which recommends that as symptoms of mild to moderate hypoglycaemia in children and young people with type 1 diabetes improves or normoglycaemia is restored 'give oral complex long acting carbohydrate to maintain blood glucose levels, unless the child or young person is about to have a snack or meal or receiving a continuous subcutaneous insulin infusion'. This already addresses your response on long-acting carbohydrate not being required if a child or young person is using an insulin pump. **Monitoring of complications (1.2.110)** Please note that the recommendations 1.2.110- 1.2.114 on Monitoring for complications and associated conditions of type 1 diabetes only recommend review from age 12 years for diabetic retinopathy (as recommended by the NHS Diabetic Eye Screening Programme), moderately increased albuminuria for diabetic kidney disease, and hypertension, for other complications and associated conditions a specific age is not provided. Recommendations for treatment of complications is beyond the scope of NICE guideline NG18, and where existing NICE guidelines exist, these have been cross-referenced. This will not be an area proposed for update. **Coeliac disease (1.2.111)** Thank you for your comments on coeliac disease, these will be logged for consideration when NICE guideline NG20 has a surveillance review. **Insulin pumps (1.2.19)** Thank you for your comment on recommendation 1.2.19 on offering 'children and young people with type 1 diabetes multiple daily

		ISPAD Consensus Guidelines (2018) https://cdn.ymaws.com/www.ispad.org/resource/resmgr/consensus_guidelines_2018_/19.other_complications_and_a.pdf American Diabetes Association (2018) Children and Adolescents: Standards of medical care in diabetes http://care.diabetesjournals.org/content/41/Supplement_1/S126 **Insulin pumps (1.2.19)** NG18 (1.2.19) should be reviewed and updated to recognise the benefit of insulin pumps with predicted low glucose suspend and hybrid closed loop systems. NG18 should be amended to be in line with the internationally recognised and accepted ISPAD consensus guidelines. ISPAD Consensus Guidelines (2018) https://cdn.ymaws.com/www.ispad.org/resource/resmgr/consensus_guidelines_2018_/21.diabetes_technologies.pdf **Effect of hypo- and hyperglycaemia on cognition (1.2.86)** The guideline should be reviewed in light of clear evidence demonstrating that hyperglycaemia, as well as hypoglycaemia, can cause cognitive impairment. The ADA has developed recommendations in this area that we suggest could be used to review and update NG18.	injection basal–bolus insulin regimens from diagnosis. If a multiple daily injection regimen is not appropriate for a child or young person with type 1 diabetes, consider continuous subcutaneous insulin infusion (CSII or insulin pump) therapy as recommended in continuous subcutaneous insulin infusion for the treatment of diabetes mellitus (NICE technology appraisal guidance 151)'. In relation to the comment that the benefits of insulin pumps with predicted low glucose suspend and hybrid closed loop systems should be recognised, recommendation 1.2.30 advises that if a child or young person with T1D does not have optimal blood glucose control, that if necessary, they can be offered an alternative insulin regimen, including an insulin pump. In relation to the consensus guidelines from ISPAD, it notes that 'Commercial availability of automated insulin delivery systems is currently limited, but patient access to these systems is anticipated to improve in the near future.' None of the evidence on hybrid closed loop systems referenced in the ISPAD guideline would meet inclusion for the surveillance review, with the RCTs that were in populations under the age of 18 years old with type 1 diabetes, having small sample sizes, however these studies were authored by Tauschmann and colleagues, who also published the results of a larger RCT which was included in the surveillance review (Tauschmann, M., et al., Closed-loop insulin delivery in suboptimally controlled type 1 diabetes: a multicentre, 12-week randomised trial. Lancet, 2018. **392**(10155): p. 1321-1329). While the study reported that the hybrid closed-loop therapy led to significant improvements in glucose control and reduced the risk of hypoglycaemia compared to sensor-augmented pump therapy in children with sub-optimally controlled type 1 diabetes, the evidence base remains limited and further evidence from larger RCTs would be required in order to consider whether this should be

		Cameron F.J. The impact of diabetes on brain function in childhood and adolescence. Paediatric Clinic North Am 2015;**62**:911–927 American Diabetes Association (2018) Children and Adolescents: Standards of medical care in diabetes http://care.diabetesjournals.org/content/41/Supplement_1/S126 **Mental health (1.2.94)** There is evidence to support further detail and recommendations being added to NG18 around mental health. Recommendations around screening for emotional distress and mental health problems in children and young people should be reviewed and the guideline updated accordingly. American Diabetes Association (2019) Children and adolescents: Standards of Medical Care http://care.diabetesjournals.org/content/42/Supplement_1/S148 There is currently no specific mention of insulin omission for weight loss (diabulimia) in NG18. Risk factors and signs that may indicate diabulimia should be reviewed and this guideline should include clear recommendations on this condition. It is not sufficient to refer to NG69: Eating Disorders as this specific 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-	an area for update. It should also be noted that both MiniMed 640G system with SmartGuard for managing blood glucose levels in people with type 1 diabetes and 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) are in the Diabetes in Children and Young people interactive NICE pathway. **Effect of hypo- and hyperglycaemia on cognition (1.2.86)** The guideline development committee for NICE guideline NG18 recognised that fluctuations in glycaemic control may cause cognitive impairment in children and young people with type 1 diabetes (see section 10.5 cognitive disorders in the full guideline for further details) and recommendation 1.2.86 highlights that diabetes teams should consider referring children and young people with type 1 diabetes who have frequent hypoglycaemia and/or recurrent seizures for assessment of cognitive function, particularly if these occur at a young age. The evidence you have highlighted is not sufficient to trigger an update and as no other relevant new evidence was identified during the surveillance review, this will not be an area for update. **Mental health (1.2.94)** In relation to adding further details around mental health, NICE guideline NG18 provides a comprehensive set of recommendations on psychological and social issues in children and young people with type 1 diabetes (recommendations 1.2.94- 1.2.109) and with type 2 diabetes (recommendations 1.3.33- 1.3.42). In the absence of evidence that meets the surveillance review inclusion criteria, this will not be considered as an area for update.

		10/Diabulimia%20Position%20Statement%202018.pdf?_ga=2.152365177.1302772124.1540908607-1362513958.1522313951&_gac=1.161746510.1537347373.CjwKCAjw54fdBRBbEiwAW28S9sPmrJFbmQVXImzZKihBxKU_NWOOnhvD2WWULL6G1Ur-O45HVfYZqBoCv3IQAvD_BwE **Medication – Type 2 diabetes** NG18 currently recommends only metformin as treatment for Type 2 diabetes. However, there is strong evidence to support the fact that children and young people with Type 2 diabetes fail to meet glycaemic targets within an average of 11 months on metformin alone. Commonly they are then prescribed insulin, but this is not mentioned in NG18. There is also new evidence to suggest that liraglutide improves glycaemic management in adolescents. Given the poor outcomes of children and young people with Type 2 diabetes, it is vital that the issue of medication is thoroughly researched, that new evidence is reviewed and recommendations made accordingly. American Diabetes Association (2018) Children and adolescents: Standards of Medical Care http://care.diabetesjournals.org/content/41/Supplement_1/S126 Copeland K C et al. (2011) TODAY Study Group. Characteristics of adolescents and youth with	We recognise the importance of 'diabulimia' and this is highlighted in Recommendation 1.2.107 which states that 'Diabetes teams should be aware that children and young people with type 1 diabetes, in particular young women, have an increased risk of eating disorders. For more guidance on assessing and managing eating disorders, see the NICE guideline on eating disorders.' Eating disorders: recognition and treatment NICE guideline NG69 does provide a set of diabetes-specific recommendations (recommendations 1.8.3-1.8.11) and is therefore well placed in dealing with this. **Medication – Type 2 diabetes** Thank you for your comments concerning the use of insulin in children with type 2 diabetes, due to the lack of RCT-level evidence exploring the effectiveness of insulin in this population, this can not currently be considered as an area for update. Please note that liraglutide is not currently licenced for use in children and so evidence on this medication is not being considered. All reports published on the TODAY trial that met the surveillance review inclusion criteria have been included. **Surgery for children and young people with Type 2 diabetes (1.3.31)** Thank you for your comments on surgery, it is however beyond the scope of NICE guideline NG18 to provide detailed recommendations on surgery. Please note that NICE guideline CG189 on Obesity: identification, assessment and management includes a set of recommendations on bariatric surgery, including considerations of its use in children (recommendations 1.10.12-1.10.17).

		recent-onset type 2 diabetes: the TODAY cohort at baseline. J Clin Endocrinol Metab:159–167 Arslanian S et. al. (2018) Evaluation and management of youth-onset type 2 diabetes: a position statement by the American Diabetes Association. Diabetes Care **41**:2648–2668 Tamborlane W.V (2019) Liraglutide in Children and Adolescents with Type 2 Diabetes. DOI: 10.1056/NEJMoa1903822 **Surgery for children and young people with Type 2 diabetes (1.3.31)** NG18 currently provides very limited recommendations on metabolic surgery for adolescents with Type 2 diabetes. The evidence in this area should be reviewed and guidelines on criteria for metabolic surgery or signposting to existing NICE guidelines should be included. American Diabetes Association (2019) Children and adolescents: Standards of Medical Care http://care.diabetesjournals.org/content/42/Supplement_1/S148 **Monitoring for complications and associated conditions of Type 2 diabetes (1.3.43)** NG18 currently provides little in recommendations for screening for complications when compared to guidelines from the ADA and ISPAD. Given the poor outcomes for children and young people with Type 2 diabetes, the	**Monitoring for complications and associated conditions of Type 2 diabetes (1.3.43)** Recommendations on monitoring for dyslipidaemia, hypertension, albuminuria (kidney disease) and retinopathy are included in NICE guideline NG18. In the absence of RCT level evidence on the treatment of these conditions in children with type 1 or type 2 diabetes, this will not be considered as an area for update. Please note that there is an existing NICE guideline on Renal replacement therapy and conservative management (NICE guideline NG107) which does include populations under the age of 18 years old with chronic kidney disease stages 4 and 5.

		incidence of co-morbidities and the faster progression to complications, it is essential that NICE reviews the evidence in this area and provides robust recommendations. NG18 should also develop recommendations regarding treating complications and co-morbidities in children and adolescents with Type 2 diabetes. Recommendations for treatment of dyslipidaemia, hypertension, albuminuria, and retinopathy should be included. American Diabetes Association (2018) Children and Adolescents: Standards of medical care in diabetes http://care.diabetesjournals.org/content/41/Supplement_1/S126 ISPAD Clinical Practice Consensus Guidelines (2018): Type 2 diabetes mellitus in youth https://cdn.ymaws.com/www.ispad.org/resource/resmgr/consensus_guidelines_2018_/3.type_2_diabetes_mellitus_i.pdf ISPAD Consensus Guidelines (2018) https://cdn.ymaws.com/www.ispad.org/resource/resmgr/consensus_guidelines_2018_/18.microvascular_and_macrova.pdf	
Do you have any comments on equalities issues?			
Stakeholder	**Overall response**	**Comments**	**NICE response**

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Sheffield Teaching Hospital NHS Foundation Trust	Yes	Those patients from more deprived areas are less likely to receive FGM or CGM unless you make a specific recommendation that both should be considered for all children, and then CCGs can set aside funds to cope with increased demand.	Thank you for your comment. The guideline highlights that children and young people with type 1 diabetes should be offered a choice of equipment for monitoring capillary blood glucose (recommendations 1.2.58-1.2.64). Consideration of the use of flash glucose monitors for children will be included as an area proposed for update in NICE guideline NG18.
Association of Children's Diabetes Clinicians	No	No comments provided	Thank you for your response.
Optical Confederation	No	No comments provided	Thank you for your response.
Institute of Child Health	Yes	There is emerging evidence that attendance to eye screening is lower in children and young people from socio-economic deprived areas.1 Special attention to these children is required.	Thank you for your comment. Measures to improve attendance for diabetic eye screening is an area for update. We will share the reference with the developers of the NICE guideline NG18 update.
Coeliac UK	No	No comments provided	Thank you for your response.
British Dental Association	No	No comments provided	Thank you for your response.
Digital Diabetes Media Ltd	No	No comments provided	Thank you for your response.

JDRF, the type 1 diabetes research charity	No	No comments provided	Thank you for your response.
Abbott Diabetes Care	No	No comments provided	Thank you for your response.
Royal Devon and Exeter NHS Foundation Trust	No	No comments provided	Thank you for your response.
Novo Nordisk	No	No comments provided	Thank you for your response.
The Royal College of Ophthalmologists	Yes	There is emerging evidence that attendance to eye screening is lower in children and young people from socio-economic deprived areas.1 Special attention to these children is required.	Thank you for your comment. Measures to improve attendance for diabetic eye screening is an area for update. We will share the reference with the developers of the NICE guideline NG18 update.
UCL Eastman Dental Institute	No	No comments provided	Thank you for your response.
Children and Young People's Wales Diabetes Network	No	No comments provided	Thank you for your response.
MedTech Europe	No	No comments provided	Thank you for your response.

Royal College of Psychiatrists (RCPsych)	Yes	As delineated above the guidelines need to create equality in their emphasis on physical health management in parity to mental health assessment and management	Thank you for your comment. As discussed in response to your previous comments, NICE guideline NG18 has a set of recommendations that address mental health assessment and management in children and young people with diabetes. There is no indication in the guideline that physical health is more important than mental health.
Association for Clinical Biochemistry and Laboratory Medicine	No	No comments provided	Thank you for your response.
Imperial College Health Care NHS Trust – St Mary's Hospital	No	No comments provided	Thank you for your response.
Perspectum Diagnostics	No	No comments provided	Thank you for your response.
Medtronic Ltd	No	No comments provided	Thank you for your response.
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 response. As discussed above, real time continuous glucose monitoring is not out of scope for NICE guideline NG18 and the guideline recommends offering a choice of equipment in order to optimise blood glucose control which includes real-time continuous glucose monitoring with alarms to children and young people with T1D who have frequent severe hypoglycaemia, or impaired awareness of hypoglycaemia associated with adverse or an inability to recognise,

			or communicate about, symptoms of hypoglycaemia (recommendation 1.2.62); and recommends considering ongoing real-time continuous glucose monitoring for neonates, infants and pre-school children, children and young people who undertake high levels of physical activity, children and young people who have comorbidities or are receiving treatments that can make blood glucose control difficult (recommendation 1.2.63). The sections on 'Insulin therapy for children and young people with type 1 diabetes' and 'Blood glucose targets and monitoring' in the surveillance review Appendix A3 describes the evidence that we identified in relation to continuous glucose monitoring, findings of which support the content of the current recommendations and will therefore not be considered as an area for update.
Royal College of Nursing	Not answered	No comments provided	Thank you.
Royal College of Paediatrics and Child Health	No	No comments provided	Thank you for your response.
Association of British Clinical Diabetologists	No	No comments provided	Thank you for your response.
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 responses to DTN and ABCD for information.

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Children and Young People's NE and N Cumbria Diabetes Network	No	Equity of access to technologies Include awareness of cultural differences and sexual orientations of children and young people	Thank you for your comments. When NICE guideline NG18 is updated an equality impact assessment will be completed which considers equality in relation to groups sharing the characteristics protected by the Equality Act (2010) and health inequalities arising from socioeconomic factors or associated with the shared circumstances, behaviours or conditions of particular groups. Identifying such groups is an aspect of NICE's compliance with both general public law requirements to act fairly and reasonably, and human rights obligations.
Diabetes UK	Yes	Language throughout the whole of NG18 should be amended to reflect the NHS England position statement 'Language Matters'. This should help to ensure that all children living with 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.

References from Institute of Child Health

1. Ibanez-Bruron MC, Solebo AL, Cumberland PM, Rahi JS. 020: Diabetic eye screening uptake in children and young people in England. The Royal College of Ophthalmologists Annual Congress 2018; Liverpool, 2018. PAPER IN PRESS

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2. Ibanez-Bruron MC, Solebo AL, Cumberland PM, Rahi JS. 016: Sight-threatening diabetic eye disease in children and young people in the UK. The Royal College of Ophthalmologists Annual Congress; Liverpool, 2017. PAPER IN PRESS
3. Uspal NG, Schapiro ES. Cataracts as the initial manifestation of type 1 diabetes mellitus. Pediatr Emerg Care. 2011;27(2):132-4.
4. Iafusco D, Prisco F, Romano MR, Dell'omo R, Libondi T, Costagliola C. Acute juvenile cataract in newly diagnosed type 1 diabetic patients: a description of six cases. Pediatr Diabetes. 2011;12(7):642-8.
5. Ibanez-Bruron MC, Solebo AL, Cumberland PM, Rahi JS, Diabetic Eye Disease in Childhood Study g. Screening for diabetic retinopathy in children and young people in the UK: potential gaps in ascertainment of those at risk. Diabet Med. 2017;34(7):1012-3.
6. Ibanez-Bruron MC, Solebo AL, Cumberland PM, Rahi JS. How well integrated is the ophthalmic care for children and young people living with diabetes in England? 27th Meeting of the European Association for the Study of Diabetes Eye Complications Study Group (EASDec); Budapest 2017.

References from JDRF, the type 1 diabetes research charity

[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] 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; Gil-Poch et al; Oct 2018 https://www.liebertpub.com/doi/10.1089/dia.2018.0199