

# Diabetes Insulin Guidance System: a real-world evaluation of new technology (d-Nav) to achieve glycaemic control in insulin-treated type 2 diabetes

**R Donnelly<sup>1</sup>**

Specialist Diabetes Pharmacist

**S Carr<sup>1</sup>**

Diabetes Research Nurse

**R Harper<sup>1</sup>**

Consultant Endocrinologist

<sup>1</sup>The Department of Endocrinology & Diabetes, The Ulster Hospital, Dundonald, Belfast, Northern Ireland, UK

## Correspondence to:

Dr Roy Harper, BSc, MD, FRCP, Consultant Endocrinologist, The Ulster Hospital, Dundonald, Belfast BT16 1RH, Northern Ireland, UK; email: Roy.Harper@setrust.hscni.net

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## Abstract

The aim was to conduct a service evaluation of the effectiveness of using d-Nav (a handheld device that automates the process of insulin dosage titration using the Diabetes Insulin Guidance System [DIGS] software) in achieving glycaemic control in patients with type 2 diabetes.

The study comprised an exploratory single-centre pilot evaluation of the use of d-Nav in patients with type 2 diabetes aged  $\geq 21$  years with an HbA<sub>1c</sub> level  $\geq 53$  mmol/mol ( $\geq 7.0\%$ ) who were receiving insulin therapy for at least one year. Patients were asked to use d-Nav to monitor their blood glucose level before every insulin injection and, when they suspected the occurrence of hypoglycaemia, to allow d-Nav to adjust their insulin dosage. At scheduled three-monthly clinic visits, HbA<sub>1c</sub> was measured and information on episodes of hypoglycaemia collected from d-Nav and by patient reporting. Patients were followed for a minimum of six months.

A total of 94 patients completed the evaluation as active users. The mean ( $\pm$  standard deviation) HbA<sub>1c</sub> for active users decreased from  $77 \pm 15$  mmol/mol ( $9.2 \pm 1.4\%$ ) at baseline to  $62 \pm 13$  mmol/mol ( $7.8 \pm 1.2\%$ ) at the three- to five-month clinic visit and to  $59 \pm 13$  mmol/mol ( $7.5 \pm 1.2\%$ ) at the six- to 12-month clinic visit. In patients for whom paired data were available, the decreases were statistically significant at both post-baseline visits (both  $p < 0.001$ ). The frequency of minor hypoglycaemia (blood glucose  $\leq 3.6$  mmol/L) was low and well within the tolerated range.

In conclusion, d-Nav is shown to be a safe and effective solution for blood glucose management in insulin users with type 2 diabetes. Copyright © 2015 John Wiley & Sons.

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## Key words

d-Nav; insulin guidance; assistive technology; type 2 diabetes

## Introduction

Optimal glycaemic control is essential in patients with diabetes mellitus in order to reduce the risk of diabetes-related complications.<sup>1–3</sup> All patients with type 1 diabetes and, eventually, many patients with type 2 diabetes require insulin therapy to maintain glycaemic control. A variety of insulin formulations with differing time to action profiles are available, providing the physician with the potential to offer effective insulin therapy according to an individual patient's requirements. However, patients with diabetes who are treated with insulin frequently fail to achieve optimal glycaemic control in clinical practice. Even in well-organised health care systems between 50–75% of patients with type 2 diabetes treated with insulin fail to achieve the HbA<sub>1c</sub> goal of  $< 53$  mmol/mol ( $< 7.0\%$ ).<sup>4</sup>

Although frequent insulin dosage titration by health care professionals (HCPs) has been demonstrated in

clinical trials as a means to achieve optimal glycaemic control,<sup>5–8</sup> this is not logistically possible in clinical practice due to limited health care resources. Furthermore, as shown in the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications study, when long-term intensive clinician support is withdrawn, maintenance of adequate glycaemic control may be compromised.<sup>9</sup> While a variety of technologies are available to allow patients with diabetes to rapidly monitor and assess their blood glucose (BG) levels, one approach that has proven to be effective is the use of specially trained nurses or pharmacists, under appropriate supervision, with authority to make medication changes without consulting the physician as long as the changes fell within approved treatment algorithms.<sup>10</sup> However, given the vast numbers of insulin users, the time it takes to

provide therapy adjustments and the shortage in diabetes HCPs, the ability to adjust patients' insulin dosage frequently and accurately is not possible in clinical practice.

To address this problem, Hygieia Inc (Ann Arbor, MI, USA) developed Diabetes Insulin Guidance System (DIGS) software to adjust insulin dosage on a weekly basis. The DIGS software incorporates algorithms that identify patterns in time-tagged glucose readings and recommends updates to insulin dosage as needed.<sup>11</sup> Bergenstal and colleagues conducted a 16-week feasibility clinical trial designed as a prospective, open-label, uncontrolled, single-arm, single-centre study that demonstrated the capacity of DIGS software to provide safe and effective weekly insulin dosage adjustments.<sup>11</sup> In this study, DIGS software was used under the close supervision of HCPs. Hygieia Inc has now developed a service using assistive technology based on DIGS in the form of a handheld device known as d-Nav (Figure 1). d-Nav is a handheld device that houses the DIGS software integrated with a BG sensor. d-Nav automates the process of unsupervised insulin dosage titration for patients on a weekly basis between clinic visits.

The d-Nav device decreases insulin dosage whenever a cluster of hypoglycaemic events is identified and increases insulin dosage in the presence of a hyperglycaemic pattern (Figure 2). This enables a small number of dedicated HCPs to support a large group of patients in improving their glycaemic control. Although there are a variety of



**Figure 1.** The handheld d-Nav insulin guidance device. d-Nav is used to check capillary blood glucose and, based on the identification of patterns in time-tagged glucose readings, provides insulin dosage guidance on a weekly basis or more frequently in the presence of hypoglycaemia or near hypoglycaemia

emerging technologies for monitoring BG and simplifying insulin therapy,<sup>12,13</sup> d-Nav is unique in providing physician-type dosage adjustments for insulin users. d-Nav is European Conformity (CE)-marked and available for clinical use; however, to date there have been no reports of its use in a real-world setting.

This paper summarises the results of an exploratory service evaluation aimed at assessing the feasibility and benefits of using d-Nav to achieve desired glycaemic control in patients with type 2 diabetes in a clinical setting with minimal health care provider support.

### Patients and methods

#### Evaluation design

This 12-month service evaluation was designed as an exploratory single-centre pilot evaluation, conducted at the Ulster Hospital, Belfast, UK. The intention was to enrol at least 100 patients for a minimum of six months' follow up per patient. As this was a service evaluation of an approved device, ethical approval was not required. Patients wishing to be part of the evaluation were provided with a d-Nav kit and sufficient BG test strips to last until their next clinic visit, scheduled three to five months after commencement of d-Nav usage. At the initiation visit, d-Nav was set up for each patient with their current insulin regimen and dosage. Each patient received

instruction on the use of d-Nav and was advised to carry out their capillary BG measurements using d-Nav. During the evaluation, patients were requested to return to the clinic for their normal scheduled visits at approximately three- to five-monthly intervals and to bring their d-Nav at each visit. Follow up of patients via telephone calls from either a diabetes specialist pharmacist or nurse typically occurred within 10–14 days after the initiation visit and approximately six weeks later. Confirmation that patients were using d-Nav correctly was obtained during follow up. At the three- to five-month clinic visit, patients were provided with sufficient BG test strips to last until their next clinic visit. Throughout the evaluation patients could contact the evaluation team with any questions as often as needed.

The patient's HbA<sub>1c</sub> level was measured at the initiation visit, and at three- to five-month and six- to 12-month clinic visits following the initiation visit. Information on the insulin dosage and BG levels was downloaded from the d-Nav device at each visit. During clinic visits, information about patients' insulin therapy experience and d-Nav use was recorded. At each clinic visit patients were asked if they had experienced symptoms of hypoglycaemia since their previous visit. The overall frequency of episodes of confirmed minor hypoglycaemia



**Figure 2.** Software available to help visualise and interpret data downloaded from a d-Nav device. Software is used to download data stored on each d-Nav device. The software displays the downloaded data in a way that assists health care professionals and patients determine appropriate device usage and visualise progress in terms of insulin dosage (upper panel), weekly average blood sugars (lower panel), and hypoglycaemic events (red dots). In this example the user is on a basal bolus insulin regimen

Characteristic	Patients		
	All	Active users	Withdrew
No. of patients	122	94	28
Sex (% male)	52.5	56.4	39.0
Age (years), mean $\pm$ SD	61.2 $\pm$ 10.9	61.3 $\pm$ 10.4	60.7 $\pm$ 12.5
Race (no.)			
White	121	93	28
African	1	1	0
Diabetes type (no.)			
Type 2	122	94	28
Duration of diabetes (years), mean $\pm$ SD	12.5 $\pm$ 6.0	12.6 $\pm$ 6.1	12.4 $\pm$ 5.8
Time on insulin (years), mean $\pm$ SD	6.0 $\pm$ 4.0	5.6 $\pm$ 3.9	7.3 $\pm$ 3.7*
Initial HbA <sub>1c</sub> (mmol/mol [%]), mean $\pm$ SD	78.7 $\pm$ 16.1 [9.4 $\pm$ 1.5]	77.3 $\pm$ 15.3 [9.2 $\pm$ 1.4]	83.5 $\pm$ 17.5 [9.8 $\pm$ 1.6]
Initial weight (kg), mean $\pm$ SD	94.6 $\pm$ 18.8	95.3 $\pm$ 19.1	92.2 $\pm$ 17.4
Initial BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	33.6 $\pm$ 6.6	33.5 $\pm$ 6.5	33.9 $\pm$ 7.1
Concomitant therapy (% of patients)			
Metformin	66		
DPP-4 inhibitors	7		
Sulphonylureas	6		
Thiazolidinediones	1		
GLP-1 agonists	2		

BMI: body mass index; DPP: dipeptidyl peptidase; GLP: glucagon-like peptide; SD: standard deviation.  
\*P<0.05 vs active users.

**Table 1.** Baseline demographics and clinical characteristics of the evaluation population

(BG <3.7mmol/L) was calculated based on information downloaded from patients' d-Nav devices and reported as episodes <3.7mmol/L and <3.0mmol/L. The incidence of severe hypoglycaemia was obtained from information provided directly from the patient as part of their scheduled clinic visits or reported during periodic telephone contacts. Severe hypoglycaemia was defined as a recorded capillary BG level <2.8mmol/L associated with symptoms (memory loss, confusion, seizures, irrational behaviour, unusual difficulty in awakening, loss of consciousness) or, in the absence of a capillary or other BG determination, these symptoms were reversed with the administration of oral carbohydrate, glucagon, or intravenous glucose by someone else.

### Use of d-Nav

During the evaluation, patients were asked to use d-Nav to measure BG before every insulin injection and to label each glucose reading (e.g. 'breakfast') based on their routine and insulin regimen. Patients were also asked to use d-Nav during the night once a week. In addition, patients were asked to measure their BG every time they suspected or felt symptoms of hypoglycaemia to allow d-Nav to immediately adjust their insulin dosage if required, with the aim of preventing further hypoglycaemic events.

### Evaluation participants

The evaluation population comprised consecutive patients attending a diabetes clinic at the evaluation site. Eligible patients were men or

women aged  $\geq$ 21 years who had a clinical diagnosis of type 2 diabetes, were currently receiving insulin therapy, and had an HbA<sub>1c</sub> level >53mmol/mol (>7.0%). Patients entering the evaluation were using one of three insulin regimens supported by d-Nav: *Regimen 1*, one or two daily injections of the long-acting insulin analogue glargine; *Regimen 2*, two daily injections of biphasic insulin (Novomix 30 [Novo Nordisk A/S, Denmark], Humalog Mix25 [Eli Lilly and Company, USA] or Humulin M3 [Eli Lilly and Company, USA]); *Regimen 3*, an injection of a short-acting insulin analogue [Novorapid [Novo Nordisk A/S, Denmark], Humalog [Eli Lilly and Company, USA], or Apidra [Sanofi SA, France]) before each meal, based on a fixed dose and correction factor and one or two injections daily of the long-acting insulin analogue glargine. If indicated, the physician could change the patient's insulin regimen during the evaluation. The device also has the capacity to support a basal bolus insulin regimen incorporating carbohydrate counting (*Regimen 4*) but this was not used by any of the patients during this evaluation.

Patients were excluded if they had experienced more than two episodes of severe hypoglycaemia in the past year or had a history of hypoglycaemia unawareness, were using <10 units of glargine daily for Regimen 1, or a total of <25 units of insulin daily for all other regimens.

The initial set-up visit included training and lasted about 1 hour per patient. Patients could withdraw from the evaluation at any time at their own request without negative consequences to their standard care, or could be withdrawn at any time at the discretion of the medical team for safety, compliance or administrative reasons. Patients were withdrawn if the medical team determined the risk of hypoglycaemia was too severe; if it was decided that the patient would benefit from a regimen not supported by d-Nav; or if the patient achieved an HbA<sub>1c</sub> level lower than that set as a goal by their physician. Patients could also be withdrawn for: missing two consecutive appointments; failing to bring

their d-Nav with them on two consecutive occasions; becoming pregnant; discontinuing use of d-Nav for more than two consecutive weeks; consistently not taking sufficient glucose readings; or if their daily total insulin requirements fell below 10 units of glargine for Regimen 1 or a combined total below 20 units daily for all other regimens.

### Evaluation outcomes

The primary outcome was absolute change in HbA<sub>1c</sub> level from baseline following three and six months' use of d-Nav in conjunction with insulin injections. Secondary outcomes included the percentage of patients achieving HbA<sub>1c</sub> ≤58mmol/mol (≤7.5%), and frequency and severity of hypoglycaemia (BG ≤3.6mmol/L).

### Statistical analysis

Standard descriptive statistical methods and paired t-tests were used to assess the significance of changes from baseline in HbA<sub>1c</sub> values and body weight in 'active users' (i.e. patients who completed the service evaluation). Changes were considered statistically significant at a p-value of <0.05 by a two-tailed test.

## Results

### Service evaluation population

Overall, 122 patients participated in the service evaluation (Table 1). Twenty-eight patients withdrew (unable to use d-Nav [n=2]; did not use d-Nav appropriately, meaning they did not use it enough, could not tag use events correctly, or did not follow d-Nav's recommendations [n=17]; the preferred insulin [Levemir] was not supported by d-Nav [n=2]; lost to follow up [n=3]; experienced severe insulin resistance resulting in insulin dosage exceeding the limit supported by d-Nav [n=1]; concern about hypoglycaemia or weight gain [n=3]). The remaining 94 patients completed the service evaluation and were defined as active users. Of these, seven used Regimen 1 (basal only), 39 used Regimen 2 (premixed insulin) and 48 used Regimen 3 (basal-bolus). As shown in Table 1, the baseline clinical characteristics were very similar between the 94 active users and all enrolled participants. The only statistically significant difference was that patients

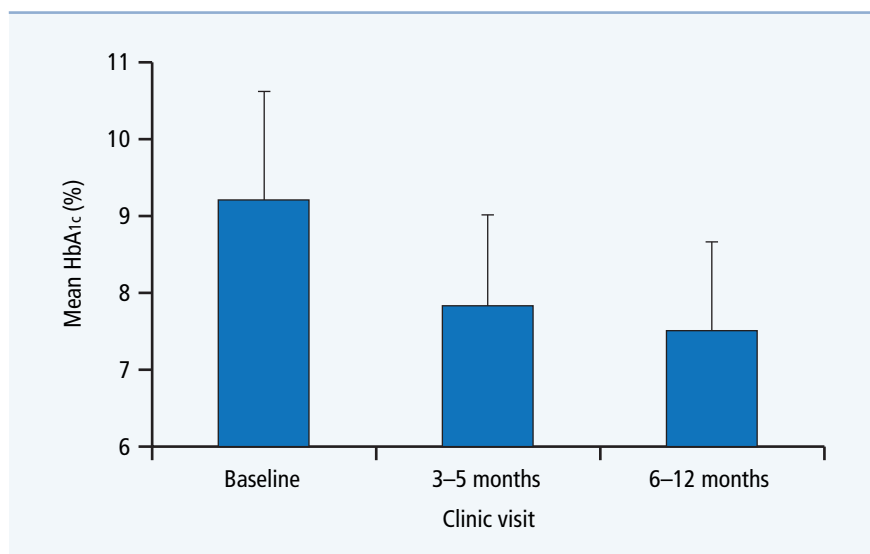


Figure 3. Mean ( $\pm$  standard deviation) HbA<sub>1c</sub> in active users of d-Nav

who withdrew had been receiving insulin for a longer time than those who completed the evaluation.

### HbA<sub>1c</sub> values

Mean HbA<sub>1c</sub> levels were stable during the year before patients enrolled in the evaluation. For all participants, during the one to six months before enrolment, the mean HbA<sub>1c</sub> level was 77±16mmol/mol (9.2±1.5%) and at seven to 12 months before enrolment the mean HbA<sub>1c</sub> was 77±15mmol/mol (9.2±1.4%); (p=0.7 vs one to six months). (Some participants had more than one HbA<sub>1c</sub> value recorded during that time.)

Intent-to-treat analysis for the 122 recruited patients was incomplete as post-baseline HbA<sub>1c</sub> data were available for 99 patients at three to five months and for 100 patients at six to 12 months. Mean ( $\pm$  standard deviation [SD]) values for HbA<sub>1c</sub> decreased between baseline (78.7±16.1mmol/mol [9.4±1.5%]) and the three- to five-month clinic visit (to 64.9±15.2mmol/mol [8.1±1.4%]), and subsequently decreased between the three- to five-month and six- to 12-month clinic visits (to 61.9±17.7mmol/mol [7.8±1.6%]).

Of the 94 active users (per protocol analysis), post-baseline HbA<sub>1c</sub> data were available for 82 patients at three to five months, and for 92 patients at six to 12 months. Mean ( $\pm$  SD) values for HbA<sub>1c</sub> decreased between baseline (77±15mmol/mol [9.2±1.4%]) and the three- to five-month clinic visit (to 62±13mmol/mol [7.8±1.2%]),

and subsequently decreased between the three- to five-month and six- to 12-month clinic visits (to 59±13mmol/mol [7.5±1.2%]); (see Figure 3).

For those active users for whom it was possible to conduct statistical comparisons, the reduction in HbA<sub>1c</sub> levels from baseline was statistically significant at both the three- to five-month and the six- to 12-month clinic visits (both p<0.001). At baseline, only 13% of patients were 'at goal' (HbA<sub>1c</sub> ≤58mmol/mol [≤7.5%]). At the three- to five-month clinic visit, 45% were at goal and at the six- to 12-month visit, 61% of patients were at goal.

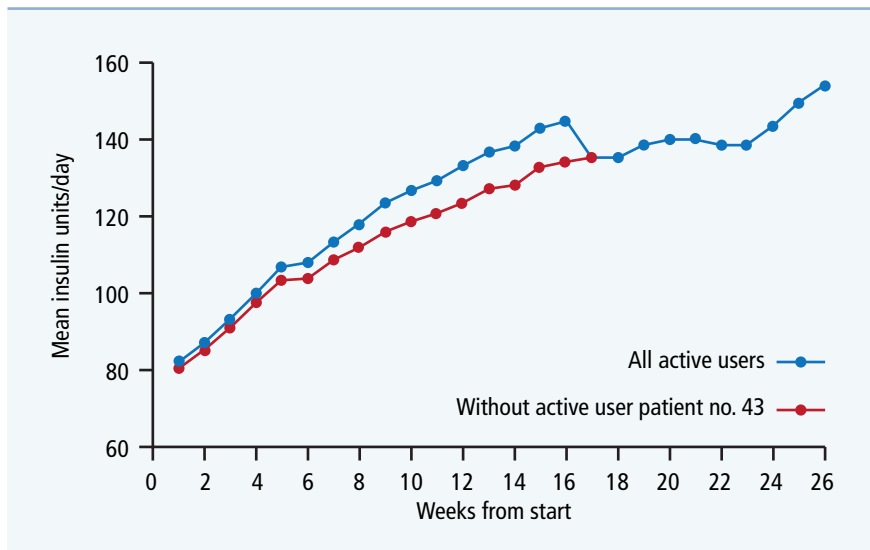
### Insulin use

During use of d-Nav, the mean daily total number of units of insulin administered per patient slowly increased to almost double the baseline value by the end of the evaluation (Figure 4). In the first week of d-Nav use, a mean of 82 units of insulin per patient were administered daily. In Week 26 of d-Nav use, a mean of 154 units of insulin per patient were administered daily. The total daily insulin dose per kg needed to achieve optimal glycaemic control was similar to that seen in previous studies of supervised insulin titration.<sup>5</sup>

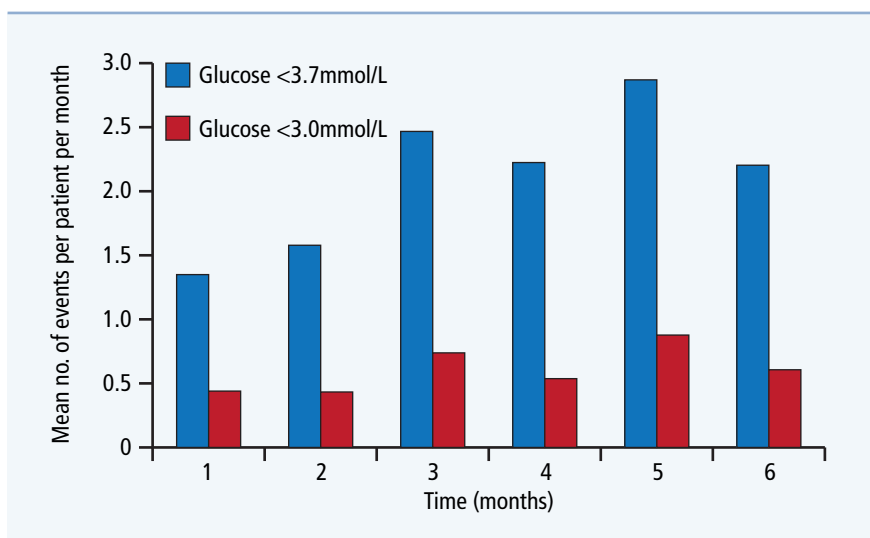
### Weight change

As might be expected with increased insulin dosage, weight gain was observed in the active-user group during the evaluation.





**Figure 4.** Mean daily insulin dose per active user by week. Daily insulin dose data were reported for each patient by d-Nav. The apparent decrease at Week 17 is attributed to one patient (no. 43) who was using significantly high doses of insulin (>500 units/day) and for whom data are not available beyond that week. Although this patient completed the evaluation, their basal insulin was changed from insulin glargine to U200 insulin degludec. Accordingly, data are shown for all active users and for all active users excluding data for active user no. 43



**Figure 5.** Frequency of hypoglycaemia in active users of d-Nav by month during the evaluation. Episodes of hypoglycaemia (blood glucose  $\leq 3.6$  mmol/L) were reported by d-Nav for each patient

The mean ( $\pm$  SD) weight at baseline was  $94.8 \pm 19.2$  kg vs  $98.3 \pm 20.9$  kg at the end of the evaluation. For those patients for whom it was possible to conduct statistical comparisons, the weight gain from baseline was statistically significant at both of the post-baseline clinic visits (both  $p < 0.001$ ).

### Frequency of hypoglycaemia

Throughout the evaluation, the frequency of documented minor hypoglycaemia (BG  $\leq 3.6$  mmol/L) events was low and well within the tolerated

range. As shown in Figure 5, there appeared to be an initial trend towards a higher frequency of hypoglycaemia from the first month to the third month, but thereafter the frequency appeared to stabilise to approximately 30 events per patient year (2.5 events per month). Furthermore, the frequency of BG measurements  $< 3.0$  mmol/L was less than 10.2 per patient-year throughout the evaluation. A comparable hypoglycaemic episode rate of 10.2 per patient-year was previously observed in patients with type 2

diabetes using insulin for more than five years.<sup>14</sup> There was one reported case of severe hypoglycaemia requiring hospital admission during the evaluation that was determined not to be d-Nav related. A 61-year-old man (BMI  $26.6 \text{ kg/m}^2$ ) with limited experience in insulin usage injected himself with biphasic insulin and then missed his planned meal, undertaking unaccustomed physical activity instead.

### Discussion

This service evaluation aimed to document changes in glycaemic control in patients with type 2 diabetes who used d-Nav as assistive technology to titrate and personalise insulin dosage. The outcomes indicate that most patients (94 out of 122) were able to use d-Nav appropriately resulting in statistically significant reductions in their HbA<sub>1c</sub> levels, while maintaining acceptable rates of hypoglycaemia.<sup>14</sup> This is the first time an insulin guidance system has been used to support insulin users. It is clear from this pilot evaluation that patients need training and ongoing support to use the device and gain benefit. The support needed was mainly reassurance that the insulin dosage adjustments recommended by d-Nav were clinically justified.

These results support those of the previously reported study of the DIGS software,<sup>11</sup> in which the software adjusted the insulin dosage on a weekly basis for patients with type 1 or type 2 diabetes, supervised by expert diabetes clinicians, based on the patients' self-reported glucose readings. Patients in this evaluation achieved statistically significant reductions in HbA<sub>1c</sub> levels accompanied by a decreased incidence of hypoglycaemic episodes compared with the study run-in phase in which they continued their pre-enrolment treatment regimens without intervention.

As previously reported, the ability to constantly match insulin dosage to BG patterns, while avoiding the dangers of hypo- and hyperglycaemia, is not sustainable for many patients. Fear of hypoglycaemia in particular is a significant barrier to patients having the confidence to self-titrate their insulin dosage.<sup>15,16</sup>

By providing dosage adjustments – reducing insulin dosage in the presence of hypoglycaemia and increasing dosage when glucose is consistently elevated – on an as-needed basis, d-Nav may, to a large extent, help allay these fears.

Optimising glycaemic control via the administration of insulin is complex, with variables such as patient behaviour and inter- and intra-patient inconsistencies in insulin pharmacokinetic profiles, necessitating individualised and flexible regimens. Frequent insulin dosage adjustments are critical for optimal glycaemic control in patients receiving insulin therapy. Inadequate control is likely to result in poor clinical outcomes, with increased incidences of retinopathy, nephropathy, neuropathy and other complications. Although frequent insulin dosage titration is known to provide optimal glycaemic control in patients with diabetes, this has typically been demonstrated in contrived clinical trial conditions involving close supervision by HCPs where participants' insulin dosage was titrated by study teams every few weeks.<sup>5–8</sup> However, weekly titration by HCPs is not feasible in clinical practice. For example, it is estimated that there are over 700 000 insulin users in the UK.<sup>17</sup> Assuming a weekly 20-minute dosage-adjustment session for each of these patients, over 12 million hours of HCP time would be required annually, i.e. over 6000 full-time professionals dedicated solely to the purpose of dosage adjustment. In contrast, there are currently approximately 1300 whole time equivalent (WTE) diabetes specialist nurses in the UK<sup>18</sup> and 739 WTE diabetes consultants.<sup>19</sup> It was estimated that in 2011 there were 2.9 million people in the UK diagnosed with diabetes; this is expected to rise to 5 million people by 2025,<sup>20</sup> with attendant increased demands on health care resources.

Obviously, improving glycaemic control with insulin intensification increases the risk of hypoglycaemia but for most patients d-Nav and the insulin guidance offered seemed to get the balance right between optimising glycaemic control while minimising hypoglycaemia. The frequency of hypoglycaemia recorded

### Key points

- d-Nav is a handheld device, registered with the Medicines and Healthcare Products Regulatory Agency, that provides physician-type dosage adjustments for insulin users
- Using DIGS software, d-Nav automates insulin dosage titration, reducing the need for clinician supervision
- Patients with type 2 diabetes who use d-Nav appropriately can achieve significant reductions in their HbA<sub>1c</sub> levels with limited clinician support over periods of up to one year
- Patients with type 2 diabetes using d-Nav maintained acceptable rates of hypoglycaemia
- d-Nav is an effective solution for optimal personalised diabetes management in type 2 diabetes insulin users

in the service evaluation was considered reasonable by the majority of patients and by HCPs, and is comparable to reported hypoglycaemia rates in studies of insulin dose optimisation.<sup>21,22</sup> With improved glycaemic control and the use of higher insulin doses, weight gain occurred as expected. The magnitude seen was similar to that demonstrated in titration studies of supervised insulin therapy.<sup>23</sup>

The single largest cause of patient withdrawal (17 of 28 withdrawals) from this service evaluation was inappropriate use of d-Nav. Some patients failed to record enough BG measurements to allow the guidance system to operate successfully and make recommendations. Some patients lacked the confidence to follow dose recommendations, perhaps as they had been used to fairly fixed insulin doses for many years and, despite sub-optimal glycaemic control, were understandably nervous to make changes. We now have a very rigorous programme of calls and visits to check that patients are using the device, using it correctly and getting benefit (as evidenced by device downloads and HbA<sub>1c</sub> checks). It is now clear that with additional patient support some withdrawals could have been avoided.

This evaluation was a pilot exploratory service evaluation in patients registered at a busy diabetes clinic and was not intended to be a clinical trial. Accordingly, it is limited in terms of the lack of a control group and modest patient numbers. However, the findings from this evaluation indicate that further investigation into the use of the d-Nav service is warranted. Further studies are planned. In addition to

evaluating patient satisfaction with the d-Nav solution, there is a need to conduct a large-scale, health-economic evaluation of the service.

In conclusion, d-Nav, accompanied by clinician support, is shown to be a highly effective solution for diabetes management for insulin users. Although it may not be suitable for all insulin users, the d-Nav service is highly scalable and could be widely used to improve patient outcomes.

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### Declaration of interests

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R Harper has acted as local investigator in a number of multi-centre studies using diabetes pharmacotherapies (Novo Nordisk A/S, Denmark; Eli Lilly and Company, USA).

S Carr has acted as research nurse and study coordinator in a number of multi-centre studies using diabetes pharmacotherapies (Novo Nordisk A/S, Denmark; Eli Lilly and Company, USA).

R Donnelly has no disclosures.

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