Digital Health and Informatics Innovations for Sustainable Health Care Systems
J. Mantas et al. (Eds.)

doi:10.3233/SHTI240349

Detailed Insights into Basal Insulin Adherence in People with Type 2 Diabetes Using a Data-Driven Assessment Method

Jannie NØRLEV[a,b,1], Thomas KRONBORG[a, b], Ole HEJLESEN[a], Morten HASSELSTRØM[a,c], Peter VESTERGAARD[b,d,e] and Stine HANGAARD[a,b]
[a] *Department of Health Science and Technology, Aalborg University, Gistrup, Denmark*
[b] *Steno Diabetes Center North Denmark, Aalborg, Denmark*
[c] *Data Science, Novo Nordisk A/S, Søborg, Denmark*
[d] *Department of Clinical Medicine, Aalborg Univerisity, Gistrup, Denmark*
[e] *Department of Endocrinology. Aalborg University Hospital, Aalborg, Denmark*
ORCiD ID: Jannie Nørlev https://orcid.org/0000-0002-0951-6949, Thomas Kronborg https://orcid.org/0000-0002-2693-0527, Ole Hejlesen https://orcid.org/0000-0003-3578-8750, Morten Hasselstrøm https://orcid.org/0000-0002-6649-8644, Peter Vestergaard https://orcid.org/0000-0002-9046-2967, Stine Hangaard https://orcid.org/0000-0003-0395-3563

Abstract. Introduction: Basal insulin non-adherence is a challenge in people with type 2 diabetes (T2D). Methods: Using injection data recorded by a connected insulin pen, we employed a novel three-step methodology to assess three aspects of adherence (overall adherence, adherence distribution, and dose deviation) in individuals with insulin-treated T2D undergoing telemonitoring. Results: Among participants, 52% were considered overall adherent. However, deviations from the recommended dose were observed in all participants, with increased and reduced doses being the predominant forms of non-adherence. Conclusions: Our study underscores the prevalence of basal insulin dosing irregularities in individuals with insulin-treated T2D undergoing telemonitoring.

Keywords. Adherence assessment, basal insulin, injection data, type 2 diabetes

1. Introduction

Achieving optimal glycemic control is vital in managing type 2 diabetes (T2D) to reduce associated morbidity and mortality [1]. Despite advancements in pharmacotherapy, insulin remains a cornerstone in the treatment regimen for many adults with T2D [2]. Nevertheless, more than 60% of people with T2D fail to attain glycemic targets, often due to non-adherence to insulin therapy [1].

Identification and a comprehensive understanding of non-adherence are crucial, as unrecognized non-adherence often leads to suboptimal treatment outcomes and increased risk of complications [3]. Nonetheless, limited data exist on the nuanced types of adherences, hindering tailored interventions, as distinct dosing irregularities signify

[1] Corresponding Author: Jannie Nørlev; E-mail: jadano@hst.aau.com.

unique behavioral entities [4]. Building upon previous research [5], this study aims to assess the adherence level among telemonitored people with insulin-treated T2D using a new comprehensive three-step methodology based on insulin injection data recorded by connected insulin pens.

2. Methods

2.1. Data Collection

Basal insulin injection data over 12 weeks were collected from 106 participants randomized to the telemonitoring intervention group in the DiaMonT trial (NCT04981808) [6]. Participants were ≥18 years of age, had a confirmed diagnosis of T2D for a minimum duration of one year, and were treated with basal insulin only or in combination with bolus insulin. The administered basal insulin injection data (dose and time) were recorded using a connected insulin pen (NovoPen6, Novo Nordisk A/S), while the recommended basal insulin injection data, including dose at baseline and continuous adjustments made during the trial, were registered by trial personnel.

Data were structured into 24-hour periods from 03:00 to 03:00 the next day. Doses less than or equal to two units were excluded because participants were instructed to test the insulin flow with a two-unit air shot after replacing the insulin cartridge [7]. The administered basal insulin doses were summed for each day and compared to the recommended dose. If no insulin injection was recorded by the connected insulin pen on a given day, 0 units were imputed.

2.2. Outcomes and Statistical Analysis

We employed the three-step methodology outlined by Nørlev et al. [5] to evaluate overall adherence (% of days with a correctly administered dose), adherence distribution (of correct, increased, reduced, and missed doses), and dose deviation (as % from recommended dose). All data analyses were performed using Python 3.8 and relevant packages (Pandas version 1.4.2, NumPy version 1.21.5, and Matplotlib version 3.5.2).

3. Results

Of the 106 participants, 55 (52.0%) were considered adherent during the 12-week trial period. See Table 1 for the baseline characteristics of the participants.

Table 1. Participant characteristics at baseline

Characteristic	N = 106
Age (years) mean ± SD	61.9 ± 10.2
Female, n (%)	44 (41.5)
Body mass index (kg/m^2), mean ± SD	33.7 ± 6.2
HbA1c (mmol/mol), mean ± SD	64.2 ± 14.5
Diabetes duration (years), mean ± SD	19.7 ± 13.9
Bolus insulin use, n (%)	49 (46.2)
Daily insulin use (IU)*, mean ± SD	69.8 ± 54.1

*Total daily insulin use including both basal insulin and contingent bolus insulin use

3.1. Step 1 – Weekly Overall Adherence Level

The weekly averaged overall adherence level ranged between 68.1% and 78.2% during the 12-week period, see Figure 1.

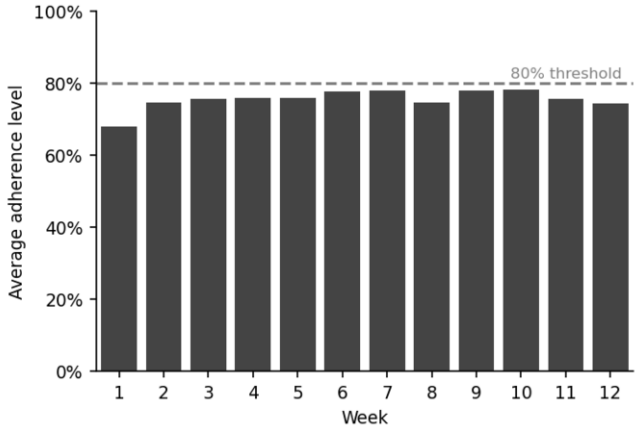

Figure 1. Overall adherence level for each trial week

3.2. Step 2 - Adherence Distribution

During the 12-week trial period, deviation from the recommended insulin dose was identified at least once in all participants. Overall, 75.6% [74.7; 76.5]$_{95\%\ CI}$ of the doses were administered correctly, while 12.4% [11.7; 13.1]$_{95\%\ CI}$ were increased doses, 8.9% [8.3; 9.4]$_{95\%\ CI}$ were reduced doses, and 3.1% [2.8; 3.5]$_{95\%\ CI}$ were missed doses, see Figure 2.

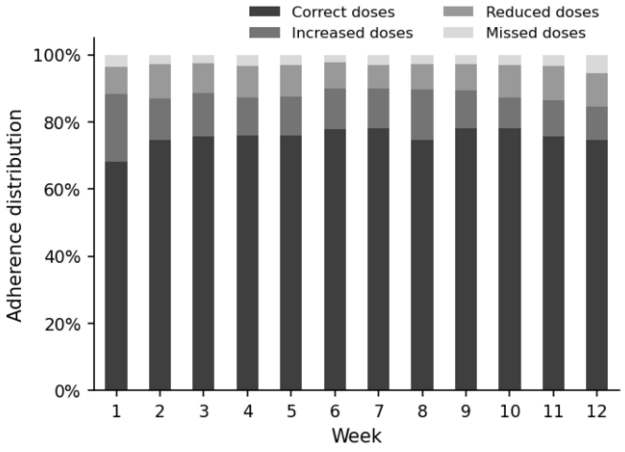

Figure 2. Adherence distribution for each trial week

Most participants administered both increased doses (92.5%), reduced doses (83.0%), and missed doses (66.0%). See Table 2 for a detailed overview. Furthermore, the analysis showed that 12.3% (n = 13) of the participants adjusted their basal insulin dose daily without instructions from the HCPs.

Table 2. Percentage [95% confidence intervals] (number) of participants with a type of non-adherence

Type of (non-)adherence	No. of participants, N = 106
Missed doses	66.0% [57.0; 75.1] (70)
Missed >5% of total doses	19.8% [12.2; 27.4] (21)
Missed >10% of total doses	6.6% [1.9; 11.3] (7)
Increased doses	92.5% [87.4; 97.5] (98)
Increased >5 % of total doses	58.5% [49.1; 67.9] (62)
Increased >10% total doses	39.6% [0.30.3; 48.9] (42)
Reduced doses	83.0% [75.9; 90.2] (88)
Reduced >5% of total doses	44.3% [34.9; 53.8] (47)
Reduced >10% of total doses	33.0% [24.1; 42.0] (35)

3.3. Step 3 – Dose Deviation

The average absolute dose deviation was 6.1 ± 10.4 units. It is worth noticing that the majority of deviations fell within ± 25% of the recommended dose, see Figure 3, and the 5% percentile was -27.6%, the 25% percentile was -5.6%, the 75% percentile was 6.4%, and the 95% percentile was 22.2%.

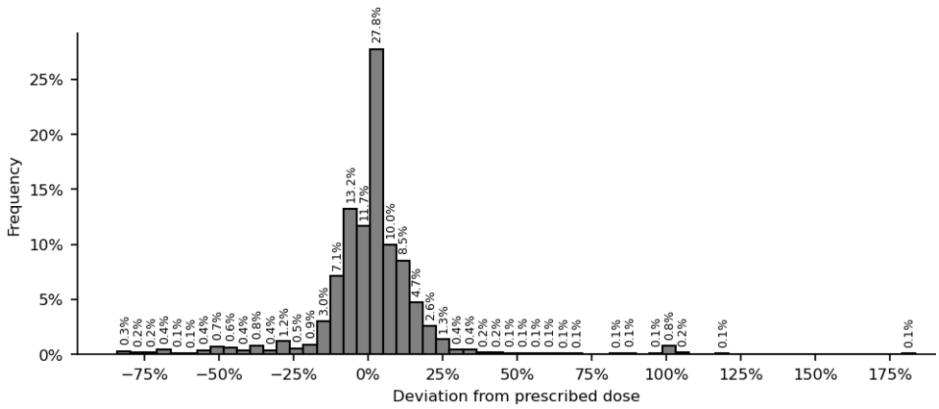

Figure 3. The distribution of percentage deviations from the recommended dose

4. Discussion

This study assessed the adherence level among people with insulin-treated T2D using a new comprehensive three-step methodology. Our results corroborate findings from previous studies [8], highlighting a high prevalence of dosing irregularities among people with insulin-treated T2D [4]. Markedly, 66% of the participants had missed at least one dose; however, only 3% of the total doses were missed, with increased and reduced doses

posing greater challenges. Yet, it must be noted that a small deviation would yield a lesser impact on glycemic control than a greater deviation [11].

Unexpectedly, a subset of participants (>10%) made daily basal insulin dose adjustments. Due to the pharmacokinetics of basal insulin, dose adjustments should only be made after several successive days with high or low blood glucose levels [12]. The daily adjustments may be explained by the potential influence of continuous glucose monitoring (CGM) and telemonitoring on participants' insulin-dosing decisions, as participants wore a CGM and were closely telemonitored during the trial [6].

Our results also demonstrate the feasibility of our three-step methodology applied to a cohort. Especially, with the methodology the size of the deviation (increased or reduced) can be considered, offering a more nuanced understanding of adherence behavior than previously.

A limitation must be noted. This study lacked data on reasons for non-adherence, warranting considerations in future research as this limitation introduces a risk of doses being erroneously counted as missed or incorrect.

5. Conclusions

Using a new methodology, we demonstrated that basal insulin dosing irregularities including missed, increased, and reduced doses are common in people with insulin-treated T2D, with increased and reduced doses being the predominant type of non-adherence. Future research should investigate reasons for non-adherence.

References

[1] Edelman SV, Polonsky WH. Type 2 diabetes in the real world: The elusive nature of glycemic control. Diabetes Care 2017;40:1425–32, doi: 10.2337/dc16-1974.

[2] ElSayed NA, Aleppo G, Aroda VR, Bannuru RR, Brown FM, Bruemmer D, et al. Standards of Care in Diabetes 2023. Diabetes Care 2022;46, doi: 10.2337/dc23-S015.

[3] Polonsky WH, Henry RR. Poor medication adherence in type 2 diabetes: Recognizing the scope of the problem and its key contributors. Patient Prefer Adherence 2016;10:1299–306, doi: 10.2147/PPA.S106821.

[4] Brod M, Rana A, Barnett AH. Adherence patterns in patients with type 2 diabetes on basal insulin analogues: Missed, mistimed and reduced doses. Curr Med Res Opin 2012;28:1933–46, doi:10.1185/03007995.2012.743458.

[5] Nørlev JTD, Kronborg T, Jensen MH, Vestergaard P, Hejlesen O, Hangaard S. A Three-Step Data-Driven Methodology to Assess Adherence to Basal Insulin Therapy in Patients With Insulin-Treated Type 2 Diabetes. J Diabetes Sci Technol 2023 Dec, doi: 10.1177/19322968231222007.

[6] Hangaard S, Kronborg T, Hejlesen O, Aradóttir TB, Kaas A, Bengtsson H, et al. The Diabetes teleMonitoring of patients in insulin Therapy (DiaMonT) trial: study protocol for a randomized controlled trial. Trials 2022;23, doi: 10.1186/s13063-022-06921-6.

[7] Novo Nordisk A/S. NovoPen 6 - User guide 2021.

[8] Cramer JA. A Systematic Review of Adherence With Medications for Diabetes. Diabetes Care 2004;27:1218–24, doi: 10.2337/diacare.27.5.1218.

[9] Sokol MC, Mcguigan KA, Verbrugge RR, Epstein RS. Impact of Medication Adherence on Hospitalization Risk and Healthcare Cost. Med Care 2005;43:521–30, doi: 10.1097/01.mlr.0000163641.86870.af.

[10] Vargas-Uricoechea H. Current State and Principles of Basal Insulin Therapy in Type 2 Diabetes. J Clin Med Res 2022;14:8–21, doi: 10.14740/jocmr4660.