Can laboratory based research regarding type 1 diabetes and exercise be applied into the real-life environment?

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Abstract  
The aim of this study was to determine whether results from laboratory based research examining glycaemic control during and after exercise can be applied to a real-life (non-laboratory) environment.

A comparative study of individuals with type 1 diabetes (n=9) using basal bolus analogue insulin regimens was undertaken. Glycaemic control before and after two 40-minute runs at 70% VO2 max, in both laboratory and real-life environments, was measured across 10 time-points during and up to 12 hours after exercise. Insulin was adjusted in all participants following a self-management algorithm.

Pooled mean glucose concentrations at each time-point were compared. There was no statistically significant difference (F[1, 8] = 1.489, p=0.257) in overall mean glucose concentrations between environments. Similarly, the exercise environment or time-point of measurement had no statistically significant effect on mean glucose concentration (F[9, 72] = 0.499, p=0.871). However, during exercise, episodes of both hypoglycaemia (<4.0mmol/L) and hyperglycaemia (>9.0mmol/L) were more frequent in the laboratory environment than in the real-life environment: 5 vs 1 and 25 vs 19 episodes, respectively; the frequency of acceptable concentrations (4.0–9.0mmol/L) was greater in the real-life environment (24 vs 34). In the 8–12 hours after exercise, hypoglycaemia occurred more frequently in the real-life environment (3 vs 8) with hyperglycaemia occurring more frequently in the laboratory environment (22 vs 14); again, there were slightly increased acceptable concentrations in the real-life environment (29 vs 33).

The exercise environment does not appear to affect overall mean blood glucose concentrations. However, it may affect the timing and frequency of hypoglycaemia and hyperglycaemia. Copyright © 2015 John Wiley & Sons.

Key words  
type 1 diabetes; moderate intensity exercise; laboratory and real-life environments; glycaemic control

Introduction  
Research relating to the effects of exercise on glycaemic control in people with type 1 diabetes has usually been performed in laboratory environments.1–5 A recent literature review was performed to identify any related research where the replication of laboratory based self-management research findings were applied into the real-life environment, and also to demonstrate any differences regarding the impact on glycaemic control between environments. It became evident that all research identified regarding self-management was based in a laboratory environment using either a treadmill or bicycle for exercise, and not applied into real-life situations.2–5 However, the knowledge generated from these laboratory based experiments underpins current self-management recommendations.2–4,6–11 From these original studies and literature review publications, a self-management algorithm for use when performing moderate intensity exercise before the evening meal was devised (see Table 1).

The aim of this current study was to compare the glucose response in participants with type 1 diabetes, during and after a 40-minute exercise session at 70% VO2 max (moderate intensity exercise) while following the self-management algorithm, in the laboratory environment using a treadmill, and while running in participants’ real-life environment. This was to evaluate the efficacy of using laboratory findings, under controlled conditions, in patient education for use in their everyday life. The significance and value of real-world data are becoming an increasingly valuable source of evidence for clinical practice.12
This supports the question of whether data collected in a controlled and possibly unrealistic laboratory environment would be replicated when performed in a real-life environment.

**Method**

The inclusion criteria for participants were: people with type 1 diabetes of over two years’ duration; aged 18–60 years old; HbA1c under 86mmol/mol (10.0%); using a basal bolus insulin regimen; hypoglycaemia awareness; and exercise twice a week or more.

The exclusion criteria were: pre-proliferative/proliferative retinopathy; neuropathy/foot ulceration; blood pressure >150/90; cardiovascular disease/history of angina; orthopaedic problems.

**Study design**

The study ran over a two-week period. On days 1 and 3 of each week, participants undertook 40 minutes of moderate intensity exercise (days 1 and 8 in the laboratory, and days 3 and 10 in real-life environments). Days 2 and 9 were rest days and participants were instructed not to perform exercise. All were instructed to follow the self-management algorithm for insulin and carbohydrate adjustment (Table 1).

**Data collection**

The data collection methods for glucose levels were:

- **Before exercise** until before evening meal: participants performed self-monitoring of blood glucose (SMBG) using a TrueResult meter (Nipro Diagnostics UK). This meter was chosen due to ease of use and small size for carrying in the exercise sessions. SMBG was chosen for this time-period as it was important to establish any immediate changes in blood glucose that may require cessation of exercise.

- **After the evening meal** until 12 hours after: interstitial glucose levels using the Minimed iPro (Medtronic) continuous glucose meter were used. This method was used as this time-period was during the night and performing SMBG would disturb participants’ sleep. The continuous glucose monitoring

<table>
<thead>
<tr>
<th>Blood glucose prior to exercise (mmol/L)</th>
<th>Amount of CHO (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Under 4</td>
<td>30</td>
</tr>
<tr>
<td>4–6</td>
<td>20</td>
</tr>
<tr>
<td>6–8</td>
<td>10</td>
</tr>
<tr>
<td>8 or over</td>
<td>0</td>
</tr>
</tbody>
</table>

**After exercise**

- **Bolus/meal insulin**
  - Eat within 2 hours of exercise and reduce the bolus/meal dose by 30%³,⁹⁻¹¹
  - After 2 hours return to usual dose

- **Long-acting insulin**
  - Take usual Lantus or Levemir dose²

- **Blood glucose**
  - If blood glucose at 8mmol/L or under before bedtime have 10–20g of CHO

**Figure 1.** A comparison of mean blood glucose concentrations in laboratory and real-life sessions. The error bars represent standard deviations.
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Data were only available by download after the study period.

In order to ensure reliability of the comparison of environments, it was important that the exercise sessions were consistent, i.e. performed at the same time of day, following the same self-management algorithm, and exercising at the same intensity. In the laboratory sessions, the treadmill was used which was considered best to replicate running in a real-life environment. The intensity was controlled by manipulating the speed and grade to ensure that 70% VO₂ max was achieved, which equates to moderate intensity exercise. This referred to the comparison of environments and this ensured the maintenance of 70% VO₂ max.

### Table 2. A summary of episode percentages and numbers in time periods for each glucose range

<table>
<thead>
<tr>
<th>Environment</th>
<th>Baseline – 40 minutes</th>
<th>Before evening meal</th>
<th>2–6 hours after</th>
<th>6–12 hours after</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood glucose under 4mmol/L</td>
<td>Lab</td>
<td>Real-life</td>
<td>Lab</td>
<td>Real-life</td>
</tr>
<tr>
<td></td>
<td>9.3% (5)</td>
<td>1.9% (1)</td>
<td>5.6% (1)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Blood glucose 4–9mmol/L</td>
<td>44.4% (24)</td>
<td>63% (34)</td>
<td>55.6% (10)</td>
<td>50% (9)</td>
</tr>
<tr>
<td>Blood glucose over 9mmol/L</td>
<td>46.3% (25)</td>
<td>35.2% (19)</td>
<td>38.9% (7)</td>
<td>50% (9)</td>
</tr>
</tbody>
</table>

*Additional hypoglycaemic episodes occurred in between the 2-hourly time-points. In the 2–6 hours after period, 2 of these occurred in the laboratory environment and 1 during the real-life environment. In the 8–12 hours after period, 1 occurred in the real-life environment. These occurrences have been included in the episode numbers.

### Mean glucose concentrations

The pooled data of mean glucose concentrations taken at the specific time-point with standard deviations in the laboratory and real-life sessions are shown in Figure 1, which displays the comparison between environments. The mean glucose concentrations revealed similar results in both environments. However, the glucose concentrations appeared to be more variable at the real-life time-points, which were recognised by the larger standard deviations, compared with the laboratory time-points.

### Differences between environments

With the overall mean glucose concentrations, the three-way ANOVA verified that the environment did not have a significant main effect on the glycaemic control of participants (F[1, 8] = 1.489, p=0.257). This referred to the comparison of all mean glucose concentrations for both environments, without examining change in blood glucose over time.

When investigating two-way interactions regarding glucose control between the variables, there were no significant effects on environments and times (F[9, 72] = 0.499, p=0.871).
The episode percentage and numbers for each glucose range at the different time periods are shown in Table 2.

During exercise. When comparing the laboratory vs real-life environment, episodes of both hypoglycaemia (5 vs 1) and hyperglycaemia (25 vs 19) during exercise in the laboratory environment were more frequent than during real-life exercise, with greater acceptable concentrations in the real-life environment (24 vs 34).

Up to 6 hours after exercise. During the before evening meal time-point and up until 6 hours after exercise, increased hypoglycaemia occurred in the laboratory environment (6 vs 2). Similar episode frequencies were demonstrated in acceptable concentrations (35 vs 34), and hyperglycaemia (33 vs 37).

8–12 hours after exercise. In the 8–12 hour time-period after exercise, when comparing the laboratory vs real-life environment, hypoglycaemia occurred more frequently in the real-life environment (3 vs 8) with hyperglycaemia occurring more frequently in the laboratory environment (22 vs 14); again, there were a slightly greater number of acceptable concentrations in the real-life environment (29 vs 33).

Descriptive analysis
The episode percentage and numbers for each glucose range at the different time periods are shown in Table 2.

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Discussed was the relationship between exercise and glucose control, with hyperglycaemia occurring more frequently during exercise than after the evening meal (22 vs 14), and hypoglycaemia occurring more frequently during exercise than before the evening meal (5 vs 1). This suggests that exercise may alter glucose control, but further investigation is needed to determine the extent of this effect.

Relevant to this discussion is the finding that hypoglycaemia episodes were more frequent during exercise than after the evening meal (25 vs 19), whereas hyperglycaemia episodes were more frequent after the evening meal than during exercise (22 vs 14). This suggests that exercise may alter glucose control, but further investigation is needed to determine the extent of this effect.

Study limitations
The addition of qualitative data would have been useful in clarifying the participants’ experiences of the two environments, which may have explained the outcomes. It could be thought that participants may have been influenced by the study setting and the presence of a researcher.

This would explain the increase in hypoglycaemia episodes during the laboratory sessions and not in real-life. However, if this was the case, the participants would not have experienced an increase in delayed hypoglycaemia after the real life sessions. It may also be viewed as more stressful running outside due to being aware of the environment and safety issues such as cars, whereas in the laboratory there were no decisions made regarding the route. Another variable which was not accounted for was that of temperature, as hot and cold temperatures could affect glycaemic control.

As statistical analysis demonstrated, the environment did not affect glycaemic control, this observation must provide reassurance that previous laboratory based research and subsequent findings can be used in patient education to advise on self-management strategies during exercising and subsequently clarify the reproducibility of clinical research in everyday life. However, it must be taken into consideration that the sample size was a limitation of this current study and, if correctly powered, results may have been different. Another reason for caution with extrapolating laboratory based statistical data would be extreme outliers of hypoglycaemia and hyperglycaemia. In the current study, extreme outliers were not highlighted in the statistical analysis, but the descriptive analysis demonstrated a difference with the patterns of hypoglycaemia and hyperglycaemia in each environment. This remains an important issue for patients, but will require further investigation using a larger sample size.

Despite the lack of power in the study, the self-management algorithm was modified to reflect the hypoglycaemia episodes; a slight increase in the carbohydrate amounts were introduced into the meal plan, but further investigation is needed to determine the extent of this effect.
Most exercise and type 1 diabetes research has been performed in a laboratory environment. Apart from case studies, no publications have been found regarding self-management and glycaemic control observing patients in real-life environments. Statistical analysis did not show a difference on the effect of glycaemic control in a laboratory environment compared to real-life. Descriptive analysis did show differences especially in relation to hypoglycaemic episodes during the exercise period and overnight. No major conclusions can be made from these findings as the study was underpowered, but it does highlight issues to consider when using laboratory data in clinical practice.

The findings described cannot be compared with other results in the literature since no studies, as far as these authors are aware, have been published comparing exercise environments in this manner. Despite this, laboratory findings regarding self-management strategies are used by health care professionals to advise patients on exercise management in daily life, although they have not been evaluated in that environment.

**Conclusion**

The initial aim of this study was to determine whether results from laboratory based research examining glycaemic control during and after exercise can be applied to a real-life (non-laboratory) environment; statistical analysis infers that this is acceptable. However, the descriptive analysis does suggest differences within the laboratory environment during exercise, and the delayed risk of hypoglycaemia after the real-life sessions 8–12 hours after the post-exercise insulin dose, as it would appear that there was a difference between environments. Hyperglycaemia frequency is also increased in the laboratory environment during exercise and 8–12 hours after exercise, whereas in real-life the increase was noticed after exercise until 4 hours after the finish of the session. When considering acceptable glucose levels, the real-life environment data do suggest better glycaemic control; however, the larger standard deviations would imply greater variability. These findings are essential for patient safety and education, especially regarding the prevention of hypoglycaemia. Nevertheless, it is acknowledged that these differences were observed patterns and thus were not statistically analysed. A larger sample size would be required to make further interpretation and conclusions. However, this does highlight issues when applying laboratory research findings into clinical care.

**Acknowledgments**

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**Declaration of interests**

There are no conflicts of interest declared.

**References**