

Journal club: The challenge of multiple daily insulin injections

Some improvements in diabetes care happen slowly, whereas others seem to happen very fast. For a number of reasons, in the last two years we have suddenly seen a dramatic change in our approach to insulin therapy. This has partly been due to the roll-out of continuous and flash glucose monitoring. This, combined with the enforced inability to see people face to face, meant we had to develop tools for remote monitoring and has resulted in a dramatic increase in data sharing between people with diabetes and clinicians, particularly with regard to glucose levels throughout the day. Instead of a meeting where a paper glucose diary with perhaps two to four readings per day is reviewed, we now have a wealth of detail about day-to-day glucose variation.

This change has shifted the conversation in clinic and, as we know, resulted in measurable improvements for the individual with diabetes. It does, however, highlight a gaping hole in the information that we need in order to give accurate advice: we know very little about the appropriateness and timing of insulin doses. At the moment, the information we have for an individual using insulin pump therapy will be very different to that available for a person using multiple daily injections of insulin. Often we can only assume that insulin has, firstly, been taken and, secondly, been taken at an appropriate time and dose for that meal. Evidence would suggest that this assumption will be incorrect for a relatively high proportion of the time.

This paper by Susan Robinson and colleagues,

reviewed below, summarises our current knowledge about the timing of insulin injections for people with both type 1 and type 2 diabetes. The results are sobering but perhaps not surprising, with one or two doses of insulin being missed per person per week. The timing of bolus insulin in relation to meals is also important and, while we often assume in the clinic that the dose is being taken at the right point, the data would suggest this is probably not the case around 50% of the time.

These are the basics of insulin self-administration that we mostly assume are understood and practised correctly before considering factors such as matching the insulin dose to the carbohydrate content of the meal, the proportion of the previous insulin injection still active, correction doses to manage the current glucose level and the effects of previous or planned physical activity. When there is a problem with glucose control, we often assume it is these complexities that need addressing, without considering that just remembering to take the insulin correctly may be a challenge.

Technology is already helping, with automated systems to help calculate insulin doses and smart pens to remind about insulin injections, but in addition the consultation needs to evolve to deal with this new conversation. To best help the person with diabetes, we need to match the wealth of glucose data with equally accurate measures of insulin dose and timing. Hopefully this will come in the near future. ■



Daniel Flanagan
Consultant Physician,
Derriford Hospital, Plymouth

Citation: Flanagan D (2021)
Journal club: The challenge of
multiple daily insulin injections.
Journal of Diabetes Nursing
25: [early view publication]

Prevalence and effects of missed and mistimed insulin doses

This systematic review was conducted to assess the extent and consequences of missed and mistimed insulin doses in people with diabetes. A total of 30 studies involving 58 617 people with diabetes were included.

Between 12% and 56% of participants with type 1 diabetes had missed one or more insulin

dose in the previous month, while 16–23% of people with type 2 diabetes had. Among the latter group, those who were on a basal–bolus regimen were more likely to miss insulin doses compared with those on premixed or basal insulin regimens.

Missed insulin doses were consistently

“When there is a problem with glucose control, we often assume it is the complexities that need addressing, without considering that just remembering to take the insulin correctly may be a challenge.”

reported to be associated with higher HbA_{1c}, whilst in one study of people with type 2 diabetes, missing around 3–4 basal insulin doses per month resulted in significantly worse glycaemic control. Missed insulin doses were associated with lower health-related quality of life in adolescents with type 1 diabetes and in adults with type 2 diabetes.

Regarding mistimed insulin doses, around 25–30% of people with diabetes (type 1 or type 2) administered their bolus insulin during or after meals, contrary to guidelines, while around 20–26% had mistimed their basal doses in the previous 30 days. Hypoglycaemia was more common in people who took their bolus insulin after meals compared with before or during, and glycaemic control was better in those who took their bolus doses regularly and before meals.

Reasons for missing or mistiming insulin included forgetfulness, disruption to routines (including travelling), obstruction of usual daily activities, fear of hypoglycaemia, stress (including diabetes distress and burnout), injection pain, and embarrassment in public or social situations. Regimen complexity and the challenges of taking insulin at the same time each day were also cited as reasons.

The authors conclude that some individuals continue to struggle with the complexities of diabetes management and the specific challenges of insulin therapy. Approaches that facilitate better diabetes management are needed.

DIABETES TECHNOLOGY & THERAPEUTICS
Volume 25, Number 12, 2021
Mary Ann Liebert, Inc.
DOI: 10.1089/dt.2021.0164



REVIEW ARTICLE

**Missed and Mistimed Insulin Doses
in People with Diabetes:
A Systematic Literature Review**

Susan Robinson, PhD,¹ Rachel S. Newson, PhD,^{2,3} Birong Liao, PhD,⁴
Tessa Kennedy-Martin, MSc,¹ and Tadej Battelino, MD, PhD⁵

Abstract
Background: Development of coordinated management approaches is important to facilitate self-care in people with diabetes (PwD). Gaining a better understanding of suboptimal insulin use is key in this endeavor. This review aimed, for the first time, to systematically identify and narratively summarize real-world evidence on the extent of suboptimal insulin use (missed and mistimed insulin) in PwD.
Methods: A systematic literature search of MEDLINE, EMBASE, and the Cochrane Database of Systematic Reviews identified studies reporting on missed and mistimed insulin dosing.
Results: From 330 studies, 37 publications reporting on 30 unique studies that involved 58,617 PwD were included. Studies were conducted across 12 different countries and most employed cross-sectional surveys. Observations regarding missed and mistimed insulin doses were reported in 25 and 10 studies, respectively. PwD reported missing insulin doses, but rates varied due to differences in reporting methods, participant populations, and insulin regimens. The association between missed dosing and glycemic control was evaluated in ten studies in which the authors reported lower glycated hemoglobin (HbA_{1c}) levels in PwD who did not omit insulin. The proportion of PwD reporting mistiming of insulin was in the range of 20–45%, depending on the study; this was associated with higher rates of hypoglycemia and higher HbA_{1c} as reported by study authors. Reasons for suboptimal insulin use were multifactorial, occurring due to disrupted daily routines, social situations, and hypoglycemia avoidance.
Conclusion: This review suggests that suboptimal insulin use is widespread and that PwD using insulin may still be struggling with disease management. There is an unmet need for better integrated support in managing the complexities of insulin therapy and for the development of systems (e.g. digital solutions) that empower people to take control of insulin-treated diabetes.

Keywords: Insulin, Diabetes, Suboptimal dosing, Missed doses, Mistimed doses, Real-world evidence.

Introduction
OVER THE PAST several decades, the management of diabetes has seen significant improvements through advances in drug development and device technology. Yet despite all the innovations, diabetes remains a significant human and economic burden.¹ In general, levels of glycemic control do not appear to have improved in recent years or have even deteriorated.^{2–4} Furthermore, evidence suggests that many insulin-treated people with diabetes (PwD) are still

¹Research, Martin Health Outcomes Limited, Brighton, United Kingdom.
²Global Patient Outcomes and Real-World Evidence, Eli Lilly, Sydney, Australia.
³Medical Affairs, Eli Lilly, Indianapolis, IN, USA.
⁴University Medical Center Ljubljana, and Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia.
⁵Presented as an oral communication at the 14th International Conference on Advanced Technology & Treatment for Diabetes (ATTD 2021) on June 2–5, 2021 (virtual conference).
NCT01311424 (https://clinicaltrials.gov/ct2/show/study/NCT01311424)

© Susan Robinson, et al., 2021. Published by Mary Ann Liebert, Inc. This Open Access article is distributed under the terms of the Creative Commons License (http://creativecommons.org/licenses/by/4.0/), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

1

[Click here to read the study in full.](#)