# SUPPLEMENTARY MATERIAL

Exploring the burden of mealtime insulin dosing in adults and children with type 1 diabetes

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# Supplementary methods

Incentives were offered in the form of reward points for participants (incentive for original survey: 20 USD/15 GBP/17 EUR/25 CAD), or bank transfer/Amazon vouchers to healthcare professionals (range value: 9–53 USD, based on local requirements and type of physician), with at least 10% of the agreed honorarium being donated to the participants’ choice of registered charities.

**Supplementary Table S1. Optimal prandial bolus timing in clinical studies**

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| --- | --- | --- | --- | --- | --- |
| **Study Reference** | **Rapid-acting insulin analogue** | **CSII or MDI** | **Time of insulin administration in relation to mealtime(min)** | **Most effective time at lowering postprandial hyperglycemia(min)** | **Postprandial glucose levels** **(mmol/L)** |
| Cobry et al. 2010 (1) | Insulin glulisine | CSII  | –20, 0, +20\*  | –20 | 11.0 ± 3.8 vs 13.7 ± 3.0 vs 13.8 ± 2.3 (max) |
| Luijf et al. 2010 (2) | Insulin aspart | CSII  | –30, –15, 0 | –15 | 11.74 ± 0.8 vs 9.26 ± 0.72 vs 12.29 ± 0.93 (max) |
| Brunner et al. 2000 (3) | Insulin aspart | MDI | 0, +15 | 0 | 11.2 (10.4–12.0) vs 13.2 (12.3–14.2) (max) |
| Jovanovic et al. 2004 (4)  | Insulin aspart | MDI | –5 to 0, +30\* | – 5 to 0 | 5.7 ± 0.5 vs 8.3 ± 0.55 (max) |
| Schernthaner et al. 1998 (5)  | Insulin lispro | MDI | –20, 0, +15\* | –20 | n/a |
| Schernthaner et al. 2004 (6) | Insulin lispro | MDI | 0, +30 | 0 | 7.71 ± 1.83 vs 8.66 ± 2.13 (mean) |

\*Up to 15, 20, and 30 min after starting to eat.

CSII, continuous subcutaneous insulin infusion; max, maximum postprandial glucose level; mean, mean postprandial glucose level; MDI, multiple daily injections; min, minutes; n/a, not available.

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**Supplementary Figure S1.** Participant flow diagram



**Supplementary Figure S2.** Main challenges associated with mealtime insulin administration according to adults with type 1 diabetes (T1D)

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Please refer to the corresponding question in Supplementary material ‘Survey Questions’ 1. (Patient/Parent Questionnaire): A3.

**Supplementary Figure S3.** The extent of impact on people with type 1 diabetes regarding challenges associated with mealtime insulin administration according to healthcare professionals

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Please refer to the corresponding questions in Supplementary material ‘Survey Questions’ 2. (HCP Questionnaire): A4.

**Survey questions**

1. Patient/parent main questionnaire (excluding screener)
* A1. Thinking about the management of your/ your child’s diabetes, **how important**, if at all, do you believe it is to take your/ their bolus insulin (mealtime insulin) accurately? *(****Answers:*** *very important, fairly important, not very important, not at all important, don’t know)*
* A2. When pre-bolusing, **how confident** do you feel in accurately estimating the amount of insulin that you need to match your/ your child’s food intake, as indicated by your healthcare professional? *(****Answers:*** *very confident, fairly confident, not very confident, not at all confident, don’t know)*
* A3. Which of the following, if any, are the **main challenges** you/ your child experience with bolus insulin (mealtime insulin)? *(****Answers:*** *Not sure what I/they will be eating (either type of meal or amount of carbohydrate) to dose accurately; Not sure when I/they will be eating to dose at the right time; Interruptions after dosing causing delays to eating (e.g. unexpected phone call, an unexpected meeting or visitor, an engagement runs longer than expected etc.); Forgetting to pre-bolus in time frame needed (and having to delay eating); Missing social events due to concerns around dosing and food intake; Dosing post meal (after start of the meal) to be more certain of when and what I/ they are eating; Having to inject more insulin after eating, due to eating more/different food than expected; Having to eat extra food after end of the meal, due to eating less/different food than expected; Completely forgetting to take the pre-bolus insulin (mealtime insulin); Not sure how much I/ they will be eating to dose accurately; Other challenge; No challenges; Don’t know)*
* A4. Do you/your child tend to dose **a fixed amount** of bolus insulin (mealtime insulin) and then adjust your meal size to match this? (***Answers:*** *Always, occasionally, rarely, never, don’t know)*
* A5. How often, if at all, do you/ your child pre-bolus according to your Healthcare Professional’s (HCP’s) guidance/instructions and **then eat less than anticipated**? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A6. How often, if at all, do you/ your child **need to consume extra food** (e.g. carbohydrates) to prevent a hypo (low blood sugar), as a result of eating a meal that had less carbohydrates than anticipated, when you pre-bolused? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A7. How often, if at all, do you/ your child pre-bolus according to your Healthcare professional’s (HCP’s) guidance/instructions and **then eat more than you anticipated**? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A8. As a result of eating more food than you/ your child anticipated you would when you were pre-bolusing, how often, if at all, do you/they **need to take extra insulin** to correct the extra food eaten? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A9. How often, if at all, do you/your child take bolus insulin (mealtime insulin) **after** the start of the meal when you know exactly what and when you/they are eating? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A10. How often, if at all, do you/ your child **forget to take** your bolus insulin (mealtime insulin) completely before a meal? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A11. How often, if at all, do you/ your child **forget to pre-bolus (within the needed timeframe)** before a meal) and have to delay eating? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A12. How often, if at all, would you say you pre-bolus and **then the situation changes** (e.g. you are unsure when, what, how much you/ they will eat, there are interruptions that prevent you/them from eating) meaning you/they end up not taking the right amount of insulin (the first time)? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A14. Thinking about the need to pre-bolus before eating, in general, to what extent if at all, does managing this **negatively impact** you/ your child in your day to day life (social life, mood, independence, life in general, relationship with others)? *(****Answers:*** *to a great extent, to some extent, hardly, not at all, don’t know, not applicable)*
* A15. How often, if at all, do you/ your child **decide not to eat out** (e.g. in restaurants, at a friend’s house, social events, at the work canteen) due to being unsure of how much bolus insulin (mealtime insulin) you need to take? *(****Answers:*** *daily, several times a week, about once a week, about once or twice a month, about once every 3 months, about once every 6 months, about once a year, less often than once a year, never, don’t know)*
* A16. Here is a list of things, both positive and negative, that some people may feel about having to take bolus insulin (mealtime insulin) at a set time before every meal. Which, if any, of the following **do you feel about you/ your child having to take bolus insulin** (mealtime insulin) at a set time before every meal? *(****List:*** *refer to Suppl. Fig 3)*
* A17. In general, how do you/ your child feel after a meal when **thinking about your post meal blood glucose levels**? *(****Answers****: I never worry about it, I occasionally worry about it, I often worry about it, I always worry about it, don’t know, none of the above)*
* A18. Given the choice, when **would you/ your child prefer** to take your bolus insulin (mealtime insulin)? *(****Answers:*** *15-20 minutes before you/they eat, immediately before you/they eat, immediately after you/they eat, no preference, don’t know, none of the above)*
* A19. If you/ your child were able to **avoid pre-bolusing** (by taking bolus insulin either immediately before your meal or after the start of your meal), what, if any, impact would this have on your/ their overall quality of life? *(****Answers:*** *a very positive impact, a fairly positive impact, no impact on my/their quality of life, a fairly negative impact, a very negative impact, don’t know)*
1. HCP main questionnaire (excluding screener)
* A1. To the best of your knowledge, how confident do you think your patients with type 1 diabetes feel in accurately estimating the amount of bolus insulin needed to match their food intake? *(****Answers:*** *very confident, fairly confident, not very confident, not at all confident, don’t know)*
* A2. Thinking about your patients with type 1 diabetes and their need to pre-bolus, to what extent, if at all, do you believe this **creates extra burden in their day to day life** with diabetes? *(****Answers:*** *to a great extent, to some extent, hardly, not at all, don’t know)*
* A3. Thinking about your patients with type 1 diabetes and their need to pre-bolus, to what extent, if at all, do you believe this **negatively impacts their emotional wellbeing**? (***Answers:*** *to a great extent, to some extent, hardly, not at all, don’t know)*
* A4. To what extent, if at all, do you believe each of the following represents a challenge faced by your patients with type 1 diabetes in relation to pre-bolusing? (***Answers:*** *Not sure what they will be eating to dose accurately (either type of meal or amount of carbohydrate; Not sure when they will be eating to dose at the right time; Interruptions after dosing causing delays to eating; Forgetting to pre-bolus in time frame needed (and having to delay eating; Missing social events due to concerns around dosing and food intake; Dosing post meal to be more certain of when and what they will be eating; Having to inject more insulin after eating, i.e. taking more insulin due to eating more/different food than expected; Having to eat extra food after end of the meal, due to eating less/different food than expected; Completely forgetting to take the mealtime insulin;* *Not sure how much they will be eating to dose accurately; The need to always dose a set amount of insulin and adjust food intake to match*)
* A5. How often, if at all, do your patients with type 1 diabetes discuss with you any challenges around mealtimes that they are facing with taking bolus insulin (e.g. timing the dose, estimating the right amount etc.)? *(****Answers:*** *always, sometimes, hardly ever, never, don’t know)*
* A6. To what extent, if at all, do you believe your patients with type 1 diabetes’ quality of life would improve if they could have a bolus insulin which they could take **immediately before their meal**? *(****Answers:*** *to a great extent, to some extent, hardly, not at all, don’t know)*
* A7. To what extent, if at all, do you believe your patients with type 1 diabetes’ quality of life would improve if they could have a bolus insulin which they could take **after the start of** their meal? *(****Answers:*** *to a great extent, to some extent, hardly, not at all, don’t know)*.

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