NICE National Institute for Health and Care Excellence

2019 surveillance of diabetes (NICE guidelines NG17, NG18, NG19 and NG28)

Surveillance report

Published: 27 June 2019
www.nice.org.uk

Contents

Surveillance decision

We will update the following guidelines on diabetes:

- Type 1 diabetes in adults (NICE guideline NG17)
- Type 2 diabetes in adults (NICE guideline NG28)
- Diabetes (type 1 and type 2) in children and young people (NICE guideline NG18)

We will not update the guideline on diabetic foot problems (NICE guideline NG19).

Reasons for the decision

It is proposed that the following areas are considered for update.

Type 1 diabetes in adults (NICE guideline NG17)

Diagnosis: classification of late-onset type 1 diabetes

New evidence and stakeholder comments indicate that people with late-onset type 1 diabetes may be at risk of misclassification of diabetes and that clinical characteristics such as age at diagnosis and body mass index (currently mentioned in recommendation 1.1.1) may not be as accurate as C-peptide tests when distinguishing between diabetes types in people aged over 35 years.

Blood glucose management: telemedicine, smartphone applications and online platforms; flash glucose monitoring; continuous glucose monitoring (CGM)

Evidence indicates that the use of smartphone applications to enhance self-monitoring and telemedicine interventions (such as remote monitoring devices, online education platforms and teleconference sessions) help people to significantly reduce their HbA1c levels.

Flash glucose monitoring measures glucose levels from a sensor applied to the skin as an alternative to routine finger-prick blood glucose testing and can produce a near-continuous record of measurements which can be accessed on demand. It can also indicate glucose level trends over time. Evidence was identified to support the use of flash glucose monitoring in people with well-controlled diabetes, which is not currently recommended in the guideline.

Evidence was also identified which supports the use of CGM in people having multiple daily injection therapy with sub-optimal glucose control. Many stakeholders also raised concerns in this

area, calling for CGM eligibility criteria in the guideline to be reconsidered.

Insulin therapy: long-acting insulin; biosimilar insulins; adjuncts to insulin; closed-loop systems

Evidence was identified which supports the use of the ultra-long-lasting insulin degludec. This was also an area raised by topic experts. The safety profiles and dosage conversions will also need careful consideration, given the advice in the corresponding drug safety update.

Evidence was identified to suggest that various biosimilar insulins may be non-inferior to original insulin formulations such as lispro and glargine. The guideline currently recommends offering insulin detemir or insulin glargine in adults with type 1 diabetes (recommendation 1.7.4). This was also an area raised by topic experts, who highlighted the potential cost savings available when switching to cheaper (but clinically comparable) insulins.

Several trials examined the effect of SGLT-2 inhibitors as an adjunct to insulin therapy; however many of the studies were related to NICE technology appraisals currently in development, so were not considered in this surveillance review. There was some evidence to suggest that canagliflozin (a SGLT-2 inhibitor currently licensed for use in type 2, but not type 1 diabetes) significantly improved HbA1c levels and body weight compared to placebo. Topic experts also highlighted this as a possible area for update. Given that the guideline does not currently have any recommendations on offering SGLT-2 inhibitors, we propose that the impact of the NICE technology appraisals is assessed when the decisions are finalised.

New evidence was identified to suggest a benefit of closed-loop insulin delivery systems, particularly in people with a high risk of hypoglycaemia and those with sub-optimally controlled diabetes. NICE has produced both diagnostics guidance and a medtech innovation briefing on these devices, however there are currently no recommendations on the use of closed-loop systems in the guideline. This was also an area raised by stakeholders, who highlighted recent evidence in this area as well as ongoing trials.

Managing complications: eye disease

New evidence was identified on the treatment of diabetic eye disease, including retinopathy and macular oedema. The evidence supports the use of anti-VEGF treatment for diabetic retinopathy and laser therapy for diabetic macular oedema. Currently the guideline has recommendations on screening and referral, but no recommendations on specific treatments. However, there are many treatments covered in NICE technology appraisal guidance, suggesting that there may be a gap in the recommendations in NICE's guideline on type 1 diabetes in adults.

For further details and a summary of all evidence identified in surveillance, see appendix A1.

Type 2 diabetes in adults (NICE guideline NG28)

Blood glucose management: first and second intensification

Evidence indicates the role of clinical characteristics in informing the choice of first intensification medication (treatment with 2 non-insulin blood glucose lowering therapies in combination: dual therapy) after failure to control blood glucose with metformin and lifestyle interventions. These include the presence of established atherosclerotic cardiovascular disease (CVD), for which there is now evidence to support the use of SGLT-2 inhibitors and GLP-1 agonist classes. Evidence was also identified indicating that other comorbidities such as heart failure or chronic kidney disease; age and frailty; safety and tolerability of medication are also important in informing the choice of first intensification medication. Many stakeholders agreed with the surveillance proposal to review the antidiabetic drug pathway with a focus on CVD, renal and other relevant clinical characteristics.

Data from key cardiovascular outcome trials on SGLT-2 inhibitors and GLP-1 agonists have now been published. This evidence can be used to inform cost-effectiveness analysis of these drugs compared to other available antidiabetic drug options in people with type 2 diabetes for first or second intensification of drug treatment (treatment with either 3 non-insulin blood glucose lowering therapies in combination [triple therapy] or any treatment combination containing insulin). It is therefore proposed that this section of the guideline is updated to consider individual drugs within classes as well as class level comparisons in terms of cardiovascular outcomes, safety, tolerability and acquisition costs. Stakeholders were very supportive of the need for an update in this area including highlighting additional ongoing trials and anticipated publication dates.

NICE's guideline on type 2 diabetes in adults stipulates a body mass index (BMI) threshold of 35 kg/m^2 prior to being able to receive a GLP-1 analogue but stakeholder comments suggested that this is not evidence-based. Evidence was identified for different BMI cut-offs for ethnic groups for medications such as GLP-1 analogues. Other inequalities in treatment, metabolic control and use of healthcare services among ethnic groups was also raised by stakeholders and should be considered in the update of the antidiabetic drug pathway.

Insulin therapy: long-acting insulins – glargine biosimilars, degludec

The guideline recommends that when insulin therapy is necessary, it should be started from a choice of insulin types and regimens: Neutral Protamine Hagedorn (NPH) insulin injected once or twice daily according to need is the preferred option; insulin detemir or insulin glargine can be considered as an alternative in certain circumstances. There are several insulin glargine products

available and new evidence indicates that biosimilars are non-inferior to glargine in reducing HbA1c and have similar safety profiles.

The price reduction of the long-acting insulin Tresiba (degludec) and evidence indicating its cost-effectiveness, in addition to the emergence of cheaper biosimilars, have implications for the health economics of insulin-based treatments. Further biosimilars are also in development. Stakeholders also highlighted evidence and were supportive of an update in this area.

Managing complications: eye disease

New evidence was identified on the treatment of diabetic eye disease, including retinopathy and macular oedema, which supports the use of anti-VEGF treatment and intravitreous injection of aflibercept for diabetic retinopathy and laser therapy for diabetic macular oedema. Currently the guideline has no recommendations on specific treatments for eye disease and stakeholders were in agreement that this area should be considered in the update.

For further details and a summary of all evidence identified in surveillance, see appendix A2.

Diabetes (type 1 and type 2) in children and young people (NICE guideline NG18)

Diabetic retinopathy in children and young people with type 1 or type 2 diabetes

Evidence was identified indicating that compared with usual care, quality improvement initiatives incorporating behaviour change techniques such as goal-setting and additional social support lead to a substantial increase in diabetic retinopathy screening attendance and are likely to be cost effective.

Flash glucose monitoring

Currently the NICE guideline does not contain any recommendations on flash glucose monitoring, however a number of topic experts and stakeholders highlighted UK guidance on its use, which indicate that children aged 4 years and older may receive a monitor (if other conditions are met): NHS England guidance on Flash Glucose Monitors for Type 1 diabetes patients, the Regional Medicines Optimisation Committee FreeStyle Libre Position Statement and Diabetes UK Type 1 diabetes technology: A consensus guideline. Stakeholders also reported that it is currently being prescribed to some children and young people on the NHS.

Fluid and insulin therapy for diabetic ketoacidosis

Evidence was identified which indicates that rapid fluid infusion at volumes higher than those currently recommended is not associated with an increased risk of cerebral oedema in children and young people with diabetic ketoacidosis; and that in the case of severe diabetic ketoacidosis, more rapid fluid infusion rates may be associated with faster improvements in mental status. This evidence, along with international guidance from the International Society for Pediatric and Adolescent Diabetes (ISPAD) and topic expert opinion, indicates that this should be an area for review.

For further details and a summary of all evidence identified in surveillance, see appendix A3.

Diabetic foot problems (NICE guideline NG19)

The majority of evidence was found to be consistent with the current guideline recommendations. Improvements were seen in the area of wound dressings for several wound healing outcomes, however there was a lack of comparison between interventions. Evidence for new treatment options was thinly spread across multiple products, with no evidence of product superiority found, which is in line with topic expert feedback. We did not look for evidence relating to the use of systemic antibiotics for the treatment of diabetic foot infection as an antimicrobial prescribing guideline is in production in this area.

For further details and a summary of all evidence identified in surveillance, see appendix A4.

Overview of 2019 surveillance methods

NICE's surveillance team checked whether recommendations in the following guidelines remain up to date:

- Type 1 diabetes in adults (NICE guideline NG17)
- Type 2 diabetes in adults (NICE guideline NG28)
- Diabetes (type 1 and type 2) in children and young people (NICE guideline NG18)
- Diabetic foot problems (NICE guideline NG19).

The surveillance process consisted of:

- Feedback from topic experts via a questionnaire.
- A search for new or updated Cochrane reviews.
- Examining related NICE guidance and quality standards and NIHR signals.
- A search for ongoing research.
- Examining the NICE event tracker for relevant ongoing and published events.
- Literature searches to identify relevant evidence.
- Assessing the new evidence against current recommendations to determine whether or not to update sections of the guideline, or the whole guideline.
- Consulting on the proposal with stakeholders.
- Considering comments received during consultation and making any necessary changes to the proposal.

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

Evidence considered in surveillance

Search and selection strategy

For details of the search and selection strategies please refer to the following appendices:

- Appendix A1 for type 1 diabetes in adults (NICE guideline NG17)
- Appendix A2 for type 2 diabetes in adults (NICE guideline NG28)
- Appendix A3 for diabetes (type 1 and type 2) in children and young people (NICE guideline NG18)
- Appendix A4 for diabetic foot problems (NICE guideline NG19).

Intelligence gathered during surveillance

Views of topic experts

We considered the views of topic experts, including those who helped to develop the guidelines. For this surveillance review, topic experts completed a questionnaire about developments in evidence, policy and services related to each of the 4 guidelines.

The following responses were received from 20 topic expert questionnaires sent for each guideline:

- Type 1 diabetes in adults (NICE guideline NG17) – 6 responses were received, 5 of the experts felt an update was needed and 1 was unsure.
- Type 2 diabetes in adults (NICE guideline NG28) – 7 responses were received, all 7 of the experts agreed that an update is needed.
- Diabetes (type 1 and type 2) in children and young people (NICE guideline NG18) – 5 responses were received, 4 of the experts felt an update was needed and 1 was unsure.
- Diabetic foot problems (NICE guideline NG19) – 7 responses were received, all 7 of the experts agreed that no update is required at this time.

For full details of the topic expert feedback for these 4 guidelines, please see appendices A1–A4.

Views of stakeholders

Stakeholders were consulted on the decision to partially update NICE's guidelines on type 1

diabetes in adults, type 1 and type 2 diabetes in children and young people and type 2 diabetes in adults, and not to update diabetic foot problems. Responses were received from stakeholders representing patient organisations, professional bodies and providers of services including royal colleges (nursing, ophthalmologists and physicians), pharmaceutical companies, professional associations, universities and charities.

Feedback received at consultation were on general themes across several guidelines as well as guideline specific comments.

General themes from consultation on 4 proposals

Individualised care

Stakeholder feedback indicated a need to further highlight person-centred and personalised lifestyle management advice across the guidelines. The guidelines will be amended with the following standard text placed at the beginning of the recommendations section:

'People have the right to be involved in discussions and make informed decisions about their care, as described in your care.

Making decisions using NICE guidelines explains how we use words to show the strength (or certainty) of our recommendations and has information about prescribing medicines (including off label use), professional guidelines, standards and laws (including on consent and mental capacity), and safeguarding.'

Oral health

Stakeholders noted the bi-directional nature of poor oral health and diabetes (that diabetes can cause oral health problems, and conversely, that poor oral health can increase the risk of diabetes). They requested further recommendations on maintaining oral health and treating complications of poor oral health in children with diabetes and adults with type 2 diabetes. The aetiology of diabetes is not within scope for NICE's guidelines on type 1 diabetes in adults, diabetes (type 1 and type 2) in children and young people or type 2 diabetes in adults. However NICE's guideline on diabetes (type 1 and type 2) in children and young people has a cross reference to NICE's guideline on dental recall. Appendix G of the full guideline on dental recall highlights diabetes as a risk factor for developing dental disease and notes that: 'People with diabetes (both type I and type II) are at increased risk of developing destructive periodontal disease and that individuals with diabetes may need a more frequent recall. Inadequate plaque control and the presence of other risk factors will modify the recall interval further'. This issue will be put forward for consideration as part of the

scoping for the update of NICE's guidelines on type 1 diabetes in adults and type 2 diabetes in adults as expert input is required to determine an appropriate way of highlighting oral health in people with diabetes.

Insulin therapy for type 1 diabetes

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

Diabetic eye screening

We initially proposed to withdraw the recommendations on diabetic eye screening in NICE's guidelines on type 1 diabetes in adults and type 2 diabetes in adults as this is covered by the National Screening Committee. However, stakeholders responded that the guideline still needs to emphasise the importance of regular screening. We will therefore add in a cross reference to the NHS Diabetic Eye screening programme for ease of reference to this guidance.

Real-world data

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

Details of comments specific to each guideline are provided below

Type 1 diabetes in adults (NICE guideline NG17)

Overall, 32 stakeholders commented. All stakeholders agreed with the decision to update the guideline, however several proposed that additional areas should be updated. Several themes emerged from the comments received at consultation which are detailed below.

Diagnosis

Some stakeholders highlighted new evidence to suggest that misclassification of type 1 diabetes may be common in adults diagnosed after the age of 35 years. Further evidence was identified on the use of C-peptide to avoid misclassification of late-onset type 1 diabetes and added to appendix A1 for consideration. They raised concerns that the guideline currently only recommends the use of C-peptide tests if there is clinical uncertainty about diagnosis, particularly as the evidence suggests this could be leading to missed diagnoses. The use of C-peptide tests was an area highlighted by the original guideline committee as needing further evidence, who at the time, made the recommendations based on a consensus agreement. In light of this feedback and the new evidence, we are proposing that this area is reviewed.

Blood glucose monitoring

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

Insulin therapy

Many concerns were raised about the proposal not to add recommendations on closed-loop pump therapies, given the emerging evidence base and other NICE guidance in this area. Further evidence was highlighted which was published after the search cut-off dates for this surveillance review and we have since included it in appendix A1 for consideration. Two ongoing trials were also brought to our attention and have been added to our review. We initially judged the evidence to be insufficient to inform recommendations at this point, noting the lack of studies with long-term outcomes and in patients with sub-optimal diabetes control. The new evidence highlighted by stakeholders has a longer follow-up period and includes people with sub-optimal diabetes control. Following the strong steer from stakeholders and the emerging evidence, we are now proposing to review this area.

Psychological support

Concerns were raised about the recommendations relating to psychological support, with some calling for specific recommendations for people with diabetes (rather than a cross reference to

other related guidelines). Currently the guideline contains recommendations on recognition and referral for psychological support, with additional signposting to relevant NICE guidelines which offer more specific advice. We therefore judge this area to be sufficiently covered by existing NICE guidance. As we did not identify any new evidence in this area during the surveillance review, the recommendations will not be changed at this point.

Other areas

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

See appendix B1 for full details of stakeholders' comments and our responses.

Type 2 diabetes in adults (NICE guideline NG28)

Overall, 39 stakeholders commented. All stakeholders agreed with the decision to update the guideline. However, several stakeholders did not agree with the sections of the guideline that were not proposed for updating. Themes that emerged from the comments received at consultation were as follows.

Patient education

A review of the wording of the patient education recommendations was suggested to emphasise the importance of evidence-based online education. However, the new evidence identified for digital interventions is consistent with the evidenced-based principles set out in the existing guideline recommendations.

Motivational interviewing and mobile phone applications were also proposed for consideration. However, evidence submitted did not meet the surveillance inclusion criteria, and evidence identified in the surveillance review was inconclusive for these interventions.

Dietary advice

Many stakeholders proposed an update of the recommendations on dietary advice. The majority of comments concerned low carbohydrate, low calorie and very low calorie diet interventions. Total diet and meal replacement interventions were also suggested for inclusion. The proposed rationale was the need to move away from the perception of type 2 diabetes as a progressive condition managed with either medicine or insulin, to one that is treatable and reversible through dietary intervention. Stakeholders highlighted the need for people living with type 2 diabetes to receive more information on remission and dietary advice.

Evidence submitted was not eligible due to indirectness of population (relating to obesity without type 2 diabetes, and to prevention not treatment), out of scope study designs, and studies published outside the surveillance search period. The aforementioned joint ADA and EASD guideline was also cited as referring to low carbohydrate and low calorie diets. However, this guideline does not explicitly recommend these diets but states that 'advice should be given of the health benefits of weight loss and encouraged to engage in a programme of intensive lifestyle management, which may include food substitution'. NICE's guideline on type 2 diabetes in adults already advises individualising recommendations for carbohydrate intake, and meal patterns, which could include low carbohydrate and low calorie diets.

Stakeholders also asserted that sufficient evidence was already available on the benefits of these diets to justify recommending them. However, the totality of evidence in this area is limited to short-term benefits of these interventions. It does not indicate that low carbohydrate diets are a superior approach to other strategies for weight loss and subsequent weight maintenance in the long-term. The surveillance impact statement is therefore retained; that the longer-term results of the DIRECT study (beyond 2 years), and other longer-term studies of low calorie and low carbohydrate diets are likely to be needed to establish any definite impact on the guideline. A joint working group of The Scientific Advisory Committee on Nutrition, NHS England and Diabetes UK, with input from the British Dental Association and royal colleges, is reviewing the evidence on low carbohydrate diets with publication expected in 2020. This will be tracked by the surveillance team and the results will be considered when available.

Blood glucose management

The inclusion of real time CGM was proposed, based on the emergence of digital platforms and new clinical evidence. However, the studies submitted could not be included due to study designs being either out of scope or being published outside the surveillance search period. The new RCT evidence identified in the surveillance review supporting the use of CGM for type 2 diabetes is limited by the 6-month duration and no impact on the guideline is anticipated until the findings are

substantiated by further longer-term studies.

Drug therapy

Many stakeholders agreed with the surveillance proposal to review the antidiabetic drug pathway with a focus on CVD, renal and other relevant clinical characteristics to ensure consideration of outcomes beyond glycaemia reduction alone. Some supporting studies were submitted and are now included in the evidence summary. Several additional studies were submitted which had already been considered in the evidence review from the 2018 guideline in the areas of SGLT-2 inhibitors and GLP-1 analogues. Other studies were outside the study design scope or search period of the surveillance review. The following specific points were raised, which will inform the proposed review of the antidiabetic drug pathway.

The need to consider drug treatment to prevent renal complications, specifically:

- The CREDENCE study covering canagliflozin for renal protection. Canagliflozin is covered by the NICE technology appraisal guidance on canagliflozin, dapagliflozin and empagliflozin as monotherapies for treating type 2 diabetes, published in May 2016. This evidence will be considered in a review of this appraisal.
- DPP-4 inhibitors, particularly linagliptin, for patients with renal impairment. Linagliptin was highlighted with supporting evidence as the only DPP-4 inhibitor that does not require dose adjustment based on a patient's level of renal function. Renal outcomes are already proposed for consideration in the review of this section of the guideline, which will include the forthcoming results of the CAROLINA trial.
- Timing of treatment intensification. The NICE guideline advises treatment escalation when HbA1c rises higher than 58 mmol/mol (>7.5%) until control is achieved. It was proposed that more information should be provided on the time a patient should spend at uncontrolled hyperglycaemia before treatment intensification, and this will be considered in the update.
- The risk-benefit profile of a medicine, rather than merely the safety and tolerability profile. The evidence base currently available may no longer support the recommendation of agents such as sulphonylureas, which can increase the risk of hypoglycaemia and weight gain and lack cardiovascular outcome trial data. This will be considered in the update of the antidiabetic drug pathway.
- The distinction between individual and fixed combinations of GLP-1 analogues and basal insulin; stakeholders indicated that it is clinically important to distinguish these treatment options and provide guidance on each. This distinction will be noted for consideration in

- update, including evidence identified in surveillance for fixed-ratio combinations of liraglutide and lixisenatide.
- For first and second intensification, semaglutide was highlighted as demonstrating cardiovascular benefit, superior glycaemic control and weight reduction versus a number of comparators across the SUSTAIN clinical trial programme. This evidence has been added to the surveillance evidence summary and evidence for drugs in the GLP-1 analogue class, including liraglutide and semaglutide, will be considered in the update. The forthcoming results of the PIONEER 6 study will be considered following publication.
- Class level comparisons between drug classes were highlighted as limited by differences within classes in terms of CVD outcomes, safety, tolerability and acquisition costs. This is already acknowledged in the surveillance review and will be highlighted for consideration in the update.
- The timing of withdrawal or switching between medications. Stakeholders highlighted the need for advice on when to withdraw or switch from ineffective medication, as well as when to initiate. However, no eligible evidence was submitted, and the research recommendation in this area remains valid.

The NICE guideline on type 2 diabetes in adults stipulates a BMI threshold of 35 kg/m^2 prior to being able to receive a GLP-1 analogue but stakeholder comments suggested that this is not evidence-based. Evidence was submitted by stakeholders to support that GLP-1 analogues consistently reduce HbA1c and body weight regardless of baseline BMI. Although this evidence was not within the scope or search period of the surveillance review it does indicate that the current recommendation may not be accurate. Other inequalities in treatment access and use of healthcare services among ethnic groups was also raised by stakeholders and should be considered in the update of the antidiabetic drug pathway.

The addition of a GLP-1 analogue to a basal insulin was proposed for inclusion as an option for people already on basal insulin who are not also on a GLP-1 analogue. However, the evidence submitted indicating safety and effectiveness was out of scope for the surveillance review. A further point was that, because the majority of diabetes management takes place within primary care, the current recommendation to seek specialist advice when adding a GLP-1 analogue to basal insulin should be removed.

In developing the NICE guideline on type 2 diabetes in adults, the committee agreed that to facilitate a flexible approach to enable access for individuals most likely to benefit, this combination should be available to people for whom obesity is a concern and only where other triple oral combinations are contraindicated or not effective. The guideline committee noted that there was a

lack of evidence for combinations of GLP-1 mimetics and insulin, and therefore agreed that this option should only be offered in a specialist care setting. The surveillance review has not identified evidence to warrant a change to this position.

Evidence supporting the use of GLP-1 analogues prior to initiating insulin therapy was submitted, demonstrating similar or greater reductions in HbA1c, greater weight loss and lower rates of hypoglycaemia compared to insulin. This was proposed as an option for patients who need greater glucose lowering benefit prior to insulin, in accordance with the ADA/EASD consensus statement. However, the evidence was not within the scope or search period of the surveillance review.

The DUAL IX study was highlighted, which demonstrated safe use of IDegLira in combination with SGLT-2 inhibitors in insulin naive patients. This study has been included in the surveillance review to inform the update decision.

Stakeholders suggested that the guideline should clearly differentiate between available basal insulins, specifically taking into consideration those people at a higher risk of hypoglycaemia and prioritising a choice of insulin with a lower risk of hypoglycaemia in line with the ADA-EASD guideline. This is consistent with the surveillance review proposal to review this area with consideration of key safety issues.

Managing complications

- Diabetic kidney disease

Stakeholder(s) proposed that specific advice be provided for chronic kidney disease (CKD) as a complication of type 2 diabetes as opposed to the existing cross reference to NICE's guideline on chronic kidney disease in adults. However, CKD and renal outcomes are already proposed for consideration in the review of the antidiabetic drug pathway. More specific advice for CKD in type 2 diabetes will be considered for inclusion in NICE's guideline on chronic kidney disease in adults, which already includes advice for type 1 and 2 diabetes and is cross-linked to from the NICE guideline on type 2 diabetes in adults. A further comment proposed consideration of urinary albumin screening for cardiovascular risk, as opposed to impending end-stage renal disease.

- Eye disease

Several points were raised about the surveillance proposal for managing eye disease in type 2 diabetes.

In updating the recommendations for diabetic retinopathy, specialist ophthalmic input was advised.

This will be passed on to the developers for consideration in the update.

It was requested that data on the use of fibrates in addition to statins are reviewed in terms of the effects on diabetic retinopathy, based on evidence from Accord and FIELD studies, where fibrates were shown to reduce the rates of progression of retinopathy. However, these studies preceded the surveillance search period and would have been available for consideration when the NICE guideline on type 2 diabetes in adults was developed. No additional evidence in this area was identified through the surveillance review but the NICE surveillance team is monitoring the ongoing Lowering Events in Nonproliferative Diabetic Retinopathy in Scotland study which also concerns fibrate use.

It was highlighted that data is emerging about digital photographic and optical coherence tomography surveillance for certain patients who had already been referred to the diabetic eye clinics ('virtual clinics'). However, no evidence was submitted or identified in the surveillance review, and therefore this area will not be prioritised as part of the update.

- Periodontal disease (see general themes from consultation on 4 proposals: oral health)

Other areas

Comments on several additional areas were submitted without supporting evidence by individual stakeholders. These included: the effect of bariatric surgery on type 2 diabetes, with the resulting remission lasting up to 15 years; concerns that drugs other than aspirin were omitted from the section on antiplatelet therapy, however, recommendation 1.5.2 has a cross reference to NICE's guidelines on cardiovascular disease and myocardial infarction for more detailed advice on antiplatelet therapy for primary and secondary prevention of CVD; the antihypertensive effect of SGLT-2 inhibitor therapy (developers will be made aware of the need to consider antihypertensive benefits of SGLT-2 inhibitors during the proposed review of the antidiabetic drug pathway); liver diseases as comorbidities of type 2 diabetes (there is a separate NICE guideline on non-alcoholic fatty liver disease, which covers NASH, and a cross reference will be added from the NICE guideline on type 2 diabetes in adults to that guideline).

See appendix B2 for full details of stakeholders' comments and our responses.

Diabetes (type 1 and type 2) in children and young people (NICE guideline NG18)

Overall, 27 stakeholders commented. All stakeholders agreed with the decision to update the guideline, however several proposed that additional areas should be updated. Several themes emerged from the comments received at consultation.

Diagnosis

A stakeholder raised concerns that the recommendations on diagnosis do not include the use of islet autoantibody testing to distinguish type 1 diabetes from monogenic diabetes. During the development of the NICE guideline, evidence on diagnosis, including the use of islet autoantibody testing was reviewed. Recommendations concerning antibody screening were not made because most of the included studies incorporated an antibody test as part of the gold standard and were not designed as diagnostic test accuracy studies (instead they were prevalence studies). Antibody testing was also described as expensive and not considered cost effective. The guideline development group noted that current practice at the time was to use C-peptide and antibody tests as part of the work-up for diagnosis. However, the evidence included in the guideline review suggested that 'such tests are of no benefit in distinguishing between different types of diabetes and so use of the tests should be discontinued'. The stakeholder provided evidence, but none of the studies were diagnostic accuracy or cost-effectiveness studies, as such this is not currently being considered as an area for update.

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

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

Insulin therapy for children and young people with type 1 diabetes

Several stakeholders requested that sensor-augmented pump therapy and closed-loop therapy be included as areas for update, however none of the highlighted evidence met the surveillance review

inclusion criteria. During the surveillance review only 1 relevant RCT was identified, as such, the evidence base remains limited and further evidence from larger RCTs would be required in order to consider whether this should be an area for update.

Blood glucose monitoring

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

Several stakeholders also responded that real time CGM should be considered as an area for update, alongside the use of technology such as smartphone applications; however the evidence provided by stakeholders had either already been considered within the surveillance review, or did not meet inclusion criteria. The evidence identified in the surveillance review in relation to CGM, including the use of smartphone applications and consideration of the psychological benefits of CGM, supports the content of the current recommendations 1.2.58–1.2.64 and will therefore not be considered as an area for update. Two pieces of relevant ongoing research that were identified by stakeholders will be considered when the results of the studies are published.

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

Medications for children with type 2 diabetes

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

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

Several stakeholders raised concerns that some psychological conditions were being prioritised over others, that physical health was prioritised over mental health and that person-centred care needed more emphasis. The NICE guideline covers issues on a wide range of psychological conditions, cross-refers to relevant existing NICE guidelines and highlights the importance of emotional wellbeing and coping in the recommendations sections on psychological and social issues in children and young people with type 1 diabetes and psychological and social issues in children and young people with type 2 diabetes.

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

Monitoring for complications and associated conditions of type 2 diabetes

One stakeholder requested that non-alcoholic fatty liver disease (NAFLD) is added as a complication to recommendations 1.3.43–1.3.45 on monitoring for complications and associated conditions of type 2 diabetes. As NICE has an existing guideline on NAFLD which recommends that children and young people with type 2 diabetes are offered a liver ultrasound, we will request an editorial amendment to cross-refer to this guideline in NICE's guideline on diabetes (type 1 and type 2) in children and young people.

Other areas

Comments were also received from single stakeholders in relation to the frequency of eye screening, the definition of hypoglycaemia, the frequency of capillary blood glucose tests per day, treatment of hypoglycemia using fast-acting and long-acting carbohydrates, treating complications of type 1 diabetes, providing more in-depth recommendations on metabolic surgery and on other NICE guidelines. These comments have not resulted in any changes to the surveillance decision due to lack of supporting evidence that meets the inclusion criteria for this surveillance review or applicability to the NICE guideline.

See appendix B3 for full details of stakeholders' comments and our responses.

Diabetic foot problems (NICE guideline NG19)

Overall, 23 stakeholders commented. Eight stakeholders agreed with the proposal not to update the guideline, 12 disagreed and 3 did not answer. Themes from stakeholder comments were as follows.

Wound dressings

Stakeholders raised concerns about recommendation 1.5.10 as they felt that the wording prevented interactive dressings such as UrgoStart being used. No evidence was found at this review that was deemed to impact on the existing recommendation, which allows the most clinically appropriate dressing to be used, including interactive dressings. Additionally, the UrgoStart dressing is covered by NICE's medical technologies guidance on UrgoStart for treating diabetic foot ulcers and leg ulcers, which is linked within the diabetic foot pathway, highlighting the benefits of this dressing to service users.

Amputations

Stakeholders highlighted that minor amputations may be avoidable, in relation to new technologies such as rheophoresis and neuromuscular electronic stimulation. No new evidence was found at this surveillance review relating to these technologies. Studies highlighted by stakeholders did not meet the inclusion criteria for this review. This issue will be noted for consideration at the next surveillance review.

Time to assessment

Increasing time to diagnosis and review times for diabetic foot problems were highlighted by 2 stakeholders. Review times were highlighted in relation to a 2018 audit which found not all new cases of diabetic foot ulcer required an urgent referral. Since consultation on this surveillance review closed, the 2019 version of the audit has published which is in support of the existing recommendations that suggest a rapid referral is made for all new diabetic foot ulcers. No new evidence was found to suggest a change to recommendations, with studies provided by stakeholders not meeting the inclusion criteria for this review.

Peripheral artery disease

Several stakeholders raised issues relating to peripheral artery disease (PAD) including interventions to address ischaemia, lack of evidence around the 10 g monofilament test for diabetic peripheral neuropathy, increase in diagnostic sensitivity when the monofilament test was

combined with Neuropad and more information requested on PAD and diabetes. Studies provided by stakeholders in this area did not meet the inclusion criteria for this review. The NICE guideline has several cross references to NICE's guideline on peripheral arterial disease, which were considered sufficient for signposting service users to there for further information.

Antimicrobial prescribing guideline (APG)

An APG is in progress for diabetic foot infection which also had a consultation period at the same time as this guideline. The APG will replace recommendations 1.6.6–1.6.15. Through the consultation for the APG, a number of stakeholder comments were raised that are relevant to the other areas of the NICE guideline. A number of these are areas that have already been considered as part of this surveillance review. Comments were raised about terminology such as including more emphasis for the clinical urgency of Charcot arthropathy and more detailed definitions for ischaemia. As no new evidence was put forward during consultation, we will log these issues and consider them again at the next surveillance review. Several stakeholders highlighted a reliance on the results of wound swabs for changing antibiotics and noted that these results may not always be representative of the causative organism. We are tracking a NIHR trial which compares wound swab diagnosis to that of tissue sampling which we hope will provide new evidence in this area. When the results are available, we will assess them against the current guideline recommendations.

See appendix B4 for full details of stakeholders' comments and our responses.

See ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual for more details on our consultation processes.

Equalities

Stakeholders raised some equalities issues, details of these and actions taken in response, can be found in reasons for the decision and in appendices B1–B4.

Editorial amendments

During surveillance of the guideline, the need for editorial amendments were identified. This included the need to add cross references to NICE guidelines, technology appraisals or pathways, clarify the meaning of recommendations, changing recommendation content to align with existing NICE guidelines, add information on any MHRA safety warnings, and minor editorial amendments to ensure broken hyperlinks are fixed.

Details of guideline specific editorial amendments can be found in appendices A1–A4.

ISBN: 978-1-4731-3449-2