Review decision

Review of DG21: Integrated sensor-augmented pump therapy systems for managing blood glucose levels in type 1 diabetes (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system)

This guidance was issued in February 2016.

The review date for this guidance is February 2019.

NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance. Other factors such as the introduction of new technologies relevant to the guidance topic, or newer versions of technologies included in the guidance, will be considered relevant in the review process, but will not in individual cases always be sufficient cause to update existing guidance.

1. Review decision

Standard update of the guidance.

At the Guidance Executive meeting of 28 January 2020, the proposal for an accelerated update of the guidance without consultation was agreed. A list of the options for consideration, and the consequences of each option is provided in Appendix 1 at the end of this paper.

2. Rationale

Both systems included in DG21 are no longer available to the NHS and successor systems are available for both technologies. These new systems have enhanced functionality to modify insulin release in response to detected glucose levels, and new studies are available to assess the impact of the systems on patient outcomes. These may allow estimation of the cost effectiveness of systems using a successor to the G4 continuous glucose monitor (there was insufficient evidence to do this for DG21). The new systems also have new costs, which could impact on cost-effectiveness estimates, as could new comparator technologies such as flash glucose monitoring that are now in use in the NHS. A standard update to the guidance is therefore proposed.
3. **Implications for other guidance producing programmes**

The proposed update has been discussed with the guidelines update team who are currently producing the diabetes guideline updates. They did not highlight any concerns, and the two teams will work closely together as work progresses.

4. **Original objective of guidance**

To assess the clinical and cost effectiveness of integrated sensor-augmented pump therapy systems (the MiniMed Paradigm Veo system and the Vibe and G4 PLATINUM CGM system) for managing blood glucose levels in people with type 1 diabetes.

5. **Current guidance**

*Adoption recommendations*

1.1 The MiniMed Paradigm Veo system is recommended as an option for managing blood glucose levels in people with type 1 diabetes only if:

- they have episodes of disabling hypoglycaemia despite optimal management with continuous subcutaneous insulin infusion and
- the company arranges to collect, analyse and publish data on the use of the MiniMed Paradigm Veo system (see section on recommendations for further research).

1.2 The MiniMed Paradigm Veo system should be used under the supervision of a trained multidisciplinary team who are experienced in continuous subcutaneous insulin infusion and continuous glucose monitoring for managing type 1 diabetes only if the person or their carer:

- agrees to use the sensors for at least 70% of the time
- understands how to use it and is physically able to use the system and
- agrees to use the system while having a structured education programme on diet and lifestyle, and counselling.

1.3 People who start to use the MiniMed Paradigm Veo system should only continue to use it if they have a decrease in the number of hypoglycaemic episodes that is sustained. Appropriate targets for such improvements should be set.
1.4 The Vibe and G4 PLATINUM CGM system shows promise but there is currently insufficient evidence to support its routine adoption in the NHS for managing blood glucose levels in people with type 1 diabetes. Robust evidence is needed to show the clinical effectiveness of using the technology in practice.

1.5 People with type 1 diabetes who are currently provided with the MiniMed Paradigm Veo system or the Vibe and G4 PLATINUM CGM system by the NHS for clinical indications that are not recommended in this NICE guidance should be able to continue using them until they and their NHS clinician consider it appropriate to stop.

Research recommendations

From section 7 of the guidance:

7.1 The Committee recommended that the company collect data on people using the MiniMed Paradigm Veo system and successor technologies with low-glucose suspend function, which should be analysed and published to show the system’s impact on improving control of disabling hypoglycaemia. Key outcomes that could be presented include frequency and duration of hypoglycaemic events, time spent in hypoglycaemia, and number and duration of low-glucose suspend events.

7.2 The Committee recommended further research to quantify the impact of hypoglycaemia on quality of life for people with type 1 diabetes and their carers. Future research should include adults and children and should capture the impact of persistent anxiety associated with the fear of catastrophic events related to severe hypoglycaemic events.

7.3 The Committee recommended further data collection to assess the impact of episodes of hypoglycaemia on healthcare resource use. The Committee noted that sources of routinely collected data, such as hospital episode statistics, the national diabetes audit and ambulance service call-out data, could be combined to meet this objective.

7.4 The Committee recommended further research to investigate the clinical effectiveness of the integrated sensor-augmented insulin pump therapy systems in younger children and pregnant women. No data are currently available for these subgroups and their inclusion in future studies is encouraged.

7.5 The Committee recommended that health economic models are developed to capture the impact of interventions on short-term outcomes such as hypoglycaemia. In addition, the feasibility of incorporating more recently
developed risk prediction models for cardiovascular disease such as QRisk2 and observational data from registries such as the Swedish National Diabetes Register into health economic models for type 1 diabetes should be explored.

6. New evidence

The search strategy from the original diagnostics assessment report was re-run on Medline (Ovid) and Embase (Ovid). References from 2014 onwards were reviewed. Additional searches of clinical trials registries were also carried out and relevant guidance from NICE and other professional bodies was reviewed to determine whether there have been any changes to the diagnostic and care pathways. Companies were asked to submit all new literature references relevant to their technology along with updated costs and details of any changes to the technology itself or the CE marked indication for use for their technology. Specialist committee members for this guidance topic were also consulted and asked to submit any information regarding changes to the technologies, the evidence base and clinical practice. The results of the literature search are discussed in the ‘Summary of evidence and implications for review’ section below. See Appendix 2 for further details of ongoing and unpublished studies.

6.1 Technologies

MiniMed Paradigm Veo system (Medtronic)

The MiniMed Paradigm Veo system is no longer available to the NHS for patients who are starting to use sensor augmented insulin pumps. Some patients are still using the system, but this will be replaced by successor technologies when due for replacement.

The CE mark for the system was updated in June 2017 to include use of new sensors. In addition to the Enlite sensor (used in the Veo system), the Guardian Sensor 3 is now licensed for use with the Veo and successor systems. The Guardian Sensor 3 replaces the Enlite sensor and is compatible with both the MiniMed 640G and MiniMed 670G systems (discussed below).

Two successor technologies have been released:

- **MiniMed 640G with SmartGuard Technology**

  Launched in 2015, this system uses predictive low glucose management using SmartGuard ‘suspend before low’ technology. This allows insulin delivery to be suspended in response to predicted hypoglycaemia within the next 30 minutes, and delivery is automatically resumed once blood glucose levels start to recover.
The MiniMed Paradigm Veo system used suspend on low technology that temporarily suspended insulin delivery when the detected glucose levels dropped below a predefined threshold level. Delivery is then automatically resumed after 2 hours, unless the user manually overrides the suspension within this time.

A NICE medtech innovation briefing on this technology was published in 2016 (MiniMed 640G system with SmartGuard for managing blood glucose levels in people with type 1 diabetes).

- **MiniMed 670G system with SmartGuard Technology**

Launched in 2018. This system uses the same ‘suspend before low’ feature as the 640G system and has an additional SmartGuard Auto Mode function which can automatically adjust basal insulin based on serum glucose values every five minutes. Some user interaction is required.

The 670G system is not licensed for use in children under 7 years of age or people who are pregnant. This device should also not be used in patients who require less than a total daily insulin dose of 8 units per day because the device requires a minimum of 8 units per day to operate safely.

**Costs**

In DG21, the estimated device cost of the MiniMed Paradigm Veo System was £2,962 (based on 2014 costs). Costs of the MiniMed 640G and 670G system components are shown in table 1.

**Table 1 Costs of MiniMed 640G and 670G systems**

<table>
<thead>
<tr>
<th>Component</th>
<th>Cost (excl. VAT)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MiniMed 640G system</strong></td>
<td></td>
</tr>
<tr>
<td>MiniMed 640G insulin pump</td>
<td>£2,995</td>
</tr>
<tr>
<td>Transmitter and charger</td>
<td>£585</td>
</tr>
</tbody>
</table>
**MiniMed 670G system**

<table>
<thead>
<tr>
<th>MiniMed 670G insulin pump with CGM Starter kit (includes five Guardian Sensor 3)</th>
<th>£3,730</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guardian Sensor 3: pack of 5</td>
<td>£275</td>
</tr>
<tr>
<td>Guardian Sensor 3: pack of 10</td>
<td>£525</td>
</tr>
</tbody>
</table>

**Vibe (Animas) and G4 PLATINUM continuous glucose monitor (CGM) system (Dexcom)**

Animas Vibe insulin pumps are no longer manufactured or for sale. Animas have statements on their website detailing timelines for transitions of patients to other insulin delivery systems by September 2019.

The G4 PLATINUM CGM system was discontinued on 1st June 2019 and has been superseded by the G6 system (discussed below). Alternative pumps are available for use with the G6 CGM system (discussed below).

**Dexcom G6 CGM System**

The Dexcom G6 CGM has been released since DG21 published. The G6 monitor can be used with the t:slim X2 Insulin Pump (Tandem Diabetes Care) and the Omnipod DASH Insulin Management System (Insulet).

When used with the Tandem t:slim X2 insulin pump, one of two different algorithms can be used to control the rate of insulin delivery. Predictive low glucose suspend (PLGS) algorithms allow automated hypoglycemia prevention. PLGS systems use CGM values to predict hypoglycemia and automatically suspend insulin delivery to help prevent hypoglycemia. The Basal-IQ algorithm acts by reducing the rate of insulin delivery in response to existing or impending hypoglycaemia. The company state that a further algorithm (the Control-IQ algorithm) that uses the same t:slim X2 hardware is under regulatory review (as of October 2019). This can attenuate hypoglycaemia in a manner similar to the Basal-IQ algorithm, and additionally acts by increasing the rate of insulin delivery in response to existing or impending hyperglycaemia. The Vibe and G4 PLATINUM CGM system assessed in DG21 did not have an automated low-glucose suspend function.

The Dexcom G6 is indicated for use for people age 2 years and older.

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Costs

In DG21, the estimated cost of the Vibe/G4 Platinum CGM system CGM transmitter was £335 and the cost of a sensor was £47 (based on 2014 costs). Costs of the Dexcom G6 components are shown in table 2. These estimates do not include costs of an insulin pump required for use of this monitor in an integrated sensor-augmented pump therapy system.

Table 1 Costs of Dexcom G6

<table>
<thead>
<tr>
<th>Component</th>
<th>Cost (excl. VAT)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dexcom G6: Receiver</td>
<td>£ 290</td>
</tr>
<tr>
<td>Dexcom G6: Transmitter</td>
<td>£200</td>
</tr>
<tr>
<td>Dexcom G6: Sensor</td>
<td>£51.25</td>
</tr>
</tbody>
</table>

6.2 Clinical practice

NICE is currently updating its guidance on diabetes (type 1 and type 2) in children and young people (NG18), type 1 diabetes in adults (NG17), type 2 diabetes in adults (NG28) and diabetes in pregnancy (NG3).

Since DG21 published, flash glucose monitoring has increased in use in the NHS. NICE published a medtech innovation briefing on FreeStyle Libre for glucose monitoring in July 2017. This technology measures interstitial glucose levels from a sensor applied to the skin. It can be used 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. This technology does not appear to link with insulin pumps to form an integrated sensor-augmented pump therapy system, so differs from the technologies assessed in DG21.

NHS England have published flash glucose monitoring guidelines for CCGs for people with type 1 diabetes in 2019. This sets out patient criteria (annex A) for which NHS England will reimburse CCGs for the ongoing costs of flash glucose sensors. This includes:

“For those with Type 1 diabetes and recurrent severe hypoglycemia or impaired awareness of hypoglycaemia, NICE suggests that Continuous
Glucose Monitoring with an alarm is the standard. Other evidence-based alternatives with NICE guidance or NICE TA support are pump therapy, psychological support, structured education, islet transplantation and whole pancreas transplantation. However, if the person with diabetes and their clinician consider that a Flash Glucose Monitoring system would be more appropriate for the individual’s specific situation, then this can be considered.

6.3 New studies

Because the original technologies in the guidance are no longer available to the NHS, new studies assessing their use have not been considered here.

In line with DG21 recommendations, Medtronic collected, analysed and published data on the use of the MiniMed Paradigm Veo system and successor systems in order to assess the efficacy of insulin pumps with automated insulin suspension systems in a real-world setting. This has been published in Choudhary et al. (2019).

The study was a retrospective analysis of data from people with type 1 diabetes in the UK (n=920) with the MiniMed Paradigm Veo (7.1%) or MiniMed 640G system (86.7%; 6.2% used both systems during the period of data collection). 43.6% of participants were over 15 years old. Three suspension modes were used:

- Sensor-augmented pump (SAP): Not using any insulin suspension mode
- Low glucose suspend (LGS): Insulin delivery is temporarily suspended if glucose levels drop below a predefined level
- Predictive low glucose management (PLGM; MiniMed 640G system only): Insulin delivery is suspended if hypoglycaemia is predicted in the next 30 minutes and delivery automatically starts once blood glucose levels recover.

<table>
<thead>
<tr>
<th>Insulin suspension model</th>
<th>Median percentage of time with sensor glucose values ≤3 mmol/l (25th to 75th percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adults (&gt;15 years)</td>
</tr>
<tr>
<td>SAP</td>
<td>0.9% (0.3 to 2.1)</td>
</tr>
<tr>
<td>LGS</td>
<td>0.3% (0.1 to 0.7)</td>
</tr>
<tr>
<td>PLGM</td>
<td>0.2% (0.1 to 0.5)</td>
</tr>
</tbody>
</table>

SAP: Sensor-augmented pump; LGS: Low glucose suspend; PLGM: Predictive low glucose management

During the observation period some participants switched between modes of insulin suspension (n=187). Benefits were reported for switching between SAP and LGS in
terms of monthly rate of hypoglycaemic events and in percentage of time with glucose values 3 mmol/l or less. Monthly rate of hypoglycaemic events was reported as decreasing further for people using the PLGM mode of suspension. The authors concluded that real world UK data shows that increasing automation of insulin suspension in these devices reduces hypoglycaemia exposure in people with type 1 diabetes.

**Data on successor technologies**

Several studies are available that assess the impact of successor versions of the technologies in DG21 on patient outcomes. Although evidence on successor versions of the technologies was not systematically identified as part of this review, evidence was submitted by clinical experts and the companies.

For example, Abraham et al. (2018) was a 6 month, multicentre, randomized controlled trial in children and adolescents (8 to 20 years old) with type 1 diabetes comparing the Medtronic MiniMed 640G pump (with predictive low-glucose management [PLGM] function; n=80) with sensor-augmented pump therapy (SAPT; n=74) alone. The PLGM group had a reduction in hypoglycaemia (percentage of time with sensor glucose less than 3.5 mmol/L; p < 0.0001). This reduction was seen both during day and night (P < 0.0001). Hypoglycaemic events also declined with PLGM (p < 0.001). There was no significant difference in glycated haemoglobin (HbA1c) at 6 months (SAPT 7.6 ± 1.0% compared with PLGM 7.8 ± 0.8%; p=0.35).

In Garg et al. (2017) participants used the MiniMed 670G system for 3 months, after an initial 2 week run in phase. Participants had type 1 diabetes and were classified by the study authors as adolescents (14 to 21 years old; n=30) or adults (22 to 75 years old; n=94). The study was done at 9 sites in the USA and 1 in Israel. From baseline run-in to the end of study phase, adolescent HbA1c levels decreased from 7.7%±0.8% to 7.1%±0.6% (p<0.001), and adult HbA1c levels decreased from 7.3%±0.9% to 6.8%±0.6% (p<0.001). The proportion of overall in-target (71 to 180 mg/dL) sensor glucose values increased from 60.4%±10.9% to 67.2%±8.2% (p<0.001) in adolescents and from 68.8%±11.9% to 73.8%±8.4% (p<0.001) in adults.

Studies have also compared the performance of different versions of Medtronic monitors. For example: MiniMed 640G and MiniMed Veo (Thomakos et al. 2019) and MiniMed 640G and 670G systems (Lepore et al. 2019).

Brown et al. (2019) was 6-month randomized, multicentre trial, patients with type 1 diabetes (n=168) were assigned to receive treatment with a closed-loop system (closed-loop group) or a sensor-augmented pump (SAP; control group). The closed-loop system group received a t:slim X2 insulin pump with Control-IQ Technology (Tandem Diabetes Care) and a Dexcom G6 continuous glucose monitor; the SAP
system was not specified in the control group. The primary outcome was the percentage of time that the blood glucose level was within the target range of 70 to 180 mg per decilitre (3.9 to 10.0 mmol per litre). This increased in the closed-loop group from 61±17% at baseline to 71±12% during 6 months and remained unchanged at 59±14% in the control group (mean adjusted difference, 11 percentage points; 95% confidence interval [CI], 9 to 14; \( p<0.001 \)).

Forlenza et al (2019) was an RCT that compared use of the compared use of the Tandem t:slim X2 insulin pump paired with a Dexcom G6 continuous glucose monitor with SAP therapy. This was a 3-day home-use trial done at two sites in the USA with children aged 6 to 12 years (n=24) with type 1 diabetes. Time in target range (70-180 mg/dL) was higher with the t:slim pump and G6 monitor (71.0% ± 6.6% compared with 52.8% ± 13.5%; \( p = 0.001 \)). There was a statistically non-significant difference in time in hypoglycaemia (less than 70 mg/dL): 1.7% versus 0.9%. Participants commented that using the t:slim pump and G6 monitor was associated with less time thinking about diabetes, decreased worry about blood sugars, and decreased burden in managing diabetes.

Additional studies on the use of the Medtronic MiniMed 640G and 670G systems and the Dexcom G6 CGM used with an insulin pump are also available.

Several trials are also underway that could provide relevant data on the performance of the successor technologies. Examples are listed in appendix 2.

6.4 NICE’s research commissioning activities

The Cedar Health Technology Research Centre produced a report in response to research recommendations 7.2 and 7.3 in DG21. The report had 2 main aims:

- To determine healthcare resource use caused by hypoglycaemic episodes in patients with type 1 diabetes,
- To present results on the effect of fear of hypoglycaemia on individuals with type 1 diabetes.

This report has not yet been published and is academic in confidence at present, but could provide new inputs to update the economic model.

7. Summary of new evidence and implications for review

Both systems included in DG21 are no longer available to the NHS. Successor systems are available for both. These new systems have enhanced functionality to modify insulin release in response to detected glucose levels. Companies claim that the new systems can cause a further reduction in hypoglycaemic events and improve the proportion of time that a person is within their blood glucose target.
range. New studies provide additional evidence of clinical benefits for the successor systems. The systems also have new costs which will impact on cost-effectiveness estimates.

Recommendation 1.4 in DG21 stated that the Vibe and G4 PLATINUM CGM system showed promise but there was insufficient evidence to support its routine adoption in the NHS. Data are now available on the successor to the G4 glucose monitor which may allow further assessment of the cost effectiveness of this system and could potentially lead to a change in the recommendation.

Since the publication of DG21, new technology for monitoring glucose levels (flash glucose monitoring) is also in use in the NHS. Consideration of this technology in an assessment as an additional comparator to represent current NHS practice may affect cost estimates of the integrated sensor-augmented pump therapy systems for managing blood glucose levels. This issue could be explored further whilst scoping any guidance update.

8. Implementation

Medtronic have indicated that both the MiniMed 640G and 670G systems are in use in the NHS. The company state that about 45% of patients with type 1 diabetes starting on a Medtronic system used the MiniMed 670G system.

It is unclear to what extent the Dexcom G6 CGM System is currently in use in the NHS.

9. Equality issues

The following potential equality issues were identified during the production of DG21:

- People with cognitive disorders and people whose vision or hearing does not allow recognition of pump signals and alarms may have difficulty in using the technologies.
- People with a disability may have difficulty in self-administering insulin injections.
- Glucose levels should be more tightly controlled in pregnancy.
- Impaired awareness of hypoglycaemia is more common in older people.

No new equality issues have been identified since the publication of the guidance.

Paper sign off: Rebecca Albrow, Associate Director, August 2020

Contributors to this paper:

Technical Lead: Thomas Walker
Technical Adviser: Frances Nixon
Project Manager: Donna Barnes
Appendix 1 – explanation of options

If the published Diagnostics Guidance needs updating NICE must select one of the options in the table below:

<table>
<thead>
<tr>
<th>Options</th>
<th>Consequence</th>
<th>Selected – ‘Yes/No’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard update of the guidance</td>
<td>A standard update of the Diagnostics Guidance will be planned into NICE’s work programme.</td>
<td>Yes</td>
</tr>
<tr>
<td>Accelerated update of the guidance</td>
<td>An accelerated update of the Diagnostics Guidance will be planned into NICE’s work programme. Accelerated updates are only undertaken in circumstances where the new evidence is likely to result in minimal changes to the decision problem, and the subsequent assessment will require less time to complete than a standard update or assessment.</td>
<td>No</td>
</tr>
<tr>
<td>Update of the guidance within another piece of NICE guidance</td>
<td>The guidance is updated according to the processes and timetable of that programme.</td>
<td>No</td>
</tr>
</tbody>
</table>

If the published Diagnostics Guidance does not need updating NICE must select one of the options in the table below:
<table>
<thead>
<tr>
<th>Options</th>
<th>Consequences</th>
<th>Selected – ‘Yes/No’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transfer the guidance to the 'static guidance list'</td>
<td>The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Diagnostics Guidance on the static list should be flagged for review.</td>
<td>No</td>
</tr>
</tbody>
</table>
Produce a technical supplement

A technical supplement describing newer versions of the technologies is planned into NICE’s work programme.

No

Defer the decision to review the guidance to [specify date or trial].

NICE will reconsider whether a review is necessary at the specified date.

No

Withdraw the guidance

The Diagnostics Guidance is no longer valid and is withdrawn.

No

Appendix 2 – supporting information

Relevant Institute work

Published

- Type 1 diabetes in adults: diagnosis and management (2015, last updated 2016) NICE guideline NG17
- Diabetes (type 1 and type 2) in children and young people: diagnosis and management (2015) NICE guideline NG18
- Diabetes in pregnancy: management from preconception to the postnatal period (2015) NICE guideline NG3
- Cardiovascular disease: risk assessment and reduction, including lipid modification (2014, last updated 2016) NICE guideline CG181
- Dapagliflozin with insulin for treating type 1 diabetes (2019) NICE technology appraisals guidance 597

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• **Safer insulin prescribing** (2017, last updated (2019) NICE key therapeutic topic 20

• **FreeStyle Libre for glucose monitoring** (2017) NICE Medtech innovation briefing 110

• **Health app: GDm-Health for people with gestational diabetes** (2017) NICE Medtech innovation briefing 131

• **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)** (2016) NICE diagnostics guidance 21

• **MiniMed 640G system with SmartGuard for managing blood glucose levels in people with type 1 diabetes** (2016) NICE Medtech innovation briefing 51

• **Diabetes in children and young people** (2016) NICE quality standard 125

• **Diabetes in pregnancy** (2016) NICE quality standard 109

• **Renin-angiotensin system drugs: dual therapy** (2015, last updated 2016) NICE key therapeutic topic 2

• **Diabetes mellitus type 1 and type 2: insulin glargine biosimilar (Abasaglar)** (2015) NICE Evidence summary 64

• **Type 1 diabetes mellitus in adults: high-strength insulin glargine 300 units/ml (Toujeo)** (2015) NICE evidence summary 62

• **Diabetes in adults** (2011, last update 2016) NICE quality standard 6

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**In progress**

• **Type 1 diabetes in adults: diagnosis and management (update)**. NICE guideline. Publication date to be confirmed

• **Diabetes (type 1 and type 2) in children and young people: diagnosis and management (update)**. NICE guideline. Publication to be confirmed

• **Diabetes update**. NICE guideline. Publication to be confirmed
## Registered and unpublished trials

<table>
<thead>
<tr>
<th>Trial name and registration number</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>An Open-label, Multi-centre, Randomised, Two-period, Crossover Study to Assess the Efficacy, Safety and Utility of 16 Week Day and Night Automated Closed-loop Glucose Control Under Free Living Conditions Compared to Sensor Augmented Insulin Pump Therapy in Older Adults With Type 1 Diabetes&lt;br&gt;NCT04025762</td>
<td>Randomised, crossover open label trial (n=36) Intervention: Day and night hybrid-closed loop control (Dana RS insulin pump + Dexcom G6 rt-GCM + smartphone with the CamAPS FX app) Comparator: Sensor augmented pump therapy (Dana RS insulin pump + Dexcom G6 rt-GCM) Primary outcome: Time spent in the target sensor glucose range Status: Recruiting Estimated completion date: June 2021</td>
</tr>
<tr>
<td>An Open-label, Multi-centre, Multi-national, Randomised, 2-period Crossover Study to Assess the Efficacy, Safety and Utility of Closed Loop Insulin Delivery in Comparison With Sensor Augmented Pump Therapy Over 4 Months in Children With Type 1 Diabetes Aged 1 to 7 Years in the Home Setting&lt;br&gt;NCT03784027</td>
<td>Randomised, crossover open label trial (n=72) Intervention: CamAPS FX (Dana insulin pump + Dexcom G6 rt-CGm + CamAPS FX app) Comparator: Sensor augmented pump therapy Primary outcome: Time in target (3.9 to 10.0 mmol/l)(70 to 180 mg/dl) Status: Recruiting Estimated completion date: June 2020</td>
</tr>
<tr>
<td>A Multi-centre, Randomised, Two-period, Crossover Study to Evaluate Home Use of Closed-loop Applying Faster Insulin Aspart Versus Standard Insulin Aspart&lt;br&gt;NCT04055480</td>
<td>Randomised, crossover trial (n=30) Intervention: Closed-loop using standard rapid-acting insulin (Dana insulin pump + Dexcom G6 rt-CGm + CamAPS FX app) Comparator: Closed-loop using faster insulin aspart (Dana insulin pump + Dexcom G6 rt-CGm + CamAPS FX app) Primary outcome: Time spent in the target glucose range from 3.9 to 10.0 mmol/l based on CGM Status: Recruiting Estimated completion date: August 2020</td>
</tr>
<tr>
<td>Trial name and registration number</td>
<td>Details</td>
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<tr>
<td>An Open-label, Multicentre, Randomised, Single-period, Parallel Design Study to Assess the Effect of Closed Loop Insulin Delivery From Onset of Type 1 Diabetes in Youth on Residual Beta Cell Function Compared to Standard Insulin Therapy NCT02871089</td>
<td>Randomised, open label trial (n=96) Intervention: 24/7 Closed loop delivery (Florence M: Medtronic 640G pump with Medtronic Elite/Guardian 3 rt-CGM and glucose suspend feature + an android smartphone app; CamAPS FX: Dana insulin pump + Dexcom G6 rt-CGM + CamAPS FX app) Comparator: Multiple Daily Injections Primary outcome: Area under the meal stimulated C-peptide curve (AUC) during a mixed meal tolerance test (MMTT) Status: Active, not yet recruiting Estimated completion date: October 2024</td>
</tr>
<tr>
<td>An Open-label, Three-center, Randomized, Two-session, Crossover Study, to Assess 4 Days Inpatient, and 6-week Follow-up Home Study Phase Under Remote Monitoring at Only French Centers, the Efficacy and the Safety of the Diabeloop Closed-loop Glucose Control Compared With Sensor-augmented Pump Therapy, in Young Children With Type 1 Diabetes. NCT03671915</td>
<td>Randomised, crossover open label trial (n=23) Intervention: DIABELOOP system (closed loop; utilize Dexcom G6) Comparator: Usual system (open loop; utilize Dexcom G6) Primary outcome: The time spent of the glucose level drop in below 70 mg/dl over the 72-h, as recorded by CGM Status: Recruiting Estimated completion date: December 2019</td>
</tr>
<tr>
<td>Assessment of the Efficacy of Closed-loop Insulin Therapy (Artificial Pancreas) on the Control of Type 1 Diabetes in Prepubertal Child in Free-life: Comparison Between Nocturnal and 24-hour Use on 18 Weeks, Followed by an Extension on 18 Weeks NCT03739099</td>
<td>Randomised trial (n=120) Intervention: Closed-loop insulin delivery 24/7, day and night Comparator: Closed-loop insulin delivery 7/7, dinner and night Primary outcome: Percent of time spent in the 70-180 mg/dl glucose range assessed on daily CGM data Status: Recruiting Estimated completion date: September 2020</td>
</tr>
<tr>
<td>Trial name and registration number</td>
<td>Details</td>
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| An Open-label, Multi-centre, Randomized, Single-period, Parallel Study to Assess the Efficacy, Safety and Utility of 6 Month Day-and-night Automated Closed-loop Insulin Delivery Under Free Living Conditions Compared to Insulin Pump Therapy in Children and Adolescents With Type 1 Diabetes  
**NCT02925299** | Randomised, open label trial (n=130)  
Intervention: 24/7 closed-loop insulin delivery  
(FlorenceX (UK): Dana insulin pump + Dexcom G6 CGM + an android smartphone app with algorithm or FlorenceM (US): Medtronic 640G pump + Guardian 3 CGM + an android smartphone app with algorithm)  
Comparator: Insulin pump therapy  
Primary outcome: Measurement of glycated haemoglobin (HbA1c) at 6 months  
Status: Recruiting  
Estimated completion date: June 2020 |
| Observational Study of Patient Important Outcomes in Pregnant Patients With Type 1 Diabetes Mellitus on Insulin Pump  
**NCT03761615** | Prospective, observational study (n=50)  
Intervention: Dexcom G6 CGM in pregnant T1D women  
Primary outcome: Time in range glucose levels as determined by CGM  
Status: Recruiting  
Estimated completion date: July 2021 |
| An Extension Study of t:Slim X2 With Control-IQ Technology  
**NCT03591354** | Randomised controlled trial (n=168)  
Intervention: Closed-control loop: t:slim X2 with Control-IQ Technology & Dexcom G6 CGM  
Comparator: Predictive-Low Glucose Suspend: t:slim X2 with Basal-IQ & Dexcom G6 CGM  
Primary outcome: Time in target range 70-180 mg/dL measured by CGM  
Status: Enrolling by invitation  
Estimated completion date: December 2020 |
| The International Diabetes Closed Loop (iDCL) Trial: Clinical Acceptance of the Artificial Pancreas in Pediatrics: A Study of t:Slim X2 With Control-IQ Technology  
**NCT03844789** | Randomised trial (n=101)  
Intervention: Closed Loop Control: t:slim X2 with Control-IQ Technology & Dexcom G6 CGM  
.Comparator: Standard of Care: Dexcom G6 with optional t:slim X2 with Control-IQ Technology  
Primary outcome: Time in target range 70-180 mg/dL measured by CGM in CLC group vs. SC group  
Status: Active, not recruiting  
Estimated completion date: March 2020 |
<table>
<thead>
<tr>
<th>Trial name and registration number</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>The VRIF Trial: Hypoglycemia Reduction With Automated-Insulin Delivery System NCT03674281</td>
<td>Observational study (n=68) Intervention: Sensor Augmented Pump (SAP; Dexcom G6) followed by Closed-Loop Control (CLC) with Control-IQ plus CGM (Dexcom G6) Primary outcome: Time of blood glucose in range 70-180 mg/dL Status: Recruiting Estimated completion date: December 2019</td>
</tr>
<tr>
<td>Safety Evaluation of the Hybrid Closed Loop (HCL) System in Pediatric Subjects With Type 1 Diabetes NCT02660827</td>
<td>Observational study (n=105) Intervention: Hybrid closed loop Medtronic 670G Primary outcome: Change in A1C from baseline to end of 3-month treatment period Status: Active, not yet recruiting Estimated completion date: December 2019</td>
</tr>
</tbody>
</table>
| Multi-center, Randomized, Parallel, Adaptive, Controlled Trial in Adult and Pediatric Patients With Type 1 Diabetes Using Hybrid Closed Loop System and Control (CSII, MDI and SAP) at Home NCT02748018 | Randomised control trial (n=1,500) Intervention: Hybrid closed loop arm (Medtronic 670G Insulin Pump) Comparator: Cohort 1: Continuous Subcutaneous Insulin Infusion (CSII cohort) Cohort 2: Multiple Daily Injections (MDI cohort) Cohort 3: Sensor-Augmented Pump therapy (SAP cohort) Primary outcome: For subjects with:  
  - Baseline A1c >8%; Change in A1C from baseline to the end of the six-month treatment period  
  - Baseline A1c ≤8%; Time with sensor glucose (SG) below 70 mg/dL (3.9mmol/L) during the six-month study period Status: Recruiting Estimated completion date: December 2021 |
<table>
<thead>
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</table>
| A Randomized Crossover Comparison of Artificial Pancreas vs. Sensor Augmented Pump/Predictive Low Glucose Suspend With Different Stress Assessments in the Outpatient Setting for Patients With Type 1 Diabetes NCT04142229 | Randomised clinical trial (n=20)  
Intervention: The AiD system (iAPS: an insulin pump, Dexcom G6 CGM and a smartphone with algorithm)  
Comparator: Sensor augmented pump therapy (insulin pump with Dexcom G6 CGM)  
Primary outcome: Time in target glucose range 70-180 mg/dL measured by CGM to determine safety and efficacy of the integrated system  
Status: Recruiting  
Estimated completion date: June 2020 |
| An Open-label, Multi-centre, Multi-national, Randomised, 2-period Crossover Study to Assess the Efficacy, Safety and Utility of Closed Loop Insulin Delivery in Comparison With Sensor Augmented Pump Therapy Over 4 Months in Children With Type 1 Diabetes Aged 1 to 7 Years in the Home Setting NCT03784027 | Randomised clinical trial (n=72)  
Intervention: CamAPS FX closed loop system (Dana insulin pump + Dexcom G6 CGM + a smartphone with CamAPS FX app)  
Comparator: Sensor augmented pump therapy (pump + CGM)  
Primary outcome: Time in target (3.9 to 10.0 mmol/l) (70 to 180 mg/dl)  
Status: Recruiting  
Estimated completion date: June 2020 |
| Comparison of the Efficacy of Sensor-augmented Pump Therapy Versus Hybrid Closed-loop Glucose Management (MiniMed 670G™) in Patients With Type 1 Diabetes at Home in a Randomized Controlled Trial NCT03815487 | Randomised clinical trial (n=40)  
Intervention: Hybrid Closed Loop system (MiniMed 670G with Auto Mode on)  
Comparator: Sensor augmented pump therapy (MiniMed 670G with Auto Mode off)  
Primary outcome: Time in Range (% of Sensor Glucose 70-180 mg/dL)  
Status: Enrolling by invitation  
Estimated completion date: December 2019 |
<table>
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| A Randomized Cross-over Clinical Trial to Assess the Efficacy of Closed-loop Control (CLC) and Predictive Low-glucose Suspend (PLGS) Compared With Sensor-augmented Pump Therapy (SAP) Among Older Adults With Type 1 Diabetes  
NCT04016662 | Randomised crossover trial (n=90)  
Intervention: Closed Loop Control (CLC) arm (the Tandem t:slim X2 with Control-IQ Technology and Dexcom G6 CGM) Predictive Low Glucose Suspend (PLGS) arm (the Tandem t:slim X2 with Basal-IQ Technology and Dexcom G6 CGM)  
Comparator: Sensor augmented pump therapy arm (the Tandem t:slim X2 and Dexcom G6 CGM without CLC or PLGS features)  
Primary outcome: Percentage of sensor glucose values <70 mg/dL  
Status: Not yet recruiting  
Estimated completion date: June 2022 |
| Randomized Cross Over Trial of the MiniMed™ 670G 4.0 Insulin Pump, Comparing Advanced Hybrid Closed Loop Mode With Sensor Augmented Pump Therapy in Type 1 Diabetes.  
NCT04073576 | Randomised control trial (n=60)  
Intervention: Closed loop algorithm contained in the MiniMed™ 670G 4.0 pump to be used in the study; includes a modified proportional integrative derivative (PID) model, with insulin feedback, an auto correction bolus feature and additional safety features.  
Comparator: Sensor Augmented Pump (SAP) Therapy Mode with Predictive Low Glucose Management (PLGM), contained in the the MiniMed™ 670G 4.0 pump to be used in the study.  
Primary outcome: Performance of the AHCL system: sensor glucose values between 3.9 - 10.0 mmol/L  
Status: Recruiting  
Estimated completion date: October 2019 |
| In Adults With Very Unstable Type 1 Diabetes, is the DBLHU Closed-Loop Insulin Delivery System Able to Improve Blood Glycemic Control Compared to Low-Glucose-Predictive-Suspend System: Two-center, Randomized, Open-label Study  
NCT04042207 | Randomised clinical trial (n=7)  
Intervention: Closed Loop System (Dexcom G6 + Kaleido insulin pump + Model Predictive Control-based glucose control algorithm)  
Comparator: Sensor augmented pump therapy with Low Glucose Predictive Suspend System (Dexcom G6)  
Primary outcome: Percentage of CGM time in glucose range 70-180 mg/dl, during 24 hours periods for the third and fourth week for each treatment period  
Status: Recruiting  
Estimated completion date: March 2020 |
### Trial name and registration number

Assessment of the Impact of Real-Time Continuous Glucose Monitoring on People Presenting With Severe Hypoglycaemia  
NCT03748433

### Details

- Randomised clinical trial (n=55)
- Intervention: Phase 1: real-time CGM (Dexcom G6)
- Phase 2: randomised to either Dexcom G6 or Tandem t:slim X2 Insulin pump
- Comparator: Phase 1: self-monitoring Blood glucose
- Primary outcome: Percentage time spent in hypoglycaemia (<3.0mmol/L, 55mg/dL)
- Status: Recruiting
- Estimated completion date: September 2020

### Additional information

Further potentially relevant guidance:


### References


