Sensor-augmented pump therapy: review of new NICE diagnostic guidance

In February 2016, NICE released diagnostic guidance about two forms of sensor-augmented pump (SAP) therapy. These integrated devices represent the first commercially available steps to a closed-loop system or artificial pancreas. The artificial pancreas seems to us the closest (c.f. replacing islet cells with stem cell or donor transplants or preventing beta cell loss with immunotherapy or technology) to achieving a ‘cure’ for type 1 diabetes (T1DM).

SAP therapy comprises an integrated system of an insulin pump (providing a subcutaneous insulin infusion) with a continuous glucose monitor and a transmitter to send the continuous glucose readings wirelessly to the pump. The sensors continuously measure interstitial glucose levels to give readings, trends and warnings against pre-set parameters. This information allows the user to make ‘real-time’ changes to their insulin therapy.

The guidance considers two systems: the MiniMed Paradigm Veo system and the Animas Vibe and G4 Platinum CGM system. Technology is moving fast in this area so that although the more ‘advanced’ MiniMed 640g is mentioned in an accompanying Medtech Innovation Briefing it is not formally assessed, for use, by this guidance. We are likely to have closed-loop systems available before long. Thabit et al. recently showed the real-life benefit of this in a 12-week free-living home trial using a closed loop system in children, adolescents and adults versus SAP therapy.1

There is a key difference between the two systems: the MiniMed system has the additional benefit of a low glucose suspend feature which stops insulin delivery for a period of up to 2 hours when the user’s blood glucose falls below a certain threshold. This is likely to revolutionise the day-to-day diabetes management for a specific cohort of patients who are regularly troubled with hypoglycaemia. Alleviating the constant worry of impending hypoglycaemia and promoting a greater sense of independence for such patients and their carers could be life changing.

Guidance (NICE DG21)
The NICE guidance approves the use of the MiniMed Paradigm Veo system and not the Animas Vibe G4 system (though noting that the latter is promising but that there is a lack of published evidence to recommend its use).

The guidance states:2
- ‘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.’
- ‘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.’
- ‘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.’

These recommendations are sensible and fit with both the evidence and current practice. The requirement for data collection is an interesting mandate to ensure the appropriate use and ongoing research of SAP therapy.

The evidence
Although there is much positive anecdote of the use of continuous glucose monitoring systems in conjunction with pumps – and many patients clearly wonder how anyone with T1DM lives without one – there is no good-quality evidence for their use in routine practice. Only one randomised controlled trial (RCT) shows improvement in HbA1c, quality of life, and fear of hypoglycaemia at 12 months.3 Of the other three studies, two show some statistical benefit of pump and sensor against pens and meter.4-6 Whether the effect is pump or sensor or both, is thus unclear.

Bergenstal et al. showed in their RCT (ASPIRE in-home study), comparing the MiniMed system with a standard integrated SAP therapy, a reduction in hypoglycaemic events at three months’ follow up (3.3±2.0 weekly events per patient compared to 4.7±2.7 weekly events per patient; p<0.001).7 This effect remained consistent when the results were confined to nocturnal hypoglycaemic events only, which tends to be a major concern for a large proportion of our patients with T1DM. The primary safety endpoint, however – change in HbA1c – was negligible in both groups in this RCT. In a younger population, Ly et al. showed that the MiniMed reduced the risk of moderate and severe hypoglycaemia when compared with capillary testing and pump therapy.8

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NICE guidelines commentary

Key points of new NICE guidelines (DG21)
- There are limited data supporting the routine use of sensor-augmented pump therapy
- NICE approves the use of an integrated sensor-augmented pump therapy (MiniMed Paradigm Veo system) for patients with disabling hypoglycaemia despite CSI
- The MiniMed Paradigm Veo System has an additional benefit of a low glucose suspend feature
- Further research to investigate the effectiveness of the integrated sensor-augmented pump therapy is needed in younger children and pregnant women
The overall evidence base to support using the integrated SAP therapy is weak, but there is some limited evidence to suggest the MiniMed system is beneficial in reducing rates of nocturnal and severe hypoglycaemia which, from a clinical setting, are a major concern for a large proportion of our patients with T1DM.

**The costs**

The IMS Core Diabetes Model which simulates disease progression was used to assess the cost effectiveness of both these systems in adults with T1DM who qualify for an insulin pump based on NICE TA151. The clinical outcomes assessed were reduction in HbA1c from baseline (mean baseline of 7.26% was used) and number of severe hypoglycaemic events, whereas cost outcomes included primary prevention and management of diabetes complications, treating diabetes and related hospital costs. Although well validated, this model favours interventions that reduce HbA1c and associated complications rather than short-term outcomes associated with reducing hypoglycaemic events; thereby underestimating its impact. The MiniMed system and the Animas Vibe system were both found not to be cost effective when compared with multiple-dose injections or pump therapy. Cost per QALY is up to ~£700 000 for SAP therapy. In subgroup analysis, surprisingly, in adults who had difficulty in maintaining target HbA1c, SAP therapy was not cost effective compared with standard multiple-dose injection regimen or pump therapy. In adults who experienced frequent hypoglycaemic events, the MiniMed system was again not cost effective compared with multiple-dose injections. However, when compared with a non-integrated system, the MiniMed system was found to be superior.

Overall, within its limitations, the current cost-effectiveness data suggest that, due to the large incremental cost of technology, it is not cost effective when compared with capillary blood testing with multiple-daily injection or pump therapy. If a patient has escalated from a multiple-dose regimen to needing non-integrated SAP therapy, it is then a cost-effective decision to switch to an integrated system such as the MiniMed system, particularly with the additional benefit of low glucose suspend.

**What does this mean in practice?**

Although as clinicians we want to optimise the care for individuals, we need to think about the wider health economy. We know from experience that clinical commissioning groups already restrict access to insulin pump therapy and continuous glucose monitoring (CGM). The combination of these which is more expensive is likely to be harder to fund. At present, with the current evidence, it appears to only be cost effective to offer this to a small subgroup of patients who experience frequent hypoglycaemia and are already on non-integrated pump devices.

We suggest a stepwise progression of treatment in the face of poor glycaemic control (hypo- or hyperglycaemia) as shown in Figure 1.

From patients’ perspectives SAP therapy is likely to be appealing. Having the ability to prospectively reduce or stop insulin delivery when hypoglycaemia is anticipated could be life changing: improving independence, and the ability to work. We also have to be mindful of the implications of children and adolescents who transition into adult services on pump therapy with or without CGM. SAP therapy is likely to be used more widely in this group than in adults. It may prove difficult to justify the restrictions on provision of SAP therapy to the general population with T1DM; hopefully, the ability to offer it to a limited number of patients who face the serious disabling hypoglycaemia will offer some relief. Alternatively, one has to be aware that funding expensive technology removes money from other important treatment options in T1DM, such as education or psychological therapy.

In today’s world, newer technologies to augment the care of people with T1DM are welcomed. However, in an overstretched, resource-limited NHS, we need to seek ways to provide the latest, yet individualised, targeted treatment for our patients within these constraints.

**References**

References are available in Practical Diabetes online at www.practicaldiabetes.com.

**Figure 1.** Schematic representation for the stepwise management of type 1 diabetes

Table: Sensor-augmented pump therapy: review of new NICE diagnostic guidance

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<td>• Continuous glucose monitoring system</td>
<td>• Pancreas or islet transplant in the face of ongoing severe hypoglycaemia despite all of the foregoing</td>
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Suchitra Raj, MBBS, Specialty Registrar in Diabetes and Endocrinology, King’s College Hospital NHS Foundation Trust, London, UK

Ali Chakera, PhD, Consultant in Diabetes and Endocrinology, Royal Sussex County Hospital, Brighton and Sussex University Hospitals NHS Trust, Brighton, UK

Declaration of interests

There are no conflicts of interest declared.
References