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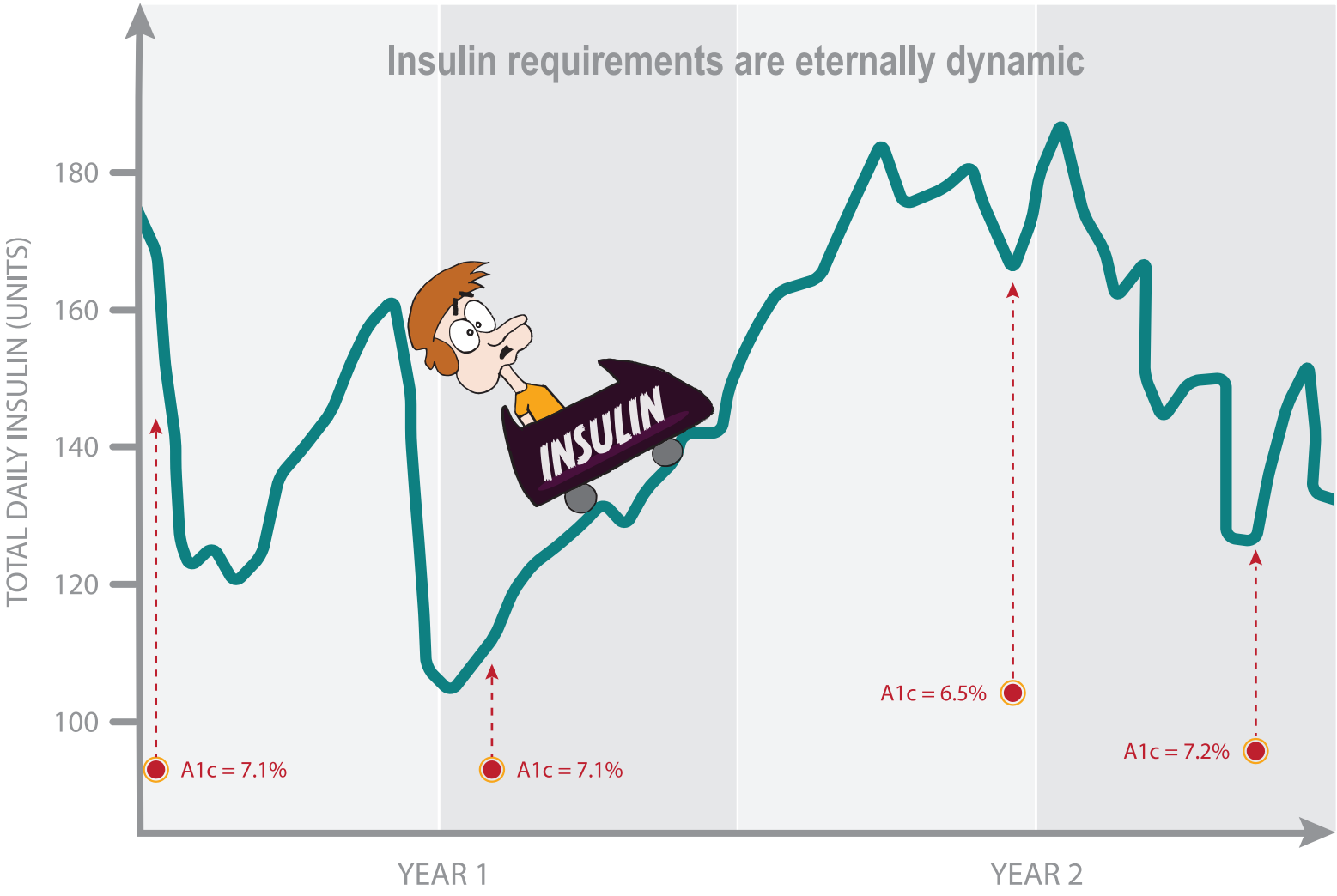

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LETTER TO THE EDITOR

WILEY

Insulin requirements are eternally dynamic

To the Editor

In the recently published paper, 'Day-to-day variability of insulin requirements in the inpatient setting: Observations during fully closed-loop insulin delivery', Boughton et al. provided data related to variability in insulin requirements in patients with type 2 diabetes admitted to hospital.[1] The group had analysed data from 67 hospitalized patients over a cumulative period of 535 days. They found considerable variability in insulin requirements in hospitalized patients that was overcome by the use of closed-loop insulin-infusion devices. The coefficient of variations of total daily insulin was found to be as high as 30%. I commend the group for providing these valuable data.

I would like to draw the attention of your audience to the fact that dynamics in insulin requirements exist at all times in day-to-day life. We have previously reported data from 246 patients with type 2 diabetes, using insulin injections in the outpatient setting over a cumulative follow-up period of 689 patient-years.[2,3] In this report, optimization and stability of glucose levels was achieved by d-Nav® (diabetes navigator) providing automatic, frequent insulin dose titrations on average 1.1 times per week. Stability in the population's HbA1c was observed after about 9 months, with HbA1c maintained at an average of about 7.2% (initial HbA1c was about 9.5%). Nearly 85% of patients achieved an HbA1c of less than 8%. The average frequency of hypoglycaemia (<54 mg/dL or <3 mmol/L) was 0.5 ± 0.6 per month. The coefficient of variations of total daily insulin was found to be as high as 75%. Major drops in insulin requirements (as defined by a total daily insulin drop of ≥25%) were found in 70.3% of patients, occurred 0.8 ± 0.5 times per year, lasted 10.0 ± 7.7 weeks, and insulin requirements declined by 39.9% ± 12.6%. These changes explained 39.9% of all hypoglycaemic events. Patients with a higher hypoglycaemic propensity tended to have more frequent occurrences of decreased insulin requirements, as previously suggested.[4] Seasons of the year, gender, age, body mass index, duration of diabetes, duration of insulin therapy, kidney function and HbA1c were not found to be predictors of reduction in insulin requirements.

The d-Nav technology has been described elsewhere.[5] Briefly, patients in their daily life (not hospitalized) use the d-Nav application, which can be housed on a cellphone or glucose meter. They use it before each insulin injection to receive a recommended insulin dose. d-Nav uses the patient glucose readings, from either a blood glucose meter or a continuous glucose monitor, to assess the patient's response to their current insulin dosage by analysing glucose patterns, and then automatically adjusts the user's next insulin dosage. Adjustments are typically made weekly. If insulin requirements drop or hypoglycaemia ensues, d-Nav makes immediate adjustments as often as needed, following the safety-first approach. d-Nav works with most insulin regimens. The number of glucose measurements needed will be equal to the number of injections required per day in each regimen (from once a day to four a day). The d-Nav care specialists follow the d-Nav data and periodically contact patients to bestow user confidence, correct usage errors, triage, and identify uncharacteristic clinical courses. Additional software tools are available to provide further insights regarding insulin dynamics. The patient's data are always available to be reviewed by the patient's physician, who continues to handle all other diabetes-related issues.

Closed-loop systems that automate the process of insulin infusion are hard to implement without significant support, which is widely available in the inpatient setting but less so in the outpatient setting. On the other hand, artificial intelligence-based frequent titration of insulin for injection regimens, such as d-Nav, has been simpler to implement, and could readily be scaled up to meet the growing needs of the large population of patients who use insulin for type 2 diabetes.[6]

Simplicity and support are the key determinants of technology scalability. For example, 40 years since its introduction, the insulin pump is used by less than 40% of patients with type 1 diabetes. Many of those with type 1 diabetes who do not use an insulin pump have tried one in the past and decided to stop. In type 1 diabetes healthcare, the ratio of the number of patients to the number of providers is comparatively low. The disease is uncommon, and physicians, nurses and diabetes educators are sufficiently available to troubleshoot sophisticated devices, such as a closed-loop system. Type 2 diabetes healthcare, however, is entirely different. The number of patients with type 2 diabetes who require insulin therapy is huge and overwhelms the limited number of providers available. The average patient who uses insulin therapy for type 2 diabetes is aged 60 years, and many are not capable or motivated to use sophisticated technology such as closed-loop systems. The simplicity of the user interface, and the fact that marginal support from physicians, nurses and diabetes educators is needed, are the fundamentals of the d-Nav technology, and therefore the key to its scalability.

Insulin requirements change over time and do not achieve a steady state, either in day-to-day life or during hospital admissions. Insulin replacement therapy is the most dynamic treatment in modern medicine. This phenomenon, which is now coming to light, needs vast implementation of frequent insulin titration.

CONFLICT OF INTEREST

Israel Hodish is a co-founder of Hygieia Inc.

PEER REVIEW

The peer review history for this article is available at https://publons.com/publon/10.1111/dom.14460.

DATA AVAILABILITY STATEMENT

Non-applicable.

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