Type 1 diabetes in adults: diagnosis and management (update) – insulin

Consultation on draft guideline - Stakeholder comments table
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Association of British Clinical Diabetologists	General	General	General	With no head to head of Degludec vs U300 in those with T1, from the available data I am not sure the differences are that stark and the evidence in the NMA is rated as low. In practice I find both U300 and degludec good options for those with high overnight variability or those who don't want a BD insulin or those in whom OD glargine runs out. These issues are sadly overlooked in treat to target trials. We published an analysis of the approach of NICE (see attached) which also raises some questions. When detemir was the comparator (as it should be given this is now standard therapy not NPH) there were no significant differences in HbA1c. This brings me back to the real world experience - where clinicians should be able to individualise based on the person in front of them.	Thank you for your comment. As highlighted, we are in agreement - no head-to-head studies were identified that compared degludec (100 units/ml) with glargine (300 units/ml). NMA results also did not identify a significant difference between glargine (300 units/ml) and other long-acting insulins for outcomes change in HbA1c, all hypoglycaemia, severe and nocturnal hypoglycaemia. Based on the findings, specific recommendations on the use of glargine (300 units/ml) were not made. The evidence did show that there was a lower proportion of nocturnal hypoglycaemic events with degludec (100 units/ml) compared to other long-acting insulins. The results of the economic modelling also showed that, when hypoglycaemia was included, degludec (100 units/ml) was consistently more cost-effective than glargine (300 units/ml). Based on this evidence, the committee recommended that degludec (100 units/ml) should be considered as an alternative basal insulin therapy if there is a particular concern about nocturnal hypoglycaemia. Additionally, recommendation 1.7.8 allows further flexibility in identifying an alternative suitable insulin regimen in situations where the regimens outlined in recommendations 1.7.3 and 1.7.4 do not meet agreed treatment goals.
Association of British Clinical Diabetologists	General	General	General	We actually use quite a lot of degludec, using it in those who despite ++ input still have sub optimal control and don't fancy bd…..most of our lot seem to	Thank you for your comment and feeding back experience from your clinical practice.

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				live in constant chaos (especially those in transition clinic)!	
Association of British Clinical Diabetologists	General	General	General	Offer people twice daily Levemir as their first choice, allowing people to make adjustments for exercise and alcohol as per principles of structured edcaiton Alternative should be Toujeo or Degludec as both are once daily and have shown lower hypoglycaemia rates than lantus alone. Consider concentrated insulins such as Insulin Toujeo or degludec 200 for those needing > 40 units of basal insulin / day.	Thank you for your comment. Recommendations on dietary advice and physical activity are covered in sections 1.4 and 1.5 of the guideline. Also, the recommendations state that deguldec (100 units/ml) should be considered if there is a particular concern about nocturnal hypoglycaemia. It is also stated that once-daily insulin such as degludec (100 units/ml) should be considered for people who need help from a carer or healthcare professional to administer injections. Recommendations further state that other basal insulin regimens for adults with type 1 diabetes can be considered if the regimens in recommendations 1.7.3 and 1.7.4 do not meet the agreed treatment goals. Additionally, only studies comparing degludec (200 units/ml) and glargine (300 units/ml) were identified. However, as the follow up time in these studies was less than 4 weeks, these studies were not included in the network meta-analysis. Due to this, recommendation on degludec (200 units/ml) could not be made. Furthermore, NMA results did not identify a significant difference between glargine (300 units/ml) and other long-acting insulins for outcomes change in HbA1c, all hypoglycaemia, severe and nocturnal hypoglycaemia. Based on the findings, specific recommendations on the use of glargine (300 units/ml) were not made.

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Association of British Clinical Diabetologists	General	General	General	Similar guidance regarding BD basal insulin use has not been produced by NICE for managing children and young people with diabetes. Our local service, for example, uses a single basal insulin dose and so patients are taking this at transition to the adult service. The is no evidence to support a transfer to a BD basal insulin regime at the age of eighteen years and so diabetes services should not be encouraged to do this by NICE. Furthermore, there is no evidence of statistical superiority of BD levemir insulin over modern once daily basal regimens, as illustrated by Bain et al (ref). So the suggestion that people with type 1 diabetes must express a 'strong preference for once-daily basal injections' is unwarranted and at-odds with patient choice. The suggestion that clinicians should routinely discuss a change in basal insulin when a less expensive biosimilar is available, indicates a lack of understanding of the work pressures in adult diabetes services. NICE should also be aware that in Wales the first biosimilar glargine insulin is now (slightly) more expensive that the original molecule; should patients be switched back? Reference: Bain SC, Feher M, Fisher M, Hex N, Lee KCS, Mahon J, Russell-Jones D, Schou H, Wilmot EG, Baxter M. A review of the NG17 recommendations for the use of basal insulin in type 1 diabetes. Diabet Med. 2020 Feb;37(2):219-228. doi:	Thank you for your comment. While the recommendation is not specific to those transitioning from paediatric care to adult services, recommendation 1.7.4 does state that an insulin regimen that is already being used by the person can be considered if it is meeting their agreed target goals (such as meeting their HbA1c targets or time in glucose range and minimising hypoglycaemia). Thank you for providing reference to Bains 2020. This review was based on the NMA conducted as part of the 2015 update and does not take into consideration the analysis conducted as part of the new update. As part of this new update, we conducted NMAs for the following outcomes: • Change in HbA1c • All hypoglycaemic events • Severe/major hypoglycaemic events • Probability that an event is nocturnal given a patient had an event. As highlighted in section 1.1.12 of the evidence review, the results from the change in HbA1c NMA could not differentiate between the different long-acting insulins and uncertainty with the evidence was also identified. However, NMAs conducted for hypoglycaemic events did highlight that there were fewer severe and nocturnal hypoglycaemic events with insulin detemir compared with NPH. Detemir twice daily was also found to be the most cost-effective treatment strategy in the economic analysis.

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				10.1111/dme.14180. Epub 2019 Nov 27. PMID: 31729775; PMCID: PMC7004078.	Recommendation on switching to biosimilars, highlights that the possibility of switching can be discussed and stresses the importance of shared decision making. The rationale and impact section has been amended to state that this discussion could take place at the person's routine review. Additionally, the rationale and impact section highlights that cost is not the only important element in decision making. The committee noted that switching should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. The committee noted the point that in some circumstances the originator product may be cheaper than subsequent biosimilars and agreed that is such circumstance it would be appropriate to use the originator product.
Association of British Clinical Diabetologists	General	General	General	My opinion is as follows:- • It's good that NICE is giving advice on long acting insulin analogue use for T1DM and highlighting situations when it might be better to consider a long acting analogue rather than twice daily levemir. • I think NICE should consider stating that twice daily levemir is a good choice in patients who exercise, particularly later in the day, or who are consuming alcohol in the evening as it allows them to reduce their evening	Thank you for your comment. As evidence was not identified which included this cohort of patients, the committee did not think it was appropriate to draft specific recommendations. However, this has been added to the committee discussion section in the evidence review.

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				background insulin dose, to reduce the risk of nocturnal hypoglycaemia, which isn't possible with longer acting insulin analogues particularly insulin degludec. Whilst it is often more convenient for patients with T1DM to take once daily background insulin it may not give them flexibility around their lifestyle. Perhaps it should be stated that this cohort of patients would not be best served with a long acting insulin analogue.	
Association of British Clinical Diabetologists	Guideline	019	020	1.7.4 – we use degludec rarely – and we limit it to those at risk of nocturnal hypos (the minority of our use), but have actually found it most useful for admission avoidance – in those (few people) who have erratic and chaotic lives for whatever reason who come in with DKA very regularly, we use degludec and have seen a significant reduction in admissions as a result.	Thank you for your comment. Recommendations state that degludec (100 units/ml) can be considered if there is a particular concern about nocturnal hypoglycaemia. Additionally, DKA was an outcome of interest identified at review protocol stage however no evidence was for this outcome. Additionally, no studies were identified in people with frequent DKA admissions. Therefore, specific recommendations could not be drafted. However, the committee did note that this was an important issue that needs to be taken into consideration. Therefore, recommendation 1.7.8 has been amended to state that DKA and adherence should also be taken into consideration when considering other basal insulin regimens for adults with type 1 diabetes only if the regimens in rec 1.7.3 and 1.7.4 do not meet their agreed treatment goals. Further discussion has also been added to section 1.1.12 of the evidence review.

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BAME Health Collaborative	Comments form	Q1	Q1	**Which areas will have the biggest impact on practice and be challenging to implement?** Clinician-related challenges • Understanding traditions • Dietary consumptions in respect to European food calorie and nutritional needs Patient-related challenges. • Individual Patient-related challenges (pyscho-social) • Taboos and fears Health care system-related challenge • Culturally targeted approach to diagnosis and management	Thank you for your comment. Your comment will be considered by NICE's Implementation team where relevant support activity is being planned.
BAME Health Collaborative	Comments form	Q2	Q2	**Please say for whom and why.** Patient, all healthcare professionals, Public health and the Commissioners	Thank you for your comment. Your comment will be considered by NICE's Implementation team where relevant support activity is being planned**.**
BAME Health Collaborative	Comments form	Q3	Q3	**Would implementation of any of the draft recommendations have significant cost implications?** No because as noted in page 45 no 6 (Why the committee made the recommendation) BHC support the valuable cost comparison because the patient had positive clinical outcomes.	Thank you for your comment. Your comment will be considered by NICE's Implementation team where relevant support activity is being planned**.**
BAME Health Collaborative	Comments form	Q4	Q4	**What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)**	Thank you for your comment. Your comment will be considered by NICE's Implementation team where relevant support activity is being planned.

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				• Psychological barriers to insulin use (sexuality, professional work-life balance, and privacy issues) • Training developing culturally informed diabetes educators to work within the community. • Encouraging and supporting parents of young children with diabetes are usually highly involved in their child's diabetes management.	
BAME Health Collaborative	Comments form	Q5	Q5	**The recommendations in this guideline were largely developed before the coronavirus pandemic. Please tell us if there are any particular issues relating to COVID-19 that we should take into account when finalising the guideline for publication.** BHC recognises that COVID-19 has amplified the need why this guideline is a necessity. The involvement of community leaders and organisations (religious leaders, ethnic representatives etc) is fundamental in the success of any rollout plan. Lead to increase employability of the community which would reduce the overall cost.	Thank you for your comment. Your comment will be considered by NICE's Implementation team where relevant support activity is being planned.
BAME Health Collaborative	Guideline	019	006	We are concerned that this recommendation may not inform the relevant clinicians in the patient pathway; the need to increase transparency throughout the insulin supply chain and several other interventions are important steps toward developing viable, long-term solutions to improve insulin access and affordability.	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess

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					hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope
British Society of Rehabilitation Medicine	Guideline	039	002 - 004	Diabetic foot problems – *The BSRM recommend liaison with the local amputee rehabilitation team if amputation is considered, for pre-amputation consultation and early access of rehabilitation, to optimise the individual's potential and reduce dependency*	Thank you for your comment. Recommendations on diabetic foot problems were outside the scope of this update.
Chelsea & Westminster Hospital NHS Foundation Trust	Guideline	017	011	On targeting blood glucose levels in patients with type 1 diabetes it is important to take into consideration the patient's comorbid conditions and frailty status. For example, with moderate to severe frailty a pre-meal target as low as 4.0 mmol/L can be harmful and a higher target is proposed in international recommendations (https://www.diabetes.org.uk/resources-s3/2019-05/Clinical%20Guideline%20for%20Type%201%20Diabetes%20for%20Older%20Adults%20-%20April%202019.pdf).	Thank you for your comment. Blood glucose targets was outside the remit of the review question and was not prioritised for an update at scoping.
Chelsea & Westminster Hospital NHS Foundation Trust	Guideline	017	011	Taking into consideration that over 20% of patients in the UK are using interstitial glucose monitoring and international guidance advising on targeting a range of continuous glucose data (3.9-10.0 mmol/L) and a Time in Range depending on risk of hypoglycaemia and pregnancy status (Battelino et al. Diabetes Care. 2019 Aug;42(8):1593-1603. doi: 10.2337/dci19-0028.	Thank you for your comment. Blood glucose targets was outside the remit of the review question and was not prioritised for an update at scoping.

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				Epub 2019 Jun 8), including a recommended time in range based on interstitial glucose measurements in the Type 1 NICE guidance is likely to be relevant and timely.	
Chelsea & Westminster Hospital NHS Foundation Trust	Guideline	017	011	It will be important to ensure that biosimilar insulins have no immunogenicity or potency differences from the originator products.	Thank you for your comment. The NICE position statement on biosimilars (originally developed for the NICE technology appraisal process to applicable to guidelines as well) states that once a biosimilar is licensed, they are assumed to only differ from the originator in terms of price. The committee agree it is important to check all these aspects when making the original determination that a biosimilar is "equivalent" but noted this was something that was not within the remit of NICE, but rather part of the licensing process for biosimilars.
Chelsea & Westminster Hospital NHS Foundation Trust	Guideline	018	006	The guidance does not make reference to intermittent interstitial glucose monitoring with the use of freestyle libre, a device that is currently used for glucose monitoring by 20-30 % of patients living with type 1 diabetes in the UK (https://www.england.nhs.uk/2019/10/tens-of-thousands-given-life-changing-diabetes-monitors-thanks-to-the-nhs-long-term-plan/). There are specific criteria on prescribing the freestyle libre on the NHS, and as over 1 in 5 patients are currently using flash glucose monitoring, reference to the criteria to consider a prescription is we believe relevant.	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope

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Chelsea & Westminster Hospital NHS Foundation Trust	Guideline	019	018 - 022	Patient centred care should we believe be at the heart of the insulin preparation choice. Whereas detemir twice daily in a patient who has received structured education on flexible insulin management and who is able to make dose adjustments is the gold standard, there are patients who are either unable to self-adjust their doses, or are unlikely to adhere to twice daily basal insulin. In these patients adhering to a blanket recommendation of twice daily detemir and then change the basal preparation once patients do not achieve their glycaemic goals may introduce delays and risk deterioration in glycaemia. There are other individual patient characteristics (frailty, comorbidities, such as chronic kidney disease), that can increase the risk of hypoglycaemia, which also need to be taken into consideration when making a choice of basal insulin. Lastly, the network meta-analysis methodology used to assess the efficacy of insulin preparations has been challenged by Bain S et al. (Diabetic Medicine. 2020 Feb;37(2):219-228. doi: 10.1111/dme.14180. Epub 2019 Nov 27). In this review the authors showed no significant differences in HbA_{1c} reduction between twice-daily detemir and other basal analogue insulin comparators in efficacy trials, and a wide variation in HbA_{1c} which undermines the statistical robustness, suggesting that with the lack of differentiating evidence to support twice-daily detemir as the basal insulin of choice for type 1 diabetes, selection of basal insulin should be personalized to individual needs.	Thank you for your comment. As highlighted in the rationale and impact section, the clinical evidence showed that there were fewer severe and nocturnal hypoglycaemic events with insulin detemir twice daily. Economic analysis identified detemir twice daily as the most cost-effective treatment strategy. Based on this evidence and their clinical expertise, the committee recommended twice-daily insulin detemir as basal insulin therapy for adults with type 1 diabetes. As highlighted in section 1.1.12, people with renal impairment were identified as a key subgroup by the committee and while no studies were identified which included evidence on this group, the committee stated that renal impairment should be taken into consideration along with other comorbidities such as age, frailty, hypoglycaemic unawareness when considering basal insulins. Other basal insulin regimens may be considered if insulin regiments highlighted in rec 1.7.3 and 1.7.4 do not help meet the agreed treatment targets. When choosing an alternative insulin regimen, person's preferences, comorbidities, risk of hypoglycaemia and the acquisition cost should be taken into account. Thank you for providing reference to Bains 2020. This review was based on the NMA conducted as part of the 2015 update and does not consider analysis conducted as part of the new update.

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					As part of this new update, we conducted NMAs for the following outcomes: • Change in HbA1c • All hypoglycaemic events • Severe/major hypoglycaemic events • Probability that an event is nocturnal given a patient had an event. As highlighted in section 1.1.12 of the evidence review, the results from the change in HbA1c NMA could not differentiate between the different long-acting insulins and uncertainty with the evidence was also identified. However, NMAs conducted for hypoglycaemic events did highlight that there were fewer severe and nocturnal hypoglycaemic events with insulin detemir compared with NPH. Detemir twice daily was also found to be the most cost-effective treatment strategy in the economic analysis.
Coeliac UK	Guideline	029	007	We are pleased to see a cross reference to the NICE guideline on coeliac disease (NG20) to raise awareness on guidance for testing for coeliac disease. However a change is needed to reflect the wide range of symptoms that people with undiagnosed coeliac disease may present with. We are disappointed that this recommendation has not been updated since we highlighted concerns during the 2019 consultation. Recommendation 1.12.1 states that adults with type 1 diabetes with a low BMI or unexplained weight loss should be assessed for coeliac disease. We are concerned that this reinforces an outdated view of coeliac disease; that people with coeliac disease are	Thank you for your comment. Recommendation 1.12.1 has amended and reference to low BMI has been removed. The recommendation does state that for guidance on testing for coeliac disease, to refer to the NICE guidance on coeliac disease. We will also pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date.

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				underweight at diagnosis. In reality, people with coeliac disease are often overweight or obese at diagnosis. A study published in 2012 reviewed records of newly diagnosed coeliac disease patients between 1999 and 2009 and found that only 3% were underweight, 53% were a normal weight, 31% were overweight and 13% were obese [1]. Only testing people with type 1 diabetes when they present with weight loss or a low BMI will miss a diagnosis of coeliac disease in many people. As highlighted within NG20, coeliac disease can present with a range of symptoms including persistent gastrointestinal symptoms, fatigue, persistent mouth ulcers and nutritional deficiencies such as iron, B12 or folate [2]. Weight loss is one symptom that may be seen in some but not all people with undiagnosed coeliac disease. As a minimum, the guideline should be updated to include the recommendation within NG20, to offer serological testing for coeliac disease to people with Type 1 diabetes at diagnosis. People with coeliac disease face unacceptable delays, an average of 13 years from onset of symptoms to diagnosis [2]. This guideline provides an opportunity to provide a more timely diagnosis of coeliac disease for adults with type 1 diabetes. [1] Tucker, E. Rostami, K. Prabhakaran, S. and Al Dulaimi, D. (2012) Patients with Coeliac Disease Are Increasingly Overweight or Obese on Presentation. J Gastrointestin Liver Dis. 2012 Mar;21(1):11-5.	

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				[2] National Institute for Health and Care Excellence, Coeliac disease: recognition, assessment and management (NG20), September 2015 [3] Violato, M. and Gray, A. (2019) "The impact of diagnosis on health-related quality of life in people with coeliac disease: a UK population-based longitudinal perspective," BMC Gastroenterology. Springer Science and Business Media LLC, 19(1). doi: 10.1186/s12876-019-0980-6.	
Dexcom	Guideline	018	006 - 009	While the update to NG17 should reference the DG21 update, it should not be based on it. The update to DG21 will only assess the value of Hybrid closed loop vs Sensor Augmented Pump systems. This assessment will not provide the committee with the appropriate information to make an informed recommendation on rtCGM's place in therapy reflective of the current evidence base. If the update to NG17 is to reflect the current evidence base, NICE will recommend that rtCGM is made available for the following indication. Type 1 diabetics with suboptimal glycaemic control: • HbA1c >58 mmol/mol [>7.5%] • And or Problematic hypoglycaemia It must be noted, at present national funding mechanisms exist for FLASH[1] glucose monitoring and Insulin pumps[2]. While people with type 1 diabetes that require rtCGM to adequately control their glucose, have no access to national and in many cases local funding. The lack of appropriate national guidelines that accurately reflects the current evidence base, results in wide variation in access to rtCGM[4]. As highlighted in the recent Dexcom G6 MIB, only 50% of	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope

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				Dexcom users have their system funded by the NHS, with 50% of people paying for the G6[5]. This leads to access and health outcomes that are driven by economic status and not clinical need, exacerbating health inequalities for people with insulin dependent diabetes. It is imperative that the NG17 update provides clinicians with the ability to prescribe rtCGM to MDI using Type 1 diabetics and to empower the person with diabetes to exercise informed choice regarding their treatment modality. As presented below, the evidence demonstrating the benefits of rtCGM for people with Type 1 diabetes independent of insulin administration modality has grown tremendously since the last guideline update in 2015. This evidence base clearly demonstrates the significant benefits of rtCGM not only for individuals with problematic hypoglycaemia (Hypoglycaemia unawareness, fear of hypoglycaemia), but also for those individual whose control is poor with HbA1c values above recommended target, or for those individuals who present high glycaemic variability. In addition to this the use of rtCGM+ MDI in Type 1 diabetics with an HbA1c ≥7.5% is highly cost effective[6]. If Type 1 Diabetes in adults: diagnosis and management guidelines are to reflect the current evidence base they should recommend that rtCGM is offered to all Type 1 diabetics with an HbA1c ≥ 7.5% or problematic hypoglycaemia.	

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				Significant CGM+MDI publications since 2015 The DIAMOND trial[7], which randomized 158 participants with T1D and mean baseline HbA1c of 70 mmol/mol [8.6%, range 58 to 85 mmol/mol [7.5% to 9.9%] treated with MDI to rtCGM or usual care with SMBG, demonstrated that individuals in the rtCGM group exhibited a 1 percentage point reduction in HbA1c after 6 months while those in the SMBG group demonstrated only a 0.4 percentage point reduction in HbA1c, a significant between-groups difference (P < 0.001). Correspondingly, mean time in range (3.9 to 10.0 mmol/L) increased for those that initiated rtCGM use, from 660 minutes/day to 736 minutes/day after treatment, while it remained steady at 650 minutes/day throughout the trial for those in the SMBG group. The GOLD RCT[9], was is a randomized, open-label, multicenter clinical trial with a crossover design including 161 patients with mean baseline HbA1c of 70 mmol/mol (8.6%). After a run-in period of up to 6 weeks, patients were randomized to receive rtCGM or conventional SMBG for 26 weeks with a 17-week washout between treatment periods. The aim of this study was to analyze the effect of rtCGM on glycemic control, hypoglycemia, well-being, and glycemic variability in individuals with T1DM treated with MDI. The outcome of this analysis demonstrated that rtCGM was associated with a 0.43% reduction in HbA1c vs conventional treatment. Interestingly HbA1c was lower in rtCGM-treated patients during both the first and second treatment periods clearly demonstrating the	

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				superiority of rtCGM. Daytime hypoglycemia was also significantly reduced by rtCGM compared with SMBG for both glucose levels evaluated. Time with daytime glucose levels below 70 mg/dL was reduced by 40% and for glucose levels <54 mg/dL by 54%. Overall hypoglycemia confidence was greater at the end of the rtCGM period than at the end of the SMBG period, 3.40 (95% CI 3.32-3.47) versus 3.27 (95% CI 3.18-3.35). rtCGM use was associated with greater confidence than SMBG use in being able to avoid serious problems due to hypoglycemia detect and respond to falling glucose levels and thus prevent hypoglycemia, and continue with one's chosen lifestyle activities despite the risk of hypoglycemia. In addition, rtCGM use was linked to greater confidence in social situations. Billings et al. (2018)[10] conducted a post-hoc analysis of the DIAMOND trial and investigated whether the previously demonstrated HbA1c reduction was still evident when participants were first stratified by baseline HbA1c. This analysis included 158 people with T1D and a mean baseline HbA1c of 70 mmol/mol [8.6%]. The analysis found that the change in HbA1c was significantly greater among participants in the rtCGM group compared to SMBG group at all predefined HbA1c thresholds at 12 and 24 weeks. Reductions in HbA1c ranged in magnitude from 1.0% to 1.4%. The evidence clearly demonstrates that rtCGM therapy improves glycemia for people with poorly controlled diabetes (HbA1c ≥58 mmol/mol (7.5%)). Importantly, the improvements seen in	

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				patients with high baseline HbA1c levels were achieved without the need for additional medications and their associated costs. Ruedy et al. (2017)[11] conducted a separate analysis of adults ≥60 years of age who completed the DIAMOND trial and found that HbA1c reductions were greater in the group assigned to CGM than in the control group. They additionally reported that CGM usage was high and concluded that CGM should be considered for older adults with diabetes using MDI. The results from the first phase of the DIAMOND trial[7] were consistent with those of the GOLD randomized controlled clinical trial[9], which used a crossover design to determine the difference in HbA1c between rtCGM and SMBG treatment for 161 MDI users with T1D. In this trial, mean baseline HbA1C was also 70 mmol/mol [8.60%]; mean HbA1c was 63 mmol/mol [7.92%] during rtCGM use and 67 mmol/mol [8.35%] during conventional treatment (mean difference, −0.43%; P <0.001). Results from the crossover design of the GOLD trial[9] highlighted that continued access to CGM is necessary to obtain continued benefit. A secondary analysis of data from the GOLD study[12] (Ólafsdóttir et al., 2018) showed the beneficial effects of CGM with respect to glycemic metrics other than HbA1c, as well as improvements in patient-reported outcomes including hypoglycemia confidence.	

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				To assess the impact of rtCGM beyond reducing HbA1c, the HypoDE RCT[13] evaluated whether rtCGM reduces the incidence of hypoglycemic events compared with SMBG in 149 high-risk adults (with a history of IAH or severe hypoglycemia) with T1D treated by MDI compared with SMBG. This RCT clearly demonstrated that rtCGM reduced the incidence of hypoglycemic events by 72% (incidence rate ratio [IRR] 0.28, (95% CI 0.20-0.39), p<0.0001), the incidence of nocturnal hypoglycemic events by 65% (IRR 0.35, (95% CI 0.22-0.56), p<0.0001) and the incidence of severe hypoglycemic events by 64% (IRR 0.36 (95% CI 0.15-0.88), p=0.0247). The HypoDE RCT adds great value to the wide body of evidence on rtCGM. Not only are T1Ds with an impaired awareness to hypoglycaemia regularly excluded from RCTs. Through the use of HypoDE and the numerous studies demonstrating the clinical value of rtCGM in T1Ds with elevated HbA1c. Health care professionals can now match the primary outcome of the various studies (risk of hypoglycaemia or elevated HbA1c) to the clinical indications for rtCGM. The recently completed MILLENIALS[14] study evaluated efficacy and usability of the Dexcom G6 rt-CGM in young people with T1D. The study demonstrated that the G6 reduced Hba1c levels by 0.54% (5.9 ± 8.0 mmol/mol) while in the same period the control group increase HbA1c by 0.24% ± 0.69% (2.6 ± 7.5 mmol/L) (mean difference CGM vs. control; -0.76% [95% CI -1.1 to -0.4] [-8.5 mmol/mol (95% CI -12.4 to -4.6); P <0.001]). Time in target blood glucose	

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				range (defined as 3.9 mmol/L to 10 mmol/L) was significantly higher for Dexcom G6 versus SMBG. The nonrandomised, prospective, real-life study by Šoupal et al[15,16]. was designed to compare the long-term efficacy of four, patient-selected, treatment modalities including sensor-augmented insulin regimens (SAIRs), i.e. sensor-augmented pump (SAP) therapy or rtCGM+MDI, insulin pump therapy alone, or MDI therapy alone in 65 patients with T1D. This study provides data from the longest-term evaluation of the efficacy of rtCGM use. At baseline, the mean HbA1c was 67 mmol/mol [8.3%]. After 52 weeks, the SAIR group had significantly lower HbA1c than baseline (54 vs 67 mmol/mol [7.1% vs 8.3%], P<0.0001). This improvement in HbA1c from study baseline was observed both in the SAP therapy subgroup (54 vs 66 mmol/mol [7.1% vs 8.2%], P=0.0025) and the MDI + rtCGM group (55 vs 69 mmol/mol [7.2% vs 8.5%], P=0.0034) and was superior to the reduction observed with insulin pump therapy alone (63 vs 68 mmol/mol [7.9% vs 8.4%], P<0.05). The reduction in HbA1C was sustained for at least 3 years: after 3 years, mean HbA1c for those in the SAIR group was 53 mmol/mol [7.0%] and was still superior to HbA1c reduction observed during insulin pump use alone (61 mmol/mol [7.7%]). Further, after three years, 48% of those in the SAIR group achieved an HbA1c of <53 mmol/mol [<7%], while only 16% of those using insulin pump therapy alone achieved an HbA1c of <53 mmol/mol [<7%]. In addition to this MDI+CGM was associated with the greatest reduction	

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				in daily SMBG utilisation [3.9 at bassline vs 2.7 at study end] P=0.02). The one-year and three-year findings show rtCGM resulted in sustained improvements in glycaemic control regardless of insulin delivery method. To support this growing body of evidence, Mulinacci et at[17] (2019) performed a retrospective analysis of 396 patients with newly-diagnosed T1D and clearly demonstrated that initiating patients on CGM within a year of diagnosis, with or without insulin pump therapy, provided superior and sustained HbA1c benefit compared to insulin pump or MDI therapy alone. At baseline, mean HbA1c did not vary significantly between groups and was ~ 102 mmol/mol [~11.5%]. For 2.5 years of follow-up, the MDI+CGM group had 16.4 mmol/mol [1.5%] lower HbA1c than the MDI-only group (61 vs 77 mmol/mol [7.7% vs. 9.2%,] [P < 0.0001]). The CSII+rtCGM group had an A1c for 2.5 years after diagnosis that was 0.7% lower than the CSII only group (LS mean ± SE A1c 8.0% ± 0.08% vs. 8.7% ± 0.07%, respectively, P< 0.0001). Furthermore, there was not a significant difference in A1c for 2.5 years after diagnosis between the MDI+rtCGM and the CSII+rtCGM users. The number of diabetes-related emergency department visits was also significantly lower among early CGM users compared with non-CGM users (P = 0.003). Because studies have shown that glycaemic control may settle into long-term patterns within the first 5 years after diagnosis, this study supports the notion that early initiation of CGM within 1 year of diagnosis may help to improve long-	

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				term control and reduce long-term complications, irrespective of insulin delivery system. Because the study found MDI+rtCGM users had better glycaemic control compared to CSII without rtCGM, the authors concluded CGM initiation alone, rather than CSII initiation with rtCGM, may be better for newly diagnosed for patients. Starting a patient with rtCGM is much easier than starting CSII during the challenging time of learning to manage diabetes. The G6 Medical Innovation Briefing[5] (MIB) comments that there is a wealth of clinical evidence and presents the results of the UK G6 cost effectiveness analysis (CEA). This CEA analysis was recently published in Diabetes Care, demonstrating the G6 to be a highly cost-effective intervention for people with uncontrolled diabetes (ICER £9,558 / QALY). This shows the G6 falls *55% under* the NICE Willingness to Pay threshold of £20,000 / QALY. "*clinical experts felt that using Dexcom G6 could reduce costs and would benefit the healthcare system. This is because it could improve long-term outcomes, reducing the need for intensive treatment and, in the short term, reducing severe hypoglycaemic events leading to hospital admissions. Remote care may reduce the need for hospital visits." (NICE Dexcom G6 MIB, 2020, p18)* **Key published clinical studies HbA1c, Hypoglycaemia, and Economic** **HbA1c**	

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				• Beck et al., Effect of Continuous Glucose Monitoring on Glycaemic Control in Adults With Type 1 Diabetes Using Insulin Injections The DIAMOND Randomized Clinical Trial. JAMA. 2017;317(4):371-378 • Beck et al., Effect of initiating use of an insulin pump in adults with type 1 diabetes using multiple daily insulin injections and continuous glucose monitoring (DIAMOND): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol. 2017 Sep;5(9):700-708. • Beck RW, Riddlesworth TD, Ruedy K, Ahmann A, Haller S, Kruger D, et al. Continuous Glucose Monitoring Versus Usual Care in Patients With Type 2 Diabetes Receiving Multiple Daily Insulin Injections: A Randomized Trial. Ann Intern Med. 2017;167:365–374.doi: 10.7326/M16-2855 • Ruedy, K. Riddlesworth, TD, Graham C. Continuous glucose monitoring in older adults with type 1 and type 2 diabetes using multiple daily injections of insulin: results from the DIAMOND trial. J Diabetes Sci Technol 2017;11:1138-1146. • Billings et al., Baseline Glycated Hemoglobin Values Predict the Magnitude of Glycemic Improvement in Patients with Type 1 and Type 2 Diabetes: Subgroup Analyses from the DIAMOND Study Program. Diabetes Technol Ther, 2018. 20(8): p. 561-565	

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				• Lind et al., Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: The GOLD randomized clinical trial. JAMA 2017;317(4):379-387 • Mulinacci et al., Glycemic Outcomes with Early Initiation of Continuous Glucose Monitoring System in Recently Diagnosed Patients with Type 1 Diabetes. Diabetes Technol Ther. 2019;21(1):6-10. • Šoupal J, Petruzelkova L, Flekac M, et al. Comparison of Different Treatment Modalities for Type 1 Diabetes, Including Sensor-Augmented Insulin Regimens, in 52 Weeks of Follow-Up: A COMISAIR Study. Diabetes Technol Ther. 2016;18(9):532-538. • Šoupal (2019). Glycemic Outcomes in Adults With T1D Are Impacted More by Continuous Glucose Monitoring Than by Insulin Delivery Method 3 Years of Follow-Up From the COMISAIR Study, DIABETES CARE 2019;43(1)37-43 • Laffel, L., et al. (2020). "Effect of Continuous Glucose Monitoring on Glycemic Control in Adolescents and Young Adults with Type 1 Diabetes." JAMA. 323(23):2388-2396 • Pratley, R., et al. (2020). "Effect of Continuous Glucose Monitoring on Hypoglycemia in Older Adults with Type 1 Diabetes." JAMA. 323(23):2397-2406	

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				• Puhr, S., et al. (2018). "The Effect of Reduced Self-Monitored Blood Glucose Testing After Adoption of Continuous Glucose Monitoring on Hemoglobin A1c and Time in Range." Diabetes Technol Ther 20(8): 557-560. • Thabit et al, Comparison of Dexcom G6 CGM with Self-Monitoring Blood Glucose in Young Adults with Type 1 Diabetes: The Millennial Study, 2020, American Diabetic Association **Hypoglycaemia** • Heinemann, L, Freckmann, G, Ehrmann, D, Faber-Heinemann, G, Guerra, S, Waldenmaier, D, Hermanns, N. Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial. *Lancet* 2018;391:1367-1377 • Riddlesworth T, Price D, Cohen N, Beck RW. Hypoglycemic Event Frequency and The Effect of Continuous Glucose Monitoring in Adults with Type 1 Diabetes Using Multiple Daily Insulin Injections. Diabetes Ther 2017; 8:947-51 • Aleppo G, Ruedy KJ, Riddlesworth TD, Kruger DF, Peters AL, Hirsch I, et al. REPLACE-BG: A randomized trial comparing continuous glucose monitoring with and without routine blood glucose monitoring in	

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				well-controlled adults with type 1 diabetes. *Diabetes Care* 2017; 40:538-45. • Reddy M, Jugnee N, El Laboudi A, Spanudakis E, Anantharaja S, Oliver N: A randomized controlled pilot study of continuous glucose monitoring and flash glucose monitoring in people with Type 1 diabetes and impaired awareness of hypoglycaemia. Diabet Med 2018;20(11):751-757. 2018;20(11):751-757. • Reddy M, Jugnee N, Anantharaja S, BSc, Oliver N, Switching from Flash Glucose Monitoring to Continuous Glucose Monitoring on Hypoglycemia in Adults with Type 1 Diabetes at High Hypoglycemia Risk: The Extension Phase of the I HART CGM Study, 2018, DIABETES TECHNOLOGY & THERAPEUTICS, DOI: 10.1089/dia.2018.0252 • Olafsdottir et al. A Randomized Clinical Trial of the Effect of Continuous Glucose Monitoring on Nocturnal Hypoglycemia, Daytime Hypoglycemia, Glycemic Variability, and Hypoglycemia Confidence in Persons with Type 1 Diabetes Treated with Multiple Daily Insulin Injections (GOLD-3). Diabetes Technology & Therapeutics 2018; DOI: 10.1089/dia.2017.0363 • Giada Acciaroli et al "266-OR: Rebound Hyperglycemia in Real-World Data and Its Mitigation with a CGM-Based Predictive Alert"	

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				presented at American Diabetes Association, 2020 **Economic** • Stéphane Roze, John Isitt, Jayne Smith-Palmer, Mehdi Javanbakht, Peter Lynch, Long-term Cost-Effectiveness of Dexcom G6 Real-Time Continuous Glucose Monitoring Versus Self-Monitoring of Blood Glucose in Patients With Type 1 Diabetes in the U.K. Diabetes Care 2020 Jul; dc192213. • Chaugule S, Oliver N, Klinkenbijl B, Graham C. An Economic Evaluation of Continuous Glucose Monitoring for People with Type 1 Diabetes and Impaired Awareness of Hypoglycaemia within North West London Clinical Commissioning Groups in England. Eur Endocrinol. 2017;13(2):81-5. • Bronstone, A. et al. "The Potential Cost Implications of Averting Severe Hypoglycemic Events Requiring Hospitalization in High-Risk Adults With Type 1 Diabetes Using Real-Time Continuous Glucose Monitoring." J Diabetes Sci Technol (2016) **10**(4): 905-913. • Charleer, S., et al. (2018). "Effect of Continuous Glucose Monitoring on Glycemic Control, Acute Admissions, and Quality of Life: A Real-World Study." J Clin Endocrinol Metab **103**(3): 1224-1232 Reference list	

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				1) Flash Glucose Monitoring: National Arrangements for Funding of Relevant Diabetes Patients, NHS England, 2019 2) Continuous subcutaneous insulin infusion for the treatment of diabetes mellitus, TA151, NICE, 2008 3) National Diabetes Insulin Pump Audit (2017-2018) NHS England and Wales, NHS Digital 2019. (https://digital.nhs.uk/data-and-information/publications/statistical/national-diabetes-audit/national-diabetes-audit---insulin-pump-report-2017-18) 4) Perera, R., Oliver, N., Wilmot, E., & Marriott, C. (2018). *Variations in access to and reimbursement for continuous glucose monitoring systems for people living with Type 1 diabetes across England. Diabetic Medicine.* doi:10.1111/dme.13766 5) National Institute for Health and Care Excellence, Dexcom G6 for real-time continuous glucose monitoring, Medtech innovation briefing [MIB233] Published date: 03 November 2020 6) Stéphane Roze, John Isitt, Jayne Smith-Palmer, Mehdi Javanbakht, Peter Lynch, Long-term Cost-Effectiveness of Dexcom G6 Real-Time Continuous Glucose Monitoring Versus Self-Monitoring of Blood Glucose in Patients With Type 1 Diabetes in the U.K. Diabetes Care 2020 Jul; dc192213	

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				7) Beck et al., Effect of Continuous Glucose Monitoring on Glycaemic Control in Adults With Type 1 Diabetes Using Insulin Injections The DIAMOND Randomized Clinical Trial. JAMA. 2017;317(4):371-378 8) Beck et al., Effect of initiating use of an insulin pump in adults with type 1 diabetes using multiple daily insulin injections and continuous glucose monitoring (DIAMOND): a multicentre, randomised controlled trial. Lancet Diabetes Endocrinol. 2017 Sep;5(9):700-708. 9) Lind et al., Continuous glucose monitoring vs conventional therapy for glycemic control in adults with type 1 diabetes treated with multiple daily insulin injections: The GOLD randomized clinical trial. JAMA 2017;317(4):379-387 10) Billings et al., Baseline Glycated Hemoglobin Values Predict the Magnitude of Glycemic Improvement in Patients with Type 1 and Type 2 Diabetes: Subgroup Analyses from the DIAMOND Study Program. Diabetes Technol Ther, 2018. 20(8): p. 561-565 11) Ruedy, K. Riddlesworth, TD, Graham C. Continuous glucose monitoring in older adults with type 1 and type 2 diabetes using multiple daily injections of insulin: results from the DIAMOND trial. J Diabetes Sci Technol 2017;11:1138-1146. 12) Olafsdottir et al. A Randomized Clinical Trial of the Effect of Continuous Glucose Monitoring on Nocturnal Hypoglycemia, Daytime Hypoglycemia, Glycemic Variability,	

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				and Hypoglycemia Confidence in Persons with Type 1 Diabetes Treated with Multiple Daily Insulin Injections (GOLD-3). Diabetes Technology & Therapeutics 2018; DOI: 10.1089/dia.2017.0363 13) Heinemann, L, Freckmann, G, Ehrmann, D, Faber-Heinemann, G, Guerra, S, Waldenmaier, D, Hermanns, N. Real-time continuous glucose monitoring in adults with type 1 diabetes and impaired hypoglycaemia awareness or severe hypoglycaemia treated with multiple daily insulin injections (HypoDE): a multicentre, randomised controlled trial. Lancet 2018;391:1367-1377 14) Thabit, et all (2020). Use of Factory-Calibrated Real-time Continuous Glucose Monitoring Improves Time in Target and HbA1c in a Multiethnic Cohort of Adolescents and Young Adults With Type 1 Diabetes: The MILLENNIALS Study, Diabetes Care 2020 Oct; 43 (10): 2537-2543. 15) Šoupal J, Petruzelkova L, Flekac M, et al. Comparison of Different Treatment Modalities for Type 1 Diabetes, Including Sensor-Augmented Insulin Regimens, in 52 Weeks of Follow-Up: A COMISAIR Study. Diabetes Technol Ther. 2016;18(9):532-538. 16) Šoupal (2020). Glycemic Outcomes in Adults With T1D Are Impacted More by Continuous Glucose Monitoring Than by Insulin Delivery Method 3 Years of Follow-Up From the	

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				COMISAIR Study, DIABETES CARE 2019;43(1)37-43 17) Mulinacci et al., Glycemic Outcomes with Early Initiation of Continuous Glucose Monitoring System in Recently Diagnosed Patients with Type 1 Diabetes. Diabetes Technol Ther. 2019;21(1):6-10.	
Diabetes UK	Guideline	020	001 -005	**1.7.4: Alternative basal insulin therapy to twice-daily insulin detemir** We agree with the two new recommendations which have been included in this section to recognise new evidence on ultra-long-acting insulin, degludec. Firstly, we support the recommendation of administering degludec for individuals where there is a particular concern about nocturnal hypoglycaemia, given new evidence demonstrating a lower proportion of nocturnal hypoglycaemic events occurring with degludec compared to long-acting insulins. Secondly, we support the recommendation to administer once-daily insulin, including degludec, for people who need help from a carer or healthcare professional to administer injections. Given the mode of action and longer duration, degludec provides greater flexibility in when the dose can be administered, allowing for an individual's care and support arrangements to be more flexible. This is pertinent in situations where twice-daily injections may be challenging or impractical to manage.	Thank you for your comment.
Diabetes UK	Guideline	020	019	**1.7.7: Considering other basal insulin regimens for adults with type 1 diabetes**	Thank you for your comment. DKA was an outcome of interest identified at review protocol stage however no

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				We support the addition of recommendations that give greater priority to personalising treatment to the needs of individuals. Given the mode of action and longer duration of degludec, people who experience frequent diabetic ketoacidosis (DKA) admissions are a group that would suit a change to this type of long-acting insulin, especially if another regimen does not meet their agreed treatment goals. We suggest adding 'frequent DKA admissions' as an additional factor for healthcare professionals to take into consideration when choosing alternative insulin regimens to those set out in recommendations 1.7.3 and 1.7.4. Whilst the guidance recommends healthcare professionals consider a person's comorbidities, explicitly highlighting DKA as a factor to consider would provide additionally clarity and aid practitioners in making these decisions.	evidence was for this outcome. Additionally, no studies were identified in people with frequent DKA admissions. Therefore, specific recommendations could not be drafted. However, the committee did note that this was an important issue that needs to be taken into consideration. Therefore, recommendation 1.7.8 has been amended to state that DKA and adherence should also be taken into consideration when considering other basal insulin regimens for adults with type 1 diabetes only if the regimens in rec 1.7.3 and 1.7.4 do not meet their agreed treatment goals. Further discussion has also been added to section 1.1.12 of the evidence review.
Diabetes UK	Guideline	General	General	Diabetes UK agrees with the updated recommendations on long-acting insulin and supports the other proposed areas for review that have been identified in the final scope for updating NG17, including diagnosis, blood glucose monitoring and periodontal disease. We look forward to participating in future consultations on these areas.	Thank you for your comment.
Healthy.io	Guideline	034	014	It is worth noting that reagant strips can be used in place of lab-based testing together with digital solutions that enable patients to test from home. This is important because there are significant issues around uptake of this test using conventional	Thank you for your comment. Diabetic kidney disease was outside the remit of this update. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date.

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				approach to taking a sample into surgery and sending to the lab for testing that is outlined here, particularly for people with T1DM. Only 33.6% of people living with T1DM were tested in first three quarters of 2020 according to the National Diabetes Audit. This number was down from 51% in 2018 and clearly impacted by COVID, but even prior to COVID, only half of people with T1DM were undertaking this test. Digital approaches, such as that offered by Healthy.io (which has a NICE Medtech Innovation Briefing) and has been adopted by the Accelerated Access Collaborative for national NHS spread, is achieving consent rates on average 75% of untested patients and achieving 85% average uptake of the testing from consented patients. An independent Health Economic evaluation undertaken by York Health Economic Consortium (Shore et al ExpertRev Pharacoecon 2019) sets out significant NHS savings through adopting this approach across the previously untested patient cohorts. It is worth mentioning in the guidance that home based testing is now available to the NHS.	
Juvenile Diabetes Research Foundation	Guideline	020	011	JDRF is pleased to see that NICE recommends a shared decision is made with the person with type 1 diabetes after discussing their preferences around biosimilars. Informed patient choice and shared decision making should be embedded throughout the recommendations.	Thank you for your comment.
Juvenile Diabetes Research Foundation	Guideline	020	015	If the use of long acting insulins are not helping a person with type 1 meet their personal targets, insulin pump therapy should be considered as an alternative when taking into account the person with type 1's preferences.	Thank you for your comment. Insulin pump therapy was outside the remit of this review.

Type 1 diabetes in adults: diagnosis and management (update) – insulin

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Juvenile Diabetes Research Foundation	Guideline	General	General	JDRF is concerned to see that this guideline update only addresses long-acting insulin and not other areas identified in the scoping document of July 2020, such as diagnosis, blood glucose management and managing complications. A timescale for consultation for those areas to be updated would be welcomed.	Thank you for your comment. As highlighted in the draft guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Recommendations on diagnosis are currently being updated and are also due to be published in 2022.
King's College Hospital NHS Foundation Trust	Guideline	005	018 - 026	The guidance implied c-peptide measurement in serum, but there is evidence from Exeter supporting the measurement of c-peptide in urine as a urinary c-peptide : creatinine ratio. NICE may want to consider indicating the different ways c-peptide can be measured, and consider providing a pathway for c-peptide and antoantibody measurement (and the role of genetic risk scores) as suggested by the Type 1 diabetes UK consortium.	Thank you for your comment. Diagnosis was outside the remit of this question. Also, as highlighted in the draft guideline, NICE is currently updating recommendations on diagnosis of type 1 diabetes and will be published in 2022.
King's College Hospital NHS Foundation Trust	Guideline	006	026	Include occupational history and driving.	Thank you for your comment. Recommendations on early care plan were outside the remit of the current review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	006	028	Suggest explicitly include diabetic ketoacidosis (DKA) and hypoglycaemia, hospital admissions and paramedic callouts for diabetes emergencies, and assess hypoglycaemia awareness e.g. Gold or Clarke score for care planning.	Thank you for your comment. Recommendations on early care plan were outside the remit of the current review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	007	006	Suggest ensure patient is enrolled on the national diabetes eye complication screening programme, if not attending secondary care ophthalmology clinics.	Thank you for your comment. Recommendations on early care plan were outside the remit of the current review question and was not prioritised for an update at scoping. Diabetes eye screening programme is covered in recommendations 1.15.1 -1.1.5.4.
King's College Hospital NHS	Guideline	007	008	Suggest include use of diabetes distress scale (DDS-2 as a screening tool; for further assessment DDS-17).	Thank you for your comment. Recommendations on early care plan were outside the remit of the current

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Foundation Trust					review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	009	001 - 018	Individual care plans should include active assessment for psychological wellbeing, including diabetes distress e.g. using diabetes distress score (with management offered if DDS-2 score 4 or above; may include peer support as well as formal psychological support) and mental health.	Thank you for your comment. Recommendations on support and individualised care were outside the remit of the current review and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	010	006 - 008	Group education in 2015 would have referred to face to face group education. Would it be possible to describe examples of alternatives of equal standard e.g. video conference based group education such as DAFNE online, online modular courses such as BERTIE online for greater access, flexible learning especially during the current COVID-19 pandemic.	Thank you for your comment. Recommendations on education and information were outside the remit of the current review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	012	012 - 014	Suggest add discuss the impact of fat and protein content of foods on post-meal glucose levels.	Thank you for your comment. Recommendations on dietary management were outside the remit of the current review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	013	013	Suggest changing "Eating Disorders" to type 1 diabetes and disordered eating [T1DE]	Thank you for your comment. Suggested change has been made to rec 1.4.13.
King's College Hospital NHS Foundation Trust	Guideline	014	023	In addition to guidance of blood glucose monitoring, reference to ketone (urine or blood) measurement should be made, so that facilities (i.e. prescriptions for the relevant test strips) are made available for monitoring ketone levels, and reference to recognised "sick day rules" e.g. DAFNE, NHS England: https://www.england.nhs.uk/london/wp-content/uploads/sites/8/2020/04/2.-Covid-19-Diabetes-Sick-Day-Rules-Type-1-MDI-06042020.pdf	Thank you for your comment. Ketone monitoring and managing diabetic ketoacidosis is covered in section 1.11 of the guideline. This section includes recommendations on ketone self-monitoring to prevent diabetic ketoacidosis (with reference to 'sick day rules'), ketone monitoring in hospital and the management of DKA.

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King's College Hospital NHS Foundation Trust	Guideline	015	016	In addition to quality-controlled blood glucose profiles, suggest for those using either flash glucose monitoring or continuous glucose monitoring, Time In Range, and Glucose Management Indicator/estimated HbA1c.	Thank you for your comment. HbA1c measurements and targets was outside the remit of this question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	015	027 - 028	"Ensure that aiming for an HbA1c target is not accompanied by problematic hypoglycaemia in adults with type 1 diabetes" – is a definition required? E.g. level of hypoglycaemia, frequency of hypoglycaemia, hypoglycaemia unawareness, fear of hypoglycaemia?	Thank you for your comment. HbA1c measurements and targets was outside the remit of the review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	016	009 - 012	Support adults with type 1 diabetes using flash glucose monitoring to scan glucose levels at least 8 times per day with at least 70% of the day using it.	Thank you for your comment. Continuous glucose monitoring was outside the remit of the review question. As highlighted in the guideline, these recommendations are due to be updated and will be published in 2022.
King's College Hospital NHS Foundation Trust	Guideline	017	002 - 005	For those using flash glucose monitoring, advise adults on personalised time in range / time above range / time below range targets, with reference to the International Consensus statement of 70% time in range of 3.9-10 mmol/L, with target >70% time in range (>50% in older, high risk frailty groups), 4% time below range, and <36% coefficient of variation: https://care.diabetesjournals.org/content/diacare/40/12/1631.full.pdf https://care.diabetesjournals.org/content/diacare/42/8/1593.full.pdf	Thank you for your comment. Continuous glucose monitoring was outside the remit of the review question. As highlighted in the guideline, these recommendations are due to be updated and will be published in 2022.
King's College Hospital NHS Foundation Trust	Guideline	018	006 - 028	Line 6-9 indicates recommendations on continuous glucose monitoring (CGM) are due to be updated, including sensor augmented pump therapy. This section needs to be distinguished from flash glucose monitoring (flash glucose monitoring should not be offered instead of CGM for those who meet the NICE	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose

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				recommendations for CGM), and include current guidance on who should be offered flash glucose monitoring.	monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope
King's College Hospital NHS Foundation Trust	Guideline	019	005 - 008	For those using continuous glucose monitoring, advise adults on personalised time in range / time above range / time below range targets, with reference to the International Consensus statement of 70% time in range of 3.9-10 mmol/L, with target >70% time in range (>50% in older, high risk frailty groups), 4% time below range, and <36% coefficient of variation: https://care.diabetesjournals.org/content/diacare/40/12/1631.full.pdf https://care.diabetesjournals.org/content/diacare/42/8/1593.full.pdf	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope

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King's College Hospital NHS Foundation Trust	Guideline	020	001 - 002	In addition to Degludec (100 units/ml), Glargine (300 units/ml) is associated with reduced frequency of nocturnal hypoglycaemia compared to Glargine (100 units/ml) and is a once daily insulin	Thank you for your comment. As highlighted in the comment, glargine U300 is an ultra-long-acting insulin making it a useful treatment option. However, no direct evidence was identified which compared glargine 300 units/ml and degludec 100 units/ml. The NMA results could not differentiate between degludec 100 units/ml and glargine 300 units/ml for outcomes change in HbA1c, all hypoglycaemia, severe/major hypoglycaemia and nocturnal hypoglycaemia. Based on the findings, specific recommendations on the use of glargine (300 units/ml) were not drafted. However, the results did show that there were fewer nocturnal hypoglycaemic events with degludec 100 units/ml when compared to detemir once daily, NPH once daily and glargine 100 units/ml once daily. Based on these findings the committee highlighted that degludec 100 units/ml can be considered if there is a particular concern about nocturnal hypoglycaemia. The committee were aware that other basal insulins not covered by recommendations 1.7.3 and 1.7.4 may be considered. In such instances, it is recommended that other basal insulin regimens can be considered if regimens in recs 1.7.3 and 1.7.4 do not meet agreed treatment target. Additionally, when choosing an alternative insulin regimen, the person's preferences, comorbidities, risk of hypoglycaemia, DKA and adherence, and acquisition cost should be considered.

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King's College Hospital NHS Foundation Trust	Guideline	020	003 - 005	For people with type 1 diabetes using more than 40 units long acting insulin per day, more concentrated preparations such as Glargine (300 units/ml) or Degludec (200 units/ml) can be considered.	Thank you for your comment. Evidence was not identified in people with type 1 diabetes using more than 40 units long-acting insulin per day. Additionally, no direct evidence was identified which compared glargine 300 units/ml and degludec 100 units/ml. Additionally, studies which assessed the effectiveness of degludec 200 units/ml were not included in the NMAs as the follow up was less than 4 weeks. The NMA results could not differentiate between degludec 100 units/ml and glargine 300 units/ml for outcomes change in HbA1c, all hypoglycaemia, severe/major hypoglycaemia and nocturnal hypoglycaemia. Based on the findings, specific recommendations on the use of glargine (300 units/ml) were not drafted. However, the results did show that there were fewer nocturnal hypoglycaemic events with degludec 100 units/ml when compared to detemir once daily, NPH once daily and glargine 100 units/ml once daily. Based on these findings the committee highlighted that degludec 100 units/ml can be considered if there is a particular concern about nocturnal hypoglycaemia. The committee were aware that other basal insulins not covered by recommendations 1.7.3 and 1.7.4 may be considered. In such instances, it is recommended that other basal insulin regimens can be considered if regimens in recs 1.7.3 and 1.7.4 do not meet agreed treatment target. Additionally, when choosing an

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					alternative insulin regimen, the person's preferences, comorbidities, risk of hypoglycaemia, DKA and adherence, and acquisition cost should be considered.
King's College Hospital NHS Foundation Trust	Guideline	020	011 - 014	This recommendation runs counter to the current policy of not changing a person's insulin without clinical indication. It should only be done after full discussion with the patient and not instituted at dispensing level, in line with present policies to prescribe insulin by brand name e.g. prescribe Lantus ® rather than Glargine. Patients should be protected against frequent changes in the source of their insulin as subtle changes in properties may be perceptible to the user. While we understand that biosimilars should be identical to the patented version, how sure are we that they are identical? As penfill cartridges for different brands of biosimilar insulins are not interchangeable between reusable pen devices, issues with device compatibility and familiarity also need to be considered.	Thank you for your comment. A new recommendation has been added (rec 1.7.9) to highlight that when prescribing, ensure that insulins are prescribed by brand name. Furthermore, recommendation 1.7.7 encourages discussions to take place around switching to biosimilars. The rationale and impact section also highlights that the possibility of switching should be discussed with people and should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached.
King's College Hospital NHS Foundation Trust	Guideline	021	009 - 011	This should also include ultra fast acting insulin analogues, e.g. where injecting 15 mins before meals is not practical with standard insulin analogues, resulting in significant post-meal hyperglycaemia.	Thank you for your comment. Recommendations on rapid-acting insulin were outside the remit of the review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	022	009 - 017	Dapagliflozin is a licenced adjunctive therapy in type1 diabetes reviewed by NICE not mentioned in the current guideline: https://www.nice.org.uk/guidance/ta597/chapter/1-Recommendations	Thank you for your comment. A cross reference to the technology appraisal has been added to recommendation 1.7. 17.
King's College Hospital NHS	Guideline	028	016	Suggest continue long acting insulin injection alongside intravenous insulin by infusion to adults with	Thank you for your comment. Management of DKA was outside the remit of the review question and was not prioritised for an update at scoping.

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Foundation Trust				DKA. Guidance is available from the Joint British Diabetes Society in 2013: https://www.diabetes.org.uk/resources-s3/2017-09/Management-of-DKA-241013.pdf	
King's College Hospital NHS Foundation Trust	Guideline	029	004	What is "continuous monitoring"? Does this refer to continuous bedside monitoring including cardiac monitoring? We do not think this refers to continuous glucose monitoring – there are no data supporting this as far we are aware.	Thank you for your comment. Current recommendations highlight that continuous glucose monitoring includes real-time glucose monitoring. Additionally, as highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Furthermore, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope
King's College Hospital NHS Foundation Trust	Guideline	030	002 - 005	This should state assessment of risk of cardiovascular disease *and lipid modification* in adults with type 1 diabetes.	Thank you for comment. Section 1.13 was outside the remit of the review question and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	030	016 - 017	Is it possible to include vaping and e-cigarettes?	Thank you for comment. Section 1.13 was outside the remit of the review question and was not prioritised for an update at scoping.

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King's College Hospital NHS Foundation Trust	Guideline	033	001 - 003	Adults with type 1 diabetes who are hospital inpatients should be enabled to use their insulin pump therapy, and own glucose monitoring (capillary blood glucose monitoring, flash glucose monitoring, continuous glucose monitoring) if they are willing and able and it safe and appropriate (e.g. not when on intravenous insulin infusion) for them to do so.	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be updated in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. **https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope**
King's College Hospital NHS Foundation Trust	Guideline	039	020 - 024	This should include explicit mention of diabetes distress, which can be screened for using the diabetes distress scale (DDS-2), as this may be misdiagnosed as depression / general anxiety.	Thank you for your comment. Recommendations on psychological problems was outside the remit of this update and was not prioritised for an update at scoping.
King's College Hospital NHS Foundation Trust	Guideline	040	010	This should be re-labelled as Type 1 diabetes and Disordered Eating, instead of "Eating disorders"	Thank you for your comment. The committee reviewed the suggested change and agreed that term 'insulin dose manipulation' should be replaced with term 'disordered eating'. Subheading for this section has also been amended to state 'disordered eating' and the term has been added to the glossary. The committee also recognised since the development of the recommendations; work has been conducted on disordered eating. We will pass your comment to the

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					NICE surveillance team which monitors guidelines to ensure that they are up to date.
King's College Hospital NHS Foundation Trust	Guideline	040	011 - 019	This should include wider spectrum of disordered eating including binge eating. Patients with disordered eating and type 1 diabetes may not necessarily have a low BMI	Thank you for your comment. Recommendation 1.15.39 has been amended to state 'disordered eating'. A definition has also been provided for disordered eating which states that examples of disordered eating includes fasting or chronic restrained eating, skipping meals, binge eating, self-induced vomiting, restrictive dieting, and laxative or diuretic misuse.
King's College Hospital NHS Foundation Trust	Guideline	041	024 - 027	Should include flash glucose monitoring, and the role of this and continuous glucose monitoring in inpatients e.g. diabetic emergencies – DKA/hypoglycaemia.	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems.
King's College Hospital NHS Foundation Trust	Guideline	042	008 - 012	Should include research into the delivery of structured education from diagnosis to 6 months (i.e. before that recommended by NICE) on retention of knowledge and clinical efficacy. Also research in structured education on continuous glucose monitoring / flash glucose monitoring.	Thank you for your comment. The delivery of structured education was not prioritised for an update at scoping. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date. This will be considered for inclusion as part of another update.
Medtronic Limited	Guideline	018	005	The published scope for this "Type 1 diabetes in adults: diagnosis and management" guideline outlined all the areas that would be reviewed in this guideline update. This included Section 1.6: Blood Glucose	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose

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				Monitoring. In the area of "Continuous Glucose Monitoring", the scope set out what NICE planned to do in this area as follows: • Review evidence and update existing recommendations 1.6.21 and 1.6.22 as needed • Review evidence and update existing recommendation 1.6.23 as needed • No evidence review: retain recommendation 1.6.24 from existing guideline • Refer to the NICE diagnostics guidance on 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) In the published draft guidance, the section on Continuous Glucose Monitoring has not been updated and a note has been added as follows: *"Recommendations on continuous glucose monitoring are due to be updated, alongside a review on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (NICE diagnostics guidance [DG21])"* When the update of this "Type 1 Diabetes in Adults" guidance started, there was also a planned update of DG21 however this update has been terminated and a new MTA process has started for "Hybrid Closed Loop Systems for managing blood glucose levels in type 1 diabetes". This guidance will assess hybrid closed	monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope

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				loop systems only and **will not assess sensor augmented pump therapy or standalone continuous glucose monitoring**. We are concerned that an update on the guidance relating to Continuous Glucose Monitoring, will not be provided by either guideline therefore we ask that the section on Continuous Glucose Monitoring is reviewed, as planned in the scope, as part of this current Type 1 Guideline update.	
NHS England and NHS Improvement	Example 5	033 - 034	025	We are strongly supportive on the emphasis on prevention and diabetic eye screening in section 1.15	Thank you for your comment.
NHS England and NHS Improvement	Guideline	019	018 - 028	Welcome the guidance on specific type of insulin to use and alternatives	Thank you for your comment.
NHS England and NHS Improvement	Guideline	020	001 - 005	Welcome the guidance on specific type of insulin to use and alternatives	Thank you for your comment.
NHS England and NHS Improvement	Guideline	020	007	MHRA link is useful reminder	Thank you for your comment.
NHS England and NHS Improvement	Guideline	020	011	Welcome the guidance on switching (for cost reasons)	Thank you for your comment.
NHS England Patient Safety Team	Guideline	011	013	We are aware of patient harm when staff have tried to 'carbohydrate count' for inpatients unable to self-manage – consideration should be given to either recommend training for staff or to advise staff should not use 'carbohydrate counting' for patients whilst an inpatient.	Thank you for your comment. Recommendations on dietary management were outside the remit of this current update and was not prioritised for an update at scoping.

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NHS England Patient Safety Team	Guideline	017	016	Consideration should be given to advise education for women using insulin pumps during pregnancy; due to unpredictability of requirements caused by hormone fluctuations after giving birth and during breast feeding.	Thank you for your comment. Use of insulin pumps is covered as part of NG3 (Diabetes in pregnancy: management from preconception to the postnatal period).
NHS England Patient Safety Team	Guideline	020	022	Incidents reported where it has not been considered that patients, unconscious or unable to communicate, may be on a continuous insulin pump device when admitted in an emergency; this has lead to patient harm.	Thank you for your comment. Recommendations on insulin pumps were outside the remit of this update. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date. This will be considered for inclusion as part of another update.
NHS England Patient Safety Team	Guideline	022	018	Please reference previous Patient_Safety_Alert_-_Withdrawing_insulin_from_pen_devices.pdf (england.nhs.uk)	Thank you for your comment. The safety alert has been added to rec 1.7.4, rationale and impact section of the guideline and evidence review.
NHS England Patient Safety Team	Guideline	026	005	Reported incidents report significant issues when diabetic patients receive a continuous variable rate insulin infusion and enteral or parenteral nutrition; as the insulin rate is often not adjusted when rates of feeding are changed, feeding regimen ends and not replaced for a significant time period, or feeding regimen suspended whilst other procedures are undertaken; often resulting in significant hypoglycaemia – please consider need for education in this area,	Thank you for your comment. Recommendations on preventing and managing hypoglycaemia were outside the remit of this update and was not prioritised for an update at scoping. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date. This will be considered for inclusion as part of another update.
NHS England Patient Safety Team	Guideline	027	018	Consider strengthening this statement to say that patients who are admitted with DKA should be referred immediately to the diabetes specialist team for assessment and review. National guidance notes that admitting teams "infrequently refer early to the diabetes specialist team and it is not uncommon for the most junior member of the admitting team, who is least likely to be aware of the hospital guidance, to be	Thank you for your comment. The comment was reviewed, and it was noted that recommendation 1.11.4 already states that professionals managing DKA in adults should have adequate and up-to-date training, and be familiar with all aspects of DKA management that are associated with mortality and morbidity. Therefore, this recommendation will not be updated.

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				given responsibility for the initial management of this complex and challenging condition." - https://www.diabetes.org.uk/resources-s3/2017-09/Management-of-DKA-241013.pdf	
NHS England Patient Safety Team	Guideline	05	018	Ongoing work with RCPath in relation to known delay in C-peptide lab results; affecting patient treatment – themes from incident review include: (a) variation in turnaround time (varies between 3hrs and 5 weeks) and (b) clinicians need to be aware to specify relevant medical history/current treatment that can affect results. Consider if this needs to be made clear in guidance.	Thank you for your comment. As highlighted in the guideline, NICE is currently updating recommendations on the diagnosis of type 1 diabetes and is due to be published in 2022.
Novo Nordisk	Evidence review	General	General	Novo Nordisk welcomes inclusion of the SWITCH 1 study[1] which is high ranking evidence in terms of both being a randomised controlled trial but also in the fact that hypoglycaemia was the primary endpoint. The study is strong evidence for insulin degludec reducing overall and nocturnal hypoglycaemia in type 1 diabetes versus glargine U100. In order to further add to the evidence for degludec reducing hypoglycaemia in type 1 diabetes we would like to highlight the real world REFLECT study[2]. This demonstrated in a routine clinical care setting, switching to degludec from other basal insulins was associated with significantly lower rates of hypoglycemia, improved glycemic control, and treatment satisfaction in patients with type 1 or type 2 diabetes. In type 1 diabetes, the 12-month follow-up/baseline rate ratios (95% CI) of overall [0.80 (0.74 to 0.88)], non-severe [0.83 (0.76 to 0.91)], severe [0.28 (0.14 to 0.56)], and nocturnal [0.61 (0.50 to 0.73)] hypoglycemia suggested significantly lower	Thank you for your comment. See comments below on the studies referenced in the comment: - Lane 2017 (SWTICH 1 study) was included in this review and contributed to the body of evidence underpinning the recommendations - Fadini 2019 (REFLECT study) is an observational study and therefore did not match the protocol for this review which states that randomised controlled trials would be considered for inclusion. - Holmes 2019 was reviewed. This study reviewed evidence comparing benefits and harms of long-acting insulins in patients with type 1 and type 2 diabetes. The review included the following studies, which were also included in our analyses: o Birkelnad 2011 o Heller 2012 o Mathieu 2013 o Lane 2017.

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				hypoglycemia rates with degludec (all *P*s < 0.001). At 12 months, HbA1c, fasting plasma glucose (FPG), and basal insulin dosage decreased significantly. We would also like to highlight a systematic review and meta analysis of long acting insulins which showed nocturnal hypoglycaemia was less probable with insulin degludec than with insulin glargine in type 1 diabetes[3] (rate ratio 0.68, 95% CI 0.56-0.81). No differences in glycaemic control were seen between insulin degludec, detemir and glargine. References 1. Lane, Wendy, Bailey, Timothy S, Gerety, Gregg et al. (2017) Effect of Insulin Degludec vs Insulin Glargine U100 on Hypoglycemia in Patients With Type 1 Diabetes: The SWITCH 1 Randomized Clinical Trial. JAMA 318(1): 33-44 2. Fadini G, Feher M, Hansen T et al (2019) Switching to Degludec from Other Basal Insulins is Associated with Reduced Hypoglycemia Rates: a Prospective Study. J Clin Endocrinol Metab. 2019 Dec; 104(12): 5977–5990. Published online 2019 Aug 9. doi: 10.1210/jc.2019-01021. Holmes, RS, Crabtree E, McDonagh MS (2019) Comparative effectiveness and harms of long-acting insulins for type 1 and type 2 diabetes: A systematic review and meta-analysis.Diabetes, Obesity and Metabolism 21.4. 2019: 984-992.	These studies contributed to the body of evidence underpinning the recommendations.

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Novo Nordisk	General	General	General	Thank you for giving us the opportunity to submit our comments to this important guideline. As a final comment and reflecting on the disproportionate impact COVID-19 has had on people with diabetes, it is more important than ever to improve care and outcomes for people living with type 1 diabetes, to reduce their risk of serious consequences and death from COVID-19 and to reduce their risks of developing potentially avoidable complications. NICE guidelines should look to provide clinicians with clear guidelines which include a clear direction to prioritise individualised care and make shared prescribing decisions with the person living with type 1 diabetes, focusing on making treatment choices that will improve their quality of life, as well as improve their health outcomes.	Thank you for your comment. Remit of this review was the update of the recommendations on long-acting insulin. The committee noted the importance of shared decision making and have highlighted the importance of patient preferences in the updated recommendations. Recommendations are based on the principle of shared decision making – a collaborative process that involves a person and their healthcare professional working together to reach a joint decision about care.
Novo Nordisk	Guideline	018	006	The final scope includes review and update to recommendations 1.6.21 and 1.6.22. There was significant support from the clinical community at the time of surveillance consultation that this part of the guideline needed to be reviewed and updated, in line with emerging evidence and new technology. This section has not been updated as part of this current update nor is there a clear timeline for when this will happen. The wording makes it unclear if it will happen concurrently with DG21 and although we recognise there is overlap with DG21, there is a significant population of people living with type 1 diabetes who would benefit from updated guidance on CGM outside of sensor-augmented pump therapy systems, We are disappointed this section has not	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-

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				been updated as part of the current update and would suggest a firm timeline is provided for when this will happen.	the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope
Novo Nordisk	Guideline	019	009	Insulins should always be prescribed by brand name for safety reasons and prescribing by brand name is recommended by both the MHRA[1] and NHS England[2] stressing the importance of this to support pharmacovigilance and patient safety. This is now even more important within this guideline update with the inclusion of biosimilars. We suggest an addition is inserted above section 1.7.1 to guide clinicians and increase insulin safety: "*Always prescribe insulins by brand name"* 1. MHRA. Biosimilar Products. December 2014. Available from https://www.gov.uk/drug-safety-update/biosimilar-products. NHS England. December 2017. Commissioning Framework for biological medicines including biosimilar medicines. Available from https://www.england.nhs.uk/wp-content/uploads/2017/09/biosimilar-medicines-commissioning-framework.pdf	Thank you for your comment. A new recommendation has been added (rec 1.7.9) to highlight that when prescribing, ensure that insulins are prescribed by brand name.
Novo Nordisk	Guideline	020	003	We welcome the new recommendation that recognises the flexibility in timing of insulin administration provided by insulin degludec. However we believe the wording in this recommendation should be made clearer to reflect the benefits provided *by* flexibility of timing. Of the long-acting insulins, degludec has the longest window in terms of duration of action (beyond 42 hours) which contributes to the	Thank you for your comment. The committee noted that the recommendation does not require changing as this is highlighted in the rationale and impact section of the guideline. The rationale and impact section states that flexible insulins, such as degludec (100 units/ml), have a long

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				flexibility in the timing of insulin administration, a minimum of 8 hours between injections should be ensured. We suggest a small amendment to the wording: "once daily insulin such as degludec for people who need help from a carer or healthcare professional to administer injections *or who would benefit from flexibility with timing of insulin administration*."	duration of action may be particularly useful as they give more flexibility in when the dose can be given.
Novo Nordisk	Guideline	020	006, 007, 008, 009, 010	We believe that the wording in section 1.7.5 should be amended to reiterate the importance of safe prescribing of insulin by brand name, to support pharmacovigilance, and to reflect national NHS England guidance that prescribing decisions should not be made on the basis of cost alone, for the reasons outlined below. **Safety of prescribing** • The link to the MHRA document in line 7 of the draft guidance takes you to a 2015 document which includes Abasaglar as the only biosimilar insulin available at that point in time. The point in the document it takes you to relates to minimising errors with high strength insulin or combination products which is not relevant for this particular recommendation. We suggest the link here is removed. • We also believe a repeated reminder about always prescribing by brand name is important to include within this section of the guideline, which refers to the prescribing of	Thank you for your comment. The MHRA alert does contain information about Abasaglar but this is because this was the only insulin biosimilar available at the time the alert was published. However, the alert does summarise general information to be considered when starting a biosimilar which can be useful to healthcare professionals. Thank you for providing wording for the recommendation. This was reviewed along with other comments and decision was made to add a new recommendation has been added (rec 1.7.9) to highlight that when prescribing, ensure that insulins are prescribed by brand name. Furthermore, as highlighted in the rationale and impact section, biosimilar medicines have shown to be safe and as effective as the original reference medicine and have the same quality. The NICE position statement on biosimilars (originally developed for the NICE technology appraisal process to applicable to guidelines as well) states that once a

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				biosimilar insulins. Prescribing by brand name is recommended by both the MHRA[1] and NHS England,[2] stressing the importance of this to support pharmacovigilance and patient safety. **Prescribing decisions should not be made on the basis of acquisition cost alone** • We do not believe it is appropriate to guide clinicians to automatically prescribe the product with the lowest acquisition cost when a biosimilar insulin is available for patients starting insulin therapy. Biosimilar medicines have a place in the range of treatment options available for clinicians to offer their patients, so that they can determine together which treatment is best suited to the individual's needs, but any decision about an individual's treatment must respect the clinical autonomy of their treating clinician and take into account all considerations (including any patient preferences), not just the cost of the medicine. • The commissioning framework for biological medicines in England stresses that "individual treatment decisions should always be made firstly on the basis of clinical judgement, with overall value offered by medicines considered as a secondary factor.[2]	biosimilar is licensed, they are assumed to only differ from the originator in terms of price. The committee agree it is important to check all these aspects when making the original determination that a biosimilar is "equivalent" but noted this was something that was not within the remit of NICE, but rather part of the licensing process for biosimilars. Based on this understanding the committee noted that when starting an insulin for which a biosimilar is available, to use the product with the lowest acquisition cost. However, clinical scenarios outlined in rec 1.7.4 would still apply to the use of insulin for which a biosimilar is available. Shared decision making is also a key part of the recommendations drafted. Recommendation 1.7.8 specifically states that when switching to a biosimilar, a shared decision should be made. The rationale and impact section also states that possibility of switching should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached. Thank you for providing the references. Please see comments below: • MHRA. Biosimilar Products. December 2014. Available from https://www.gov.uk/drug-safety-update/biosimilar-products. – **Not included in review as we have provided a**

				• It is important to recognise that the "overall value" of a medicine relates to more than just its acquisition cost. For example, different formulations of similar insulins will be associated with different administration devices. Differences in administration devices that may affect patient preference and improved adherence to medication include the availability of insulin pen devices rather than vial and syringe[3 4] and the availability of novel devices for certain patient groups.[5] • Insulin administration devices are continuously upgraded by companies based on user feedback, often showing more positive user feedback when comparing within-brand progressions.[6] • As insulin devices have continued to evolve and improve, developments have expanded beyond physical upgrades and subsequently there is a growing body of evidence on the benefits of additional, software-based functionality such as memory function and connectivity with other relevant patient data (for example connected smart insulin pens that can be used to record insulin doses or in combination with a patient's glucose data to help manage their diabetes)[7]. The new NICE strategy recognises the emergence of new hybrid technologies and products where the impact of innovation extends beyond the use of a medicine alone. This highlights the need for future consideration of the cost-	**reference to the MHRA advice on biosimilar insulin products.** • NHS England. December 2017. Commissioning Framework for biological medicines including biosimilar medicines - **Not included in review as we have provided a reference to the MHRA advice on biosimilar insulin products.** • Davies (2013) – **Study focused on adherence to insulin therapy which was not the objective of the review.** • De Luis (2004)- **study focuses on patients with type 2 diabetes which is outside the remit of this question.** • Sommavilla (2011)- **Study investigated preference between insulin pens which was not the focus of our review** • Heinemann (2021) - **Study was a literature review of smart insulin pens which is not the focus of our review.**

				effectiveness of an insulin to take in to account the overall value offered to the patient and the NHS, when a particular delivery device is used in combination with the medicine. • Overall value provided from a medicine may also relate to other factors, such as any services that pharmaceutical companies provide to support patients using their insulin products. **In summary** Further to the evidence outlined above, we suggest that the link to the MHRA is removed. We also suggest amending the wording at section 1.7.5 as follows: *"When starting an insulin for which a biosimilar is available, use the product with the lowest acquisition cost where possible, basing prescribing decisions on clinical judgement, taking into account the needs and preferences of individual patients. Always prescribe insulins by brand name."* References 1. MHRA. Biosimilar Products. December 2014. Available from https://www.gov.uk/drug-safety-update/biosimilar-products. 2. NHS England. December 2017. Commissioning Framework for biological medicines including biosimilar medicines. Available from https://www.england.nhs.uk/wp-	

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				content/uploads/2017/09/biosimilar-medicines-commissioning-framework.pdf 3. Anderson BJ, Redondo MJ. What can we learn from patient-reported outcomes of insulin pen devices? J Diabetes Sci Technol. 2011;5(6):1563-1571. Available from https://journals.sagepub.com/doi/pdf/10.1177/193229681100500633 4. Davies M.J. et al. Real-world factors affecting adherence to insulin therapy in patients with Type 1 or Type 2 diabetes mellitus: a systematic review *Diabet. Med.* 30, 512– 524. 2013. Available from https://onlinelibrary.wiley.com/doi/full/10.1111/dme.12128 5. D.A de Luis et al. Effect on quality of life with a new insulin injection device in elderly patients with diabetes mellitus type 2. Journal of Diabetes and its Complications, Volume 18, Issue 4, 2004, Pages 216-219. Available from https://doi.org/10.1016/S1056-8727(03)00089-8 6. Sommavilla B, Pietranera G. A randomized, open-label, comparative crossover handling trial between two durable pens in patients with type 1 or 2 diabetes mellitus. Journal of Diabetes Science and Technology, Vol 5, Issue 5, September 2011. Available from https://journals.sagepub.com/doi/pdf/10.1177/193229681100500529 7. Heinemann L et al 2021, Digital Diabetes Management: A Literature Review of Smart Insulin Pens. Journal of Diabetes Science and Technology. Available from	

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				https://journals.sagepub.com/doi/pdf/10.1177/1932296820983863	
Novo Nordisk	Guideline	020	011, 012, 013	**Shared decision making and individual patient needs** • We welcome the reference to shared decision making between clinicians and patients in considering the potential switching of patients to a biosimilar insulin. Novo Nordisk believes however that the wording could be clearer in ensuring individual patient preferences and circumstances are taken into account. • The commissioning framework for biological medicines in England makes clear "the decision to prescribe a biological medicine for an individual patient, whether a reference or biosimilar, or to change between the two, rests with the responsible prescriber in consultation with the patient, in line with the principles of shared decision making"[1]. However, research recently conducted by the Patients Association found more than one in three patients had not been consulted by their doctor prior to being moved onto a biosimilar medicine[2]. Similarly, Diabetes UK has stressed the importance of decisions about the prescribing of biosimilar insulins always being made on a case by case basis and that there should be no blanket changes to local prescribing policies[3] and equally the Position Statement from the Association of British Clinical Diabetologists (ABCD) states that	Thank you for your comment. The committee reviewed the suggested wording and noted that this is already covered in the rationale and impact section of the guideline. The rationale and impact section highlights that the possibility of switching could be discussed with people during their routine review and should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached.

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				changing patients' insulin for entire clinics or GP practice populations should not take place for non-clinical reasons[4]. • Additional complexities include the fact that an insulin pen delivery devices may be unique to a particular insulin and that patients will need to be instructed on the correct use of a new device; furthermore, any change in insulin necessitates additional monitoring and support from the diabetes team and for this reason, ABCD includes in their Position Statement that following a switch to a biosimilar insulin it is recommended that arrangements are made for patients to be reviewed and to have ongoing supervision by a specialist team[4]. Self care and management for people with type 1 diabetes is complex and impacts on their daily lives. A principle common to both Diabetes UK and ABCD within their Position Statements re-iterates that patients on an established insulin regime who are achieving their HbA1c without hypoglycaemia should not be automatically switched to a biosimilar insulin[4] and similarly that patients already on an insulin who are well managed should continue with that treatment[3] **In summary** We suggest therefore that for the reasons given above, the wording is amended to provide clearer	

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				advice for healthcare professionals and patients considering a biosimilar: *"When people are already using an insulin for which a lower cost biosimilar is available, discuss the possibility of switching to the biosimilar, taking into account their individual needs and preferences and in line with the principles of shared decision making".* And additionally adding: *"When considering switching to a biosimilar it is important to factor in any change in device and time and any additional monitoring needed to make this switch safely".* References 1. NHS England. December 2017. Commissioning Framework for biological medicines including biosimilar medicines. Available from https://www.england.nhs.uk/wp-content/uploads/2017/09/biosimilar-medicines-commissioning-framework.pdf 2. Patients Association (2018) Understanding patient needs in switching from biologic to biosimilar medicines, Dec 2018. Available from https://www.patients-association.org.uk/Handlers/Download.ashx?IDMF=b17810ee-8470-4173-8efc-e7c13d117fbe	

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				3. *Diabetes UK, Position statement on biosimilar insulins, updated Aug 2019. Available from https://www.diabetes.org.uk/professionals/position-statements-reports/diagnosis-ongoing-management-monitoring/biosimilar-insulins* 4. *Association of British Clinical Diabetologists, (2018) Position statement on the use of biosimilar insulin. Available from https://bjd-abcd.com/index.php/bjd/article/view/346/541*	
Novo Nordisk	Methods	General	General	The following points are related to the "NICE NG17 Economic model report" and the network meta-analysis performed as part of the "NICE NG17 Evidence reviews underpinning recommendations 1.7.3 to 1.7.7 and research recommendations in the NICE guideline" • There is a lack of clarity on the methods used for the estimation of baseline effects and whether the economic modelling follows the NICE methods on the derivation of the baseline effects from baseline natural history models, as described in the NICE DSU TSD 5. The estimation of the baseline effect is crucial in a cost-effectiveness model, as all the other absolute treatment effects are derived from it to form the efficacy component of the model. • The economic model uses different HbA1c level change per treatment based on NMA results. This is surprising since the treat-to-target trial design of diabetes trials will have an impact on efficacy outcomes with the	Thank you for your comments. The responses for each of the points raised with regard to the economic model report are listed below. **Baseline effects:** The baseline effects were calculated by synthesising the event rates in the Detemir twice daily arms from the included RCTs in R, with treatment effects from the NMA applied to these baseline rates. The methods section of the document (section HE 2.3.3.1) has been updated to explain this more clearly. We did initially look for observational cohort studies reporting baseline rates as the preferred source of this data, but no suitable studies were identified, and the committee agreed that suitably applicable UK cohorts are unlikely to exist, as these studies are unlikely to report event rates for a particular type of insulin. Therefore, the committee agreed that using the detemir twice daily arms from the RCTs was the most appropriate choice. **Use of HbA1c levels from NMA:** Whilst we agree that many of the trials follow a treatment to target design, this was not felt to be a substantive concern

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				forced titration of insulin dosages to achieve a prespecified treatment goal often resulting in comparable glycaemic control between treatments. The use of different change in HbA1c levels for each treatment together with the unclear approach on the estimation of baseline effects could potentially have led in inaccurate ICERs considering patients' life years in the model are mainly driven by HbA1c change. • We would like to highlight the economic model uses dosing data for degludec and glargine U100 that are contradictory to the results of the meta-analysis by Vora et al, 2014[1]. This showed In Type 1 diabetes basal bolus, the total daily dose of insulin was significantly lower, by 12%, with degludec compared with glargine ($p \leq 0.0001$). Statistical analyses were performed for both basal and bolus insulin doses to clarify the relative contribution of each to the observed reduction in total dose. These showed that the daily basal and bolus doses were both lower with degludec, with relative rates (degludec versus glargine) as follows: daily basal dose, 0.87; daily bolus dose, 0.88 (both $P < 0.05$). • The Core Diabetes Model is a well-established, validated economic model traditionally used to estimate the cost-effectiveness of diabetes treatments using long term clinical effects. Given that many clinical trials for diabetes have a treat-to-	as it reflects real-world practice in diabetes care. The model used has been designed in a way that takes into account treatment effects both in terms of changes in HbA1c levels and hypoglycaemic events which occur during the lifetime of the patients. Whilst the trials are designed on a treat to target approach, it does provide valuable comparative information on how insulins reduce HbA1c levels (as a trade-off against hypoglycaemia rates). The CORE model then uses these reductions in HbA1C levels to determine the incidence of long-term complications via its risk equations, hence helping capture differences in long-term effects between insulin therapies. **Dosing data for Degludec and Glargine U100:** The paper quoted by Vora at al (2014) was a meta-analysis published in 2014 and hence would not include information from more recent trials such as Lane et al (2017)[1]. There is a lack of clarity on the trials included by Vora et al to calculate the treatment ratio, to pinpoint exactly where the differences are coming from. It should also be pointed out that Vora et al have included trials reporting the combined basal/ bolus dose (since this was the endpoint reported) whereas we have looked at trials reporting basal and bolus dose separately (which was a requirement in our costing exercises since basal and bolus insulins differ in prices). Our analysis will also take into account any indirect evidence available as the dosing ratios are calculated using a network meta-analysis.

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				target design implementing a similar level of glycaemic control across treatments, we would like to highlight that a short-term approach could be considered a more appropriate modelling option to assess insulins. For example, the DOSE model is a simple and transparent Excel-based model that has been used in many publications[2,3] and offers a short-term approach focusing on important additional parameters such as hypoglycaemia and dosing, enabling economic evaluations based on data from treat-to-target clinical trials. In summary we believe the economic report should include a more detailed description of the methods used for the estimation of baseline effects and a justification of the inclusion of HbA1c level differences per treatment. Additionally, we would like to point out the Vora (2014) meta-analysis that found lower dosing of degludec vs glargine U100 is in contrary to the results used for the NICE economic modelling report and we recommend considering the DOSE model as an alternative approach to the economic modelling of diabetes which enables economic modelling based on data from treat-to-target clinical trials while focusing on parameters such as hypoglycaemia events and dosing. <u>References:</u> 1. Jiten Vora, Torsten Christensen, Azhar Rana, Steve C Bain. Insulin degludec versus insulin	**Use of a short term model:** The papers quoted by Evans et al did come up in our literature review, and the DOSE model was presented to the committee as a potential option. However the committee was of the opinion that a short-term approach such as this would not factor in the long-term complications of type 1 diabetes, which have substantial cost and quality of life implications. A short-term model of this nature will also not factor in any differences in changes in HbA1c levels between insulin therapies which regardless of the nature of the trials, is an important factor as it dictates the occurrence of a range of long-term complications. **References:** [1]Lane, W., Bailey, T.S., Gerety, G., Gumprecht, J., Philis-Tsimikas, A., Hansen, C.T., Nielsen, T.S. and Warren, M., 2017. Effect of insulin degludec vs insulin glargine U100 on hypoglycemia in patients with type 1 diabetes: the SWITCH 1 randomized clinical trial. Jama, 318(1), pp.33-44.

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				glargine in type 1 and type 2 diabetes mellitus: a meta-analysis of endpoints in phase 3a trials. Diabetes Therapy. 2014. Available at DOI 10.1007/s13300-014-0076-9 2. Evans M, Chubb B, Gundgaard J. Cost-effectiveness of Insulin Degludec Versus Insulin Glargine in Adults with Type 1 and Type 2 Diabetes Mellitus. Diabetes Ther. 2017 Apr;8(2):275-291. doi: 10.1007/s13300-017-0236-9. Epub 2017 Feb 16. PMID: 28210866; PMCID: PMC5380498. Evans, M., Mehta, R., Gundgaard, J. et al. Cost-Effectiveness of Insulin Degludec vs. Insulin Glargine U100 in Type 1 and Type 2 Diabetes Mellitus in a UK Setting. Diabetes Ther 9, 1919–1930 (2018). https://doi.org/10.1007/s13300-018-0478-1	
Renal Association	Guideline	007	007	NICE CKD guideline CG182 recommends that urinary protein should be assessed using ACR. We recommend that urine albumin excretion and urine protein should be removed and urine ACR should be inserted. CG182 also states that renal excretory function should be assessed with eGFR rather than serum creatinine. To maintain consistency, "serum creatinine" should be changed to "eGFR"	Thank you for your comment. Bullet point 13 in recommendation 1.1.7 has been amended to state urine albumin: creatinine ratio (ACR) and estimate glomerular filtration rate (eGFR).
Renal Association	Guideline	029	021	The CV risk assessment recommends that "albuminuria" be assessed. We feel that a specific instruction to measure urine ACR is preferable. Furthermore, no mention is made of checking eGFR. This is inconsistent with the advice given later in (para 1:15:6 of this document) where it is recommended	Thank you for comment. The first bullet point in rec 1.13.2 has been amended to state eGFR and ACR.

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				that measurement of serum creatinine should accompany a check of ACR. An annual check of ACR and eGFR is an important element of CV risk assessment. We therefore recommend that "albuminuria" should be amended to read: "eGFR and urine ACR" with a reference to para 1:15:6.	
Renal Association	Guideline	034	024 - 028	The use of undefined terms ("particularly", "suddenly", "significant") in this section may not be clinically useful. We offer this as a suggested amendment: *Suspect other renal disease if:* • *Diabetic retinopathy is absent* • *Blood pressure is very high or resistant to treatment* • *ACR increases above 30mg/mmol within a year of first becoming abnormal* • *Persistent non-visible haematuria is present (+ or more on dipstick testing)* • *The person is systemically unwell. [2004]*	Thank you for your comment. The committee reviewed the suggested changes and noted that evidence would need to be reviewed to make the changes. However, recommendation 1.15.7 has been amended and a link to the NICE guideline on chronic kidney disease has been added. Additionally, We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date
Renal Association	Guideline	034	021	NICE CKD guideline CG182 recommends that renal excretory function should be assessed with eGFR rather than serum creatinine. To maintain consistency, "serum creatinine" should be changed to "eGFR"	Thank you for your comment. The recommendation has been amended based on feedback.
Renal Association	Guideline	035	003 - 007	Para 1:15:9 uses the terms "moderately increased albuminuria" (which has no definition) and "microalbuminuria". Use of the latter term should be discouraged because an ACR>3mg/mmol is now established as **significant** albuminuria, identifying people at demonstrable risk. Use of "Microalbuminuria" implies something other than "true"	**Thank you for your comment. The recommendation has been amended to bring it in line with CG182.**

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				albuminuria (which historically was defined using urine dipsticks). This distinction is no longer appropriate. The following wording is therefore preferred:- *Start angiotensin-converting enzyme (ACE) inhibitors and, with the usual precautions, titrate to full dose in all adults with type 1 diabetes who have confirmed nephropathy with ACR>3mg/mmol.* This brings the recommendation in line with NICE guideline CG182	
Renal Association	Guideline	035	013 - 014	The recommendation in Para 1.15.12 is contentious. Clinical studies in humans exploring the effect of high dietary protein intake on CKD progression have so far yielded inconclusive results. Accordingly, the NICE guideline for management of CKD (CG182) makes no mention of potential harm arising from high dietary protein intake and makes no recommendation on this issue. It would therefore be difficult to follow the recommendation (given here) to advise adults with type 1 diabetes and nephropathy about "the advantages" of avoiding a high-protein diet; these advantages are unknown. It is not accepted practice to advise a reduction of dietary protein in early CKD and tight protein restriction is actively discouraged (CG182 states: *Do not offer low-protein diets (dietary protein intake less than 0.6 to 0.8 g/kg/day) to adults with CKD)* The recommendation in para 1.15.12 therefore does not confer proven benefit and may confuse	Thank you for your comment. The full CG182 guideline stated that low protein diets (0.6-0.8g/kg) were compared with higher protein diets (greater than 0.8g/kg, free or unrestricted diet). The GDG also noted that the evidence indication that a high protein intake is potentially harmful for CKD patients, but this aspect was not part of the review protocol. Additionally, specific recommendations were not developed for people with type 1 diabetes. Based on this, this recommendation was not updated. Additionally, we will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date

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				practitioners and patients (the distinction between avoiding high protein diet and recommending a low protein diet is not obvious). Besides, it would be odd for a NICE guideline on type 1 diabetes to make a recommendation relating to CKD which is notably absent from the specific NICE guideline on CKD. We therefore believe this recommendation is not necessary and should be removed.	
Renal Association	Guideline	035	015	Referral criteria for patients with nephropathy are clearly described in the NICE CKD guideline CG182. It would be preferable to reference that document in order to maintain consistency between these NICE guidelines. This would also make the document more clinically useful; it is obvious that local specialists should agree referral criteria (it is difficult to conceive a situation where they would agree to differ) and a cross reference to CG182 would define best practice with specific regard to nephropathy.	Thank you for your comment. A link to CG182 has been added to the recommendation.
Royal College of General Practitioners	Guideline	018	010	NICE maintain within the guidance the very clear instruction not to offer continuous monitoring routinely to patients (1.6.21), yet state that the technology review is due. The wording may lead professionals actively discouraging continuous monitoring if this is released before the technology review is updated. Can the panel consider waiting to publish this guidance until after the review on continuous monitoring is complete to ensure the recommendation is updated appropriately and the guidance is only issued once, after the complete review to prevent confusion?	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-

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					therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope
Royal College of Nursing	General	General	General	The Royal College of Nursing (RCN) welcome the proposal to develop NICE guidance for Type 1 diabetes in adults: diagnosis and management. The RCN invited members who work with people in these settings and care for people with this condition to review and comment on the draft guidelines on our behalf. The comments below, reflect the views of our reviewers.	Thank you for your comment.
Royal College of Nursing	Guideline	020	003	Once daily insulin like Degludec could also be considered for people who struggle with adherence	Thank you for your comment. As evidence was not identified in this cohort, specific recommendations could not be drafted. However, the committee did note that this was an important issue that needs to be taken into consideration., Therefore recommendation1.7.8 has been amended to state that DKA and adherence should also be taken into consideration when considering other basal insulin regimens for adults with type 1 diabetes only if the regimens in rec 1.7.3 and 1.7.4 do not meet their agreed treatment goals. Further discussion has also been added to section 1.1.12 of the evidence review.
Royal College of Nursing	Guideline	020	011	When considering a switch to a biosimilar and after shared decision making, the new regimen should be reviewed to ensure the person is tolerating the new biosimilar	Thank you for your comment. Recommendation 1.7.7 states that when switching to a biosimilar, a shared decision should be reached. Additionally. the rationale and impact section of the guideline, the committee agreed that switching to the biosimilar should be carefully planned, taking into consideration

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					the dose switching protocols and monitoring. The committee also noted that healthcare professionals should also refer to the summary of product characteristics for further information when considering switching to biosimilars.
Royal College of Nursing	Guideline	020	019	Take into account the persons capacity also	Thank you for your comment. Recommendation 1.7.7 states that when people are already using an insulin for which a lower cost biosimilar is available, discuss the possibility of switching to the biosimilar. This recommendation stresses the importance of shared decision making. The rationale and impact section in the guideline highlights that switching to biosimilars should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen, and a shared decision reached.
Royal College of Physicians and Surgeons of Glasgow	General	General	General	The Royal College of Physicians and Surgeons of Glasgow although based in Glasgow represents Fellows and Members throughout the United Kingdom. While NICE has a remit for England, many of the recommendations are applicable to all devolved nations including Scotland. They should be considered by the relevant Ministers of the devolved governments. The College welcomes this update on guidance on Type I Diabetes in Adults, diagnosis and management.	Thank you for your comment.
Royal College of Physicians and Surgeons of Glasgow	Guideline	008	016	While commendable, this service may not be available in all areas. Consider adding 'if available' to the wording	Thank you for your comment. This recommendation is outside the remit of the current review question. The committee noted that recommendation 1.2.3 is an aspirational recommendation outlining services that

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					can be provided to adults with type 1 diabetes. The committee agreed that 'if available' could not be added without reviewing the evidence. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date.
Royal College of Physicians and Surgeons of Glasgow	Guideline	008	026	While commendable, this may not be practical in many areas/centres. Perhaps 'if possible' should be added.	Thank you for your comment. Recommendations on support and individualised care were outside the remit of the current review question and was not prioritised for an update at scoping.
Royal College of Physicians and Surgeons of Glasgow	Guideline	General	General	Blood Glucose Monitoring There is no mention of 'Flash Blood Glucose Monitoring' anywhere in the guideline. This is an integral part of self-management for many individuals with Type 1 Diabetes and is considered different from 'Continuous Glucose Monitoring'.	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope
Sanofi UK	Evidence Review	352		Nocturnal hypo data for glargine U100 once daily versus Degludec U100 once daily (>6month) is referenced to the 104- week study (Bode et al 2015). The data is taken from the interim 52-week analysis of the same study (Heller et al, 2012).	Thank you for your comment. As noted in appendix K, the probability that an event is nocturnal given a patient had a hypoglycaemic event was modelled. To model this data, only studies that reported both all hypoglycaemic events and nocturnal hypoglycaemic

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					events could be included. While it is true Bode 2013 (extension trial for Heller 2012) did report data on nocturnal hypoglycaemic events at 104 weeks, it did not provide data for the rate of all hypoglycaemic events for the two arms of the trial. Due to this, data from Heller 2012 was used, which did provide arm data for all hypoglycaemic events and nocturnal hypoglycaemia.
Sanofi UK	Evidence Review	350		Severe hypoglycaemia rate data for pairwise analysis for detemir twice daily versus Glargine U100 once daily does not accurately reflect full trial data available and is not In line with the stated NMA methodology - where trials report data at multiple time-points, the data from the longest time point should be used in the analysis. For Pieber et al, 2007 severe hypo data was selected from a 20-week maintenance period rather than the full 26-week trial data which is also available within the manuscript. If full trial data was used in this analysis the corresponding estimated rate ratio would be 0.41.	Thank you for your comment. Several studies were identified which included a titration phase as part of the treatment period. These studies only reported data from the maintenance phase of the trial. For example, Pieber 2005 was a 16-week trial but the first 4 weeks were regarded as the titration phase. This study only reported data on hypoglycaemia for the last 12 weeks of the treatment (maintenance phase). Pieber 2007 on the other hand, reported titration and maintenance phase data separately. To remain consistent with these trials, data from the maintenance phase was extracted. It was also noted that data from the maintenance phase was also more relevant as in practice patients would be on a fixed dose during treatment. Appendix B has been amended to highlight this decision.
Sanofi UK	Evidence Review	352		Data included in pairwise meta-analysis for Glargine U100 Once daily vs Degludec U100 Once daily is incorrect. The event rate data recorded for Bode et al 2013 (Begin trial) have been incorrectly assigned to the wrong intervention arm in the trial resulting in a	Thank you for your comment. Our calculations were reviewed and double checked and were found to be correct. However, a presentational issue was identified in the forest plot. The labels of the forest plot have been amended which now show Bode 2013 to

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				rate ratio that favours Degludec U100 over Glargine U100. If the data is used correctly, the estimated RR from this study would be 1.13 in favour of Glargine U100.	favour glargine U100. This change does not affect the data underpinning the recommendations.
Sanofi UK	Evidence Review	352		Event data for pairwise analysis between Glargine U100 Once daily versus Degludec U100 once daily does not accurately reflect full trial data available Lane et al 2007 (SWITCH-1) nocturnal hypo data was selected from a 16-week maintenance period rather from the full 32-week trial data, which is also available within the manuscript. Full 32-week trial data should be included as part of the pairwise meta-analysis where possible.	Thank you for your comment. As highlighted in appendix B, if available, data from the first period of crossover trails would be utilised. Lane 2017 provided data from the first maintenance period. As our methods (appendix B) specify that data from the first period would be used, we opted to use data from the first maintenance period.
Sanofi UK	Evidence Review	354		Only 52-week data for Glargine u300 (EDITION 4 and EDITION JP-1 extension studies) is utilised for inclusion in the severe hypoglycaemia network meta-analysis. This is in comparison to detemir twice daily comparator studies which have an average follow-up time of 20.3 weeks (median: 18 weeks, range: 16-43 weeks), Degludec once daily comparator studies of 32.33 weeks (median: 21 weeks, range: 6-104 weeks) and glargine u 100 comparator studies of 33.09 weeks (median: 26 weeks, range: 6-52 weeks). As such, the network analysis provided is weighted in favour of those trials which have a shorter follow up time. Severe hypoglycaemia rate data (which is available to comply with the pairwise analysis methodology) from the original 26-week randomised control trial EDITION 4 (Home et al 2015) and EDITION JP-1 (Matsuhisa et a 2016) could be captured separately from the extension study into the analysis to provide more balanced and comparable data in the network meta-analysis.	Thank you for your comment. As detailed in appendix K, the committee discussions highlighted that long-acting insulins are quick acting and therefore there would not be expected to be meaningful differences in the long-term and short-term comparative effectiveness of different insulins. Based on this discussion, it was agreed that all follow up data should be combined in the NMAs.

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Sanofi UK	Evidence Review	354		Bergenstal et al 2017 severe hypo data is incorporated as risk data based on severe hypoglycaemia incidence reported in the trial manuscript. Severe hypoglycaemia rate data is also available in the Bergenstal et al 2017 manuscript and this data should be incorporated into the accompanying rate analysis in line with the documented NMA methodology where all hypoglycaemia rate data is preferred where possible.	Thank you for your comment. In Bergenstal 2017 rate data was presented for outcome confirmed or severe hypoglycaemic during the nocturnal interval, which does not match with our protocol outcome of just severe hypoglycaemia.
Sanofi UK	Evidence Review	355		Nocturnal hypoglycaemia event data for pairwise analysis for detemir twice daily versus Glargine U100 once daily does not accurately reflect full trial data available and is not in line with the stated NMA methodology "where trials report data at multiple time-points, the data from the longest time point should be used in the analysis". Pieber et al, 2007 severe hypo data was selected from a 20-week maintenance period rather than the full 26-week trial data which is also available within the manuscript. Full 26-week trial data should be included as part of the pairwise meta-analysis where possible.	Thank you for your comment. Several studies were identified which included a titration phase as part of the treatment period. These studies only reported data from the maintenance phase of the trial. For example, Pieber 2005 was a 16-week trial but the first 4 weeks were regarded as the titration phase. This study only reported data on hypoglycaemia for the last 12 weeks of the treatment (maintenance phase). Pieber 2007 on the other hand, reported titration and maintenance phase data separately. To remain consistent with these trials, data from the maintenance phase was extracted. It was also noted that data from the maintenance phase was also more relevant as in practice patients would be on a fixed dose during treatment.
Sanofi UK	Evidence Review	357		The pairwise analysis comparing the event numbers in EDITION 4 (Home et al 2018) and EDITION JP-1 (Matsuhisa et al 2016) is incorrect. The event numbers recorded in both trials have been incorrectly assigned to the wrong intervention arm in both trials resulting in an odds ratio that favours glargine 100 units/ml over Glargine 300 unit/ml in nocturnal hypoglycaemia risk. If	Thank you for your comment. The forest plot and corresponding value in table 10 (relative effectiveness of all pairwise comparisons) have been updated. This change did not have an impact on the data underpinning the recommendations.

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				the data is used correctly, the estimated OR from EDITION 4 trial would be 1.2 (95% CI: 1.12-1.28) and the estimated OR from the EDITION JP-1 trial would be 1.06 (95% CI 0.97-1.16).	
Sanofi UK	Evidence Review	423		The Pairwise analysis captured in Table 10 for Glargine U100 once daily versus Glargine U300 once daily is incorrect (OR 0.88). Results presented this table are based on the pairwise analysis documented on page 357. The pairwise analysis comparing the event numbers in EDITION 4 (Home et al 2018) and EDITION JP-1 (Matsuhisa et al 2016) is incorrect. The event numbers recorded in both trials have been incorrectly assigned to the wrong intervention arm in both trials resulting in an odds ratio that favours glargine 100 units/ml over Glargine 300 unit/ml in nocturnal hypoglycaemia risk. If the data is used correctly, the estimated OR from EDITION 4 trial would be 1.2 (95% CI: 1.12-1.28) and the estimated OR from the EDITION JP-1 trial would be 1.06 (95% CI 0.97-1.16).	**Thank you for your comment. The forest plot and corresponding value in the NMA analysis has been amended.** This change did not have an impact on the data underpinning the recommendations.
Sanofi UK	Evidence Review	423		Only 52-week data for Glargine U300 comparator studies (EDITION 4 and EDITION JP-1 Extension studies) are utilised in the nocturnal hypoglycaemia network meta-analysis. This is in comparison to detemir twice daily comparator studies which have an average follow-up time of 20.3 weeks (median: 18 weeks, range: 16-43 weeks), Degludec U100 once daily comparator studies of 23.7 weeks (median: 21 weeks, range: 6-52 weeks) and glargine U100 comparator studies of 28 weeks (median: 26 weeks, range: 6-52 weeks). As such, the NMA provided is weighted in favour of those trials which have a shorter	Thank you for your comment. As detailed in appendix K, the committee discussions highlighted that long-acting insulins are quick acting and therefore there would not be expected to be meaningful differences in the long-term and short-term comparative effectiveness of different insulins. Based on this discussion, it was agreed that all follow up data should be combined in the NMAs.

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				follow up time. Nocturnal hypoglycaemia event data (which is available to comply with the pairwise analysis methodology) from the original 26-week EDITION 4 randomised control trial (Home et al 2015) and EDITION JP-1 (Matsuhisa et a 2016) should be captured separately from the extension studies to provide comparable data in the NMA.	
Sanofi UK	Evidence Review	General	General	Notes: We have organised our comments below into 3 themes: • Comments 14, 15 and 16 related to errors in the analysis of the evidence base. These errors must be corrected in the final document • Comments 17 to 22 related to comparing 'like with like' for the duration of the data observed between trials. • Comment 23 relating to the use of risk vs. rate data	Thank you for your comment. Your specific points have been responded to where they appear.
Sanofi UK	Guideline	009	027	The guidance recommends Dose Adjustment for Normal Eating (DAFNE) as the sole example of an evidence-based structured education programme. The emphasis of a single programme is unhelpful. DAFNE is not available nationally, it has been suggested that the cost and governance involved in delivering DAFNE are prohibitive in some areas. Although data from the DAFNE program is available it tends to reflect completer–finishers and no head-to-head trials of programmes have been performed. We therefore suggest that the section on structural education programs should be more inclusive and avoid specific or implied preference to any structured educational programme.	Thank you for your comment. Recommendations on education and information were outside the remit of the current review question and was not prioritised for an update at scoping.

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Sanofi UK	Guideline	018	006 - 016	Sanofi is concerned that the upcoming review of diagnostics guidance [DG21] may mean the 2015 recommendations in this guidance will be out of step. NICE should present a clear understandable pathway for the use of these technologies to drive clinician confidence. Diabetes UK's 'Future of Diabetes' 2017 survey found that 28% of respondents reported problems getting the medication or equipment they need to manage their diabetes. It is critical that this guidance alongside the upcoming diagnostics guidance avoids any doubt that might drive unwarranted variation – as seen for example with availability of insulin pumps currently.	Thank you for your comment. As highlighted in the guideline, recommendations on continuous glucose monitoring are due to be updated and will be published in 2022. Additionally, NICE diagnostic guidance on integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (DG21) is being updated. The update will assess hybrid closed loop technologies which will be replacing integrated sensor-augmented pump therapy systems. https://www.nice.org.uk/guidance/DG21/documents/type-1-diabetes-integrated-sensoraugmented-pump-therapy-systems-for-managing-blood-glucose-levels-the-minimed-paradigm-veo-system-and-the-vibe-and-g4-platinum-cgm-system-final-scope
Sanofi UK	Guideline	019	018 - 019	The directive offering of a twice daily basal insulin may run counter to patient preference in some cases. Reference to the role of patient preference in basal insulin choice at this stage would uphold the principle of personalised care.	Thank you for your comment. Recommendations do state that once- daily glargine (100 unit/ml) can be considered if insulin detemir is not tolerated or the person has a strong preference for once-daily basal injections. Additionally, rec 1.7.8 states that when choosing an alternative insulin regimen, take account of the person's preferences, comorbidities, risk of hypoglycaemia, diabetic ketoacidosis and concerns around adherence, and the acquisition cost.
Sanofi UK	Guideline	019	018 - 019	This statement omits the word "consider" which is the preface of all subsequent decision points. It therefore is seen as a directive statement. Sanofi suggests that this specific statement be modified to reflect a statement of guidance and emphasise that other	Thank you for your comment. The evidence showed that there were fewer severe and nocturnal hypoglycaemic events with insulin detemir twice daily. It was also found to be the most cost-effective treatment strategy. Based on these findings the committee recommended that detemir should be

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				clinical factors can influence therapy choice, including personalised treatment.	offered as basal insulin therapy for adults with type 1 diabetes. The committee were also aware that there are situations in which an insulin other than twice-daily insulin detemir might be preferred and set out specific clinical scenarios where alternative long-acting insulins could be used. These are set out in rec 1.7.4. Furthermore the use of the term 'offer' acknowledges the experience of people who are directly affected by the recommendation (and family members, carers or advocates), and their role in decision-making. In keeping with the principles of shared decision-making, people may choose whether or not to accept what they are offered.
Sanofi UK	Guideline	020		The guidance recommends Once-daily insulin such as degludec (100units/ml) for people who need help from a carer or healthcare professional to administer injections. [2021]. The basis for this guideline as stated in the evidence reviews "insulin degludec may have some advantages in this population, as the longer duration of treatment effect means there is more flexibility in when during the day the insulin is delivered, as opposed to basal insulins with less than 24-hour coverage that may result in periods of no insulin coverage". Using the same rationale, Glargine U300 could also offer value to people who need help from a carer or healthcare professional to administer injections. According to information included in the summary of product characteristics, the effect of	Thank you for your comment. As highlighted in the comment, glargine U300 is an ultra-long-acting insulin making it a useful treatment option. However, no direct evidence was identified which compared glargine 300 units/ml and degludec 100 units/ml. Additionally, the NMA results could not differentiate between degludec 100 units/ml and glargine 300 units/ml for outcomes change in HbA1c, all hypoglycaemia, severe/major hypoglycaemia and nocturnal hypoglycaemia. Based on the findings, specific recommendations on the use of glargine (300 units/ml) were not drafted. However, the results did show that there were fewer nocturnal hypoglycaemic events with degludec 100

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				Glargine U300 is beyond 24 hours (up to 36 hours) at clinically relevant doses. Glargine U300 can also be given, when needed, up to 3 hours before or after the persons usual time of administration.	units/ml when compared to detemir once daily, NPH once daily and glargine 100 units/ml once daily. Based on these findings the committee highlighted that degludec 100 units/ml can be considered if there is a particular concern about nocturnal hypoglycaemia. The committee were aware that other basal insulins not covered by recommendations 1.7.3 and 1.7.4 may be considered. In such instances, it is recommended that other basal insulin regimens can be considered if regimens in recs 1.7.3 and 1.7.4 do not meet agreed treatment target. Additionally, when choosing an alternative insulin regimen, the person's preferences, comorbidities, risk of hypoglycaemia and acquisition cost should be considered. Additionally, the results of the economic modelling also showed that, when hypoglycaemia was included, degludec (100 units/ml) was consistently more cost-effective than glargine (300 units/ml). Therefore, degludec (100 units/ml) was identified as an adequate treatment in people who need help from a carer or healthcare professional to administer injections, but the recommendation is not limited to the use of deguldec. Based on feedback, the recommendation has been amended to state that 'once daily ultra-long-acting insulin such as degludec (100 units/ml) can be considered in people who need help from a carer or healthcare professional to administer injections'.
Sanofi UK	Guideline	020	010 - 020	In keeping with the wording of the 'What is a Biosimilar Medicine' guide (2019), reference to a	Thank you for your comment. As recommendations specifically focus on biosimilars, this term was used

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				lower cost option should utilise the language of 'best value biologic' rather than any association with the biosimilar.	instead of the term 'biological medicines' or 'biologic'. NICE recognises that biosimilar medicines have the potential to offer the NHS considerable cost savings and therefore provide increased value for money.
Sanofi UK	Guideline	020	010 - 020	Sanofi recognise the biosimilar rapid-acting insulins will also be on the market in addition to long-acting insulins. We would appreciate information from NICE about whether the principles outlined in relation to long-acting insulins will also be reviewed in relation to rapid-acting insulins or where the evidence points to a different approach.	Thank you for your comment. NICE guidelines are evidence-based and undergo a rigorous development process. Guidelines are reviewed through the surveillance process to check that the guidelines are up to date. NICE maintains an event tracker containing information on key events, such as ongoing studies, that are judged to be relevant to the guideline content. Based on the evidence identified as decision is made to update the guideline. The surveillance decision for NG17 highlighted that new evidence identified for rapid-acting insulins was unlikely to impact the current recommendations. Based on this finding, recommendations on rapid-acting insulins were not reviewed as part of this update.
Sanofi UK	Guideline	020	011 - 014	Ensuring that shared decision making underpins any conversation around switching is a key principle of the 'What is a Biosimilar Medicine' guide (2019) endorsed by NHS England and NICE alongside other key stakeholders. NICE should outline here more detailed information that exists around what a shared decision-making conversation should look like, including recognition of the use of different devices. Consistency with existing guidance produced by patient organisations such as Diabetes UK and the Patients Association - as well as core NHS guidance is critical to ensure that patient outcomes are upheld and clinicians can make appropriate clinical decisions.	Thank you for your comment. The committee drafted recommendation 1.7.7 to encourage discussions to take place around switching to biosimilars. The rationale and impact section also highlights that the possibility of switching should be discussed with people during their routine review and should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached. Furthermore recommendation 1.7.7 is based on the principle of shared decision making – a collaborative

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					process that involves a person and their healthcare professional working together to reach a joint decision about care. This is in agreement with the 'What is a Biosimilar Medicine' guide (2019) which also highlights that the decision to prescribe a biological medicine for an individual patient is in line with the principles of shared decision making (page 9).
Sanofi UK	Guideline	040	001 - 004	A survey of 100 people with Type 1 Diabetes, conducted by Sanofi in 2019 found that 3% regularly see a mental health professional in relation to the emotional impact of diabetes self-management. The language of this guideline should be reviewed to avoid any clinical barriers to referral for psychological support.	Thank you for your comment. Recommendations throughout the guideline have been amended and term such as 'psychological disorders', 'psychological difficulties' and 'psychological problems' have been replaced with the term 'mental health problems'.
Sanofi UK	Guideline	General	General	Sanofi is keen to ensure that NG17 meets the requirements of providing individualised, holistic care and support for self-management for people living with Type 1 Diabetes. It is our belief that these three things are paramount to improving patient outcomes.	Thank you for your comment and for providing useful feedback for improving patient care. Your commentscomment regarding the role of individualised care will be considered by NICENICE's Implementation team where relevant support activity is being planned.
Sanofi UK	Guideline	General	General	90% of patients with type 1 diabetes fail to achieve the NICE stated glycaemic target (less than 15% achieve the target). Recognition of the role of individualised care, as well as newer outcome measures in future guidance (such as Time in Range) is critical to improving outcomes.	Thank you for your comment. HbA1c measurements and targets was outside the remit of this question and was not prioritised for an update at scoping. Your comment regarding the role of individualised care will be considered by NICE's Implementation team where relevant support activity is being planned.
Sanofi UK	Guideline	General	General	Currently, England and Wales sit behind other developed countries around improving glycaemic control for young people with type 1 diabetes. According to Anderzen et al (2020), mean HbA1c at ages 15-17 in England (8.9%) and Wales (9.1%) was higher than other developed countries such as	Thank you for your comment. HbA1c measurements and targets was outside the remit of this question and was not prioritised for an update at scoping.

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				Germany (8.2%), Austria (8.2%), Denmark (8.2%), Sweden (7.8%), the United States (8.8%) and Norway (8.4%). It is important that the changes in this guideline reflect the pathway outlined in NG18 to ensure that it supports self-management and individualised care during transition where outcomes are traditionally poor.	
Sanofi UK	HE model report	017 - 018		The committee initially agreed that the frequency of dosing is likely to be associated with a quality of life decrement and this sentiment is reflected in the final guidance which recognises that in cases where the person has a strong preference for once-daily basal injections, twice daily insulin detemir should not be offered. However, we believe that the evidence for disutility associated with multiple daily injections has not been properly considered. We recognise that the direct evidence base to demonstrate such a utility decrement is small however the key high-quality study by Evans identified in the literature search is an important contribution that should not be ignored. The committee dismissed this evidence because the survey did not disaggregate Type 1 and type 2 diabetes and also did not consider adaptation. However, there are key aspects of the survey that the committee should be aware of: • More people with Type 1 diabetes were included in the relevant population (with basal-bolus therapy) than Type 2 (265 vs. 200).	Thank you for your comment. As pointed out, the study by Evans et al was not used in the analysis as it may not provide an accurate reflection of the impact on the quality of life by dosing regimens on type 1 diabetes patients as the results are reported for a mixed population due to the differences in demographics and treatment regimens between type 1 and type 2 patients. This was presented again to the committee in the post-consultation committee meeting where it was confirmed that the impact of the dosing frequency on quality of life is likely to differ by the patients type of diabetes. It is also worth noting that Evans et al measures the QoL at one time point (as an example the flexible injection health state was defined as – "You must give yourself one insulin injection each day. This can be taken at a time of your choosing", and does not provide evidence on whether these differences in QoL between dosing regimens will hold over time. Hence given these limitations in the information available, the committee decided to not factor in the results from Evans et al on the impact on QoL due to the frequency of dosing. They agreed that, since

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				• The similar response from the general population (0.022 utility decrement) and the population with diabetes (0.021 utility decrement) increases the face validity of the results. • The additional burden of SMBG has also been shown to decrease quality of life The reasons put forward by the committee to ignore the impact on quality of life because of the aggregation of the type 1 and type 2 populations are not sufficient to discount the clear signal arising from this study. Indeed, it is likely that given the younger average age of type 1 patients the additional impact on lifestyle of an extra injection per day would be more keenly felt than for older type 2 patients. Similarly, whilst the Evans study was cross sectional in nature the average duration of diabetes was 16.6 (+/-14.4) years for people with type 1 diabetes and 8.7 (+/-7.9) years for those with type 2 diabetes. Any argument to say that adaptation had not occurred in these patients is clearly spurious given their duration of disease. It is particularly important to consider all aspects of uncertainty in the current analysis. The committee has noted the inherent uncertainty in the hypoglycaemia rates, which are the key driver of cost-effectiveness. However not including a quality of life decrement due to multiple daily dosing risks increasing decision uncertainty and may result in decision error. Therefore, it is surprising to us that the impact of	different individuals will have very different strengths of preferences around numbers of injections, this was better captured by the references to patient choice and preferences within the recommendations.

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				dosing frequency on utility was not examined at least in sensitivity analysis. We urge the committee to consider additional analyses using the disutilities identified by Evans et al.	
Swansea Bay University Health Board	Guideline	019	017	1.7.3 in our view, there is no need for such a specific recommendation of twice-daily detemir as basal therapy in all cases. Similar guidance regarding BD basal insulin use has not been produced by NICE for managing children and young people with diabetes (NG18). Our local service, for example, uses a single basal insulin dose and so people with diabetes are taking this at transition to the adult service. The evidence to support an automatic transfer to a BD basal insulin regime at the age of eighteen years is non-existent and so diabetes services should not be being encouraged to do this by NICE.	Thank you for your comment. While the recommendation is not specific to those transitioning from paediatric care to adult services, recommendation 1.7.4 does state that an insulin regimen that is already being used by the person can be considered if it is meeting their agreed target goals (such as meeting their HbA1c targets or time in glucose range and minimising hypoglycaemia).
Swansea Bay University Health Board	Guideline	019	020	1.7.4 Furthermore, there is no evidence of statistical superiority of BD detemir insulin over modern once daily basal regimens, as illustrated by this reference (Bain SC, Feher M, Fisher M, Hex N, Lee KCS, Mahon J, Russell-Jones D, Schou H, Wilmot EG, Baxter M. A review of the NG17 recommendations for the use of basal insulin in type 1 diabetes. Diabet Med. 2020 Feb;37(2):219-228). So the suggestion that people with type 1 diabetes must express a 'strong preference for once-daily basal injections' (page 19, line 27) is unwarranted and at-odds with patient empowerment. The BD detemir regime will undoubtedly suit some people but the directive in this guideline is too strong.	Thank you for providing reference to Bains 2020. This review was based on the NMA conducted as part of the 2015 update and does not consider analysis conducted as part of the new update. As part of this new update, we conducted NMAs for the following outcomes: • Change in HbA1c • All hypoglycaemic events • Severe/major hypoglycaemic events • Probability that an event is nocturnal given a patient had an event. As highlighted in section 1.1.12 of the evidence review, the results from the change in HbA1c NMA could not differentiate between the different long-

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					acting insulins and uncertainty with the evidence was also identified. NMAs conducted for hypoglycaemic events did highlight significant findings which were used in the decision-making process. Clinical and cost effectiveness evidence demonstrated that detemir twice daily is the optimal treatment strategy for the majority of people with type 1 diabetes. Based on this finding the committee recommended detemir twice daily as basal insulin therapy for adults with type 1 diabetes. However, the committee were aware that there are situations in which an insulin other than twice-daily insulin detemir might be preferred. Based on this understanding the committee set out specific clinical scenarios where alternative long-acting insulins can be considered. In these scenarios, patient preference is also highlighted as an important factor. Furthermore the use of the term 'offer' acknowledges the experience of people who are directly affected by the recommendation (and family members, carers or advocates), and their role in decision-making. In keeping with the principles of shared decision-making, people may choose whether or not to accept what they are offered.
Swansea Bay University Health Board	Guideline	020	011	1.7.6 The suggestion that medical and nursing staff should routinely discuss a change in basal insulin when a less expensive biosimilar is available, suggests a lack of understanding of the current work pressures in adult diabetes services. NICE should	Thank you for your comment. The committee drafted recommendation 1.7.7 to encourage discussions to take place around switching to biosimilars and stresses the importance of shared decision making. The rationale and impact section also highlights that

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				also be aware that in some parts of the UK the first biosimilar glargine insulin is now (slightly) more expensive that the original reference molecule; should patients be switched back?	the cost is not the only important element in decision making. The committee noted that switching should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached. The committee noted there would be costs associated with switching but that discussing this as part of routine reviews (rather than having additional appointments for this purpose) would minimise these costs, and were confident the savings from the use of biosimilars would outweigh these additional costs. The committee noted the point that in some circumstances the originator product may be cheaper than subsequent biosimilars and agreed that is such circumstance it would be appropriate to use the originator product.
Training, Research and Education for Nurses in Diabetes	General	General	General	It is disappointing that the entire guideline has not been reviewed rather than just making small changes- will HCPs have to wait a further 5 years for a more robust revision when the ADA updates annually	Thank you for your comment. As highlighted in the NICE methods manual, NICE guidelines are evidence-based and undergo a rigorous development process. Guidelines are reviewed through the surveillance process to check that the guidelines are up to date. Some topic areas are fast moving, and this increases the risk of guidelines having out-of-date recommendations. Therefore, NICE maintains an event tracker containing information on key events, such as ongoing studies, that are judged to be relevant to the guideline content. Ongoing studies are identified for the event tracker through the standard

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					check and also through NICE's engagement with the National Institute for Health Research. As part of this update, recommendations on continuous glucose monitoring and diagnosis are due to be updated and will be published in 2022. Furthermore, updates have been planned for the management of complications in adults with type 1 and type 2 diabetes as well as in children and young people with type 1 and type 2 diabetes. It is anticipated that this work will also publish in 2022.
Training, Research and Education for Nurses in Diabetes	General	General	General	This guideline line has not taken into account the possibility of some early form of structured education soon after diagnosis rather than six months later. Would the panel be willing to consider some initial form of structural education to support newly diagnosed individuals with diabetes. This could include early information regarding carbohydrate counting and prepare the way for more intensive education after 6 months	Thank you for your comment. Education and information were outside the remit of the review question and was not prioritised for an update at scoping. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date.
Training, Research and Education for Nurses in Diabetes	Guideline	019	018	Page 1.7.3 It is disappointing that twice daily intermediate acting insulin is still to be offered to newly diagnosed individuals when once daily longer acting is readily available. This is recognised and carries lower risks of nocturnal hypoglycaemia and involves only a once daily basal injection. so reduces the injection burden	Thank you for your comment. Recommendations state that twice-daily inulin detemir can be offered to adults with type 1 diabetes but once-daily glargine (100 units/ml) can be considered if insulin detemir is not tolerated or the person has a strong preference for once-daily basal injections. Additionally, recommendations also state that degludec (100 units/ml) can also be considered if there is a particular concern about nocturnal hypoglycaemia. The committee noted the results of the economic model were consistent that, when hypoglycaemia was

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					considered, detemir twice daily was the most cost-effective treatment option, ahead of once daily insulins, include ultra-long-acting ones.
Training, Research and Education for Nurses in Diabetes	Guideline	020	011	1.7.6 Switching an individual who has stable glycaemic control to a biosimilar just because of cost, needs to take into account the cost of extra appointments and disruption to that individual as well as the cost of insulin	Thank you for your comment. The committee drafted recommendation 1.7.7 to encourage discussions to take place around switching to biosimilars. The rationale and impact section also highlights that the possibility of switching should be discussed with people during their routine review and should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached. The committee noted there would be costs associated with switching but that discussing this as part of routine reviews (rather than having additional appointments for this purpose) would minimise these costs, and were confident the savings from the use of biosimilars would outweigh these additional costs.
Training, Research and Education for Nurses in Diabetes	Guideline	022	025	Advice given in section 1.8.3 is outdated – there is no evidence to suggest that people with diabetes who are insulin treated need any other needle length than 4 mm. All children and thin adults should be advised to use a lifted skin fold to prevent intramuscular injections. If insulin is being given by a third party with a syringe the lifted skin fold is necessary to prevent intramuscular injections. Needles are only for single use – warn against reuse of needles	Thank you for your comment. Section 1.8 of the guideline was outside the remit of the review question. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date.
Training, Research and Education for	Guideline	024	025	1.10.8 Include advising 'not to drive' if hypo unaware	Thank you for your comment. Section 1.10 of the guideline was outside the remit of the review question and was not prioritised for an update at scoping.

Type 1 diabetes in adults: diagnosis and management (update) – insulin

Consultation on draft guideline - Stakeholder comments table
21/04/2021 – 19/05/2021

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Nurses in Diabetes					
Training, Research and Education for Nurses in Diabetes	Guideline	027	006	1.11.1 Suggest change 'Consider' to 'Encourage'	Thank you for your comment. Standard NICE wording was used when drafting the recommendation. This recommendation was out of scope for this review. Furthermore, the NICE guideline manual outlines that the term 'consider' reflects the strength of the evidence and is used if there is a closer balance between benefits and harms.
Training, Research and Education for Nurses in Diabetes	Guideline	029	007	1.12.1 Add in assess for Eating Disorder	Thank you for your comment. Section 1.10 of the guideline was outside the remit of the review question and was not prioritised for an update at scoping.
Training, Research and Education for Nurses in Diabetes	Guideline	030	027	1.13.8 The hypertension advice needs to sign post to the NICE Management of Hypertension guideline (2019)	Thank you for your comment. A link to NICE guideline on hypertension in adults has been added.
Training, Research and Education for Nurses in Diabetes	Guideline	034	017	1.15.6 This needs to link with the latest KDIGO guidance - the other outdated reference included in this revision will contribute to loss of confidence in the new guideline	Thank you for your comment. A hyperlink has been added to the chronic kidney disease in adults guideline (CG182).
Training, Research and Education for Nurses in Diabetes	Guideline	039	006	1.15.33 what advice are the panel giving for sexual dysfunction in women – lack of support and taboo in this area.	Thank you for your comment. Recommendation 1.15.33 was outside the remit of this update and was not prioritised for an update at scoping.
UK Clinical Pharmacy Association	Guideline	011	021	1.4.3 Dietary and lifestyle advice has altered and there is increased focus on low CHO diet in diabetes, albeit less so for those with T1DM. If specific diets are	Thank you for your comment. Recommendations on dietary management were outside the remit of the

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Diabetes & Endocrinology Committee				being highlighted then this should be expanded to include these or the recommendation should be removed to prevent confusion.	current review question and was not prioritised for an update at scoping.
UK Clinical Pharmacy Association Diabetes & Endocrinology Committee	Guideline	016	023	1.6.12 Patients testing as often as 10 times a day are now switched to use Libre to provide better data. It seems astonishing that Libre and its use to support patients with hypoglycaemia and labile CBG has not been mentioned throughout this section. NHSE have put in place recommendations and support for its use – these should have been included in this guidance with a review of the latest evidence. This omission will lead to misunderstanding of best practice and what we are encouraging our patients to achieve.	Thank you for your comment. Frequency of self-monitoring of blood glucose was outside the remit of this question and was not prioritised for an update at scoping.
UK Clinical Pharmacy Association Diabetes & Endocrinology Committee	Guideline	017	001	1.6.13 There has been no acknowledgement of the target for 'time in range' which is increasingly the preferred measure for patients with T1DM. Although not all patient will have access to Libre and CGMS, it should be included to ensure education of less specialist practitioners and a clear standard for those who have been given access. HbA1c and blood glucose targets - although they have stated about individual targets for HbA1c there is no specific mention of frail/older patients where these tight targets would not be appropriate. There is no alternative NICE guidance in which these are specified / stated.	Thank you for your comment. Blood glucose targets was outside the remit of the review question and was not prioritised for an update at scoping.
UK Clinical Pharmacy Association Diabetes &	Guideline	019	020	1.7.4 Toujeo (glargine 300units/ml) should be considered alongside degludec if there is a particular concern about nocturnal hypoglycaemia. The BRIGHT study compared insulin glargine 300 units/ml vs. insulin degludec 100 units/ml in a head-to-head RCT,	Thank you for your comment. The BRIGHT study assessed the efficacy and safety of glargine 300 units/ml and degludec 100 units/ml in people with uncontrolled type 2 diabetes. As the focus of the

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Endocrinology Committee				results showed non-inferior HbA1c reduction for Toujeo vs degludec. Hypoglycaemia rates were lower for degludec compared to Toujeo in the initial phase (0 - 12 weeks), but hypoglycaemia event rates were similar in the maintenance phase (13 - 24 weeks). Toujeo has a slightly lower per unit cost than degludec. Toujeo could also be considered where assistance is required, as it also gives flexibillity in dosing time. When needed, Toujeo can be given up to 3 hours before or after their usual time of administration. In the evidence summary and economic model there was virtually no difference between the two. Given that alternatives to detemir have been listed for the specific circumstances listed it seems very odd to have excluded an insulin that performs well against all other alternatives, especially in the population of patients that require significant insulin doses (such as obesity), where Toujeo often outperforms the others listed.	current review is on type 1 diabetes, this study did not meet the inclusion criteria. NMA results also did not identify a significant difference glargine (300 units/ml) and other long-acting insulins for outcomes change in HbA1c, all hypoglycaemia, severe and nocturnal hypoglycaemia. Based on the findings, specific recommendations on the use of glargine (300 units/ml) were not drafted. The evidence did show that there was a lower proportion of nocturnal hypoglycaemic events with degludec (100 units/ml) compared to other long-acting insulins. Based on this evidence, the committee recommended that degludec (100 units/ml) should be considered as an alternative basal insulin therapy if there is a particular concern about nocturnal hypoglycaemia. Additionally, the results of the economic modelling also showed that, when hypoglycaemia was included, degludec (100 units/ml) was consistently more cost-effective than glargine (300 units/ml). Therefore, degludec (100 units/ml) was identified as an adequate treatment in people who need help from a carer or healthcare professional to administer injections, but the recommendation is not limited to the use of deguldec. Based on feedback, the recommendation has been amended to state that 'once daily ultra-long-acting insulin such as degludec (100 units/ml) can be considered in people who need help from a carer or healthcare professional to administer injections'.

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UK Clinical Pharmacy Association Diabetes & Endocrinology Committee	Guideline	020	011	1.7.6 We strongly endorse the consideration of biosimilars for use in T1DM in order to reduce costs without altering efficacy.	Thank you for your comment.
UK Clinical Pharmacy Association Diabetes & Endocrinology Committee	Guideline	024	017	1.10.6 This needs to be adjusted for frail / elderly patients. We would fully expect targets to be relaxed in an older patient where they would no longer see the benefits of tight control and are more likely to adverse outcomes secondary to hypos particularly those with cognitive impairment.	Thank you for your comment. Section 1.10 of the guideline outside the remit of the review question. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date.
UK Clinical Pharmacy Association Diabetes & Endocrinology Committee	Guideline	029	015	1.13 The section on cardiovascular risk only considers ischaemic heart disease and has not mentioned nor considered heart failure. Given the high population of patients with diabetes and heart failure there is likely to be an increasingly elderly population where both need assessment and practitioners understand the difference between T1DM and T2DM. New data considers the use of adjunctive therapies such as SGLT2-inhibitors in T1DM and it seems remiss to not review the current data and make recommendations. Diabetes is not considered well in cardiovascular guidelines with only a recommendation to control blood glucose.	Thank you for comment. Section 1.13 was outside the remit of the review question and was not prioritised for an update at scoping. We will pass your comment to the NICE surveillance team which monitors guidelines to ensure that they are up to date.
Welsh Endocrine & Diabetes Society	Guideline	019	018	Offer twice daily detemir as basal insulin therapy for adults with type 1 diabetes This may be helpful to assist in the management of exercise and alcohol Caution may be needed in those with known insulin omission and frequent attendance with DKA as a	Thank you for your comment. As evidence was not identified in people who need assistance in managing exercise and alcohol intake, the committee did not think it was appropriate to draft recommendations for this cohort of patients. However, this has been added

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				longer acting insulin such as degludec may be preferred. Alignment with paediatric guidance is recommended for those transitioning from paediatric to adult services as swapping insulin at the time of great upheaval may be deleterious If basal requirements are high then a concentrated insulin such as degludec U200 or glargine U300 may be preferred.	to the committee discussion section in the evidence review. Additionally, DKA was an outcome of interest identified at review protocol stage however no evidence was found for this outcome. Additionally, no studies were identified in people with frequent DKA admissions. Therefore specific recommendations could not be drafted. However, the committee did note that this was an important issue that needs to be taken into consideration. Therefore, recommendation 1.7.8 has been amended to state that DKA and adherence should also be taken into consideration when considering other basal insulin regimens for adults with type 1 diabetes only if the regimens in rec 1.7.3 and 1.7.4 do not meet their agreed treatment goals. Further discussion has also been added to section 1.1.12 of the evidence review. Additionally, while the recommendation is not specific to those transitioning from paediatric care to adult services, recommendation 1.7.4 does state that an insulin regimen that is already being used by the person can be considered if it is meeting their agreed target goals (such as meeting their HbA1c targets or time in glucose range and minimising hypoglycaemia).
Welsh Endocrine & Diabetes Society	Guideline	019	020	Alternative basal insulin therapy. This seems very reasonable	Thank you for your comment.
Welsh Endocrine &	Guideline	020	006	Starting biosimilar at lowest cost.	Thank you for your comment. The committee drafted recommendation 1.7.7 to encourage discussions to

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Diabetes Society				This seems reasonable. The following should be considered: Switching insulins based on cost alone is unlikely to be cost effective as significant staff time is required for such a switch to be safe. However, if other factors such as using the engagement and staff time to improve outcomes then this may have dual benefit. Acquisition costs often vary over a short period of time. Sometimes familiarity of staff with an insulin may be a partial barrier to using an unfamiliar insulin.	take place around switching to biosimilars. The rationale and impact section also highlights that the possibility of switching should be discussed with people during their routine review and should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached.
Welsh Endocrine & Diabetes Society	Guideline	020	011	See comments above Switching insulins based on cost alone is unlikely to be cost effective as significant staff time is required for such a switch to be safe. However, if other factors such as using the engagement and staff time to improve outcomes then this may have dual benefit.	Thank you for your comment. The committee drafted recommendation 1.7.6 to encourage discussions to take place around switching to biosimilars. The rationale and impact section also highlights that the possibility of switching should be discussed with people during their routine review and should be carefully planned, taking into consideration the dose switching protocols, monitoring and the person's concerns about switching from their existing regimen. It is also emphasized that a shared decision should be reached. The committee noted there would be costs associated with switching but that discussing this as part of routine reviews (rather than having additional appointments for this purpose) would minimise these costs, and were confident the savings from the use of biosimilars would outweigh these additional costs.
Welsh Endocrine & Diabetes Society	Guideline	020	015	Consider other basal insulin if 1.7.3 and 1.7.4 does not meet needs Suggest recommending degludec for those with frequent insulin omission	Thank you for your comment. As evidence was not identified in people with frequent insulin omission, the committee did not think it was appropriate to draft recommendations for this cohort of patients. .

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				Suggest degludec U200 or glargine U300 for those with high basal insulin requirements	Additionally, DKA was an outcome of interest identified at review protocol stage however no evidence was for this outcome. Additionally, no studies were identified in people with frequent DKA admissions. Therefore, specific recommendations could not be drafted. However, the committee did note that this was an important issue that needs to be taken into consideration. Therefore, recommendation 1.7.9 has been amended to state that DKA and adherence should also be taken into consideration when considering other basal insulin regimens for adults with type 1 diabetes only if the regimens in rec 1.7.3 and 1.7.4 do not meet their agreed treatment goals. Further discussion has also been added to section 1.1.12 of the evidence review. Only studies comparing degludec (200 units/ml) and glargine (300 units/ml) were identified. However, as the follow up time in these studies was less than 4 weeks, these studies were not included in the network meta-analysis. Due to this, recommendation on degludec (200 units/ml) could not be made. NMA results could not differentiate between glargine 300 units/ml and other long-acting insulins. Therefore, specific recommendations on the use of glargine 300 units/ml were not formed. The committee were aware that other basal insulins not covered by recommendations 1.7.3 and 1.7.4 may

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					be considered. In such instances, it is recommended that other basal insulin regimens can be considered if regimens in recs 1.7.3 and 1.7.4 do not meet agreed treatment target. Additionally, when choosing an alternative insulin regimen, the person's preferences, comorbidities, risk of hypoglycaemia, DKA and adherence, and acquisition cost should be considered.

None of the stakeholders who comments on this clinical guideline have declared any links to the tobacco industry.