NICE advice

d-Nav insulin management app for type 2 diabetes

Medtech innovation briefing
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Summary

- The **technology** described in this briefing is d-Nav. It is an app used for guiding insulin dosing for adults with type 2 diabetes.
- The **innovative aspects** are the insulin dose can be calculated and adjusted based on a person's current and historic blood glucose levels on a weekly basis and without healthcare professional approval.
- The intended **place in therapy** would be to help optimise insulin dosage in people with type 2 diabetes.
- The **main points from the evidence** summarised in this briefing are from 4 studies (including 1 randomised controlled trial, 2 retrospective studies and 1 prospective pilot study) including a total of 611 adults with type 2 diabetes who use insulin. They show that d-Nav can reduce haemoglobin A1c (HbA1c) levels in people when their current insulin dosing regimen is not reaching HbA1c targets.

- **Key uncertainties** around the evidence or technology are that the 3 UK-based studies are non-comparative. This means it is difficult to compare outcomes with standard care in the NHS. All evidence uses a version of the software installed on a physical d-Nav device with built-in glucose meter.
- **Experts advised** that the technology could automate daily insulin dosage requirements when there is not enough staff resource or frequent enough clinical visits to regularly titrate insulin dosage. However, patients need to be carefully selected and would need access to a smartphone and internet.
- The **cost** of d-Nav is about £100 per person per month (excluding VAT). This technology would be used in addition to routine diabetes monitoring appointments.

The technology

d-Nav (Hygieia) is a phone app that aims to guide insulin dosing in adults with type 2 diabetes. It is primarily indicated for those needing insulin in which blood glucose or haemoglobin A1c (HbA1c) targets are not being reached. The technology comprises of 2 elements, a phone app for the person with type 2 diabetes and the d-Nav website for use by healthcare professionals.

The phone app is used by the patient to a enter glucose reading and get a recommended insulin dose. The blood glucose reading is taken from any blood glucose meter or a continuous glucose monitor. It is entered into the app either manually through the phone keypad or through the cloud from a linked blood glucose meter. Based on glucose readings and the user's current insulin instructions and history of events, the d-Nav Get-Dose Library algorithm calculates a new recommended insulin dose and updates current insulin instructions if needed.

The app is set up by a healthcare professional using the d-Nav website. Setup consists of entering the prescribed starting insulin dose instructions and sending the information to the patient's app. Insulin instructions include the treatment plan, insulin drug type, and dose(s).

The d-Nav app is available for both iOS and Android devices.

The d-Nav app is a replacement of the d-Nav device. The device was comprised of a handheld device with a built-in glucose meter. The app uses the same software and

Get-Dose Library algorithm as the device but allows additional connectivity with the healthcare professional website and a linked blood glucose meter through the cloud.

Innovations

The device is designed to help optimise insulin dosing to reduce high HbA1c levels into the target range while reducing the rate of hypoglycaemic events. The company states that the d-Nav app includes safety checks to stop insulin dose changes if the total daily dose exceeds the healthcare professional's set threshold.

Current care pathway

NICE's guideline on type 2 diabetes in adults: management states that insulin-based treatment for people with type 2 diabetes is considered as an option for the second intensification of drug treatment when current treatments have not been able to control HbA1c levels. The type of insulin and dose prescribed depends on factors including the ability to administer treatment, HbA1c levels, the likelihood of becoming hypoglycaemic, and the use of other glucose-lowering drugs.

When starting insulin therapy in adults with type 2 diabetes, a structured programme is recommended which includes:

- continuing telephone support
- self-monitoring
- dose titration to target levels
- dietary understanding
- management of hypoglycaemia
- management of acute changes in plasma glucose control
- support from an appropriately trained and experienced healthcare professional.

The following publications have been identified as relevant to this care pathway:

- NICE's guideline on type 2 diabetes in adults: management

- NICE's guideline on diabetes (type 1 and type 2) in children and young people: diagnosis and management
- NICE's technology appraisal guidance on continuous subcutaneous insulin infusion for the treatment of diabetes mellitus.

Population, setting and intended user

d-Nav is intended to be used to help optimise insulin dosage for people with type 2 diabetes. The person's insulin treatment plan would be entered by an appropriately trained healthcare professional through the d-Nav website. The patient would use the device at home alongside a glucose meter or continuous glucose monitor. People would need a smartphone and regular internet access to use the device and get the Get-Dose Library updates from the cloud.

The company provides training for healthcare professionals and patients when they start using d-Nav. The company also provides ongoing technical support with a freephone service.

Costs

Technology costs

The cost of the d-Nav app has not yet been decided for the NHS in England. The company has advised that the list price of the technology will be about £100 per person per month (excluding VAT).

Costs of standard care

Standard care would be the cost of appointments with a healthcare professional to change insulin dosage. If seen by a specialist nurse the cost would be between £79 (if the appointment was face to face) and £39 (if the appointment was not face to face; N15AF and N15AN; National schedule of NHS costs for 2019 to 2020). A non-admitted face-to-face follow-up appointment would cost £154.32 (WF01A; National schedule of NHS costs for 2019 to 2020). Follow-up care in primary care or in the community may be less costly. The d-Nav technology would be used in addition to routine follow ups with healthcare professionals.

Resource consequences

The physical version of the device has been in use in the NHS in Northern Ireland since 2013. There, GPs can refer people directly to the d-Nav service or refer them to the hospital diabetes services to consider suitability for using d-Nav.

The app alone version of the device has been used in the US for over 3 years. The technology is recommended in the US by the American Diabetes Association's standards of medical care in diabetes (2021) as an alternative to continuous glucose monitoring, to help people with insulin dosing improve HbA1c with minimal hypoglycaemia.

d-Nav would be used in addition to standard care. Adopting d-Nav could improve management of type 2 diabetes and reduce the time needed by clinicians to optimise insulin dosage. This could help maintain optimal HbA1c levels and reduce the number of hypoglycaemic events. This could reduce the likelihood of developing diabetes-related complications, reduce hospitalisation and reduce additional NHS resource use. Better control of HbA1c levels could also reduce the need for additional blood glucose control medications.

A cost-effectiveness analysis of the d-Nav device in people with diabetes in the NHS who are at high risk of foot ulcers (defined as those who have an HbA1c of 9% or greater) has been reported by Green and Taylor (2016). It found that d-Nav was cost-saving by £1,278 and produced more quality-adjusted life years (0.009) than standard care. One further US cost analysis (Schneider et al. 2018) was published looking at the impact of d-Nav on non-insulin pharmaceutical expenses. It found that device use led to a reduction in cost associated with the need for additional diabetes medications. Both studies were based on the physical device rather than the app.

Regulatory information

The d-Nav app is a CE-marked class IIa medical device. The previous physical version of the device is a CE-marked class IIb medical device.

Equality considerations

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and

others.

The technology is intended to benefit people with type 2 diabetes. The d-Nav app needs internet access and a smartphone or tablet that can run the app. People with visual or cognitive impairment, problems with manual dexterity or a learning disability or who are unable to read or understand health-related information (including people who cannot read English) may need additional support to use the technology. Disability is a protected characteristic under the Equality Act 2010.

Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the interim process and methods statement for medtech innovation briefings. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

Published evidence

There are 4 studies summarised in this briefing, including 1 randomised controlled trial, 2 retrospective studies and 1 prospective pilot study. In total, there were 611 people included in these studies. In addition to the studies presented in full, there is 1 feasibility study in 46 people (Bergenstal et al. 2012) and a pilot study in 14 people (Bashan et al. 2012). These included people with type 1 or type 2 diabetes and are not presented here in detail.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

Overall assessment of the evidence

These studies were done in appropriate populations and reported relevant outcome measurements. Three of the studies were done in the UK and so are generalisable to NHS practice. Two of these provided longer term data over a period of more than 2 years. However, these UK-based studies were single-arm, meaning there is no comparable evidence to standard care in the UK. One study was a randomised controlled trial and used an appropriate comparator. However, it was limited by a 6-month follow-up period

and the study was done in the US. This study showed a reduction in HbA1c levels in the intervention group compared with the control, with no statistical difference in hypoglycaemic events. The company highlights that reducing HbA1c levels while not increasing the risk of hypoglycaemia is a key benefit of the technology. All studies were limited by the evidence being on the physical device rather than the app. Although the company states that the software is the same in both versions of the device, there is no evidence showing whether the app version alone would affect efficacy of the technology.

Bergenstal et al. (2019)

Study size, design and location

Prospective, open-label, multicentre randomised controlled study of 181 people with type 2 diabetes who use insulin in the US.

Intervention and comparator

Intervention: d-Nav insulin guidance system (a handheld device that contains a glucose meter and software that adjusts insulin dose) and healthcare professional support.

Comparator: healthcare professional support alone.

Key outcomes

The study was done over a 6-month period. At baseline, mean HbA1c was 8.7% (standard deviation [SD] 0.8%) in the intervention group and 8.5% (SD 0.8%) in the control group. The mean decrease in HbA1c after 6 months was 1% (SD 1%) in the intervention group and 0.3% (SD 0.9%) in the control group ($p<0.0001$). There was a similar frequency of hypoglycaemic events per month in each group ($p=0.96$).

Strengths and limitations

This multicentre randomised controlled study used an appropriate comparator, and baseline characteristics between groups appear similar, although no statistical comparisons were done. However, this study is limited by a relatively short (6-month) follow-up period and the study was done in the US, which could limit generalisability to the NHS. This study was also done on the device version rather than the app for this technology.

Harper et al. (2018)

Study size, design and location

Retrospective cohort study of 246 people with type 2 diabetes who use insulin in the UK.

Intervention and comparator

Intervention: d-Nav insulin guidance system (a handheld device that contains a glucose meter and software that adjusts insulin dose); no comparator.

Key outcomes

Patient data was collected for 2.8 years (plus or minus 0.9). There were 70.3% of people who went through periods when their total daily dose was reduced. HbA1c decreased from 9.4% (plus or minus 1.6%) at baseline to 7.1% (plus or minus 0.9%). The frequency of hypoglycaemic episodes (less than 54 mg/dl) was low at 0.5 (plus or minus 0.6) episodes per month.

Strengths and limitations

This study was done in the UK and included people who have used the service for more than 19.5 months who have had no gap in insulin dosage information greater than 3 months. However, the study was observational and had no comparator group. Because the data was collected retrospectively, there was also a lack of information on additional glucose-lowering medications. This study was funded by the company and used the d-Nav device rather than the app.

Donnelly et al. (2015)

Study size, design and location

Single-centre pilot study of 122 people with type 2 diabetes who have used insulin for at least 1 year in the UK.

Intervention and comparator

Intervention: d-Nav insulin guidance system (a handheld device that contains a glucose meter and software that adjusts insulin dose); no comparator.

Key outcomes

There were 28 people who withdrew from the study, 19 of which were related to not being able to use the device correctly. Of the 94 people who completed the study, the mean (and standard deviation) HbA1c decreased from 77 mmol/mol (plus or minus 15 mmol/mol; 9.2% plus or minus 1.4%) at baseline to 62 mmol/mol (plus or minus 13 mmol/mol; 7.8% plus or minus 1.2%) at the 3-to-5-month clinic visit and to 59 mmol/mol (plus or minus 13 mmol/mol; 7.5% plus or minus 1.2%) at the 6-to-12-month clinic visit. The study reported a low frequency of minor hypoglycaemia (blood glucose less than or equal to 3.6 mmol/litre).

Strengths and limitations

Because this was a pilot study, it is limited by having no control group. This study was also funded by the company and was on the d-Nav device rather than the app.

Harper et al. (2016)

Study size, design and location

Retrospective analysis of 62 people who had used the d-Nav technology for more than a year in the UK.

Intervention and comparator

Intervention: d-Nav insulin guidance system (a handheld device that contains a glucose meter and software that adjusts insulin dose); no comparator.

Key outcomes

People were studied over an average of 2.1 years (plus or minus 0.5 years' standard deviation). After 9 months, stability in HbA1c level was achieved with an average HbA1c of 7.4% plus or minus 0.2% (57.4 mmol/mol plus or minus 1 mmol/mol). On average, insulin dose decrease events happened in 56.5% of people, with an average of 0.8 (plus or minus

0.4) events per year.

Strengths and limitations

Although this study was done in the UK, it is limited by being a retrospective study with no comparator group. The analysis was also limited to people who have used the service for more than 1 year and excluded those who had 2 or more episodes of severe hypoglycaemia in the past year. This study was also funded by the company and was on the d-Nav device rather than the app.

Sustainability

The company claims the technology will allow more people with type 2 diabetes needing insulin to be supported without the need for additional appointments. There is no published evidence to support these claims.

Recent and ongoing studies

No ongoing or in-development trials were identified.

Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Two of the 3 experts were familiar with or had used the physical device version of this technology before.

Level of innovation

Two experts stated that this technology is innovative because it can automate daily insulin dosage recommendations, which is not feasible through current healthcare professional input. Two experts said that currently people have infrequent dose adjustment advice at 6- or 12-monthly clinic reviews with a specialist diabetes nurse. One expert said that in between reviews people can make some additional adjustments to their insulin dosing,

based on advice from a diabetes nurse. However, HbA1c often remains elevated or gradually increases. One expert said that there is a lack of educational support for using and titrating insulin in those with type 2 diabetes. One expert said that there is good evidence to show that patient adjustment of insulin dosing after appropriate education can lead to better glycaemic control compared with periodic contact with healthcare professionals. They said that this app could help support people with effective insulin titration for a variety of insulin regimens, but the supporting evidence is limited.

One expert said that d-Nav is a way to allow frequent insulin dose adjustment and the resultant HbA1c improvement, without affective staff resources. They stated that d-Nav could replace the current standard of insulin dose optimisation. This would allow clinic reviews to be less frequent and would allow more time to focus on other areas of diabetes management. Another expert said that help and support from healthcare professionals would still be needed to ensure safe and continued use of the technology.

Potential patient impact

Two experts said that this technology could benefit most patients using insulin for type 2 diabetes who need good glycaemic control. All experts said that the main benefit is improved glycaemic control and the resultant reduction in diabetic complications. One expert said that making insulin dosing easier would also be better for patients. One expert said that through using the technology, people learn more about their relationship between eating and insulin requirements and become more knowledgeable about their type 2 diabetes and insulin therapy. One expert acknowledged that people would need to be able to afford a smartphone and have internet access, which is an equality consideration. They would also need to be feel confident in using technology.

Potential system impact

One expert said that the technology can reduce the burden on primary care and secondary care diabetes teams. By improving the glycaemic control for many patients, the technology can reduce the complications associated with diabetes. This would reduce the number of people who need additional, and potentially more invasive, treatments or procedures. One expert agreed that the technology could reduce reliance on healthcare professionals for insulin titration as well as reduce the number of referrals to secondary care and hospital outpatient visits. Another expert agreed but said that there are still some d-Nav users who need additional support and encouragement to use the service

consistently and safely, which leads to more support and healthcare professional interactions.

All experts said that the use of the d-Nav technology would lead to cost savings in the NHS. This would be as a result of reductions in the cost of other drugs used and from a reduction in costs because of complications and morbidity from poorly controlled diabetes.

One expert said that no additional clinical facilities are needed as the d-Nav technology comes with a support team to support the patient in using the device. All experts said that patients and healthcare professionals need training in how to use the device. One expert said that this would include training for healthcare professionals on setup and how to use the web-based services to monitor usage, set limits and reset insulin dosages. All experts said that clinicians also need guidance on who the technology would be appropriate for. One expert noted that additional costs would be incurred for staff training and patient education. One expert said that additional work is needed to set up an insulin titration support service and that patients would need initial and ongoing support to use the technology safely and successfully.

General comments

One expert said that the device is simple and straightforward to use. They have seen a wide range of people who have been able to use it successfully. However, they stated that some healthcare professionals may find it hard to understand how a device or algorithm can adjust insulin dose, meaning reassurance is needed. One expert said that patient selection is very important because they need to be able to understand the technology and the dosage guidance it gives. They said the technology would be for those who would benefit from an HbA1c score less than 53 mmol/litre who have good hypoglycaemic awareness.

One expert said that although there was a randomised controlled trial done in the US, further evidence is needed in the form of long-term comparative studies in the UK to show that the technology is better than standard care.

One expert who uses the physical device said that moving to the d-Nav phone app would improve usability and reduce the workload associated with the physical device such as setup, resets, device replacements and provision of test strips. However, they were concerned whether people will enter blood glucose readings into the app because the

glucose meter is built into the physical device.

Patient organisation comments

A representative from Diabetes UK gave the following comments.

People with type 2 diabetes increasingly use apps to support self-management of their condition. The d-Nav technology could offer benefit to people with type 2 diabetes because calculations involved in administering insulin can be complicated, especially when people use different insulin to carbohydrate ratios at different times of the day. Additionally, an individual's insulin dosage requirements can change over time, making it difficult to calculate how much insulin they should administer. Decisions on insulin dosing are currently made during clinician appointments 1 to 4 times a year. Because insulin dosing needs to be updated more frequently than this, people often struggle to meet their target glycaemic range and HbA1c.

The d-Nav technology could reduce patient burden of calculating insulin dosages and could also lead to fewer clinician appointments and improve quality of life. The technology could particularly benefit those who have difficulties with the numeracy involved in calculating insulin doses and those who struggle to attend clinical appointments because of geography, work or disability. However, the key limitations are that the technology needs a minimum level of digital skill and access to a compatible mobile phone. Clinicians also need to be trained to support patients using d-Nav. Using the technology may be challenging for those with a visual impairment or for those with a learning disability.

Expert commentators

The following clinicians contributed to this briefing:

- Dr Steven Kinnear, GP managing partner, Silverbirch Medical Practice. Dr Kinnear has previously worked as a paid consultant to Hygieia.
- Dr Niall Furlong, consultant diabetologist, St Helens and Knowsley Teaching Hospitals NHS Trust. Did not declare any interests.
- Dr Roy Harper, consultant endocrinologist, South Eastern Health and Social Care Trust. Did not declare any interests.

Representatives from Diabetes UK also contributed to this briefing.

Development of this briefing

This briefing was developed by NICE. The interim process and methods statement for medtech innovation briefings sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

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